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Review Article

Digital Therapeutics and AI in Clinical Trials

Chirag Wani*, Manasi Chavan, Sneha Dhurandhar, Rahul Patil

Department of Pharmacy, Shri Gulabrao Deokar College of pharmacy, Jalgaon, Maharashtra, India

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ABSTRACT

Artificial intelligence (AI) and digital therapeutics (DTx) are drastically changing clinical research and current healthcare. Evidence-based therapeutic interventions powered by top-notch software programs intended to prevent, manage, or treat medical conditions are referred to as "digital therapeutics." DTx improves patient engagement and adherence by enabling real-time feedback, individualized treatment, and continuous patient monitoring through wearable technology, cloud-based platforms, and mobile applications. The clinical value of DTx in the management of chronic illnesses is demonstrated by platforms like Somryst and reSET. Artificial intelligence is simultaneously transforming clinical trials by improving decision-making, efficiency, and accuracy. Artificial intelligence (AI) technologies, including as machine learning, deep learning, and natural language processing, support real-time data analysis, optimize trial design, facilitate patient recruitment, and enable predictive modelling. By examining electronic health records (EHRs), AI-driven technologies can find appropriate patient populations, cutting down on recruiting time and increasing trial success rates. By facilitating decentralized or virtual trials, enhancing patient retention, and guaranteeing high-quality data gathering, the integration of DTx with AI in clinical trials offers a synergistic advantage. While AI algorithms examine massive datasets to find trends, forecast results, and customize interventions, wearable sensors and mobile health technology enable continuous monitoring of physiological indicators. Notwithstanding these benefits, issues like algorithm openness, data privacy, regulatory compliance, and integration with current healthcare systems continue to be major obstacles. To assure safety and effectiveness, regulatory agencies such as the U.S. Food and Drug Administration are actively creating frameworks to assess and approve DTx and AI-based solutions. In conclusion, a paradigm shift in clinical trial technique is represented by the convergence of digital pharmaceuticals and artificial intelligence, providing more patient-centric, effective, and scalable solutions. These technologies have enormous potential to change the direction of precision medicine, speed up medication development, and enhance clinical results.

***Corresponding Author:** Chirag Wani
Address: *Department of Pharmacy, Shri Gulabrao Deokar College of pharmacy, Jalgaon, Maharashtra, India.*
Email ✉: wani1999chirag@gmail.com

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INTRODUCTION

1. ARTIFICIAL INTELLIGENCE (AI)

The area of engineering science known as artificial intelligence (AI) is concerned with developing intelligent machines, especially intelligent computer programs. It is the capacity of a computer or robotic computer-enabled system to process information and generate results in a way that is comparable to how humans pay attention when learning, making decisions, and solving issues[1]. The goal of artificial intelligence (AI), a subfield of computer science, is to build intelligent machines that will play a crucial role in the technology sector. The pharmaceutical industry has seen a significant transformation thanks to AI. It is heavily exploited in every industry, medical field. This technology is the result of combining computer processing and human intelligence. It is a sophisticated form of computer-aided technique that involves gathering data from multiple sources, creating guidelines to be adhered to when handling the necessary data, and sketching potential outcomes to ascertain suitable outcomes and procedures that can mimic human behavior. It is made up of components that make working with neural networks easier, like machine learning and deep learning[2].

The pharmaceutical industry has undergone a significant shift thanks to artificial intelligence (AI). It is widely used in every aspect of healthcare. Due to a lack of funding and the high expense of research, many pharmaceutical companies are currently facing significant challenges in the discovery and development of new treatments. AI technology is therefore beneficial for effective medicine development1. This technology is the result of combining computer processing with human intellect[3].

It is a sophisticated sort of computer-aided methodology that entails gathering data from multiple sources, creating guidelines to be adhered to when managing the necessary data, and sketching potential outcomes to ascertain suitable outcomes and findings. AI uses a variety of statistical techniques to make computer programs and procedures more like human behavior. It includes elements that make working with neural networks easier, such machine learning and deep learning. Artificial intelligence approaches are used at every step of the process, from hit series recognition to lead molecule determination to drug molecule formulation and clinical trials[4].

Artificial intelligence (AI) has the potential to transform how drug development and clinical trials are conducted. The 2025 Infectious Disease Clinical Research Network with National Repository (iCROWN) Symposium held in Japan on January 26, 2026 brought together experts from academia, industry, and research ethics to discuss current applications, limitations, and ethical considerations of AI in clinical trials, with a particular focus on emergency infectious disease research[5]. Presentations highlighted a wide range of use cases for generative AI, including protocol writing; generating and reviewing clinical trial documents such as the statistical analysis plan (SAP) and the clinical study report (CSR); patient matching; data monitoring; and query creation. These applications are expected to accelerate and streamline clinical trials while maintaining quality and reducing costs. Standardization of digital data flows in clinical trials further facilitates the adoption of AI. Drawing on the FDA–EMA guiding principles for good AI practice, discussions emphasized the importance of accountability, explainability, fairness, and generalizability, while addressing risks such as overreliance, bias, and deskilling. The symposium concluded that while AI may enable more efficient

clinical trial deployment during future public health crises, its challenges must be recognized and addressed. From an academic perspective, generative AI use cases included automated generation of the statistical analysis plan (SAP) and the clinical study report (CSR) based on study protocols[6].

Table 1: Milestones in the Artificial Intelligence Process

Sr. No	Year	Milestone
1.	1943	When neurons are joined as a network, they can perform logical operations like "and," "or," and "not." Warren McCulloch and Walter Pitts demonstrated this procedure.
2.	1951	Marvin Minsky created the first neural network to tackle a real-world problem, the SNARC (Stochastic Neural Analog Reinforcement Computer).
3.	1956	At Dartmouth college conference the term “Artificial Intelligence” was coined.
4.	1958	Perceptron (neural networks that transmit information in one direction) was created by Frank Rosenblatt which is the origin for todays AI progress.
5.	1969	Minsky supported the symbolic representation of problems in his book- “Perceptron’s”.
6.	1974 - 1980	This period, known as the "First AI Winter," saw a decline in interest in AI.
7.	1986	Georey Hinton created the back propagation algorithm, which is currently used extensively in deep learning.
8.	1987 - 1993	This phase is called as “AI Winter”
9.	1997	This year, Russian grandmaster Garry Kasparov was defeated by IBM Deep Blue.
10.	2013	Google conducted effective photo research using British technology.
11.	2016	Go Champion Lee Sedol was defeated by Google DeepMind and software AlphaGo.
12.	2026	Isomorphic Labs (the Alphabet/Google DeepMind spinoff) officially began its first human clinical trials.

1.1 Role of artificial intelligence in drug development

The bridge between medication development and discovery is expanding daily as the process of discovering new therapeutic compounds becomes more challenging and time-consuming due to the bigger chemical space. Therefore, methods based on the principles of artificial intelligence offer significant advantages in various stages of drug development, including the identification and validation of drug targets, the modeling of pharmaceuticals, and the enhancement of their druggable qualities. It also plays a crucial part in creating clinical trials for patients, which maximizes the decision-making approach. One of its applications, known as "Open Targets," is a new strategic effort to investigate the connections between genes and diseases as well as the association between therapeutic targets and diseases[7].

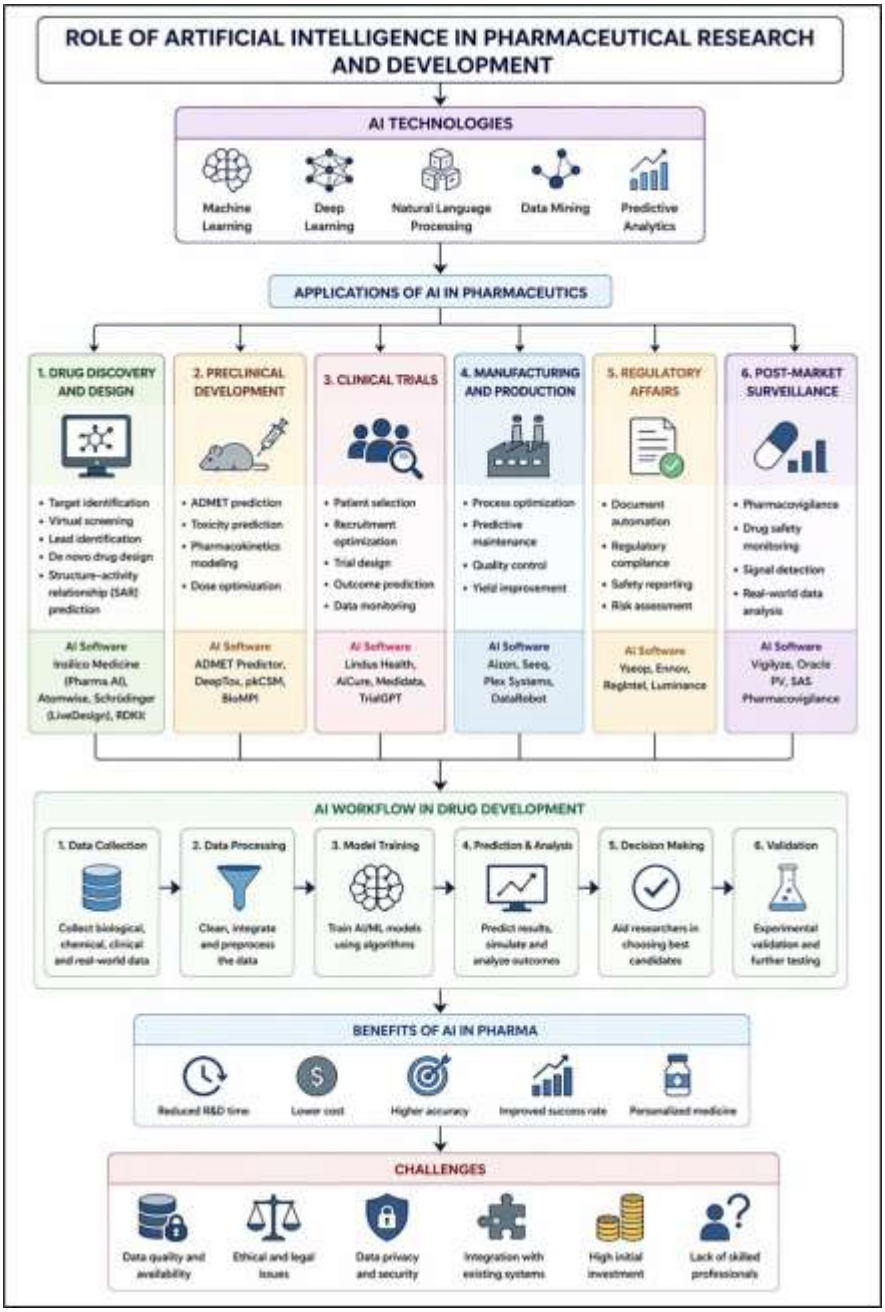


Fig. 1 Role of artificial intelligence in pharmaceutical research and development

It offers a path that would direct the identification of either the disease that is related to the target or the target that is associated with the disease. Lipinski's rule of five must be followed by the drug-like molecule. In light of this, novel neural network method, 3N-MCTS (Monte Carlo Tree Search), offers an advantage over computer-aided retro synthesis systems. This allowed for the quick development of several synthesis pathways with fewer steps to be taken.

An artificial intelligence method called SPIDER is being utilized to assess the function of natural compounds and how to exploit them in medication discovery. It was designed primarily to forecast the targets of pharmacological molecules, such as β-Lapachone, and therefore demonstrated that β-Lapachone is responsible for the reversible and allosteric inhibition of 5-Lipoxygenase. More sophisticated methods like Read Across Structure Activity Relationship (RASAR) are being utilized

to assess the toxicity of unknown substances. It is a prestigious instrument that is being created based on establishing and determining the connection between molecular structure and characteristics that could cause toxicity. This is carried out with the help of the chemicals database[8].

1.2 AI in Drug Discovery and Development

1.2.1 Target Identification

Target Identification AI finds disease-relevant genes and pathways by integrating multi-omics datasets. Network-based target prioritization is made possible by systems biology techniques [9].

1.2.2 Virtual Screening and Antibiotic Discovery

AI's potential in antimicrobial resistance research has been demonstrated by the effective identification of novel antibiotic candidates using deep learning techniques[10].

1.2.3 Generative AI in Medicinal Chemistry

Generative AI models explore chemical space beyond traditional libraries, designing novel compounds with optimized properties.

1.2.4 Drug Repurposing

AI-assisted analytics identify new therapeutic indications for existing drugs using real-world evidence and network pharmacology approaches.

1.2.5 Clinical Trial Optimization

AI enhances clinical trial risk monitoring, enrollment forecasting, and patient selection. Methodological rigor is ensured by standardized reporting criteria like CONSORT-AI[11].

1.3 Tools

1.3.1 Robot Pharmacy

UCSF Medical Center uses robotic technology for drug preparation and tracking with the goal of enhancing patient safety. They claim that the system has successfully prepared 3,50,000 doses of medication. In terms of both size and medication delivery accuracy, the robot has proven to be significantly superior than people. Robotic technology can prepare injectables and oral medications, including hazardous chemotherapy agents. This has allowed UCSF's nurses and pharmacists to use their skills by concentrating on providing direct patient care and collaborating with the doctors[12].

1.3.2 MEDi Robot

The abbreviation for Medicine and Engineering Designing Intelligence is MEDi Robot MEDi. Tanya Beran, a Community Health Sciences professor at the University of Calgary in Alberta, oversaw the development of the pain management robot. Working in hospitals where children scream during medical procedures gave her the idea. Ten When youngsters scream during a medical treatment, the robot first establishes a bond with them. It instructs them on what to do, how to breathe, and how to handle the medical treatment. The robot can be programmed to appear to have AI even though it is incapable of thinking, planning, or reasoning[12].

1.4 Advantages of Artificial Intelligence:

- **Error Reduction:** AI aids in minimizing errors and enhancing precision, particularly in space exploration where intelligent robots withstand harsh conditions.
- **Facilitates Exploration:** AI is instrumental in sectors like mining and fuel exploration, as

well as in oceanic exploration, overcoming errors introduced by humans.

- **Efficiency in Repetitive Tasks:** Machines excel in multitasking and rapid analysis, adjusting parameters like speed and time as needed.
- **Medical Advancements:** AI aids physicians in assessing patient conditions, analyzing medication effects, and provides training through surgical simulators.
- **Versatility:** Machines equipped with AI can perform diverse tasks efficiently without emotional constraints.
- **Early detection:** AI-powered diagnostic tools can assist in the early detection of diseases like cancer, Alzheimer's, diabetes, and cardiovascular conditions, potentially leading to earlier intervention and improved patient outcomes.
- **Everyday Applications:** From GPS navigation to predictive text on smartphones, AI simplifies daily tasks and assists in spell-checking.
- **Digital Assistants:** Organizations leverage AI-driven digital assistants to streamline operations and decision-making without being influenced by human emotions.
- **Continuous Operation:** Unlike humans, AI-powered machines can work tirelessly for extended periods without breaks or fatigue.
- **Technological Advancement:** AI fuels innovation across various industries, contributing to the development of computational models, molecule discovery, and drug formulations.
- **Risk Mitigation:** AI minimizes risks in hazardous environments such as fire stations, with repairable machine parts in case of mishaps.
- **Assistance:** AI serves as round-the-clock aids for children and elders, acting as both educators and companions[13].

1.5 Disadvantages of Artificial Intelligence:

- **Expensive Execution:** The initial investment in AI is substantial, encompassing complex design, maintenance, and software updates, leading to prolonged and expensive R&D processes.
- **Limited Human Replication:** While AI-equipped robots excel in tasks devoid of emotions, they may struggle with unfamiliar scenarios, lacking the ability to think and provide accurate responses.
- **Inability to Learn from Experience:** Unlike humans, AI lacks the capacity to improve with experience, unable to discern hardworking individuals from non-workers.
- **Lack of Original Creativity:** Machines with AI lack emotional and sensory capabilities, hindering their ability to think creatively or use intuition.
- **Potential Unemployment:** Widespread AI adoption may lead to significant job displacement, impacting human creativity and work habits negatively[14].

1.6 Challenges and Implementation Barriers.

Adoption of AI confronts obstacles despite quick invention, such as:

- Limitations on interoperability and data heterogeneity
- Restricted prospective validation
- Costs associated with infrastructure and implementation
- Concerns regarding ethics and medico-legal issues[11].

1.7 Future Perspectives

Emerging research directions include :-

- Responsible AI innovation will be fueled by collaborative interdisciplinary ecosystems
- Federated learning for privacy-preserving model training.
- AI-assisted vaccine development; deep learning for drug–drug interaction prediction.
- AI-enabled predictive analytics in hospital pharmacy operations and integration of wearables and IoT technologies[11, 15].

1.8 Digital Therapeutics

In its October 2018 white paper, the Digital Therapeutics Alliance (DTA), an organization that defines and oversees DTx, defined DTx as follows: "Digital therapeutics offer patients evidence-based therapeutic interventions through qualified software programs to prevent, manage, or treat medical conditions." To improve results, they can be used alone or in conjunction with other therapies, such as drugs or technologies. The terms "(1) high-quality software programs, (2) evidence-based, and (3) therapeutic interventions" are noteworthy in the definition of DTx. With the exception of DTx-like digital wellness goods, these set DTx apart from digital medicine[16]. DTx are software-based and fall under the category of Software as a Medical Device (SaMD), which is categorized as a medical device on its own without an FDA-approved medical device; instead, it makes use of consumer mobile devices like tablets and smartphones[17].

This idea is described as "software used for one or more medical purposes without hardware" by the International Medical Device Regulators Forum (IMDRF). In other words, FDA-regulated hardware is not necessary for DTx.It must be "evidence-based," which is the second important feature. In contrast to products in other digital health categories including pure-play adherence, diagnostics, and telehealth, the Alliance highlights that DTx constitute a distinct category of evidence-based products amid a broad range of medical therapeutic solutions in the digital health domains[18]. Digital medicine, which incorporates DTx sequentially, falls within the larger area of digital health. Because the products in these categories have varying degrees of danger, DTx has a higher clinical risk. For digital health solutions that pose greater risks, higher levels of evidence and regulatory monitoring are therefore required. Software applications known as "digital therapeutics" (DTx) are used to treat illnesses.

DTx are becoming more and more integrated into medical care, and the FDA regulates them as Software as a Medical Device (SaMD) in the US healthcare system. For the majority of DTx, randomized controlled trials (RCT) continue to be a crucial stage in the creation of evidence. However, there are two main reasons why it has been difficult to develop a unified approach to the design of suitable control conditions: (1) control condition definitions from pharmacotherapy and medical device RCT may not directly apply, and (2) difficulties in establishing control conditions for psychosocial interventions that form the

foundation of many DTx. Control conditions are frequently less strict throughout the early stages of clinical development[19]. Waitlist or no-intervention control groups, for instance, have been employed. These will account for effects associated with the illness's natural course, regression to the mean effects, effects from frequent social interaction with study trial staff, or effects from other study procedures like repeated assessments or just feeling observed during a trial (i.e., the Hawthorne effect). Studies using these control groups, however, do not account for the expectation of benefit because they are not blinded[20].

1.9 Relationship between Digital Health, Digital Medicine, and DTx

In general, digital health is the integration of technology and healthcare. To improve the positioning and usefulness of these goods in the market, it is crucial to distinguish between digital health, digital medicine, and DTx in order to prevent confusion among digital health stakeholders as well as the producers and developers of these products[21].

Digital medicine, which includes DTx, is included under the umbrella term "digital health." Different levels of claims and hazards are conveyed by products that fall under each of these categories. Additionally, they have differing standards for clinical evidence and regulatory supervision. Digital health encompasses a wide range of platforms, methods, and technologies that include consumers for wellness, lifestyle, and health-related objectives. Clinical activities can be supported by the collection, storing, and transmission of health data by digital health entities. Health information technology, telehealth systems, consumer health information systems, and clinical care management tools are a few examples of digital health systems. In contrast, digital medicine uses technology or software that is usually backed by data to measure or improve human health. Digital pharmaceuticals include things like remote patient monitoring devices, digital biomarkers, and digital diagnostics[22].

As previously stated, DTx includes evidence-based treatment approaches for managing, treating, or preventing a disease or medical condition. Digital sensors, wearable technology, some virtual reality, and artificial intelligence (AI) devices are examples of DTx applications[23].

However, it might be incorrect to assume that digital health products are risk-free in comparison to digital medicine or DTx products. Commercial digital health technologies may have their own set of problems, although the latter two depend on more evidence and regulatory control due to increased clinical risk. Therefore, the classification of products under digital health, medicine, and therapeutics warrants further work to explore their potential to enhance healthcare delivery as it may help all the stakeholders to thoroughly understand the purpose and clinical value of these products[24].

1.10 Digital Therapeutics in Active Clinical Trials

To find ongoing clinical trials looking at DTx, a search was done on clinicaltrials.gov. The searches were restricted to "Interventional Studies (Clinical Trials)" under the "Study type" category and carried out under "Other Terms" using the search terms "Digital Therapeutic OR Digital Therapy." "Not yet recruiting," "Recruiting," "Enrolling by invitation," and "Active, not recruiting" were among the trials having an active status. Since the clinical studies of relevance were restricted to the previous ten years, additional choices were made. At first, 456 clinical studies were found. Excluded were trials that used the terms "digit," "digital

angiography," or "digital" without using interactive software or unrelated to DTx. Following screening, a total of For additional examination, 317 trials of interest were found[25].

1.11 Regulation of digital therapeutics

The International Medical Device Regulators Forum (IMDRF) member states' DTX-related regulations were examined in six guidelines and one policy statement. Since the FDA believes that DTx do not provide an excessive danger, it has declared that it will allow the distribution and use of devices during public health emergencies without submitting a premarket notice under section 510(k)25. The Ministry of Food and Drug Safety (MFDS, South Korea) released six guidelines. The 2020 guidelines gave instructions on what DTx was and what paperwork needed to be completed in order to get DTx approval in the Korean regulatory system[26].

The safety and performance evaluation techniques for DTx for alcoholism, depressive disorder, insomnia, nicotine use disorder, and panic disorder are then suggested by five guidelines that were published between 2021 and 2022. Each guideline also includes design examples of clinical trial protocols with primary endpoints, sample size, and hypothesis. The ongoing cases of approval through regulatory bodies in the US, Europe, and Japan indicate that approval is possible within the current regulatory framework for general medical devices, even though there are no particular rules, with the exception of Korea[27].

Nonetheless, experts are proposing the creation of a DTx-appropriate regulatory framework. DTx regulation does not ensure usability and ongoing adoption14, and researchers contend that the regulatory framework is significantly ambiguous or inadequate. An analysis of stakeholders about the growth of the DTx sector stated that it is crucial to create permission standards and create a streamlined regulatory framework after receiving financing for research, indicating that the government's participation is significant[28]. Additionally, in order to enhance the quality and safety of DTx3, experts recommended the creation of a globally unified regulatory model[29].

1.12 Prescription digital therapeutics

Like other therapeutic items, digital therapies can be either prescription or over-the-counter. State-level health authorities regulate the beginning of prescription medications, which must be done by a licensed healthcare provider. The FDA's evaluation of the product and a number of other variables determine the prescription need[30]. Treatment of serious illness, the use of higher-risk equipment, the necessity for a secure diagnosis by a qualified practitioner, monitoring and follow-up to determine adequate response, and/or comparison of treatment options to find optimal treatment techniques may all require prescriptions. PDTs are software-based therapies that target the behavioural aspects of numerous illnesses and disorders and are administered via tablets or smartphones[17]. In 2017, reSET® was the first FDA-approved PDT to make therapy claims for patients with substance use disorders. The number of payors covering this new class of therapy is growing quickly[19].

Total size of the market. The global market for digital therapeutics was assessed by Research and Markets in January 2022 to be worth $3.35 billion in 2021 and projected to grow to $12.1 billion by 2026.Although PDTs were the first software-based therapies, non-prescription digital treatments are comparable, and some of them have been approved for sale by the FDA. For instance, Natural Cycles, a non-prescription software program that allows women to monitor their menstrual cycles, was approved as a Class II

device through the de novo pathway, whereas Clue, another non-prescription menstruation tracker, was approved through the 510(k) pathway using Natural Cycles as a predicate device[31].

PDTs are regulated by the FDA and classified as Class II devices since, in contrast to health and wellness apps, they expressly treat disorders. Even though PDTs and digital therapeutics in general differ technologically from conventional medical devices, CDRH currently reviews and authorizes them using regulatory pathways and procedures that aren't always in line with the quick, dynamic, and iterative nature of software-based treatments. Digital therapies are software-driven, evidence-based therapeutic treatments intended to prevent, manage, or treat illnesses or medical conditions.

To provide evidence-based therapy interventions and therapies for a range of medical disorders, these interventions make use of digital technology such as online platforms or mobile apps. Digital therapies, in contrast to conventional health and wellness applications, go through stringent clinical validation and regulatory procedures to guarantee their efficacy and safety. Software as a medical device (SaMD) that offers evidence-based treatment interventions for the avoidance, management, or cure of illnesses and/or medical conditions. They can help with a variety of issues, including as chronic ailments like diabetes and hypertension, mental health issues, age-related illnesses, pain management, and physical exercise[32].

In the medical field, digital therapies provide a number of advantages. First of all, they offer therapies that are practical and easy for patients to incorporate into their everyday routines. This implies that patients can conveniently receive the required interventions in the comfort of their own homes. Additionally, by providing individualized therapies based on each patient's needs, digital medicines have the potential to enhance health-care results. Digital therapies have the potential to enhance medical results. By utilizing technology and evidence-based therapies, they have the potential to completely transform the prevention, management, and treatment of diseases[33].

Table No:2 Digital therapeutics products that have received FDA approval clearance or EUA designation

Product Name (Trial Name)	Manufacturer	Approved Indications	Subtype	FDA Designation	Year
Psychiatry					
Somryst® (SHUTi)	Pear Therapeutics	Chronic insomnia	Mobile App	510(k)	2020
NightWare™	NightWare	PTSD-related sleep disturbance	Device / Algorithm	De Novo	2020
Freespira	Palo Alto Health Sciences	Panic disorder, PTSD	Mobile App / Device	510(k)	2018
EndeavorRx® (STARS-ADHD)	Akili Interactive	ADHD (Pediatric)	Video Game	De Novo	2020
Deprexis®	Orexo / GAIA AG	Depression	Web Application	EUA	2020
SparkRx®	Limbix	Depression (Adolescent)	Mobile App	EUA	2021
Addictions					
reSET®	Pear Therapeutics	Substance Use Disorder (SUD)	Mobile App	De Novo	2017
reSET-O®	Pear Therapeutics	Opioid Use Disorder (OUD)	Mobile App	510(k)	2018

Vorvida®	Orexo	Alcohol Use Disorder	Web Application	EUA	2020
Neurology					
Nerivio®	Theranica	Migraine (Acute & Preventive)	Wearable / App	De Novo	2019
MindMotion™ GO	MindMaze	Neuro-rehabilitation	Virtual Reality	510(k)	2017
Endocrinology					
iSage Rx	Amalgam Rx	Type 2 Diabetes (Insulin dosing)	Mobile App	510(k)	2017

2. LITERATURE REVIEW

(Bairagi, Singhai et al. 2024)AI is transforming medicine delivery systems and allowing specific, personalized, and flexible treatments. Pharmaceutical researchers and medical professionals can improve patient outcomes, reduce side effects, and increase therapeutic efficacy by utilizing AI's data analysis, pattern identification, and optimization skills. Pharmacokinetics and pharmacodynamics have been revolutionized by AI-based methodologies, which have many advantages above conventional experimental techniques. AI models are capable of simulating drug distribution and clearance inside the body, predicting pharmacokinetic parameters, and optimizing medication dosage and administration methods. By delivering a more effective, economical, and data-driven method, computational pharmaceutics, enabled by AI and big data, transforms the medication delivery process. In the end, it improves drug manufacturing processes and patient outcomes by facilitating the optimization of drug formulations, tailored therapy, regulatory compliance, and risk mitigation.

(Patel, Patel et al. 2021)Healthcare has also been impacted by AI, which has played a significant role in clinical research by predicting negative outcomes. This also gathers information about the patient. As a result, it offers quick test results and reports that help determine the best course of action for the patient. As a result, the field of artificial intelligence may contribute to the creation of new software and technologies that will enhance the development of pharmaceutical products and health management techniques in the future.

(Raval, Rana et al. 2026)Healthcare delivery and pharmaceutical sciences are being radically transformed by artificial intelligence. AI technologies provide never before seen chances to improve patient outcomes and healthcare efficiency, from speeding up molecular pharmacovigilance discoveries to improving customized treatment. However, responsible implementation still requires strict validation, regulatory supervision, and ethical governance. Interdisciplinary cooperation, open procedures, and fair deployment techniques will be essential to future advancement.

(Fürstenau, Gersch et al. 2023)We encourage the BISE/IS community to further our discipline through DTx research in light of the exciting advances that lie ahead. Healthcare IT research has a lengthy history: In addition to studying large-infrastructural technologies like electronic health records (EHRs) and health information exchanges, it has also focused more on how important consumers are to healthcare journeys. DTx is carrying on this trend and occupying a conceptually intriguing space between wearables and consumer-grade mobile apps and software that

is controlled for quality and safety as a medical device. Although earlier research on healthcare IT will serve as a great starting point, their focus on the intersection of two domains makes it worthwhile to look at DTx and to advocate for studies to It is worthwhile to look at DTx and to advocate for research to comprehend its features and both intended and unintentional repercussions.

(Huh, Oh et al. 2022)We discovered that clinical trials, which are the norm for evaluating medications and medical devices, were employed in the majority of DTx clinical evaluation examples. However, new methods utilizing digital biomarkers and real-world data are also being developed. The future course of DTx is suggested by a comparison between its components and those of chemical medications [37]. The component that exhibits a therapeutic effect is known as the "active ingredient" of DTx, and its effectiveness must be confirmed using the previously specified clinical evaluation techniques. The "excipient" of DTx is the user interface that optimizes the active ingredient's effectiveness. The significance of the "excipient," or user interface, cannot be understated because DTx products necessitate more active patient participation than medications. To put it another way, in order to obtain the intended therapeutic benefits, it is important to consider the sociocultural background of the patients who will use DTx. Global guidelines for the clinical assessment of the efficacy of the "active ingredients" must be developed in order for DTx to be approved worldwide, and local factors pertaining to "excipients" must also be taken into account.

(Yao, Liao et al. 2024)DTx's promise in healthcare is highlighted by the rise in clinical research. Standardization, regulation, and clinical efficacy are still problematic, nevertheless. To guarantee effectiveness and enhance healthcare services, a uniform worldwide classification of digital therapies and standardized clinical trial procedures are required.

(Knapen, van Kruchten et al. 2026)Conventional trial methods struggle with growing complexity, longer timelines, and higher costs, especially in oncology. Against this backdrop, our review charts how AI can be incorporated from protocol design to data analysis, aiming to ease logistical bottlenecks, cut expenditure, and shorten development cycles. When properly applied, AI can make trials more efficient and help effective treatments reach patients sooner. Snehaa

(Szymanski 2025)Tremendous manual effort is spent analyzing site risks and generating “action items” to mitigate those risks. AL and ML concepts can alleviate these pressures by manually assessing the risk environment and delivering predictive analytics to generate more effective clinical monitoring insights. Advanced analytics provide composite site rankings for holistic risk assessments of sites, allowing for more specific identification of risks and removal of false positives. Using the composite evaluation of site risks across the study to produce a simple output quickly shows high risk sites, key risk indicators (KRIs) and site risk rank.

(Olawade, Fidelis et al. 2025)Realising the full potential of AI in clinical trials requires addressing Significance implementation barriers, including technical challenges, regulatory uncertainty, and stakeholder trust issues. Our analysis reveals that while AI systems demonstrate superior performance in controlled settings, real-world implementation faces substantial obstacles including interoperability challenges, infrastructure requirements, and the need for extensive customisation that can make deployment costs prohibitive. The development of explainable

AI systems, privacy-preserving methodologies, and comprehensive validation frameworks will be essential for widespread adoption.

3. AIM AND OBJECTIVE

3.1 Aim Digital therapeutics and AI in Clinical Trials

3.2 Objective:

1) Verifying that a software-based intervention may successfully cure, manage, or prevent a medical condition is the primary objective.

2) Clinical validation is the process of demonstrating a clear connection between the use of software and better health outcomes (e.g., lowering anxiety levels or HbA1c in diabetics).

3) Continuous Monitoring: Using wearables and app interactions, a 24/7 data stream will replace "snapshots" of patient health.

4) Behavioral Modification: Delivering a "just-in-time" intervention by using AI to pinpoint the precise moment a patient is likely to disengage or relapse.

3.3 Need:

- **Quick Recruitment**: Using medical records, AI rapidly finds qualified individuals.
- **Improved Trial Design:** Aids in maximizing study success rate, sample size, and protocol.
- **Real-Time Analysis:** Makes judgments more quickly by rapidly analyzing massive amounts of trial data.
- **Predictive analytics**: forecasts treatment response, side effects, and dropout risk.
- **Data quality:** Enhances accuracy by identifying inaccuracies and missing data.
- **Remote Monitoring:** DTx continuously gathers patient data from home using wearables and applications.
- **Improved Adherence:** Increases compliance by sending reminders for activities and medications.
- **Personalized Support:** Offers therapy that is tailored to the needs and development of the patient.
- **Lower Cost:** Lowers trial costs overall and hospital visits.

4. MATERIAL AND METHOD

4.1 AI for Clinical Trial Design

4.1.1 Gathering information

Researchers look to ongoing and finished trials for ideas when designing new ones. The efficiency and accuracy of obtaining data necessary for clinical trial design have been improved using large language models (LLMs). LLMs are used by SEETrials to extract safety and efficacy information from intricate clinical reports[34].

In the same way, CliniDigest shows how AI can condense extensive clinical trial reports into clearly understandable summaries. This endeavor is further advanced by AI programs like AutoCriteria, which automate the extraction of eligibility criteria and help trial designers find pertinent participant attributes and trial parameters[35].

Literature synthesis can now be streamlined by using LLMs to extract structured population, intervention, comparator, and outcome (PICO)

data at scale from large numbers of abstracts. Systematic reviews are increasingly utilizing these generative skills, employing AI for data extraction and abstract screening activities that have historically been performed by humans, though human oversight is still necessary in complex or nuanced situations[36].

4.1.2 Determining eligibility criteria

Overly strict and occasionally unnecessary qualifying requirements frequently lead to limited enrollment in clinical trials, which restricts trial generalizability and slows accrual. Recent developments use real-world data (RWD) and LLMs to systematically optimize and rationalize these criteria[37]. By creating eligibility criteria, integrating scalable knowledge through in-context learning, and offering explicit reasoning chains for improved interpretability, AutoTrial leverages LLMs to support clinical trial design. Evaluations of more than 70,000 clinical trials demonstrated that AutoTrial generates eligibility criteria that are clinically accurate, coherent, and fluid for the intended trial. In a different study, eligibility criteria from clinical trial protocols that are accessible in the registry were clustered and encoded using LLM embeddings[38].

The results show that sentence embeddings optimized on biomedical texts efficiently compress eligibility criteria information, attaining 95% reconstruction performance and maintaining up to 97% classification accuracy. AI is being used to predict results prior to trial initiation since low clinical trial success rates provide significant ethical and financial challenges. In order to forecast outcomes ranging from early termination to approval, modern models employ both structured and unstructured features, such as protocol design, eligibility criteria, molecular targets, and historical context. By combining chemical and target-based properties, PrOCTOR predicts drug toxicity, above standard drug-likeness rules [area under the curve (AUC) = 0.83] and correlating with the severity of adverse events (AEs)[39].

Another study employed machine learning (ML) with statistical imputation to provide strong prediction performance for medication approval (AUC = 0.78-0.81) and identified significant markers such as trial results, sponsor history, and prior approvals.22 By employing hierarchical graphs to encode multimodal data, such as moleculesctively, the Hierarchical Interaction Network (HINT) obtains F1-scores of 0.665, 0.620, and 0.847 in phases I, II, and III, respectively[40].

With an AUC of 0.88 and 79% accuracy, InClinico, a transformer-based generative AI platform, combines omics, design, text, and molecular data to forecast phase II results examined machine learning (ML) techniques for phase transition prediction and used supervised ML and natural language processing (NLP) to predict results with over 80% accuracy by analyzing trial characteristics, protocol design, and eligibility difficulty across therapeutic areas.26. These developments imply that AI-driven trial outcome prediction is developing, with increasing implications for increasing the effectiveness of research and development and lowering attrition[41].

4.2 AI for patient accrual

The most time-consuming aspect of clinical trials is patient recruitment, and 20%–40% of oncology trials end early due to delayed recruitment, which has a negative impact on science, society, and the economy. Additionally, even successful trials surpass the estimated accrual time by a factor of 1.5–3. AI tools may shorten the time required to find a patient who qualifies. Additionally, AI

techniques can help with patient prescreening following the patient-trial matching procedure, for instance by assessing laboratory test findings or biomarker analysis utilizing digital pathology[42]. AI tools may shorten the time required to find a patient who qualifies. Furthermore, AI techniques can help with patient prescreening following the patient-trial matching process, for instance by analyzing biomarkers using digital pathology or assessing laboratory test findings. Various systematic reviews and meta-analyses on AI tools for trial enrolment have been published[42].

The majority of research to date has assessed the accuracy of patient-trial matching using AI technologies in comparison to physician-performed manual screening. These AI technologies often leverage both unstructured data processing from clinical records and plain text from research protocols using natural language processing (NLP) and structured data, such as age, sex, laboratory findings, cancer diagnosis, and stage, that may be collected from electronic health records (EHRs). Patient-trial matching can be carried out in two ways: either a specific clinical trial is used as a starting point and a matching algorithm provides all potentially eligible patients from electronic patient records, or an individual patient is used as a starting point and a matching algorithm provides a set of available trials for which the patient is eligible[43].

Examples of available patient-trial matching algorithms capable of processing unstructured data are DeepEnroll IBM Watson, CTM tool, and Criteria2Query.

4.3 AI for patient retention

Clinical trial dropout is a common issue that may result in biased findings reporting. A study examined 72 clinical trials with missing outcome data that were published in four highly regarded medical journals. In 89% of the trials, they reported any missing outcome data, and in 18% of the studies, more than 20% of the patients had missing outcome data. AI may help reduce the number of patients who leave clinical trials by identifying those who are most likely to do so before or during the trial, as well as by providing targeted interactions that emphasize patient adherence and retention. This would make it possible to provide participants with individualized support and prompt interventions[44].

Predicting dropout

No research on using AI to forecast clinical trial dropout was found. However, AI has been effectively used in other domains as proof of concept, such as identifying college students who are at high risk of dropping out and directing focused retention efforts[45].

4.3.1 Personalizing interactions

Twelve ways for keeping research participants were found by Robinson et al. Four of these strategies depend on direct, one-on-one interaction: study identity, determined study personnel, participant-preferred contact, and personalized reminders. These individual approaches are frequently used in trials with high retention rates, according to Abshire et al. LLM chatbots are an example of conversational generative AI, which now provides patients and physicians with individualized advice and real-time help. Driven by this potential, numerous start-ups and well-established digital firms are rapidly integrating these tools into healthcare procedures and solutions. Xue et al.'s scoping review listed 36 conversational. AI models but stressed the need for a thorough assessment of their efficacy, safety, and equity[46].

4.4 AI for clinical trial conduct

4.4.1 Passive data collection techniques

Mobile devices, biosensors, and smartphones are examples of digital health technologies (DHTs) that make it possible to continuously collect physiologic and behavioral data in real-world settings with minimal effort. They facilitate the validation of new digital biomarkers and lessen reliance on clinic visits, which makes trials more convenient for study teams and participants. Between 2019 and 2024, the use of sensor-based DHT measurements in industry trials increased tenfold, with >100 acting as primary endpoints. Atrial fibrillation burden was approved by the US Food and Drug Administration (FDA) in 2024 as the first Medical Device Development Tool based on a sensor-based DHT[47].

DiMe's new V3+ technique, incorporating usability testing into the pillars of verification, analytical validation, and clinical validation, reflects regulators' current emphasis on validation, usability, and governance of DHT-derived data.However, depending too much on DHTs might continue inequality: inequalities in digital literacy, internet access, and device ownership run the risk of removing participants and restricting generalizability[48].

4.4.2 AI enabling decentralized and hybrid trials

While the requirements of Good Clinical Practice stay the same, decentralized components (telehealth, home visits, local providers, remote data gathering) can increase access but also complicate operations. AI can help scale outcome/safety collection by converting wearable/smartphone data into validated measures and supporting near-real-time safety surveillance, enhance remote consent through more interactive and understandable eConsent experiences, and support remote recruitment and onboarding (EHR-enabled prescreening, trial matching). By using anomaly detection to identify contradictory data patterns, deviations, or possible integrity problems across distant settings, AI can also supplement risk-based monitoring. AI-enabled decentralized clinical trial designs should address privacy, cybersecurity, and prospective validation of AI tools and digital endpoints in addition to providing options for participants with restricted digital access in order to prevent growing gaps[49].

4.4.3 Consent processes

Although understanding and participation issues are frequent, the informed consent procedure is essential to conducting clinical trials in an ethical manner. Participants can benefit from AI-driven solutions, such as LLMs, which can simplify complicated papers, offer real-time explanations, and customize information according to each participant's literacy level. A recent study assessed the ability of Generative Pre-trained Transformer 4 (GPT-4) to produce patient-friendly summaries and comprehension tests from consent forms guided by cancer trials.53. After reading the AI-generated summaries, over 80% of participants in a study said they had better comprehension and were more interested. Multiple-choice questions created by AI showed >85% agreement with human annotations. But when the model went beyond the original text, mistakes happened, highlighting the necessity of human review[49]. Crucially, these AI-powered strategies don't have to be restricted to the first consent interaction. After permission, such tools can facilitate continued patient education and trial navigation, improving knowledge of study protocols and expectations during participation. As will be covered in more detail in the section on "AI for Patient Retention," such continuity is consistent

with the idea of informed consent as a continuous process and may help maintain engagement and lower dropout rates.

4.5 AI for clinical trial analyses

4.5.1 Digital pathology and radiological imaging

The two most developed data fields are radiological imaging and digital pathology. Using histopathological evaluation and/or immunohistochemistry as the reference standard, a systematic review and meta-analysis of AI tools for digital-pathology whole-slide images assessed 100 diagnostic-accuracy studies (48 included in quantitative synthesis) covering >152,000 slides across multiple diseases. Due to insufficient reporting of case selection, data partitioning, and raw performance metrics, almost all studies displayed at least one high or unclear risk of bias or application, despite pooled sensitivity and specificity being 96.3% and 93.3%, respectively[50].

The findings demonstrate significant diagnostic potential and emphasize the necessity of more well planned and openly reported evaluations prior to general clinical implementation. The technical and legal advancements that are making it possible to incorporate digital pathology into standard oncological practice are outlined in a recent review[51]. Coordinated efforts to standardize the upstream procedures that depend on algorithm performance are supporting AI readiness in radiological imaging. Simultaneously, recent developments in generative modeling provide high-fidelity synthetic pictures that enhance and anonymize clinical scans, lowering obstacles to data sharing and privacy in multicenter research. If picture realism, deidentification, and regulatory control are strictly maintained, these data support acquisition-standardization efforts by boosting training diversity and facilitating modality translation and contrast synthesis.

A modified Delphi process was used in a consensus statement from the European Society of Radiology (ESR) and the European Organization for Research and Treatment of Cancer (EORTC) to establish minimum technical and procedural requirements for lesion segmentation. These requirements included signal-to-noise and spatial resolution thresholds, system performance certification, required reference standards, and operator training and revalidation (≥75% expert agreement).57. These recommendations reduce a significant source of variability by standardizing image acquisition and segmentation logistics across centers. This allows for the reliable deployment of deep-learning models as quantitative biomarkers or adaptive-trial endpoints, as well as the reproducible extraction of radiomics features[51]. The ESR Imaging Biomarker Alliance (EIBALL), in collaboration with organ-specific European radiology societies, maintains an open-access Biomarkers Inventory to add to these segmentation standards. It lists validated semiquantitative and quantitative imaging biomarkers, rates the supporting data, and is updated on a regular basis[52].

4.5.2 Pharmacometrics workflows

Pharmacometrics workflows in trials can be improved by using AI-driven methods in clinical pharmacokinetic/pharmacodynamic (PK/PD) modeling. Large PK/PD datasets can be quickly analyzed by ML algorithms to find intricate covariate correlations that underlie interpatient variability. Sixty For instance, an elastic-net model reduced 75 baseline variables into a single risk score in 127 patients with hepatocellular carcinoma receiving the fibroblast growth factor receptor 4 (FGFR4) inhibitor roblitinib. This risk score, when added to a population PK/PD tumor-

growth-inhibition model, eliminated unexplained variability in the resistance parameter by 19% and in the dose required for tumor stasis by 32%.61. Dosing and trial design decisions can be influenced by our ML-enhanced PK/PD framework, which also improves patient-specific response predictions[53].

In a simulated trial for a FGFR inhibitor, an RL agent using PK/PD simulations beat standard dose-adjustment guidelines, boosting treatment effectiveness and safety endpoints by >10%.62 This is an example of how reinforcement learning (RL) frameworks have been used to customize adaptive dosing procedures. Accordingly, a recent scoping review of precision dosing in oncology found a number of ML-driven dosing techniques that showed promise in maximizing anticancer treatment efficacy while decreasing toxicity in comparison to conventional dosing, with RL algorithms being particularly prominent[54].

4.5.3 Multimodal predictive and prognostic modelling

In recent years, integrated machine learning frameworks that incorporate radiological, histological, molecular, and clinical data into a single model have replaced unimodal feature extraction as the analytical focus in oncology. Such multimodal architectures consistently achieve higher concordance indices (C-indices) or area under the receiver operating characteristic curve for endpoints such as overall and progression-free survival, disease recurrence, pathologic complete response, and treatment benefit than models trained on any single data source, according to comparative studies compiled in recent high-impact reviews. The improvement in performance is ascribed to the complementing biological data and patient-level variables recorded across modalities, which collectively offer a more thorough depiction of tumor behavior and treatment context[55].

Current state-of-the-art evidence currently covers a variety of malignancies. By combining whole-slide hematoxylin-eosin images with the International Federation of Gynecology and Obstetrics (FIGO) stage in 2072 endometrial cancer patients, the Histopathology-based Endometrial Cancer Tailored Outcome Risk network (HECTOR) achieved C-indices of 0.79-0.83 for 10-year distant-recurrence-free survival, outperforming molecular-pathology risk scores and identifying the subgroup that benefits from adjuvant chemotherapy.66 With AUCs of 0.88 in pooled external and 0.93 in prospective test cohorts, the Multimodal Integrated Fully Automated Pipeline System (MIFAPS) predicted pathologic complete response to neoadjuvant chemotherapy by integrating preoperative magnetic resonance imaging, digital pathology, and clinicopathological variables in 1004 breast cancer patients.

An ensemble that combines lesion-level computed data for high-grade serous ovarian cancer. The external RECIST-based response AUC increased from 0.47 (clinical model) to 0.78 using CT radiomics with circulating-tumor-DNA metrics and baseline clinical data, while the volumetric-response error decreased by 8%. Self-supervised radiology and histopathology encoders were paired with adaptive aggregation in the FoMu foundation-model architecture. Trained on 712 multicenter ovarian cancer cases, it generalized to four independent hospitals with C-indices ≥0.78 for overall and progression-free survival without recalibration. Lastly, an explainable neural network that integrated EHR variables, computed tomography-derived body composition biomarkers, and tumor mutational profiles in a pan-cancer study of 15,726 real-world patients

identified 114 important prognostic variables and 1373 cross-modal interactions, demonstrating scalability to routine data streams[56].

4.6 AI for simulating clinical trials

Simulations powered by AI have the potential to supplement conventional oncology studies. Virtual testing of medicines is made possible by methods such in silico trials and digital twins (DTs), which may speed up research. According to Katsoulakis a healthcare DT is a dynamic virtual representation of an individual that allows treatment strategy simulation and health trajectory prediction based on multimodal data (e.g. clinical, genetic, molecular, and environmental). They provide a summary of the existing uses of DTs in healthcare in their most recent scoping assessment.

They came to the conclusion that while there have been a number of DT programs in the government, military, and industry, DT for health care is still in its infancy. Tumor genetics, imaging, and clinical history can all be incorporated into patient-specific DTs in oncology to predict therapy response and disease progression. According to the most recent narrative review by Giansanti and Morelli, early implementations have shown possible decision making and optimized therapeutic regimens employing oncology DTs. For instance, DTs have been used to forecast each patient's unique chemotherapy reaction, so generating a virtual "trial" that directs individualized care[57].

Using artificial cohorts of virtual patients, in silico clinical trials replicate complete trial populations. Computational models or DTs are used in these simulations as experimental arms and proxy controls to test interventions. According to Kolla causal AI-driven in silico trials can mimic the efficacy and control arms of cancer studies, helping with dose optimization and patient selection. In silico trials facilitate the quick in silico assessment of novel cancer treatments across a variety of patient profiles by utilizing comprehensive clinico-genomic databases and mechanistic models.

By eliminating the need to expose actual patients to poor therapies, this method can supplement or even partially replace some features of traditional trials (e.g., utilizing a synthetic control arm in place of a placebo group). Real-world trials cannot now be completely replaced by AI-driven simulations. To guarantee that models accurately reflect the intricate biology of cancer and treatment toxicities, they must be thoroughly verified against clinical data. Therefore, it is currently agreed upon that these technologies are supplements to conventional phase I–III enabling more efficient hypothesis generation and trial design refinement rather than outright replacement of human trials[58].

4.7 Regulatory and health technology assessment considerations on AI in medicine development.

Both the FDA and the European Medicines Agency (EMA) have issued position papers and discussion documents aimed at facilitating the integration of AI-enabled tools across the drug-development life cycle. These documents emphasize that AI-based approaches remain subject to established requirements, for example, for data management, statistical integrity, and traceability. Accordingly, AI models should be prospectively specified; subsequent modifications ought to be version-controlled; and, where feasible, algorithms and training data should be made publicly accessible. Early, iterative dialogue with regulators regarding how an AI tool will be embedded in a development programme is encouraged by both agencies. When AI is used to derive trial outcomes, such as quantitative measures derived from imaging or pathology,

DHT endpoints, or NLP-extracted symptoms from EHR text, the algorithm's context of use should be prospectively defined (e.g., exploratory versus confirmatory endpoint; adjudication support versus autonomous scoring), and its credibility should be backed by proof that it is appropriate for the intended trial setting[59].

These ideas also apply to AI-based AE data extraction from unstructured EHR clinical narratives: sponsors should be able to show that the AI solution consistently detects AE concepts and attributes without clinically significant under-capture, maintains provenance to the original source, and supports controlled downstream safety processes (medical review, coding, reconciliation, and, if applicable, expedited reporting), including explicit definitions of human oversight and accountability. Regulators are likely to prepare for characterisation of mistake mechanisms (including overlooked major adverse events), documented validation against standard procedures, and a human-in-the-loop workflow where qualified staff members verify the seriousness, cause, and coding of adverse events. As these requirements are satisfied and human expert monitoring is maintained as necessary, an increasing amount of regulatory experience indicates that AI-assisted endpoint measurement may be acceptable. The viability of this pathway is demonstrated by the recent qualification by the EMA's Committee for Medicinal Products for Human Use (CHMP) of an AI algorithm that measures disease activity in metabolic dysfunction-associated steatohepatitis. This is the first AI-based diagnostic that has been approved as a trial endpoint[60].

Interest in external or "synthetic" control arms derived from RWD has increased in oncology due to the increasing use of expedited approval processes for targeted medicines, especially in situations where randomized controls may be impractical or unethical.84. A number of organizations, including regulatory bodies, have described frameworks in which generative and causal-inference AI models could create or augment such datasets in a predetermined, auditable manner, despite the fact that the majority of published external-control studies have up to now relied on conventional epidemiological methods. By substituting parts of the recruited population in nine completed oncology trials while maintaining concordance with the initial efficacy and safety outcomes, a sequential-synthesis AI model has already proven proof-of-concept.As of right now, no marketing authorization has directly relied on data created from scratch by an AI system. However, recent rulings demonstrate that well selected RWD can supplement traditional evidence packages and eventually help set precedents for the acceptance of evidence that includes AI-generated assessments. For instance, the FDA examined Flatiron Health EHR data when considering palbociclib for male patients with metastatic breast cancer; while residual confounding limited causal interpretation, the exercise illustrated the usefulness of integrating large-scale RWD into regulatory review. The same lack of comparable data makes payment decisions more difficult from the standpoint of health technology assessment (HTA)[61].

As demonstrated by the alcedinid versus ceritinib analysis in anaplastic lymphoma kinase (ALK)-positive lung cancer, hybrid approaches that combine single-arm trial results with RWD also show how RWD-based external control construction could provide decision-grade comparative effectiveness estimates in the future. Regulatory and HTA frameworks are progressively moving toward evidence standards that may eventually allow AI-derived data to be assessed with methodological scrutiny comparable

to that applied to traditional sources by fusing the lessons learned from current RWD applications with new approaches to AI-generated synthetic cohorts[62].

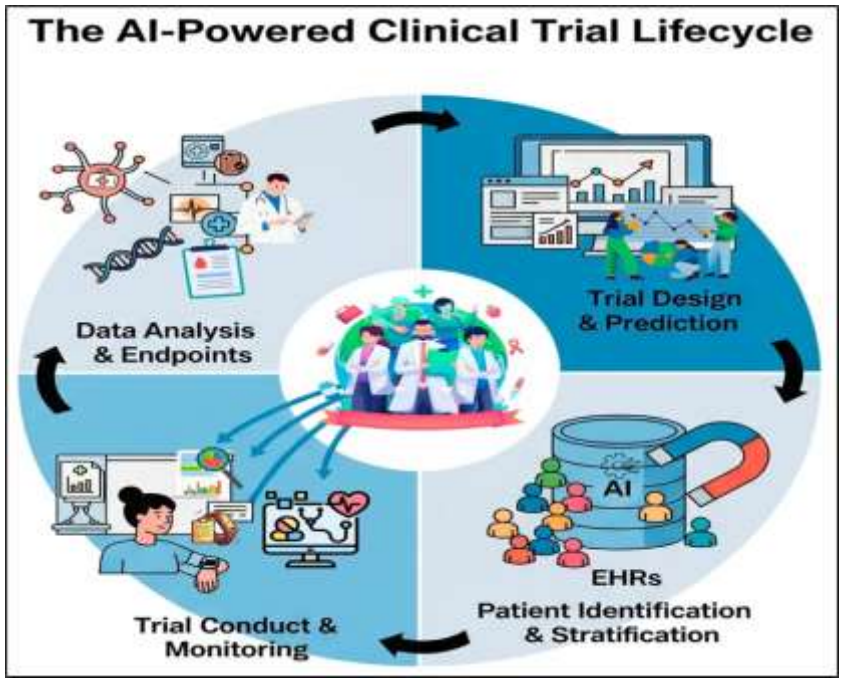


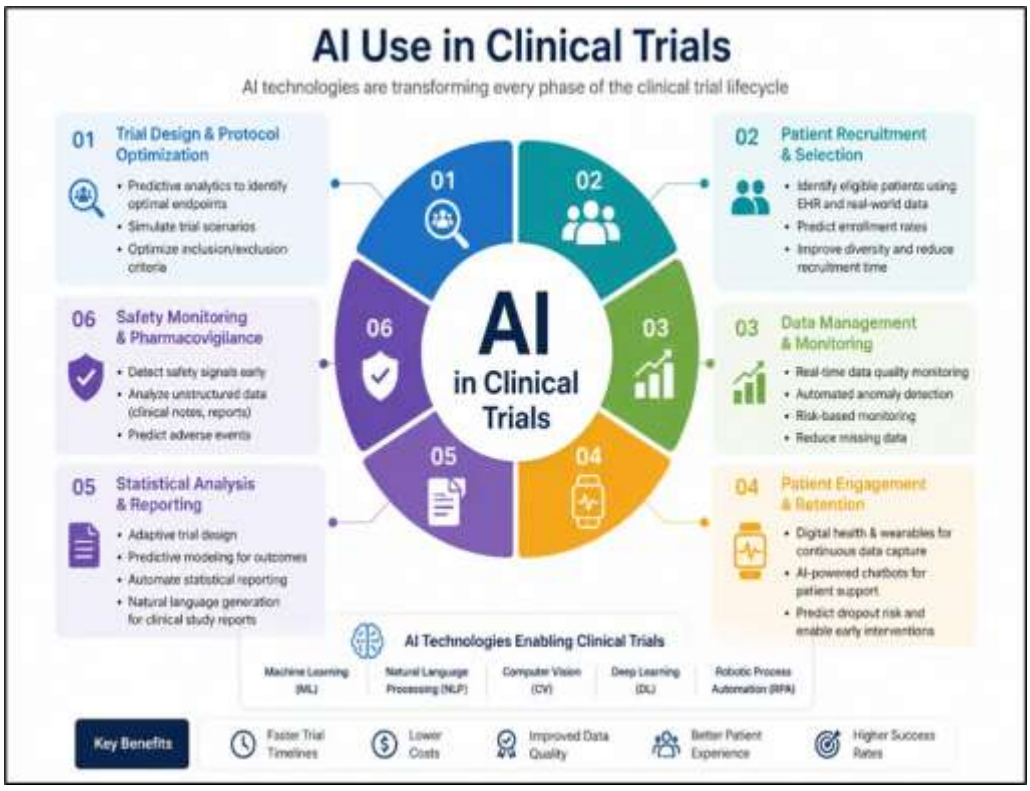
Fig No.2 The AI Powered Clinical Trial Lifecycle

5. RESULTS AND DISCUSSION

5.1 Results

The results of integrating AI into DTx clinical trials typically fall into three measurable categories: operational efficiency, data quality, and patient outcomes.

- **Operational Efficiency & Timelines:** Reduced Trial Duration: Recent data suggests that AI-optimized trials can reduce overall duration by 20–30%. In specific phases, AI compound screening and patient matching have reduced timelines by up to 59%.
- **Protocol Automation:** The adoption of "Agentic AI" in 2026 has automated the interpretation of clinical protocols. This has minimized manual data entry errors and slashed the time required for protocol amendments—traditionally one of the biggest bottlenecks.
- **Site Selection:** AI models now predict site performance with 80–90% accuracy, identifying locations with the highest likelihood of successful patient recruitment.
- **Digital Biomarkers:** AI effectively processes high-frequency data from wearables to identify "digital biomarkers." These provide a continuous view of patient health rather than the "snapshot" view provided by traditional clinic visits.
- **Synthetic Control Arms:** Results show an increasing use of AI-generated synthetic control arms, which reduce the number of patients needed for a trial while maintaining statistical rigor.



Graph No.1 AI Use in Clinical Trials

5.2 Discussion

The Shift to "Predictive" Trials: Traditionally, clinical trials were reactive (waiting for data to be collected, then analyzed). The integration of AI has made them proactive. By simulating a trial end-to-end before it even begins, sponsors can expose potential bottlenecks or eligibility criteria issues early. This shift represents a fundamental change in the "biological plausibility" of DTx.

Patient-Centricity and the Placebo Effect: Interestingly, DTx often leverages the "digital placebo effect"—where the high level of engagement with an app can improve outcomes. AI personalizes this engagement, making the therapeutic feel "bespoke" to

Challenges: The "Refractory Period" of Regulation: While technology has moved fast, regulatory policy in 2026 is in a "slow recovery" phase. Discuss the gap between technical capability (what AI can do) and regulatory acceptance (what the FDA allows). This gap remains the primary hurdle for the widespread commercialization of AI-driven digital therapeutics

6. CONCLUSION

Clinical trials have undergone a fundamental paradigm shift with the combination of AI and Digital Therapeutics (DTx). The "snapshot" era of medicine, in which data is gathered during sporadic clinic visits, is giving way to a period of ongoing, predictive, and patient-centered research.

- **Operational Transformation:** AI has effectively transformed clinical trials from a difficult, manual procedure into a data-driven pipeline, drastically cost reductions and speeding up the release of life-saving digital solutions.

- **Data Revolution:** Previously impossible levels of accuracy and data integrity are

ensured by the shift from subjective patient diaries to objective digital biomarkers.

- **The Ethical Mandate**: Transparency is crucial to this field's success as we move to 2030. The crucial obstacles that researchers and developers must overcome are assuring shifted objective datasets and using Explainable AI (XAI) to solve the "Black Box" problem.

7. RECENT AND FUTURE PERSPECTIVES

7.1 Recent Perspectives (2025–2026)

- **From "Pilots" to Infrastructure:** By 2026, AI has moved from experimental "pilot programs" to the standard operating system for testing. Companies now question how to incorporate AI into every phase, from protocol writing to data monitoring, rather than if they should utilize it.

- **Living Protocols:** "Living Protocols"—AI-powered systems that may automatically update and modify trial parameters (such as dosage or frequency of digital intervention) depending on real-time data intake—are now used in modern trials, greatly minimizing the need for manual changes.

- **Regulatory "Refractory Period":** While technology has advanced rapidly, regulatory bodies like the FDA are in a "recovery phase." There is a high demand for Explainable AI (XAI); regulators are rejecting "black box" models in Favor of traceable logic where every AI-supported decision is transparent and auditable.

- **Decentralization as Standard:** Hybrid models—where patients participate from home using DTx apps and wearables—are now the industry standard. This has improved participant diversity and trial accessibility across global regions.

7.2 Future Perspectives (2027–2030)

- **Digital Twin Populations:** By 2030, the use of "Digital Twins" (virtual replicas of patients based on their genetic and medical history) will allow researchers to simulate drug and DTx interactions before a single human is enrolled. This could potentially replace traditional placebo arms in some studies.

- **The Rise of Non-Traditional Players:** Expect big tech companies (Apple, Google, Amazon) to become major "Site Operators." Their ability to collect continuous health data through consumer devices will give them a competitive edge over traditional clinical sites.

- **Hyper-Personalized Interventions:** Future AI will not just monitor trials; it will dynamically tailor the digital therapeutic to the individual's lifestyle, culture, and biological response in real-time, making "one-size-fits-all" trials obsolete.

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