Vol. VII, **No.** I (2022) **Pages:** 1 – 7 **ISSN** (Print): 2788-4961 **ISSN** (Online): 2788-418X

Citation: Gul, P., Kausar, W. A., Noorzai, Z., Rehman, Z. U., & Bibi, A. (2022). Virtual Clinical Trials- An Overview. *Global Immunological & Infectious Diseases Review*, *VII*(I), 1-7. https://doi.org/10.31703/giidr.2022(VII-I).01

Parsa Gul [a] Warda Arooj Kausar [b] Zarmash Noorzai [c]

Zia-ur-Rehman [d] Amina Bibi [e]

Virtual Clinical Trials: An Overview

Abstract *The production of successful and promising innovation in pharmaceutical and clinical care delivery is subjected to factual and efficient clinical trials. The most crucial step for a successful trial is dependent on subject participation. The extent of subject participation has a high impact on the conclusions of a trial. The biggest challenges with the conventional trials are patient enrollment and retention, inefficiency, costly and time-consuming methods. A new concept of digitalizing the clinical research process, 'Virtual Clinical Trials' (VCTs), has captured the attention of researchers with its phenomenal time and cost-saving attributes along with the advantage of data collection from multiple sources, ease of access to restricted study sites breaking the location barriers, increased patient retention and automated data collection. The concept of virtual trials is not fully explored yet and seems to face various challenges but is expected to revolutionize the methods of clinical research with its potential benefits.*

Key Words: Virtual Trials, Emerging Technologies, Patient-Centred Care, Digital Globe, Challenges

Introduction & Background

The term VCT refers to a new method of data collection (safety and efficacy), from clinical participants, via modern technologies of communication and monitoring devices and using online programs of social consultation. This method of research aims to conduct each stage with the comfort of a patient with an emphasis on patient retention and maximum enrollment in a speedy and cost-effective manner. It can also contribute to providing effective and efficient data for developmental stages of a drug, and the decision of termination or approval of drug manufacturing could be made mode faster. As the globe seems to digitalize day by day, so the concept of digitalizing the clinical or research trials would prove to be a revolutionary step in the health care department. Ordinal wellbeing programs deliver aid to the patients and analyze the information for a magnified evaluation. The most significant progress of virtual reality (VR) exists in the clinical area, where it enhances wellbeing and fitness. The most advanced concept of digital trials is eFormulations, pharmaceutical products with enhanced efficiency. (Balevic, 2021)

In the year 2015, an initiative was taken by Sanofi and eClinical health for evaluation of Mendor digital diabetes monitor by enrolling 60 patients. In 2016, Mytrus selected for ADAPTABLE aspirin trial and enrolled 20,000 patients. Also, GSK announced a study of research kit about rheumatoid arthritis. In 2017-18, Novartis announced partnership for more than 10 virtual trials and IQVIA launched virtual research solutions. In the year 2019 -20 JnJ and Apple announced and launched HEARTLINE study by enrolling 150,000 participants, VISITOR study was also launched. A collaboration of world-renowned pharma is seen in recent spell for the establishment of VCTs with maximum enrollments of participants. (Lehrach, 2015)

VCTs have the capability to substantially reduce the animal requirements in prescreening stages and ensuring the enrollment of only those participants who are supposed to respond positively to the testing formulations. Virtual trials are expected to play a spectacular role in support of

[a] Undergraduate Student (pharm D) Department of Pharmacy, Faculty of Biological Sciences, Quaid I Azam University, Islamabad, Pakistan.
[b] Undergraduate Student (pharm D) Department of Pharmacy, Faculty of Biological Sciences, Quaid I Azam University, Islamabad, Pakistan.
[c] Undergraduate Student (pharm D) Department of Pharmacy, Faculty of Biological Sciences, Quaid I Azam University, Islamabad, Pakistan.
[d] Undergraduate Student (pharm D) Department of Pharmacy, Faculty of Biological Sciences, Quaid I Azam University, Islamabad, Pakistan.
[e] Senior Chief Pharmacist, Federal Government Polyclinic Institute, Islamabad, Pakistan. Email: amnabibi@qau.edu.pk

pharmaceutical and biotech companies by their application of personalized medications, drug repositioning, drug rescue, and expeditious data provision about the drug developmental stages. (Persky, 2020)

Components

VCTs can fulfil the requirement for thorough clinical trials by utilizing appropriated innovative arrangements that dispose of the requirement for an actual trial site. The advantages of utilizing VR are to give a "virtual site" for VCTs, a common vivid centre where the members of virtual clinical trials could encounter components of the trial and associate with the trial group.

VR is a communication technology that has been arising close by the advancement of VCTs, in spite of the fact that they have never been converted in a considerable manner. VR excels in the virtual clinical trials paradigm. VR conditions are standardized and decisively uniform, the innovation permits the introduction of an endless set of stimuli and arrangement of improvements to member's visual and auditory frameworks, and VR frameworks are proficient at catching exact development and conduct information.

In spite of the fact that VR has not yet discovered its way into VCTs, a significant part of the preparation for such incorporation has been laid through research and mechanical improvement accomplished in the previous few years. Future execution of VR inside VCTs could move us from site-less preliminaries to those with a virtual site filling in as a center for trial data arrangement, association with preliminary agents, organization of assessments and evaluations, and that's only the tip of the iceberg.

Many organizations like Oracle Health Sciences and CNS Summit are studying virtual clinical trials. The participants in these studies had experience with clinical trials and technologies that are used in virtual clinical trials.

The participants seemed satisfied with virtual clinical trials results. It appears that data obtained through virtual clinical trials are more accurate and have better quality. Virtual clinical trials also seemed to provide improved patient convenience.

Well, members likewise wrote about how challenges in fusing innovation and technology have slowed the clinical trial process and neglected to understand the maximum capacity of "virtual components" in a trial. In any case, they accept that the arrangement lies in cross-industry endeavors to normalize phrasing and information models, just as a slow joining of computerized endpoints and patient-confronting advances in Phase II and, later, Phase III trials.

Process

VR Research Relevant for Remote Interactions

With the continuous growth of the population, assessment and treatment in-home settings have become a significant concentration inside the VR industry. For instance, researchers have started to survey the capability of patients to utilize VR applications for physical and occupational therapy self-assessment and activities in the home, with great outcomes. This exploration has reasonably happened essentially in areas where mobility can be an issue and where locally situated or home-based exercises are, as of now, the standard. This is a likely beginning stage for VR-based movement or mobility assessment in VCTs where interventions under investigation impact these processes.

In a functional VR development community around wellbeing, medical services, and health, there are many use cases destined to be ready to go. For instance, VR assessments of neuropsychological processes and results have been created both with regards to non-interventional characteristic history trials and in drug trial contexts. For instance, in lab-based work, specialists have utilized VR study halls and driving test systems to assess impacts of psychostimulants. Analysts have likewise evolved VR conditions to inspire and evaluate pressure reactivity in both research center/laboratory standard and in naturally reasonable ways. Psychological and executive function assessment is another space of dynamic VR improvement, where testing happens in an exact virtual climate (e.g., a virtual supermarket) to give consistency among trials and between patients.

Interpersonal factors in VCTs

Social factors of clinical trials are critical, alongside the trust that can create among members and researchers. A VR-based communication center point for VCTs could re-insert a portion of the human component into these conveyed examines. Numerous scientists have made VR clinical settings that could be utilized as natural and trustworthy contexts in which to pass on clinical information to patients. Exploration on social VR, just as work on telemedicine, has shown the capacity of VR to help genuine social co-operations and remedial/therapeutic alliance. Utilization of VR to help interpersonal collaboration among patients and preliminary/trial staff could likewise be gainful on account of single-blind preliminaries/trials, wherein communication could be separated, or components could be automated to diminish worries about scientist assumptions saturating the experience. Despite the fact that VR can convincingly impersonate a clinical association, there may likewise be motivation to adorn and investigate additional opportunities in these data trades. Patient instruction could be improved by bringing VCT members into VR instructive conditions, for instance, to assist patients with picturing and visualizing wellbeing and clinical information. Clinical trialists could have a full stockpile of VR perceptions and exhibitions while clarifying preliminary/trial strategy, infection measures, operations, treatment techniques, etc.,

within the consent process and as trials continue. _(9. Senbekov, 2020)

VCT are just a modification of clinical trials, and they are not something novel. They employ faster, enhance retention and boost participant diversity and representation.

The future of clinical trials as virtual has swiftly become the incredible urgent present due to the nowadays ongoing global pandemic giving a huge slap to planned studies.

Data Collection

Gadgets and technology are the core of virtual clinical research. In today's world, it is supported by smartphone apps, vestures and customized e-diaries. The data provided by these devices is the heart of clinical trials, as the study cannot be carried on without data. In a lot of cases, the data is gathered and sent for analysis spontaneously, which removes the element of concealing the work plans.

Patient Enrollment

About 30% of Phase III failures happen due to patient enrollment problems as it is a pressure on clinical research to use the precious time and energy to recruit patients for tests and trials.

Therefore, this problem can be solved by decentralization, and this process can be fastened. As the patron of patient recruitment, social media allows for global contact with potential subjects and the training of them using a glut of AI-driven tools.

Virtual setups do not need sites; this also increases the enrolment speed as the patients have no need of travelling for the trials recruitment and consent given. The rise up of eConsent solutions has made it even simpler and cooler. Virtual trial enrollment has a comfortable scenario considering that patients can be approached without visiting, especially when it comes to the elderly patient groups. This provides the virtual setup with an edge on traditional enrollment.

Medical Imaging

VCTs are an efficient working substitute to the clinical trials for the evaluation of imaging technologies. In this technology, the human body is swapped with a virtual digital phantom. This system consists of a virtual scanner instead of an imaging system, and there is virtual interpretation. VCT is carried on rapidly and essentially on a computer device that provides a controlled facility. This is only feasible in a virtual domain where scientists and researchers understand the answers to the basic questions through practical ways.

The optimization of existing and new imaging technologies, which include both hardware and software and their usage (tasks), is thereby done by the virtual trials.

VCTs Success Requires an Integrated Approach

- Develop digital patient recruitment methodologies.
- Employ At-home patient visits.
- Unveiling virtual patient interactions.

Oncology

Electronic consent platforms have been found with elevated achievement and minimal fault ratios. It has been very much efficacious in the determination of patient communication preferences upfront in breast cancer surgery.

Virtual trail models also support this pandemic era by improving the capacity of studies. For example, they provide grown access to RPM technologies which allows the turning of intermittent to endless volumes in research. This could have a large impact on the description of long-lasting poisonousness synopses of chemotherapeutical mediators and offer real-time information regarding their side effects. (Kadakia, 2021)

VCTs: Case studies

Case study# 01: REMOTE

In 2011 Pfizer performed virtual clinical trials for overactive bladder disease considering the tolterodine ER versus Placebo as the interventions

The main goal of the studies is validation which involves the analysis to see whether the future clinical trials would be beneficial to conduct. In the first randomized clinical trial (REMOTE), Patient enrollment, recruitment, and collection of data were done by using the web and mobile phones without requiring the patient to visit any study site and with a lack of human involvement. But in order to study recruit older patient who was less literate with technology, there was a need for digital health technology in a trial.

So, there were only 18 patients Pfizer was able to enrol, but some primary and secondary outcomes were observed, such as mean no. of micturition per 24 hours were changed when observed for 24 hours.

Though Pfizer's REMOTE was a failure, it gave us some important lessons. It taught us the possibility to design and conduct randomized trials based on patients and make them acceptable for regulatory agencies. And the other most important thing is that is totally relying on technology without the involvement of human-to-human interaction can impact the results negatively.

Case Study# 02: VERKKO

In 2015 Sanofi performed VCTs for Diabetes. This study was performed in order to check the ability of an online platform and test the use of a 3G capable wireless glucose meter. The main purpose of this trial was to assess the efficacy of an

online patient investigator communication system. These clinical trials were approved by European regulatory agencies and were named VERKKO.

It proved that by using virtual platforms, retention, compliance, and convenience could be increased.

In this study, all 60 patients were recruited via Facebook, and the results were definitely unexpected in many areas as 74 persons showed interest, and out of them, 60 got enrolled. The recorded average age of patients was 56 years old, and most importantly, time in study coordination was less than 66%, with improvement in compliance up to 18%.

Case Study# 03:

In 2016 William Stone performed VCTS on depression, considering behavioral interactive, media-based problem-solving treatment as an intervention using computer-based digital health technology.

This computer-based treatment has many advantages, which include its standardization and consistent approach and its ability to use it anywhere. As it is fully automated, so it did not require a live clinician, and it provides access to those patients who are deprived of good living conditions and traditional therapy.

When this trial was conducted, the actual enrolled participants were 45. The main purpose of these trials was to know about the impact of electronic problem-solving treatment on depressive symptoms of the person using it, and comparison is done with a control group.

Case Study# 04

Some of VCTs are ongoing, and one of them is telemonitoring of rheumatoid arthritis, which was started by Frederiksberg University Hospital in 2018.

The aim of the study is to know about the effectiveness of telemonitoring of rheumatoid arthritis in order to reduce the joint destruction, symptoms and disability using home-based interventions and then to perform a comparison with standard clinical disease activity assessment.

Benefits

The major advantage of VCTs is to improve patient engagement, record, and data of the patient. Virtual trials are used for data collection. It provides an advantage to the clinical research team. It provides comfort and decreases the patient dropout rate. The purpose of virtual trials is to make it easier for people living in backward and far areas. It becomes easy for patients who belong to socio-economic backgrounds as their cost and time, and distance coverage is to be reduced.

By using virtual methods and virtual platforms, it provides ease for patients causes faster recruitment. Recruitment models are to be the longest ones reduces by the virtual trials. It lowers cost and staff. In virtual clinical trials, data is to be accumulated by using technology and electronics. Mobile technology reduces time in research provides speedy and effective research.

Challenges

A rare disease, which affects a rare population is to be a big challenge under clinical trials. Diseases their site, treatment are to be present in abroad is costly. A recent example of the corona virus as we all face many difficulties and challenges when it comes to clinical trials. We are able of dealing with a large amount of data and challenging the perspective of its analysis. We are challenging the perspective of data storage and accumulation. We are trying to convert traditional trials into virtual trials.

Major challenges are banned on technology in some countries, interaction with a doctor in dealing tests, examinations and methods. Other challenges are data collection, analyzing and handling. Major efforts are improving the virtual sites, methods and platforms by introducing regular ways by increasing patient involvement and interest in research.

Future

In 2000 about 2000 clinical trials were being conducted in United States (US), whose number had reached almost 320000 along with trial complexity in 2019. The trial complexity means the cost of drug development is increasing day by day, and according to recent estimation, it sits around 2.6 billion US dollars. It's not only a matter of cost but a higher percentage of failure of trials. All these things demand technology adoption in clinical trials.

In very recent years, the pandemic (COVID 19) has accelerated the virtual clinical trials by highlighting them and now is making the research studies totally dependent on the virtual trial technologies, which are running efficiently along with providing convenience for patients. FDA, NIH and other regulatory agencies are supporting these efforts related to the virtual services. Investment in the VCTs is also increasing, and in future, it will further progress. All the leading companies along the startups have conducted various VCTs. Companies realize the benefits of modern technological solutions in clinical research, and that's why they invested about 1B US dollars in 2019.

As we all know that on every coming day, technology is making its way up to higher and helping to conduct much faster, accessible and cheaper research by making the providers implement new software tools. In the upcoming 5 years, many clinical research professionals are going adopt the clinical trial software's as Al (artificial intelligence) and Big Data are driving the trend in town. In future, its use will increase for geographically dispersed groups or rare populations where traditional models have failed. It's not an

easy road, but with continuous evolution in studies, the scope of virtual studies will definitely increase in sensors and diagnostic areas.

While thinking of patient limitations in a virtual clinical trial, there is none because by using technologies including electronic questionnaires, electronic consent, video conferencing and telehealth, home kits for lab testing and microsampling, different devices such as mobiles tablets, wearable sensors which can easily be used to collect data, these things make virtual trials more effect from cost time patient retention and maximized enrollment point of view.

There are some major concerns which we have to deal with even in the future as a number of people in different areas have low computer literacy, which acts as a great hurdle in the collection of data, retention and recruitment of patients. So, it is being advised that we keep in view the circumstances we move towards the virtual clinical trials. Meanwhile, a great relief site is that virtual studies are here to augment the traditional studies, not to replace them, so traditional studies can be continued at any time. (Kumar, n.d.)

Conclusion

VCTs can achieve patient centered care which is the ultimate priority of all stakeholders of health care. It can provide open and sustained engagement of patients with more reliable outcomes. VCTs give the impression of being augmenting the conventional study methods. Perhaps in the future of the 'digital globe', they may replace the old conventional studies due to their divergent and peculiar properties of cost-effectiveness, time-saving and more efficient data collection. Virtual trials being an innovation, are likely to face regulatory, operational and analytical challenges, including developing the trust of the population and understanding the digital ecosystem. The next generation of millennial patients may expect virtualization as an only alternate, so it is vital for us to move the needle in that direction.

References

Balevic, S. J., Singler, L., Randell, R., Chung, R.J., Lemmon, M.E. and Hornik, C.P., (2021). Bringing research directly to families in the era of COVID-19. *Pediatric Research*, *89*(3), pp.404-406.

Chiamulera, C., Mantovani, E. and Tamburin, S., (2021). Remote clinical trials: A timely opportunity for a virtual reality approach and its potential application in neurology.

Elangovan, P., Mackenzie, A., Dance, D. R., Young, K. C., Cooke, V., Wilkinson, L., Given-Wilson, R. M., Wallis, M. G. & Wells, K., (2017). Design and validation of realistic breast models for use in multiple alternative forced choice virtual clinical trials. *Physics in Medicine & Biology*, *62*(7), p.2778.

Giustini, D., (2012). Social media and clinical trials recruitment: potential benefits and challenges. *Journal of the Canadian Health Libraries Association/Journal de l'Association des bibliothèques de la santé du Canada*, *33*(3), pp.140-145.

Jones, S. H., (2015). Benefits and challenges of online education for clinical social work: Three examples. *Clinical Social Work Journal*, *43*(2), pp.225-235.

Kadakia, K. T., Asaad, M., Adlakha, E., Overman, M. J., Checka, C. M. & Offodile, A. C., (2021). Virtual Clinical Trials in Oncology—Overview, Challenges, Policy Considerations, and Future Directions. *JCO Clinical Cancer Informatics, 4*, pp.421-425.

Lehrach, H., (2015). Virtual clinical trials, an essential step in increasing the effectiveness of the drug development process. *Public Health Genomics*, *18*(6), pp.366-371.

National Academies of Sciences, Engineering, and Medicine, (2019). Virtual clinical trials: challenges and opportunities: proceedings of a workshop.

Persky, S., (2020). A virtual home for the virtual clinical trial. *Journal of medical Internet research, 22*(1), p.e15582.

Sebenkov, M., Saliev, T., Bukeyeva, Z., Almabayeva, A., Zhanaliyeva, M., Aitenova, N., Toishibekov, Y. & Fakhradiyev, I. (2020). The Recent Progress and Applications of Digital Technologies in Healthcare: A Review. *International journal of telemedicine and applications*, 2020.