Original Research Paper

Volume - 13 | Issue - 04 | April - 2023 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Clinical Research

RECENT ADVANCEMENTS IN CLINICAL TRIALS AND IMPLEMENTATION

Kanukuntla Supriya* Pharm D, Student, Clinosol Research Pvt Ltd*Corresponding Author

Kumari Ankita M. Pharma, Student, Clinosol Research Pvt Ltd

ABSTRACT Clinical trials are an elementary tool used to estimate the safety and efficacy of new medicinal products, medical devices and other health system interventions. The traditional clinical trial system acts as a quality channel for the development and implementation of new medicines, devices and health system interventions. The concept of a "digital clinical trial" leverages digital technology to improve participant access, engagement, trial-related measurements, and/or interventions. The digital trial has the potential to transform clinical trials by reducing the cost of trials. Bringing together experts in clinical trials, digital technology, and digital analytics to demonstrate strategies to apply the use of digital technologies in clinical trials while considering implicit challenges. This paper describes the current state of the art for digital clinical trials including defining digital clinical trials, describing recruitment and retention using digital technology, outlining data collection elements including wearable technologies, mobile health, digital transmission of data, and consideration of regulatory oversight and guidance for data privacy, security, and remotely provided informed consent, elucidating digital analytics and data science approaches leveraging artificial intelligence and machine learning algorithms, Recruiting and retaining participants in randomized controlled trials (RCTs) is challenging. Digital tools like social media, data mining, email or text messaging, electronic health records, electronic medical records, and registry data could improve recruitment or retention.

KEYWORDS : Recruitment and Retention, Informed consent, Data capture and processing, Real-world data, Artificial intelligence.

1 Introduction

Earlier, clinical trials, including recruitment, delivery of interventions, retention and data collection have been conducted using conventional "face-to-face" approaches. Such as radio advertisements or newspapers are used to recruit participants, telephone calls or emails are used to conduct follow-up assessments, interventions are delivered in person, and data are collected using paper-and-pencil instruments. Clinical trials have been slow to incorporate modern technology that utilizes the Internet or mobile devices, into the design and execution of studies. [1]

Clinical trials are fundamental steps in advancing new treatments and improving outcomes. With greater participation, trials can be conducted more rapidly and efficiently and new therapies can be discovered more quickly, benefitting all patients. Moreover, trials allow patients to access the latest available treatments, so access to trials should be equitable and easy for patients. [2]

Clinical trials are essential to estimate the efficacy and safety of drugs, devices and new medical treatments. Still, traditional clinical trials pose challenges that can hamper the effective conduct of experimentation to develop a knowledge base supporting products for patient communities.

The complexity and costs associated with conducting clinical trials have not only increased exponentially over time but also threaten to stifle the development of new drugs and devices. The wide use of electronic health records (EHRs), and the rising number of available mobile applications and wearable devices, as well, offer significant promise for making clinical trial operations more pragmatic, more efficient, and less costly. Optimism for these technology-enabled approaches can be seen in many ways. Move into health and healthcare research. Although technology-enabled pragmatic trials may offer significant promise for the future, implementing technological innovations in clinical trials is still a challenge. [3][4]

This paper aims to provide a general overview of the use of technologies in clinical trial research, specifically within the last decade. [1]

1.1 When is a clinical trial considered digital?

Digital technologies speed up the information gathered from formal clinical studies. Through its capability to empower and profit experimenters and trial teams, digital technology can increase the effectiveness of clinical trials

2.0 Recruitment and Retention

A key determinant of a successful clinical trial is proficiently recruiting and retaining a sufficient number of the study population. However, worldwide clinical trial professionals face several challenges and pressure concerning the recruitment and retention of participants. Surprisingly, participant enrollment issues are the significant reasons for trial terminations.[5]

Informed consent, recruitment and retention of participants are major stumbling blocks to the timely completion of clinical trials. Multiple reasons live to help explain this lack of enrollment, including financial difficulties, lack of clinician involvement, and restrictive eligibility criteria.

The use of digital tools to help in recruitment, especially for purposes of medicinal intent trials, is a crucial step to more effective trials, but to move forward, collaboration with the Office of Human Research Protections is evaluative. While guidance has been issued concerning the use of new technologies in the informed consent process, similar guidance for recruiting potential study volunteers is lacking. Such guidance is necessary to address the use of novel communication tools and social media as recruitment tools by local institutional review boards (IRBs) while allowing investigators to react and respond in real time.

Subject retention may be adversely impacted for other causes, including concerns regarding assignment to a placebo arm, and randomization, lack of understanding related to lack of remuneration, poorly executed informed consent, and lack of understanding of the clinical trial process. Digital technologies have the potential to assist address all of these issues. Proposed interventions range from tracking applications to allow for more efficient subject outreach and improved opportunities in the use of video and other visual formats to aid informed consent and participation in trials without returning to the research centre. Where payments are envisioned, efforts to provide payment should enhance the use of currently available technologies, bearing in mind the necessity of any relevant taxation limits and revenue for study volunteers. [1]

2.1 Social media

Recruiting subjects for clinical trials can be difficult, thus research teams and sponsors should consider incorporating social media into their recruitment strategy. Recruitment plays an important role throughout the drug development process, starting with protocol development and continuing to the end of the process when the team reaches their final goal of enrolling its last participant. This procedure involves a feasibility study that will help the team to understand who comprises their target population, the optimal geographic locations for

recruiting these participants, how to educate the participants regarding the benefits and risks of participating in a clinical trial, and how to retain the enrolled participants throughout the clinical trial to reduce the withdrawal rate. Recruiting participants for a clinical trial study normally combines numerous approaches. In addition to traditional methods, such as social media can increase or complement a comprehensive strategy, by offering a stream of new, continuously evolving technological tools. These tools can help minimize recruitment times; reduce screen failure rates, and meet recruitment goals, therefore allowing the research team to gain valid outcomes and credible data results that meet regulatory requirements.

2.2 Mobile devices

The general population is increasingly comfortable with engaging in a variety of activities on smart phones, including health and wellness mobile apps and downloading. Mobile technology such as smart phone applications, telehealth, and wearable devices offers an opportunity to enhance the efficiency and reach of clinical trial processes, including remote consent, evaluation of interventions, and collection of outcome data. [6]

2.2.1 Data Collection, Analysis, and Interpretation

The Structure and volume of data gathered remotely and continuously are much greater than what is typically gathered in a traditional trial. Thus, marketing authorization holder must engage the expertise of data scientists and biostatisticians in opinions regarding protocol design, data collection, analysis of data, and interpretation of data. Only high-quality, clinically meaningful data that are evaluated properly can inform robust conclusions. Appropriate data quality optimization approaches will help reduce missing data captured from mobile technology, minimize data variability, and make sure that data are gathered from the intended participant. CTTI's recommended strategies for optimizing data quality give the finest practices for sponsors.

2.2.2 Data management

CTTI's resources illustrate the complex inflow of data in clinical trials using mobile technologies and offer strategies for promoting and guarding data integrity across the entire data life cycle. Data must be secured both during the transfer of data and on mobile technology. Marketing authorization holders are eventually responsible for data operation, but numerous data operation processes may be carried out by, or in cooperation with, contract research organizations or other third parties, similar to information technology service providers (e.g., Platform as a Service, Software as a Service, and Infrastructure as a Service) and mobile technology manufacturers. Therefore, it is crucial to have a full understanding of the data inflow and know who is responsible for the data and accountable for data integrity at each step during the data life cycle.

2.2.3 Protocol design and Execution

When incorporating mobile technologies for data collection in trials, marketing authorization holders will make opinions on whether or how to share real-time data with study subjects. It is necessary that any data sharing preserves trial integrity and internal validity and doesn't affect the quality, safety, and feasibility of the study. CTTI has developed a decision support tool that sponsors can acclimate to their specific trial needs for data participating with subjects. Utilizing mobile technologies for collection of clinical data remotely offers the possibility of gathering complete safety information about an investigational medical product in a timely manner. The usage of mobile technologies raises new implicit issues related to safety signals that marketing authorization holder should consider. The first is around safety signals not observed before using traditional protocol design and monitoring. The alternative is on data gathered and observed by the study subject, in the absence of context supplied by clinicians, which may lead to difficulty distinguishing between normal data and a possible adverse event. CTTI has developed a frame of options and approaches to help sponsors seeking to optimize their approach for managing atypical data, including those data captured outside of the intended use of mobile technology. Study participants must be well informed regarding safety monitoring through mobile technologies.

2.2.4CTTI Recommendations for FDA submission and inspection

Summarizes and data collected and data processes information that should generally be included in a marketing submission. To ensure success in a premarket submission for a new medicine or medical device that includes studies using mobile detector technology for data collection. The most applicable strategy for gathering and sharing data with the FDA will probably be trial-specific and require an open dialogue previous to and during trial conduct.Source data should generally be the primary data resource given to the FDA. This data should be the first level of data that is both clinically applicable to the trial and interpretable, and this should be prespecified in the data collection plan. Metadata and inspection trails should be maintained and retained. [18]

3.0 History of informed consent

The first event follows the Nazi party's tortuous medical experimentation throughout World War II. Herein, Nazi Doctors killed and tortured camp victims in the name of scientific research. This 'research' consisted of such horrific acts as killing Jews for anatomical studies, and utilizing non-consenting prisoners for experiments involving exposure to deadly diseases, and poisons, simulated high altitude, and immersion in freezing water. After the end of the Second World War, in 1946, these evil acts were tried before a board of three American judges in a trial known as 'The Medical Case'. This resulted in the accountability of the responsible medical physicians, and the introduction of the Nuremberg Code, wherein it was stated that “the voluntary consent of the human subject is essential”, and that research subjects “should be so situated as to capable of expressing free power of choice”, and that they “should have enough knowledge and understanding of the elements of subject matter”. While the Nuremberg Code was incorporated into several human rights legislations, it did little to guide the behavior of researchers dealing with human participants. Still, over time, its circular influence urged the medical exploration community to develop its guidelines for mortal- subject research, which latterly came the protestation of Helsinki. It now includes provisions for the privacy of identifiable human materials and data and the dissemination of their results. [7]

3.1 The definition of informed consent

It is the process by which a subject voluntarily expresses his or her willingness to participate in a clinical trial, after having been fully informed about all the aspects of the clinical trial that are relevant to the subject's decision to participate in the trial. Study subjects must understand the purpose, procedures, benefits and potential risks of their involvement. Informed consent is a document that participants must sign before participating in a clinical trial.

3.2 Mandatory elements of informed consent

Informed consent is a crucial aspect of any research involving human subjects. According to the ethical guidelines, several mandatory elements must be included in informed consent. These include voluntary participation, where the subject must be informed that their participation is voluntary and they are free to withdraw from the research at any time without any penalty. The purpose of the research and the description of the procedures must also be clearly explained to the subject. Risks associated with the research must be disclosed along with the potential benefits. Confidentiality of the subject's personal information must also be ensured. Financial considerations must be made clear to the subject, and they must be informed of any compensation or incentives offered for their participation. The subject must be informed of their right to withdraw from the research at any time without penalty and of any alternatives to participation that may be available. Finally, contact information for the researcher or research team must be provided in case the subject has any questions or concerns. Ensuring that all of these mandatory elements are included in informed consent is essential for ethical and responsible research involving human subjects. [8]

3.3 Online consenting

Electronic approaches are getting more extensively used tools to gain informed consent for research participation. E-consent provides an adaptable and accessible approach to the consenting process, which can be enhanced with interactive features and audio-visual to enhance subject understanding and engagement of study procedures. Greatest practice guidance sustained by ethical principles is needed to make sure the effective implementation of e-consent for use in research.

3.4 E-consent

E-consent uses electronic processes which include digital media (e.g. videos, audio) and/or interactive interfaces (e.g. websites or tablets) to increase the presentation of information and enable prospective research participants to give informed consent for recruitment. A variety of e-consenting approaches can be used simultaneously, offering versatility to researchers who can customize them to suit their project's needs. The provision of information between face-to-face and

electronic methods can be interchangeable such as hardcopy documents can be posted for tele-consenting or e-consenting media can be used for traditional consenting. E-consenting resources can be used during tele-consenting or in person. The process of tele-consenting includes prospective participants "meeting" with study researchers through a video call to discuss study procedures (having previously been sent relevant electronic material), before completing an online document that can be electronically signed immediately, and digitally saved. E-consenting platforms have also been modified by researchers to enable subjects to record their consenting preferences across multiple studies. There are a variety of custom-built platforms for entirely virtual consenting as well as commercial software programs such as Redcap.

E-consent benefit

E-consent may enhance research workflows by reducing the physical burden of the collection of hardcopy-signed consent data, reducing errors associated with storing paper-consent forms and archiving, facilitating search ability of data for enabling easier audit, and recruitment and quality control checking. [9]

3.5 Audio-visual recording of the informed consent process

A-V recording of the informed consent process is anticipated to serve as a means to better document understanding by potential subjects. It also serves as a legal record for the investigator regarding the information provided to the subject in detail and can act as an effective tool for the ethics committees, sponsors, and regulators during the processes of monitoring, inspections, or auditing. During development in the quality of the conduct of the informed consent process and transparency can be viewed as potential benefits of Audio-Video consenting, the process can present significant challenges.

Challenges include

- Operational challenges during the recording process.
- When infants and neonates are subjects.
- Testing the participants' understanding.
- Training of study personnel.
- Storage, retrieval, and archival. [10]

4.0 Data capture and Processing

Why consider using digital devices in clinical trials?

The use of wearable technologies has skyrocketed in recent times. We define wearable technologies here as sensors and/or software applications (apps) on smartphones and tablets that can collect health-related data remotely, i.e., outside of the healthcare provider's office. The data can be gathered passively or may need a user's input. An accelerometer fixed in a cell phone or a wristband is an example of a sensor passively collecting data about a person's movement and physical activity. Software e.g., ePRO (electronic Patient Reported Outcome)) can output a patient's report capturing health-related information, collected by means of a cell phone app or a web-based interface. In addition, some technologies, such as smart-cap bottles designed to monitor medication adherence, can use a combination of app-based data collection and sensors. A user action triggers the event recording (opening the bottle), but the data is passively transmitted from a sensor to a server via Bluetooth. [11]

4.1 Wearable and continuous Sensors

The largest source of individual health data is likely to be from sensors that record information about a person continuously for days or years. Numerous similar sensors are being integrated into wearable devices to measure movement and heart rate or into objects in the environment, similar to beds at home that record sleep-time activity or beds in a hospital's intensive care unit that measure intracranial pressure. Whether or not these data find their way to the institutional EHR or technical storage for streamed data, patients and clinicians will expect to be able to view derived and or summary measures and also have decision support such as alerts driven from the derived data or primary. Still, the reality of the growth in the wearable industry (e.g., Fitbit or Apple Watch) has vastly outstripped any standardization efforts, which suggests that the initial sets of apps for these data streams will remain confined to their separate platforms and also integrate with EHR data in very limited ways. [12]

4.2 Telemedicine, Telehealth, and Mobile Health

Telemedicine allows clinical services to leverage information technologies, telecommunication linkages, and video imaging to enable physicians to provide healthcare services at a distance. In comparison to telemedicine, which is narrowly defined as the provision of medical services at a distance by a doctor, telehealth is an umbrella term that covers telemedicine and a variety of non-healthcare services, including telepharmacy and telenursing. Mobile health is a newer concept that describes services supported by mobile communication devices, such as smart phones, wireless patient monitoring devices, tablet computers, and personal digital assistants. Mobile applications (apps) and, in some instances, sensors and companion mobile devices are the enablers of mobile health and the drivers of the systems. [13]

4.3 Telehealth: It is the use of telecommunication technologies like telemonitoring to enhance the provision of care. This allows for care to be supplied at a distance and for that reason to maintain clinical contact with patients at home without requiring the same amount of resources to be dispensed. Examples of telehealth are blood glucose–monitoring machines tethered to an EHR that integrate blood glucose values which are taken by the subject at home into the EHR automatically, and progressively mobile health data gathered by wearable devices. [14.

Clinical significance-

- Telehealth, telemedicine, and mobile health could fundamentally change the way medical services are delivered.
- Teleradiology, the first telemedicine service, currently brings diagnostic radiology to millions of rural and urban patients.
- New models of health care delivery, like telestroke, bring critical services to underserved populations.
- Many state legislatures have mandated that third-party payers reimburse for telehealth services. [13]

4.4 Electronic health record (EHR)

EHRs are electronic platforms that contain health-related data collected during medical care in practices, clinics and other medical settings from various sources, connected to form a network of patient clinical data. EHRs can also incorporate software that allows straightforward physician ordering practices (CPOEs), even including safety features, or that guide physicians through clinical decision-making with up-to-date guidelines (CDSS).

4.5 Electronic medical records (EMR)

Electronic medical records **(**EMRs) are frequently collected data sources that contain standard clinical and medical data gathered during medical care in an individual location of a clinic, practice, or another medical setting. When the data are divided among different units and locations, it becomes a network and is regarded as an EHR for example an electronic chart system in a primary care practice that cannot be accessed by any other entity is an EMR, wherein a hospital system in which affiliated clinic charts, laboratory data, etc., are all accessed under one platform is an EHR.

4.6 Applications

- **Electronic patient-reported outcomes (ePRO)**

Electronic patient-reported outcomes **(**ePRO) are health-related data recorded by the patient themselves in electronic form, often through an application or website. Since ePRO has frequently been used in clinical trials, we also consider ePRO to be any data collected by the patients themselves and confined to an EHR or PHR. An example would be a patient pain diary, in which a pain score and information are entered daily on a website or via a smart phone application, and the data are added to an EHR, which clinicians monitor and consult during a visit.

Personal health records (PHR)

PHRs are electronic platforms (often online interfaces such as websites) that securely store patients' health information and allow them to engage actively in their health. Time and again, they can add information to a PHR and can exchange it with health providers, see test results, make appointments or receive educational information. We consider PHRs to be the only platforms that are confined to an EHR, where information can be exchanged in both directions; otherwise, if patients are simply adding data and not viewing any of their data, then it is considered an ePRO.

Computerized physician order entry (CPOE) system

CPOE systems are electronic ordering technologies in which physician orders can be entered and processed computerized, often mimicking the workflow in clinical settings. CPOE systems can be the latest and identify order mistakes. It also displays preferred treatments

by individual patient EHR queries, or indeed set up blocks with drug-interaction orders. [14]

5.0 Participant Privacy

Patient and participant privacy remain crucial concerns with the digital approaches in research and community engagement. Since digital approaches to community engagement hold promise in reaching diverse participants who are generally underrepresented in clinical trial research, privacy protections need to shift in tandem with potentially heightened vulnerabilities that such communities face. For e.g., individuals who are socioeconomically disadvantaged may face obstacles in negotiating confidentiality and digital privacy and require tailored frameworks to uphold data governance principles and mitigate risks to privacy. Therefore, privacy concerns may come into the picture from digital crowd-sourcing methods and qualitative approaches, as open calls rely on the use of online systems as well as principles of open access to materials and information. These may pose ethical risks if privacy safeguards are taken into concern. Potential safeguards include limiting the identifying information collected as part of digital engagement and not requiring the use of real names when taking part in the trial, which allows the participants to opt out of specific questions and still join a clinical trial study or engagement project, and co-create study protocols with communities in considering the ethics and study design to minimize potential risks. [16]

5.1 Data security

In the practical consideration of security, privacy, and compliance, it can be helpful in separating compliance from security and privacy, as compliance tends to be retrospective in nature, but ensures that privacy and security must be proactive and forward-looking. Much has been written about general and advanced security and privacy with respect to devices and medical data.

Specifically focusing on wearable devices and sensors, the guide deems it essential that all personally identifiable information (PII) and all personal health information (PHI) must be kept secure, and that the devices themselves are secured from any form of outside interference, whether accidental or malicious. The predominant generic issues include the device security of any tablets, mobile devices, and cell phones that are used to collect, store, or transmit data; the potential complications of merging study sponsor collected PHI on the personally owned device of a research study participant; secure account management; data encryption; secure data transmission and receipt; data blinding; and device fidelity and data backup. It is necessary to understand that these phenomena are generic by necessity. Specific solutions will always be required which can rely on the exact device model, the intended method of network connectivity, the specific device operating system, the intended data capture and processing strategy, and many other variables that will be study-specific. [11]

6.0 Data Analytics

What is Real World Evidence (RWD)?

"Clinical evidence about the possible benefits or risks and also utilization of a medical product which is derived from exploration of real-world evidence (RWD)". [16]

What is Real World Data?

The data is related to patient health status and/or the delivery of health care and is routinely collected from a variety of sources including claims and billing, EHR, product and disease registries, activities, but also patient-generated data via in-home-use settings and also gathered from health monitoring devices and medical

6.1 Types of RWD

There are many various types of RWD. Here are a few common RWD types, Such as Electronic health records (EHRs), registry data claims data, patient-reported outcome (PRO) data, and data collected from wearable's.

1) EHRs

These are collected as part of routine care across hospitals, clinics, and healthcare institutions. EHR data are typical RWD which is heterogeneous, noisy, structured, and unstructured (e.g., imaging, text,), dynamic, and require intensive and careful pre-processing efforts. EHRs have created unprecedented opportunities for data-driven approaches to learning patterns, making new discoveries, assisting preoperative planning, diagnostics, and clinical prognostication, among others improving predictions in selected outcomes especially if linked with administrative and claim data and usage of proper machine learning techniques, and validate and replicate findings from clinical trials.

2) Registry data

These have various types. Such as health services registries consist of patients who have had a common procedure or hospitalization, product registries include patients who have been exposed to a biopharmaceutical product or medical device, and disease registries contain information about people diagnosed with a specific type of disease. Registries data enable sharing and the identification of best clinical practices, provide valuable data and improve the accuracy of estimates for supporting regulatory decision-making. Especially for rare diseases where clinical trials are often of small size and data are subject to high variability, registries provide critical information for confirmatory clinical trial design and translational research to develop treatments and improve patient care and provide a valuable data source to help understand the course of a disease.

3) Claims data

This refers to data generated during the processing of healthcare claims from practice management systems or in health insurance plans. Despite claims data are collected and stored primarily for payment purposes originally, they have been used in healthcare to understand patients and prescribe behavior and how they interact, to estimate disease prevalence, to learn medication usage, disease progression, drug-drug interactions and disease diagnosis, replicate and validate findings from clinical trials. The data fraud problem can be eased with the adoption of modern statistical and detailed audits, ML techniques and data mining for fraud detection.

4) PRO data

PRO assesses a range of issues including functional health, symptoms, psychological issues and well-being from the case's perspective, without interpretation by a clinician. PRO data may provide benefits for patients and society. Still, in practice, there is relatively less proof demonstrating directly attributable and indirect real-world PRO-related investigation impact. In part, this is due to the wider challenges of measuring the impact of investigation and PRO-specific issues around design, conduct, analysis and reporting. PRO instruments include patient journals and validated questionnaires that are used to capture data directly from patients and can be in the form of ePRO. PRO measures are generally developed with input from numerous stakeholders like clinicians and psychometric experts to ensure that the questions address issues in an objective manner without any bias.

5) Wearable devices

Generate continuous streams of data. When combined with contextual data such as location data, and social media they give an opportunity to conduct extensive research studies that are large in scale and scope that would be otherwise infeasible in controlled trials. Examples of using wearable RWD to induce RWE include applications in environmental health and neuroscience. The wearable's generate huge amounts of data. Efficient battery technology, advances in data storage and real-time processing capabilities would be significant for theutilization of wearable data. [17]

7.0 AI and ML in clinical R&D

These technologies have a wide range of applications in clinical research and development. Applications of machine learning today include finding patient populations that fit inclusion/ exclusion criteria, identifying molecules that have the most potential, claims reports, reviewing scans, and other healthcare data to interpret trends to improve and accelerate decision-making. However, these incredible technological capabilities can only be leveraged by organizations that have access to the tools, expertise and expansive healthcare data sets to design and build effective algorithms and accurately interpret the results. Nevertheless, healthcare data collected is frequently unstructured and difficult to access, requiring more protection to ensure privacy.

7.1 The benefits of AI: Enhancing operational efficiencies

Artificial intelligence and Machine learning are already providing meaningful quality, time, and cost benefits across many aspects of the clinical research process.

Table 1: benefits of AI: Enhancing operational efficiencies

Study design	The study design has a tragic impact on the effectiveness, cost and success eventuality of clinical trials. Using huge healthcare data sets, we can use Machine learning, Artificial intelligence and natural language processing (NLP) tools to assess and select primary and secondary endpoints in study design, to make sure the most applicable protocols for regulators, patients and payers are defined. This will help to optimize the site strategies and study design by informing the ideal country, patient recruitment, enrollment models and start-up plans. Better study design leads to reduced cycle time for protocol development, more predictable results, advanced efficacy throughout a study, and fewer protocol amendments. It also results in fewer non-enrolling sites, improved recruitment rates, and smaller protocol amendments. These improvements increase the chances of success and facilitate realistic and accurate planning.
Site identification and patient recruitment	Relating trial sites to successfully perform a clinical trial with access to enough participants who meet inclusion/ exclusion criteria is an ongoing challenge. As studies target more specific populations, recruiting goals become even harder to achieve, driving costs up, increasing timelines, and raising the risk of failure. According to the Center for the Study of Drug Development (CSDD), nearly half of all spots miss registration targets. One of the ways AI and ML can alleviate these risks is by recognizing the sites with excessive reclamation potential and suggesting appropriate recruitment strategies. This involves mapping patient populations and proactively targeting spots with high prognosticate potential to deliver the most cases – before a single site is opened – and recognizing the best avenues to recruit them. This means marketing authorization holders can open hardly any sites, accelerate recruiting, and reduce the threat of under-enrollment
Pharmacovigilance (PV)	In PV, massive amounts of organized and unorganized data must be integrated and reviewed in order to make sure quality and oversight. AI and ML technologies are addressing numerous of the challenges that PV units face in employing the power of this data via new situations and visionary analytics to enhance quality and oversight. These tools can be used to automate highly manual processing tasks, translate and digitize adverse drug reaction (ADR) documents and safety case processing to make them more usable. They can also perform data listening tasks to monitor conversations on social media and other platforms, ensuring adverse events are promptly identified
Clinical monitoring	Tremendous tactical effort is spent examining site risks and generating “action items” to reduce those risks. AL and ML concepts can alleviate these pressures by manually evaluating the risk environment and delivering anticipated analytics to induce further effective clinical monitoring perceptivity.

Conclusion

In the past twenty years, people have increasingly adopted new and innovative solutions that utilize the convenience, reach, and values of digital technologies. Many interactions with professionals that were once conducted face-to-face, such as those with travel agents or bank tellers, are now commonly done from the comfort of one's home using a computer or smart phone. While the healthcare industry has been slower to transition from legacy systems to digital technologies, a variety of digital tools have recently become available that can be used to improve healthcare and clinical research. These technologies are expanding rapidly, and key components such as medical-grade personal sensors, individual access to and control of health records, and personalized digital communications are already being utilized in small pilot programs for clinical research. Although many challenges remain and there is much to learn as digital research moves into the mainstream, the numerous benefits of clinical research highlight the importance of supporting digital methods and focusing on learning the most effective and efficient ways to utilize them.

REFERENCES

1. Inan, O. T., Tenaerts, P., Prindiville, S. A., Reynolds, H. R., Dizon, D. S., Cooper-Arnold, K., ... & Califf, R. M. (2020). Digitizing clinical trials. NPJ digital medicine, 3(1), 101.
2. Unger JM, Vaidya R, Hershman DL, Minasian LM, Fleury ME. Systematic Review and Meta-Analysis of the Magnitude of Structural, Clinical, and Physician and Patient Barriers to Cancer Clinical Trial Participation. J Natl Cancer Inst. 2019 Mar 1;111(3):245-255. doi: 10.1093/jnci/djy221. PMID: 30856272; PMCID: PMC6410951.
3. Marquis-Gravel G, Roe MT, Turakhia MP, Boden W, Temple R, Sharma A, Hirshberg B, Slater P, Craft N, Stockbridge N, McDowell B, Waldstreicher J, Bourla A, Bansilal S, Wong JL, Meunier C, Kassahun H, Coran P, Bataille L, Patrick-Lake B, Hirsch B, Reites J, Mehta R, Muse ED, Chandross KJ, Silverstein JC, Silcox C, Overhage JM, Califf RM, Peterson ED.
4. Technology-Enabled Clinical Trials: Transforming Medical Evidence Generation. Circulation. 2019 Oct 22;140(17):1426-1436. doi: 10.1161/CIRCULATIONAHA.119.040798. Epub 2019 Oct 21. PMID: 31634011.
5. Desai M. Recruitment and retention of participants in clinical studies: Critical issues and challenges. Perspect Clin Res. 2020 Apr-Jun;11(2):51-53. doi: 10.4103/picr.PICR_6_20. Epub 2020 May 6. PMID: 32670827; PMCID: PMC7342339.
6. Rosa C, Marsch LA, Winstanley EL, Brunner M, Campbell ANC. Using digital technologies in clinical trials: Current and future applications. Contemp Clin Trials. 2021 Jan;100:106219. doi: 10.1016/j.cct.2020.106219. Epub 2020 Nov 17. PMID: 33212293; PMCID: PMC8734581.
7. Dankar FK, Gergely M, Dankar SK. Informed Consent in Biomedical Research. Comput Struct Biotechnol J. 2019 Mar 25;17:463-474. doi: 10.1016/j.csbj.2019.03.010. PMID: 31007872; PMCID: PMC6458444.
8. Wilbanks, J. T. (2020). Electronic Informed Consent in Mobile Applications Research. The Journal of Law, Medicine & Ethics, 48(1_suppl), 147–153. https://doi.org/10.1177/1073110520917040
9. Skelton E, Drey N, Rutherford M, Ayers S, Malamateniou C. Electronic consent for conducting research remotely: A review of current practice and key recommendations for using e-consenting. Int J Med Inform. 2020 Nov;143:104271. doi: 10.1016/j.ijmedinf.2020.104271. Epub 2020 Sep 13. PMID: 32979650; PMCID: PMC7487205.
10. Shetty PA, Maurya MR, Figure BH, Thatte UM, Gogtay NJ. Audiovisual recording of the consenting process in clinical research: Experiences from a tertiary referral center. Perspect Clin Res. 2018 Jan-Mar;9(1):44-47. doi: 10.4103/picr.PICR_172_17. PMID: 29430418; PMCID: PMC5799953.
11. Izmailova ES, Wagner JA, Perakslis ED. Wearable Devices in Clinical Trials: Hype and Hypothesis. Clin Pharmacol Ther. 2018 Jul;104(1):42-52. doi: 10.1002/cpt.966. Epub 2018 Apr 2. PMID: 29205294; PMCID: PMC6032822.
12. Mandl KD, Mandel JC, Kohane IS. Driving Innovation in Health Systems through an Apps-Based Information Economy. Cell Syst. 2015 Jul;1(1):8-13. doi: 10.1016/j.cels.2015.05.001. PMID: 26339683; PMCID: PMC4556429.
13. Weinstein RS, Lopez AM, Joseph BA, Erps KA, Holcomb M, Barker GP, Krupinski EA. Telemedicine, telehealth, and mobile health applications that work: opportunities and barriers. Am J Med. 2014 Mar;127(3):183-7. doi: 10.1016/j.amjmed.2013.09.032. Epub 2013 Oct 29. PMID: 24384059.
14. McCord KA, Hemkens LG. Using electronic health records for clinical trials: Where do we stand and where can we go? CMAJ. 2019 Feb 4;191(5):E128-E133. doi: 10.1503/cmaj.180841. PMID: 30718337; PMCID: PMC6351244.
15. Tan, R.K.J., Wu, D., Day, S. et al. Digital approaches to enhancing community engagement in clinical trials. npj Digit. Med.5, 37 (2022). https://doi.org/10.1038/s41746-022-00581-1
16. Baumfeld Andre E, Reynolds R, Caubel P, Azoulay L, Dreyer NA. Trial designs using real-world data: The changing landscape of the regulatory approval process. Pharmacoepidemiol Drug Saf. 2020 Oct;29(10):1201-1212. doi: 10.1002/pds.4932. Epub 2019 Dec 10. PMID: 31823482; PMCID: PMC7687110.
17. Liu, F., Demosthenes, P. Real-world data: a brief review of the methods, applications, challenges and opportunities. BMC Med Res Methodol22, 287 (2022). https://doi.org/10.1186/s12874-022-01768-6
18. Coran P, Goldsack JC, Grandinetti CA, Bakker JP, Bolognese M, Dorsey ER, Vasisht K, Amdur A, Dell C, Helfgott J, Kirchoff M, Miller CJ, Narayan A, Patel D, Peterson B, Ramirez E, Schiller D, Switzer T, Wing L, Forrest A, Doherty A. Advancing the Use of Mobile Technologies in Clinical Trials: Recommendations from the Clinical Trials Transformation Initiative. Digit Biomark. 2019 Nov 6;3(3):145-154. doi: 10.1159/000503957. PMID: 32095773; PMCID: PMC7011727.
19. Artificial Intelligence in clinical development available at https://www.iqvia.com/-/media/iqvia/pdfs/library/white-papers/ai-in-clinical-development.pdf