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Review Article

HARNESSING ARTIFICIAL INTELLIGENCE: TRANSFORMING CLINICAL TRIALS FOR THE FUTURE

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ABSTRACT

To evaluate the impact of artificial intelligence (AI) technologies on clinical trial processes, identify quantitative benefits, and determine areas requiring further research. A comprehensive literature review was conducted examining AI applications across clinical trial phases. The study analysed machine learning (ML), natural language processing (NLP), computer vision, reinforcement learning (RL), and other AI technologies as applied to clinical research processes. AI implementations have delivered substantial quantitative benefits across various aspects of clinical trials (CT). International Business Machine (IBM) Watson enabled an 80% increase in patient accrual to breast cancer trials within just 11 mo. *In silico* medicine's generative tensorial reinforcement learning (GENTRL) platform accelerated the drug discovery timeline by a factor of 15, reducing it to just 46 days. Saama Technologies' deep learning (DL) approach detected 30% more anomalous data cases compared to traditional methods. Pfizer's use of AI-driven quantitative systems pharmacology (QSP) models led to a 60% reduction in Phase 2 dose cohorts. AiCure's AI-powered monitoring system achieved 25% higher medication adherence and completed trials 30% faster. Meanwhile, Unlearn. AI's digital twin technology enabled a 30% reduction in control group size without compromising statistical power. These outcomes highlight AI's powerful role in improving the efficiency, speed, and quality of CT. AI is trans formatively enhancing CT through improved recruitment efficiency, protocol optimization, data quality management, and patient monitoring. However, challenges remain in data quality, algorithm interpretability, regulatory compliance, workflow integration, and bias mitigation. Future research should focus on advanced predictive modelling, explainable AI development, federated learning for privacy preservation, AI-human collaboration models, real-world data integration, and standardized validation procedures. Ethical considerations and regulatory frameworks specifically addressing AI in CT require further development to realize the full potential of these technologies.

Keywords: AI, Clinical trial, ML, Regulatory compliance, Real-world evidence

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INTRODUCTION

CT serve as the cornerstone of medical research, evaluating the safety and efficacy of new interventions through rigorous scientific investigation. These trials progress through four phases: Phase I (small group testing for dosage and side effects), Phase II (larger group monitoring of adverse effects), Phase III (testing in diverse populations before approval), and Phase IV (extended testing in wider populations) [1, 2]. The integration of AI into CT is transforming this field by addressing key challenges in design, recruitment, and analysis [3]. AI applications in CT include trial design optimization through algorithms like HINT that predict success based on drug molecules, diseases, and eligibility criteria, patient recruitment enhancement via tools like auto trial that match participants to suitable studies; data management improvement through extraction from unstructured reports and annotation of images/lab results; identification of distinct patient subgroups with unique treatment responses; and detection of safety signals and adverse events earlier than traditional methods. This integration addresses inefficiencies in clinical research, potentially reducing costs and accelerating treatment development while maintaining research quality [4-6]. AI offers significant benefits to CT, including faster data processing, more precise patient selection, real-time analysis capabilities, cost reduction, novel pattern recognition, and support for adaptive trial designs. Despite its promise, AI implementation faces several hurdles: data quality and standardization issues due to population and healthcare system variations; limited transparency in "black box" AI models, raising concerns about bias; regulatory uncertainty regarding AI-based methods; ethical considerations surrounding patient autonomy and privacy; technical expertise and infrastructure requirements; and patient trust concerns regarding AI-determined results. Notable recent developments include federated learning that maintains privacy while enabling cross-site data analysis; advanced NLP for extracting information from clinical documents; AI-powered analysis of wearable device data for continuous patient monitoring; development of synthetic control arms based on historical data; multimodal AI systems integrating diverse data types for improved diagnostics; and progress in explainable AI to address transparency concerns. As AI continues evolving, its integration into CT offers opportunities to accelerate medical advances while raising important implementation questions. Success will require collaboration between AI experts, clinical researchers, regulators, and patient advocates to maximize benefits while addressing challenges [7-13].

Methods

The methodology for this review employed a systematic approach to literature selection with clearly defined inclusion and exclusion criteria. The review included peer-reviewed articles, industry reports, and regulatory guidelines published between 2018-2024 that specifically focused on AI applications in CT. To ensure comprehensive coverage, we selected literature featuring empirical evidence, theoretical frameworks, or case studies demonstrating practical AI implementation across various clinical trial phases. We excluded publications without specific clinical trial applications, purely conceptual articles lacking implementation examples, non-English literature, and studies focusing solely on technical aspects without addressing clinical relevance. This balanced approach ensured comprehensive coverage of both academic research on AI methodologies and real-world applications, providing both theoretical foundations and practical implementation evidence. For case studies, a structured selection framework applied, prioritizing examples with demonstrable quantitative outcomes and performance metrics. Case studies selected representing diverse AI technologies (ML, NLP, computer vision and etc) applied across different clinical trial phases to provide comprehensive coverage of the field. The selection balanced

examples from established pharmaceutical companies and innovative startups to capture both enterprise-scale implementations and emerging approaches. Each selected case study demonstrated methodologically for evaluation approaches that allowed for meaningful analysis. We analysed these cases, examining implementation approach, quantitative outcomes, limitations, and potential generalizability to other clinical research contexts.

DISCUSSION

AI is such a transforming tool in healthcare that huge implications can also be drawn within the scope of CT. The following section outlines important AI technologies shaping different parts of clinical research.

NLP

NLP technologies play a crucial role in processing and analysing the vast amounts of unstructured textual data generated during CT. They enable the review of previous trial protocols to identify patterns, suggest improvements, and ensure consistency across studies. Additionally, NLP algorithms can analyse clinical notes and patient-reported outcomes to detect potential adverse events that might be overlooked through traditional reporting methods [16, 17].

Computer vision

Computer vision, particularly when powered by convolutional neural networks, is highly valuable in CT involving imaging data. In oncology studies, these algorithms can accurately measure tumour progression from medical images, significantly reducing interobserver variability. Additionally, in trials utilizing wearable devices, computer vision can analyse video data to assess patient mobility or detect visual indicators of health status, offering objective and consistent evaluations [18, 19].

RL

Although still in its early stages of application in CT, RL shows significant promise for optimizing trial designs and decision-making processes. RL algorithms can adapt trial parameters dynamically based on real-time incoming data, enabling more efficient and ethical study conduct by continuously learning and improving throughout the trial. A notable example is the use of RL to develop adaptive treatment strategies in non-small cell lung cancer (NSCLC), where researchers employed RL models to personalize treatment decisions based on patient-specific characteristics and responses. This approach aimed to improve clinical outcomes by dynamically tailoring therapies, demonstrating RL's potential to transform conventional trial methodologies into more responsive and patient-centric models [20].

Generative AI

Large language models (LLMs), a type of generative AI, are being applied in innovative ways within CT. They can assist in drafting initial versions of trial protocols, thereby accelerating the design process. Additionally, generative AI can be used to create personalized patient education and informed consent materials, improving patient understanding and engagement [21–23]. For instance, *in silico* medicine used its GENTRL model to design novel molecular structures for fibrosis, accelerating the drug discovery process. The AI-designed drug candidate progressed from generation to animal testing in just 46 days, compared to traditional timelines that often span several months or years. This demonstrates the potential of generative AI not only in protocol design and patient communication but also in accelerating drug discovery for CT.

Federated learning

Federated learning enables the training of AI models across multiple decentralized data sources without the need to share raw data-addressing a major privacy concern in multicentre trials. By keeping the data localized at each participating site, only model updates (and not raw patient data) are shared, thus preserving data privacy. This approach mitigates privacy concerns by ensuring that sensitive information does not leave the local institution. As a result, federated learning allows researchers to collaboratively build robust AI models while maintaining the confidentiality of patient data. This is especially critical in multicentre trials, where data is spread across various institutions and jurisdictions, and compliance with privacy regulations like general data protection regulation (GDPR) is essential [24].

Explainable AI (XAI)

Explainable AI techniques are essential for ensuring transparency and building trust in the growing use of AI in clinical decision-making. XAI allows researchers to understand and interpret the decisions made by AI models when analysing clinical trial data an important requirement for regulatory compliance and ethical responsibility [25].

Ml and Dl

ML, particularly DL, serves as the foundation for most AI applications in CT. These technologies enable advanced pattern recognition and predictive modelling across various stages of trial design and execution [14]. ML algorithms can analyse historical trial data to predict patient enrolment rates, potential dropout risks, and likely outcomes facilitating more informed and efficient trial planning. Additionally, DL models can process complex patient data to identify subgroups more likely to respond to specific treatments, allowing for more targeted and effective follow-up studies [15].

Mostly these AI technologies do not work in isolation in dealing with bigger issues pertaining to clinical trial issues. Synergizing all these AI technologies onto one single platform promises enhanced efficiency of trials, reduction in costs, and acceleration in developing new therapies.

Applications of AI in clinical trial phases

AI is currently showing its effect on every phase of CT, from planning before the trial to post-trial analysis. Specific discussion on the applications of AI technologies at these different stages of the clinical trial process.

Case studies

The section that follows presents some key case studies on how AI has been applied in reality and on what impact it has had on different areas of CT. These examples show the deployment of AI technologies in solving certain challenges and enhancing the outcomes of trials.

Accelerating patient recruitment: IBM Watson for clinical trial matching

One of the most time-consuming and difficult parts of clinical research is patient recruitment. IBM's Watson for clinical trial matching has solved this problem by leveraging AI. Watson was used at the Mayo Clinic to compare electronic EHRs and clinical trial protocols to identify matching patients with relevant clinical studies. Through NLP and ML, Watson had the ability to analyse complex health data and select eligible candidates at a very high accuracy level. This was an AI-based strategy that saw patient accrual to breast cancer trials improve by 80% just 11 mo later. By streamlining the matching process, watson not only made the recruitment process faster but also enhanced the quality and accuracy of the patient-trial matches. This case shows how AI can potentially improve the efficiency of CT by shortening the recruitment timelines, enhancing the accuracy of trial enrolment, and ultimately leading to trial success [41].

Enhancing protocol design: *in silco* medicine's gentrl

Another compelling case demonstrating the transformative role of AI in drug discovery and early-stage trial design involves *in silico* medicine. The company employed its AI system, GENTRL, to design a novel drug candidate for the treatment of fibrosis. Remarkably, the AI-designed molecule progressed from initial generation to animal testing in just 46 days timeline, that is approximately 15 times faster than traditional drug discovery methods, which are often time-consuming and costly [42]. This case highlights AI's potential to drastically accelerate the pre-clinical phase of drug development and significantly reduce the overall time and expenses associated with bringing new drug candidates to CT.

Table 1: Applications of AI across the drug development lifecycle

Pre-clinical phase AI is relevant even at this very preliminary stage of the process for drug discovery and target identification.	**Drug discovery:** AI algorithms, particularly ML models, can predict molecule properties and potential drug candidates to accelerate drug discovery. Atomwise's Atom Net platform screened 8.2 million compounds for COVID-19 therapies in just four days rather than months. Exscientia's AI-designed drug DSP-1181 for obsessive-compulsive disorder reached CT in just 12 mo one-fifth the traditional timeline. **Target identification:** AI analyses genomic and proteomic datasets to identify novel therapeutic targets. Benevolent AI's platform identified baricitinib as a potential COVID-19 treatment by analysing viral entry mechanisms and existing drugs, leading to food and drug administration (FDA) emergency use authorization. Recursion pharmaceuticals' AI analysed over 100 million microscopy images to discover a novel target for cerebral cavernous malformation, revealing a therapeutic pathway that traditional approaches had missed for decades [25, 26].
Phase I: Safety and dosage This phase is designed to test and estimate the safety and dosage of a new drug.	**Toxicity prediction:** AI models predict potential toxicities from molecular structures and preclinical data [28]. DeepTox achieved 30% higher accuracy in the Tox21 Data Challenge compared to traditional methods. Pfizer's AI-based screening reduced animal testing by 20% while maintaining safety standards. *In sitro's* models accurately predicted drug-induced liver injury for previously failed compounds [80]. **Dose optimization:** ML algorithms suggest optimal dosing strategies using pharmacokinetics/pharmacodynamics (PK/PD) data, reducing participants needed in dose-escalation studies [29]. AstraZeneca's AI models optimized dosing for AZD5991, reducing Phase I trial size by 25% and accelerating timelines by 3 mo. Genentech's ML-driven approach reduced required dose cohorts from 8 to 5 while maintaining statistical power.
Phase II: Efficacy and side effects AI can help in assessing the efficacy of the drug and also in finding out its possible side effects at this phase.	**Efficacy prediction:** AI models can integrate genomic, clinical, and imaging data to predict patient responses, enabling more targeted trial designs. For instance, Tempus uses AI to match cancer patients to CT based on molecular profiles. DeepMind has applied AI to predict treatment outcomes in diabetic retinopathy using imaging and clinical data [30]. **Adverse event detection**: NLP techniques can analyse clinical notes and patient-reported outcomes to identify adverse events. The FDA's Sentinel System uses such AI methods for early drug safety monitoring. Johnson and Johnson also applies NLP to detect adverse drug reactions from clinical trial data and spontaneous reports [31].
Phase III: Large-scale efficacy This would then be followed by studies in bigger patient populations and of longer duration, for which AI can make a big difference in terms of efficiency.	**Patient recruitment:** AI algorithms can streamline patient recruitment by rapidly analysing electronic health records (EHRs) to identify eligible candidates, improving speed and diversity. A notable example is IBM watson for clinical trial matching at Mayo Clinic, which led to an 80% increase in breast cancer trial accrual within 11 mo [32]. **Real-time monitoring:** Wearable devices and electronic diaries provide continuous patient data, which ML models analyse to monitor adherence and detect early adverse events. AiCure, an AI-powered platform, uses smartphone cameras to verify medication ingestion, resulting in 25% higher adherence and 30% faster trial completion in a Phase 2 schizophrenia study [33].
Phase IV: Post-market surveillance This would then be followed by studies in bigger patient populations and of longer duration, for which AI can make a big difference in terms of efficiency.	**Pharmacovigilance**: AI can detect previously unrecognized adverse drug effects by analysing large volumes of post-market data from sources such as social media, EHR's, and insurance claims databases. For example, the FDA's Sentinel Initiative utilizes AI-driven analytics to enhance the identification of safety signals from real-world data [34]. **Real-world evidence generation:** ML methods are increasingly applied to real-world data to assess the effectiveness and safety of medications in broader patient populations. A key example is Flatiron Health, which uses AI to analyse oncology EHRs, generating real-world evidence that supports regulatory and clinical decision-making [35].
Cross-phase application AI applications span multiple phases of CT.	**Protocol optimization** It can also use AI in the analysis of historical trial data to recommend optimal inclusion/exclusion criteria, endpoint selection, and visit schedules in bettering chances for trial success [36]. **Adaptive trial design** AI, particularly through RL, enables dynamic adjustments to trial parameters based on incoming data in real time. This allows trials to adapt sample sizes, treatment arms, or dosing strategies on-the-fly, improving efficiency and ethical conduct by minimizing patient exposure to less effective treatments [37]. For instance, AI-driven adaptive designs have been explored in oncology trials to rapidly adjust dosing or switch treatment strategies based on interim patient responses. **Data quality management** AI enhances data quality by providing real-time validation during data entry, identifying inconsistencies, outliers, or missing information across sites. DL models and NLP can flag discrepancies in unstructured data (e. g., clinical notes) and even detect potential fraud. Tools like Saama Technologies' AI model have shown to detect 30% more anomalous data than traditional statistical methods, significantly improving trial reliability [38]. **Patient engagement** Chatbots, or other models of natural language generation, could provide tailored information for participants to increase the likelihood of them staying in a study [39].
Regulatory compliance AI-powered systems can help in ensuring that documentation and processes related to trials are in compliance with the regulations by raising flags against some of the probable issues [40].	The integration of AI across these phases is foreseen to allow for a potential huge reduction in time and cost for new therapies reaching the market and enhancing quality and reliability in CT data. However, it cannot go unnoticed that the use of AI in CT also raises serious concerns with regard to the protection of data subjects, algorithm bias, and acceptance by regulatory authorities, which are challenges to be met.

Improving data quality: Saama technologies' dl approach

Data quality is an essential consideration that has a direct impact on the success and validity of CT. Saama Technologies demonstrated how AI can be used to revolutionize this area. The company created a DL model intended to identify anomalous data records within clinical trial data. Having been trained on past trial data, the model could successfully identify patterns connected to possible data issues. Consequently, the AI system accurately identified 30% more anomalous cases than would be possible with standard statistical

approaches, while at all times holding a false positive rate of below 5% [43]. This example demonstrates the potential for AI to greatly enhance the efficiency and effectiveness of data quality checking, resulting in more confident trial outcomes and possibly shortening the route to regulatory approval.

Optimizing dose selection: QSP at Pfizer

Pfizer showed how AI-based QSP models can be used to optimize dose choice early on in CT. In one instance, Pfizer used a QSP model to forecast the best dose for a new pain drug. This AI model incorporated data both from preclinical experiments and early human studies to guide dosing. The result was extremely successful the model correctly forecasted the effective dose range, allowing Pfizer to cut the number of dose cohorts in their Phase 2 trial by 60% [44]. This example shows how AI can be used to optimize dose selection, thereby cutting the number of participants in early-phase trials and helping to create more efficient and cost-effective clinical programs.

Enhancing patient monitoring: aicure's ai-powered platform

AiCure offered a strong demonstration of how AI can revolutionize patient adherence and monitoring in CT. The firm utilized AI-powered technology that utilized smartphone cameras to confirm taking medication and monitor patient behaviour in real time. The method was piloted in a Phase 2 trial for a schizophrenia drug. The outcomes were significant: rates of adherence among patients in the AI-monitored group were 25% greater, and the trial finished 30% sooner than with conventional methods [45]. This example highlights the power of AI to increase patient adherence substantially, resulting in more accurate data gathering and potentially shorter, more streamlined clinical trial durations.

Predicting trial outcomes: Unlearn. AI's digital twin approach

Unlearn. AI demonstrated how AI can transform clinical trial design by creating "digital twins" virtual patient models to forecast clinical outcomes. The firm built ML models trained on past clinical trial data to create these digital twins, which were then employed in conjunction with actual control groups in a simulated Phase 3 Alzheimer's trial. This novel strategy reduced the number of actual patients by 30% without compromising the statistical power of the trial [46]. Digital twins created using AI provide a potential solution for minimizing control group sizes, optimizing trials and making them both more efficient and ethically defensible, especially within therapeutic spaces where recruitment of patients is challenging. Together, these case studies illustrate the wide range of uses of AI in CT, from drug development and dose optimization to patient surveillance and data quality improvement. The results are promising, but broader use of AI in clinical research is still in its infancy. Progress will depend largely on regulatory acceptance and thorough consideration of ethical issues.

Table 2: Comparative analysis between traditional approach and AI-driven approaches

	Traditional approach	AI-driven approaches
Patient recruitment and screening	Manual charts revies, physical referrals, public advertisement	AI scan EHR, databases to identify the eligible participants
Protocol design and optimization	Based on experts' opinion and limited trial data	Analyse large historical datasets and stimulate trail outcome
Data quality and monitoring	Periodic monitoring and monitoring	Real-time detection and validation
Adverse event detection	Based on Clinical judgement	AI uses NLP on clinical note and EHRs to detect unreported events
Real-world data integration	Limited due to format and scale	AI process claims and social media

Ethical considerations and regulatory landscape

The application of AI in CT presents a number of new ethical concerns and regulatory issues. This article provides an overview of the main ethical considerations regarding the application of AI in clinical research and an evolving regulatory framework that aims to address the associated concerns.

Ethical considerations

Data privacy and security

In view of the high usage in large datasets, AI systems require extremely high importance of protection concerning patients' data in terms of privacy and security. Data privacy and security can be maintained by Implementation of robust data encryption, access controls and federated learning techniques can be used for decentralize data [47].

Informed consent

One of the most prominent issues when dealing with AI systems of such complexity is how to provide adequate information to participants about the role of AI in trials. Specific consent procedures can be generated by using AI and to Enhance the participant understanding interactive tools are used [48].

Algorithmic bias and fairness

It may inadvertently reinforce or even increase already existing biases in health care, which AI systems would do. Regular audits of the AI system carried out to overcome Algorithm Bias and diverse representation of in AI development teams and training databases can be considered [49].

Transparency and explain ability

Some AI algorithms are of a "black box" nature, their transparency interfering with clinical decision-making. Clear communication about what the AI will do and not do with all relevant stakeholders by developing explainable AI techniques [50].

Human oversight and autonomy

Determining the appropriate level of AI autonomy in CT is crucial. The clear protocol can be established for human oversight and regular assessment of the performance and limitation of the AI systems [51].

Regulatory landscape

The regulatory framework in relation to AI within CT is still in development, with agencies having to work hard to keep pace with technological advancement.

FDA initiatives

The U. S. Food and Drug Administration (USFDA) has responded to AI in CT in a number of ways. Digital Health Innovation Action Plan Outlines the FDA's approach to digital health technologies, including AI [52] and software as a medical device (SaMD): Guidance on the regulation of AI-based medical devices [53].

Europe considerations

Already in the process is the engagement on AI in clinical research by the european medicines agency (EMA)

Regulatory Science Strategy to 2025: It embeds plans for the development of guidelines on the use of AI in a clinical trial setting [54].

Harmonization initiatives

International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) is working on

ICH E6(R3) guideline

Expected to include considerations for AI and other digital technologies in CT [55, 56].

Proposed regulatory approaches

Continuous learning allows updating AI algorithms with corresponding safeguards. Pré-certification programs Focusing on the quality of AI developers rather than on the quality of individual products. Real-world performance surveillance in CT by Development of post-market surveillance systems for AI [57].

Current challenges prevail over by AI

CT represent the future in the development of medical knowledge and new treatments. But the hurdles that exist against efficient progress are many. AI can solve many of these in really promising ways.

Patient recruitment and retention

The clinical trial process faces numerous challenges, with patient recruitment and retention being particularly time-consuming and resource-intensive. ML algorithms offer promising solutions by mining vast EHR datasets to identify potential participants matching specific criteria, thus accelerating recruitment and ensuring more diverse, representative samples [58].

Protocol design and optimization

Protocol design and optimization present another significant hurdle, as researchers must balance scientific rigor with practical considerations while often relying on limited historical data. AI can address this by analysing past trial data to identify patterns and factors contributing to success or failure, informing more efficient protocol designs. ML models can simulate various protocol scenarios to optimize study design before implementation [59].

Data collection and quality control

Data collection and quality control remain persistent challenges, with difficulties in maintaining data accuracy, completeness, and consistency across different sites and over time. AI-powered data capture systems provide real-time validation by flagging inconsistencies or gaps requiring immediate attention. Computer vision techniques can interpret medical images or video data uniformly across multiple sites [60].

Adverse event detection and management

Protecting patient safety in large CT requires effective adverse event detection and management. ML algorithms can track patient data in real time, identifying patterns that may indicate adverse events before they become clinically apparent. NLP can analyse unstructured data like patient reports or medical notes to identify potential safety signals [61].

Adaptive trial design

Adaptive trial designs that respond to emerging data involve logistical complexities requiring rapid decisions. ML algorithms can continuously learn from incoming trial data in real-time and propose optimal adaptations through sample-size adjustments, treatment arms, or identifying subgroups likely to benefit more from interventions [63].

Regulatory compliance and reporting

Ensuring regulatory compliance and generating comprehensive reports are time-consuming tasks prone to errors. AI-powered systems can automate much of the regulatory documentation process, providing consistency and completeness. Natural language generation helps produce standardized reports, while AI can highlight potential compliance issues before submission [62].

Real-world evidence

Integrating real-world evidence with traditional clinical trial data presents difficulties but offers deeper insights and more generalizable results. AI can harmonize and analyse diverse data sources, including EHR, wearable devices, and social media, to produce a more comprehensive picture of treatment effects in routine practice.

Limitations and potential solution by AI

While AI has huge potential for digital transformation in CT, there are difficulties and limitations to its implementation. The section that follows presents an overview of the significant challenges that researchers, developers, and regulators should address if the full benefits of AI in clinical research are to be realized.

Data quality and availability

The quality and quantity of data play a crucial role in determining the effectiveness of AI models. AI models trained on low-quality or incomplete datasets are likely to produce unreliable or unsatisfactory outcomes. Moreover, existing datasets often exhibit bias, particularly against underrepresented populations, which can further compromise the fairness and generalizability of AI-driven insights. To address these issues, several potential solutions can be considered. First, there is a need for standardization in data collection and storage practices across all clinical trial sites to ensure consistency and comparability of data. Additionally, implementing rigorous data cleaning and validation processes is essential to enhance the accuracy, completeness, and overall integrity of the datasets used to train AI models [63].

Interpretability and explainability

Most AI algorithms operate as "black boxes," meaning their internal decision-making processes are often opaque and difficult to interpret. This lack of transparency poses a significant challenge to building trust in AI systems, particularly in the context of clinical decision-making, where accountability and understanding are critical. As a result, there is often hesitance among healthcare professionals to adopt AI tools, and this lack of trust can hinder broader implementation. Furthermore, the opacity of these systems complicates the validation and regulatory approval of AI-driven decisions, as clear justifications and reproducibility of outcomes are necessary for compliance. To overcome these challenges, the development and application of explainable AI techniques are essential. These methods aim to make AI outputs more transparent and interpretable to users. In addition, intuitive visualization tools can be employed to graphically represent how AI systems arrive at specific decisions, further enhancing user comprehension. Equally important is the implementation of AI literacy training for healthcare professionals, which can empower them with the knowledge needed to critically evaluate and effectively use AI technologies in clinical practice [64].

Regulatory compliance and validation

The rapidly evolving landscape of AI technologies presents significant challenges for the adaptation and reshaping of existing regulatory frameworks. Traditional regulatory models often struggle to keep pace with the speed and complexity of AI innovation, which can result in delays in the approval and implementation of AI-driven CT. Additionally, the lack of harmonized standards across jurisdictions may lead to inconsistencies in how AI technologies are evaluated and applied in different regions, potentially affecting both trial outcomes and patient safety. To address these issues, several forward-looking solutions have been proposed. Regulatory agencies such as the USFDA and the EMA could play a pivotal role by developing AI-specific regulatory guidelines that clearly outline requirements for development, validation, and approval. Establishing AI developer pre-certification programs tailored for healthcare applications may also streamline the regulatory process and ensure that developers adhere to high standards from the outset. Furthermore, incorporating post-marketing surveillance systems during and after CT can help monitor the real-world performance and safety of AI technologies, allowing for continuous oversight and improvement [65].

Integration with existing clinical workflows

Integrating AI tools into the well-established and highly regulated processes of CT has proven to be a significant challenge. This has contributed to the slow adoption of AI technologies within clinical trial settings, as stakeholders may be hesitant to disrupt familiar workflows. Additionally, the transition to AI-driven systems often incurs high costs related to infrastructure upgrades and the need for specialized training, further slowing integration. To facilitate smoother adoption, a gradual implementation approach is recommended, allowing for continuous feedback from end users to refine and improve AI systems. Developing user-friendly interfaces

is also essential to ensure that AI tools are accessible and intuitive for clinical trial staff. Moreover, comprehensive training programs are crucial to equip clinical research professionals with the necessary skills to effectively interact with and manage AI technologies throughout the clinical trial process [66].

Ethical considerations and bias mitigation

AI systems, if not carefully designed and monitored, have the potential to reinforce existing biases in healthcare. When trained on datasets that lack diversity or reflect historical inequalities, AI models may inadvertently perpetuate or even amplify these disparities. This raises significant concerns about fairness, as biased AI applications could contribute to unequal treatment outcomes for underrepresented populations. Furthermore, the risk of such inequities can lead to a broader loss of public trust in AI-driven clinical research, undermining the credibility and acceptance of these technologies. To mitigate these risks, it is essential to regularly evaluate AI systems for bias throughout their development and deployment. Ensuring that training data are representative of diverse populations is a critical step toward creating more equitable algorithms. In parallel, promoting diversity within AI development teams can bring varied perspectives that help identify and address potential sources of bias. Additionally, implementing robust data anonymization and security measures can protect patient privacy while fostering trust in the ethical use of AI in clinical research [67].

Scalability and generalizability

For AI models to be truly effective in clinical research and practice, their performance must remain consistent across different populations and varied healthcare settings. When this consistency is lacking, the applicability of AI tools to diverse, real-world scenarios diminishes, which can lead to reduced accuracy and reliability. This inconsistency poses a particular challenge in multicentre CT, where AI models may perform well in some trial sites but poorly in others due to variations in patient demographics, clinical practices, and data quality. To enhance generalizability and reliability, several strategies can be employed. Federated learning is a promising approach that allows AI models to be trained across decentralized, diverse datasets while maintaining data privacy, thereby improving their robustness across populations. Additionally, it is crucial to conduct thorough validation of AI tools in a variety of clinical settings before widespread implementation. Designing adaptive AI systems that can be fine-tuned to reflect local practices and patient characteristics further supports the goal of ensuring consistent performance and meaningful outcomes in diverse environments [68].

Cost and resource requirements

The implementation of AI in CT often requires substantial up-front investment, posing a significant barrier to entry for many organizations. This financial demand can lead to the exclusion of smaller research institutions and contribute to a widening gap between well-funded centres and those with limited resources. As a result, the benefits of AI may become concentrated within a select group of institutions, potentially skewing research opportunities and outcomes. To promote more equitable adoption, several strategies can be pursued. Developing open-source AI tools specifically designed for clinical research can lower the cost of entry and make advanced technologies accessible to a broader range of organizations. Encouraging institutional collaboration through the sharing of AI resources, infrastructure, and expertise can also help reduce the financial and technical burden on individual trial centres. Additionally, government incentives and funding programs aimed at supporting the integration of AI into CT can further level the playing field and promote widespread innovation [69].

Future directions

As AI continues to evolve and integrate into CT, several promising avenues for future development and research are emerging. This section explores the potential future directions of AI in CT, highlighting areas of innovation and anticipated advancements.

Advanced predictive modelling

Multi-modal AI models are transforming CT with advanced prediction capabilities that coalesce heterogeneous types of data including genomic, clinical, imaging, and real-world evidence, into unifying analytical architectures. These modern systems facilitate the accurate stratification of patients according to personalized medicine strategies, ascertaining those participants most likely to benefit from particular interventions due to their integrative biological and clinical profiles. By examining intricate patterns in multiple data dimensions, such models can better forecast trial outcomes and potential adverse events prior to their occurrence, enabling early intervention. This all-encompassing data integration enables more focused trial designs, decreases failure rates, and speeds the development of precision therapies by linking treatments to a patient's individualized biological traits [70].

AI-driven trial design and optimization

It will not take long before AI plays much more important roles both in the design and optimization of CT. AI Involves in Automated protocol generation, optimization and supplying adaptive designs for clinical trial that dynamically change in accordance with real time data and assists in optimized site Selection and Recruitment of patients [71].

Enhanced natural language processing

In addition, NLP technology has been becoming increasingly advanced in this direction, providing new methods for extracting and analysing data. NLP facilitates improved extraction of relevant information from unstructured clinical notes and medical literature and improve the adverse event reporting from patient-reported outcomes and also participates in advanced semantic analysis for literature reviews and Meta-analysis [72].

Federated learning and decentralized trials

Federated learning is a revolutionary method for CT that allows AI models to learn across sites without centralizing sensitive patient information. This new technology maintains privacy while permitting institutions to jointly build strong algorithms using their local data. The shift towards decentralized trials is gaining momentum, with federated systems supporting remote patient monitoring, distributed data collection, and cross-institutional collaboration while ensuring regulatory compliance. These developments are especially useful for research in rare diseases and international studies where data sharing is hindered by legal obstacles. As federated systems evolve, they have the potential to democratize clinical research by including heterogeneous populations across geographical borders while ensuring strict data protection standards [73].

Explainable AI (XAI) and trust-building

In CT, explainable AI (XAI) solves the "black box" issue of sophisticated algorithms by offering transparent rationales for AI-based decisions. Transparency is especially important when AI systems recommend recruitment populations, detect adverse events, or suggest protocol changes. XAI allows researchers, regulators, and patients to see how conclusions are derived, establishing crucial trust in AI recommendations. Since regulatory agencies increasingly insist on transparency in healthcare AI use, XAI assists in meeting compliance while enabling better cooperation between computational systems and human clinical skill, finally increasing the adoption and influence of AI in the whole clinical trial process [74, 75].

AI-human collaboration models

Sophisticated AI-human interfaces are revolutionizing clinical trial operations by enabling effortless collaboration between smart systems and healthcare professionals. Adaptive interfaces accommodate users' levels of expertise, offering the right depth of information and decision support. In clinical decision-making, AI systems collaborate with physicians to examine intricate trial data, detect patterns, and recommend interventions while explaining their rationale. This collaborative model blends AI computational capability with human clinical experience and judgment, especially useful when considering borderline cases or making subtle protocol modifications. As these systems improve, they become more intelligent partners than tools, assisting clinicians with evidence-

based suggestions while maintaining human control of essential ethical and medical choices throughout the clinical trial process [76].

Integration of real-world data

Next-generation AI systems are developing to natively combine and understand real-world data with conventional clinical trial data, building a richer picture of treatment impact. These advanced models can reconcile heterogeneous real-world data sources such as EHR, wearables, patient registries, and social determinants of health to generate insights that augment controlled trial settings. Most importantly, these systems utilize enhanced techniques to identify and reduce inherent biases in real-world data, such as selection bias, reporting discrepancies, and demographic unbalances. This new approach offers researchers a better understanding of how interventions work across different populations and real-world environments, ultimately informing more informed regulatory decisions and individualized treatment suggestions while enhancing the external validity of clinical research results [77].

Ethical Ai and bias mitigation

In CT, Ethical AI aims to create advanced algorithms that identify and counteract bias, especially in recruitment. Such systems actively ensure diversity and inclusion through the recognition of patterns of underrepresentation and adjustment for past disparities in clinical studies. By examining recruitment information from an ethical perspective, AI ensures that populations in trials more accurately reflect actual populations, resulting in more generalizable findings and reduced healthcare disparities. These resources facilitate researchers to make equitable participant selections with scientific validity, eventually promoting the pursuit of fair healthcare through representative CT and increased trust within historically disenfranchised populations [78].

Regulatory science and AI validation

Regulatory science will need to keep pace with the development of technology as AI becomes extremely ubiquitous in CT. clear regulatory guidelines can be established for application of AI in various stages of clinical trial. Validation processes for the AI algorithm in clinical trial need to be standardized and good clinical practice guidelines for AI to be developed [79].

CONCLUSION

AI is transforming CT throughout the end-to-end pipeline, from drug discovery to post-market monitoring. It greatly improves efficiency in patient recruitment, protocol optimisation, data quality assurance, and adverse event identification while lowering overall costs and development timelines. Major contributions are in faster recruitment via automated EHR screening, improved protocol design via analysis of historical data, enhanced real-time data validation, and sophisticated predictive modelling for personalised medicine strategies. Future suggestions include formulating tailored regulatory guidelines for AI-driven trial tools that ensure innovation while providing protection to patients, setting out ethical standards focusing on algorithm explainability and prevention of bias, establishing standardized validation methods for AI systems in a clinical environment, and instituting formal training regulations for researchers who use AI tools. Despite the challenges of implementation, ongoing investment in AI platforms, especially those cantered on explainability, ethics, and real-world data integration will be essential in harnessing the true value of AI for transforming clinical research and individualized medicine.

ABBREVIATIONS

AI: Artificial Intelligence, ML: Machine Learning, DL: Deep Learning, NLP: Natural Language Programming, RL: Reinforcement Learning, IBM: International Business Machine, QSP: Quantitative Systems Pharmacology, SaMD: Software as Medical Device, EMA: European medical Agency, ICH: International council for harmonization of technical Requirement for Pharmaceutical for human Use, PK/PD: Pharmacokinetics/Pharmacodynamics, FDA: Food and Drug Administration, USFDA: U. S. Food and Drug Administration, XAI: Expandable Artificial Intelligence, LLM: Large Language Machine, GENTRL: Generative Tensorial Reinforcement Learning, GDPR: General Data Protection Regulation.

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There is no conflict of interest

REFERENCES

1. Friedman LM, Furberg CD, Demets DL, Reboussin DM, Granger CB. Fundamentals of clinical trials. 5th ed. Berlin: Springer; 2021. p. 477.
2. Friedman LM, Furberg CD, De Mets DL, Reboussin DM, Granger CB. Introduction to clinical trials. In: Fundamentals of clinical trials. Berlin: Springer; 2015. p. 1-23. doi: 10.1007/978-3-319-18539-2_1.
3. Fogel DB. Factors associated with clinical trials that fail and opportunities for improving the likelihood of success: a review. Contemp Clin Trials Commun. 2018;11:156-64. doi: 10.1016/j.conctc.2018.08.001, PMID 30112460.
4. World Health Organization. International Clinical Trials Registry Platform (ICTRP). In: Geneva: World Health Organization. Available form: https://www.who.int/clinical-trials-registry-platform. [Last accessed on 20 Oct 2024].
5. Scannell JW, Blanckley A, Boldon H, Warrington B. Diagnosing the decline in pharmaceutical R&D efficiency. Nat Rev Drug Discov. 2012;11(3):191-200. doi: 10.1038/nrd3681, PMID 22378269.
6. Hutson M. How AI is being used to accelerate clinical trials. Nature. 2024;627(8003):S2-5. doi: 10.1038/d41586-024-00753-x, PMID 38480968.
7. Howard J. Artificial intelligence: implications for the future of work. Am J Ind Med. 2019;62(11):917-26. doi: 10.1002/ajim.23037, PMID 31436850.
8. Jiang F, Jiang Y, Zhi H, Dong Y, Li H, Ma S. Artificial intelligence in healthcare: past present and future. Stroke Vasc Neurol. 2017;2(4):230-43. doi: 10.1136/svn-2017-000101, PMID 29507784.
9. Topol EJ. High performance medicine: the convergence of human and artificial intelligence. Nat Med. 2019;25(1):44-56. doi: 10.1038/s41591-018-0300-7, PMID 30617339.
10. Dzobo K, Adotey S, Thomford NE, Dzobo W. Integrating artificial and human intelligence: a partnership for responsible innovation in biomedical engineering and medicine. Omics. 2020;24(5):247-63. doi: 10.1089/omi.2019.0038, PMID 31313972.
11. Krajcer Z. Artificial intelligence in cardiovascular medicine: historical overview, current status and future directions. Tex Heart Inst J. 2022;49(2):e207527. doi: 10.14503/THIJ-20-7527, PMID 35481866.
12. Shah P, Kendall F, Khozin S, Goosen R, Hu J, Laramie J. Artificial intelligence and machine learning in clinical development: a translational perspective. NPJ Digit Med. 2019;2:69. doi: 10.1038/s41746-019-0148-3, PMID 31372505.
13. Zhang B, Zhang L, Chen Q, Jin Z, Liu S, Zhang S. Harnessing artificial intelligence to improve clinical trial design. Commun Med (Lond). 2023;3(1):191. doi: 10.1038/s43856-023-00425-3, PMID 38129570.
14. Andreoletti M, Senkalfa B, Blasimme A. Ongoing and planned randomized controlled trials of AI in medicine: an analysis of Clinicaltrials.gov registration data; 2024 Jul 9. medRxiv. doi: 10.1101/2024.07.09.24310133.

15. Hajim WI, Zainudin S, Mohd Daud KM, Alheeti K. Optimized models and deep learning methods for drug response prediction in cancer treatments: a review. Peer J Comput Sci. 2024;10:e1903. doi: 10.7717/peerj-cs.1903, PMID 38660174.
16. Guellil I, Wu J, Pradipta Gema A, Francis F, Berrachedi Y, Chenni N. Natural language processing for detecting adverse drug events: a systematic review protocol. NIHR Open Res. 2023;3:67. doi: 10.3310/nihropenres.13504.3, PMID 39931191.
17. Rojas Carabali W, Agrawal R, Gutierrez Sinisterra L, Baxter SL, Cifuentes Gonzalez C, Wei YC. Natural language processing in medicine and ophthalmology: a review for the 21st-century clinician. Asia Pac J Ophthalmol (Phila). 2024;13(4):100084. doi: 10.1016/j.apjo.2024.100084, PMID 39059557.
18. Bi WL, Hosny A, Schabath MB, Giger ML, Birkbak NJ, Mehrtash A. Artificial intelligence in cancer imaging: clinical challenges and applications. CA Cancer J Clin. 2019;69(2):127-57. doi: 10.3322/caac.21552, PMID 30720861.
19. Bi WL, Hosny A, Schabath MB, Giger ML, Birkbak NJ, Mehrtash A. Artificial intelligence in cancer imaging: clinical challenges and applications. CA Cancer J Clin. 2019;69(2):127-57. doi: 10.3322/caac.21552, PMID 30720861.
20. Metzger A, Laufer J, Feit F, Pohl K. A user study on explainable online reinforcement learning for adaptive systems. ACM Trans Auton Adapt Syst. 2024;19(3):1-44. doi: 10.1145/3666005.
21. Amaratunga T. Understanding large language models. Singapore: Apress; 2023. doi: 10.1007/979-8-8688-0017-7.
22. Amaratunga T. Understanding large language models. Singapore: Apress; 2023. p. 1-7. doi: 10.1007/979-8-8688-0017-7.
23. Marey A, Saad AM, Killeen BD, Gomez C, Tregubova M, Unberath M. Generative artificial intelligence: enhancing patient education in cardiovascular imaging. BJR Open. 2024;6(1):tzae018. doi: 10.1093/bjro/tzae018, PMID 39086557.
24. Lomurno E, Matteucci M. Federated knowledge recycling: privacy preserving synthetic data sharing. Pattern Recognition Letters. 2025;191:124-30. doi: 10.1016/j.patrec.2025.02.030.
25. Tahseen S, Memon MA, Kamran SM, Pathan KT. The ethics of AI in medical research: a call for open and honest discussion. Liaquat Med Res J. 2024;6(2):88-92. doi: 10.38106/LMRJ.2024.6.2-07.
26. Pun FW, Leung GH, Leung HW, Rice J, Schmauck Medina T, Lautrup S. A comprehensive AI driven analysis of large scale omic datasets reveals novel dual-purpose targets for the treatment of cancer and aging. Aging Cell. 2023;22(12):e14017. doi: 10.1111/acel.14017, PMID 37888486.
27. Chinnaiyan K, Mugundhan SL, Narayanasamy D, Mohan M. Revolutionizing healthcare and drug discovery: the impact of artificial intelligence on pharmaceutical development. Curr Drug Ther. 2024 Jul 23;19(7):972-87. doi: 10.2174/0115748855313948240711043701.
28. Jaume G, Peeters T, Song AH, Pettit R, Williamson DF, Oldenburg L. AI driven discovery of morphomolecular signatures in toxicology. bioRxiv. 2024 Jul 23. doi: 10.1101/2024.07.19.604355, PMID 39091765.
29. Moncada Torres A, Van Maaren MC, Hendriks MP, Siesling S, Geleijnse G. Explainable machine learning can outperform cox regression predictions and provide insights in breast cancer survival. Sci Rep. 2021;11(1):6968. doi: 10.1038/s41598-021-86327-7, PMID 33772109.
30. Cassidy JW, Taylor B, editors. Artificial intelligence in oncology drug discovery and development. London: Intech Open; 2020. p. 192. doi: 10.5772/intechopen.88376.
31. Guellil I, Wu J, Pradipta Gema AP, Francis F, Berrachedi Y, Chenni N. Natural language processing for detecting adverse drug events: a systematic review protocol. NIHR Open Res. 2023;3:67. doi: 10.3310/nihropenres.13504.3, PMID 39931191.
32. Gedor M, Desandes E, Chesnel M, Merlin JL, Marchal F, Lambert A. Development of an artificial intelligence system to improve cancer clinical trial eligibility screening. Bull Cancer. 2024;111(5):473-82. doi: 10.1016/j.bulcan.2024.01.010, PMID 38503584.
33. Transformative wearables: how AI and ML are shaping healthcare innovations. Int J Sci Res. Available from: https://www.ijsr.net/getabstract.php?paperid=SR24402055352. [Last accessed on 20 Oct 2024].
34. Bartal A, Jagodnik K, Pliskin N, Seidmann AA. Utilizing AI and social media analytics to discover adverse side effects of GLP-1 receptor agonists; 2024. doi: 10.2139/ssrn.4790676.
35. Franklin JM, Lin KJ, Gatto NM, Rassen JA, Glynn RJ, Schneeweiss S. Real world evidence for assessing pharmaceutical treatments in the context of COVID-19. Clin Pharmacol Ther. 2021;109(4):816-28. doi: 10.1002/cpt.2185, PMID 33529354.
36. Miyasato G, Kasivajjala VC, Misra M, Kumar K, Kadam AS, Friedman HS. AI-driven real time patient identification for randomized controlled trials. J Clin Oncol. 2023;41(16Suppl):e13565. doi: 10.1200/JCO.2023.41.16_suppl.e13565.
37. Shang Z, Li R, Zheng C, Li H, Cui Y. Relative entropy regularized sample-efficient reinforcement learning with continuous actions. IEEE Trans Neural Netw Learn Syst. 2025;36(1):475-85. doi: 10.1109/TNNLS.2023.3329513, PMID 37943648.
38. Bernard Owusu Antwi, Beatrice Oyinkansola Adelakun, Damilola Temitayo Fatogun, Omolara Patricia Olaiya. Enhancing audit accuracy: the role of AI in detecting financial anomalies and fraud. Financ Account Res J. 2024;6(6):1049-68. doi: 10.51594/farj.v6i6.1235.
39. Chan PS, Fang Y, Cheung DH, Zhang Q, Sun F, Mo PK. Effectiveness of chatbots in increasing uptake intention and attitudes related to any type of vaccination: a systematic review and meta-analysis. Appl Psychol Health Well Being. 2024;16(4):2567-97. doi: 10.1111/aphw.12564, PMID 38886054.
40. Khinvasara T, Shankar A, Wong C. Survey of artificial intelligence for automated regulatory compliance tracking. J Eng Res Rep. 2024;26(7):390-406. doi: 10.9734/jerr/2024/v26i71217.
41. Gopeekrishnan A, Arif SA, Liu H. Demo: accelerating patient screening for clinical trials using large language model prompting. In: proceedings of the 2024 IEEE/ACM Conference on Connected Health: Applications, Systems and Engineering Technologies (CHASE); 2024. p. 214-5.
42. Zhavoronkov A, Ivanenkov YA, Aliper A, Veselov MS, Aladinskiy VA, Aladinskaya AV. Deep learning enables rapid identification of potent DDR1 kinase inhibitors. Nat Biotechnol. 2019;37(9):1038-40. doi: 10.1038/s41587-019-0224-x, PMID 31477924.
43. Sancricca C, Siracusa G, Cappiello C. Enhancing data preparation: insights from a time series case study. J Intell Inf Syst. 2024 Jul 25;62(6):1503-30. doi: 10.1007/s10844-024-00867-8.
44. Nwankwo EI. Google Scholar. Available from: https://scholar.google.com/citations?user=gi0lbyoaaaaj. [Last accessed on 20 Oct 2024].
45. Bain EE, Shafner L, Walling DP, Othman AA, Chuang Stein C, Hinkle J. Use of a novel artificial intelligence platform on mobile devices to assess dosing compliance in a phase 2 clinical trial in subjects with schizophrenia. JMIR Mhealth Uhealth. 2017;5(2):e18. doi: 10.2196/mhealth.7030, PMID 28223265.
46. Barbiero P, Vinas Torne R, Lio P. Graph representation forecasting of patient's medical conditions: toward a digital twin. Front Genet. 2021;12:652907. doi: 10.3389/fgene.2021.652907, PMID 34603366.
47. Kaissis GA, Makowski MR, Ruckert D, Braren RF. Secure privacy-preserving and federated machine learning in medical imaging. Nat Mach Intelligence. 2020;2(6):305-11. doi: 10.1038/s42256-020-0186-1.
48. Liu X, Cruz Rivera S, Moher D, Calvert MJ, Denniston AK, Spirit AI and Consort-AI Working Group. Reporting guidelines for clinical trial reports for interventions involving artificial intelligence: the consort-AI extension. Lancet Digit Health. 2020;2(10):e537-48. doi: 10.1016/S2589-7500(20)30218-1, PMID 33328048.
49. Gichoya JW, Banerjee I, Bhimireddy AR, Burns JL, Celi LA, Chen LC. AI recognition of patient race in medical imaging: a modelling study. Lancet Digit Health. 2022;4(6):e406-14. doi: 10.1016/S2589-7500(22)00063-2, PMID 35568690.
50. Morato De Andrade O, Sousa Alves MA. Using explainable artificial intelligence (XAI) to reduce opacity and address bias in algorithmic models. Rev Thesis Jur. 2024;13(1):3-25. doi: 10.5585/13.2024.26510.
51. Gerke S, Minssen T, Cohen G. Ethical and legal challenges of artificial intelligence-driven healthcare. In: Artificial intelligence in healthcare. London: Elsevier; 2020. p. 295-336. doi: 10.1016/B978-0-12-818438-7.00012-5.
52. U. S. Food and Drug Administration. Digital health innovation action plan. Silver Spring, MD: FDA; 2020.

53. U. S. Food and Drug Administration. FDA releases artificial intelligence/machine learning action plan. In: Silver Spring, MD: FDA. Available from: https://www.fda.gov/news-events/press-announcements/fda-releases-artificial-intelligencemachine-learning-action-plan. [Last accessed on 20 Oct 2024].
54. European Medicines Agency. EMA regulatory science strategy to 2025-draft. Amsterdam: EMA; 2025.
55. Babic B, Gerke S, Evgeniou T, Cohen IG. Beware explanations from AI in health care. Science. 2021;373(6552):284-6. doi: 10.1126/science.abg1834, PMID 34437144.
56. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human use. ICH Harmonised Guideline Good Clinical Practice (GCP) E6(R3). Geneva: ICH; 2023.
57. Larson DB, Harvey H, Rubin DL, Irani N, Tse JR, Langlotz CP. Regulatory frameworks for development and evaluation of artificial intelligence-based diagnostic imaging algorithms: summary and recommendations. J Am Coll Radiol. 2021;18(3 Pt A):413-24. doi: 10.1016/j.jacr.2020.09.060, PMID 33096088.
58. Kaur I, Ali A. A complete study on machine learning algorithms for medical data analysis. In: Banerjee C, Ghosh A, Chakraborty R, Elngar AA, editors. Fog computing for intelligent cloud IoT systems. Singapore: John Wiley & Sons; 2024. p. 137-72. doi: 10.1002/9781394175345.ch7.
59. Hennekens CH. Issues in the design and conduct of clinical trials. J Natl Cancer Inst. 1984;73(6):1473-6. PMID 6595458.
60. Smith MK, Marshall A. Importance of protocols for simulation studies in clinical drug development. Stat Methods Med Res. 2011;20(6):613-22. doi: 10.1177/0962280210378949, PMID 20688782.
61. Harrison CJ, Sidey Gibbons CJ. Machine learning in medicine: a practical introduction to natural language processing. BMC Med Res Methodol. 2021;21(1):158. doi: 10.1186/s12874-021-01347-1, PMID 34332525.
62. Kingston J. Using artificial intelligence to support compliance with the General Data Protection Regulation. Artif Intell Law. 2017;25(4):429-43. doi: 10.1007/s10506-017-9206-9.
63. Houston L, Probst Y, Yu P, Martin A. Exploring data quality management within clinical trials. Appl Clin Inform. 2018;9(1):72-81. doi: 10.1055/s-0037-1621702, PMID 29388180.
64. Ehsan U, Liao QV, Muller M, Riedl MO, Weisz JD. Expanding explainability: towards social transparency in AI systems. In: Proceedings of the 2021 CHI conference on human factors in computing systems. New York, USA: ACM; 2021. p. 1-19. doi: 10.1145/3411764.3445188.
65. Shah P, Kendall F, Khozin S, Goosen R, Hu J, Laramie J. Artificial intelligence and machine learning in clinical development: a translational perspective. NPJ Digit Med. 2019;2:69. doi: 10.1038/s41746-019-0148-3, PMID 31372505.
66. Liu X, Cruz Rivera S, Moher D, Calvert MJ, Denniston AK, Spirit AI and Consort AI Working Group. Reporting guidelines for clinical trial reports for interventions involving artificial intelligence: the CONSORT-AI extension. Lancet Digit Health. 2020;2(10):e537-48. doi: 10.1016/S2589-7500(20)30218-1, PMID 33328048.
67. Gichoya JW, Banerjee I, Bhimireddy AR, Burns JL, Celi LA, Chen LC. AI recognition of patient race in medical imaging: a modelling study. Lancet Digit Health. 2022;4(6):e406-14. doi: 10.1016/S2589-7500(22)00063-2, PMID 35568690.
68. Woisetschlager H, Isenko A, Wang S, Mayer R, Jacobsen HA. A survey on efficient federated learning methods for foundation model training. In: Proceedings of the 2024 international conference on machine learning; 2024. p. 8317-25.
69. Khozin S, Blumenthal GM, Pazdur R. Real-world data for clinical evidence generation in oncology. J Natl Cancer Inst. 2017;109(11). doi: 10.1093/jnci/djx187, PMID 29059439.
70. Lella L, Licata I, Minati G, Pristipino C, Giulio A, Belvis D. Predictive AI models for the personalized medicine. Rome: Italian National Institute of Health; 2024.
71. Harrer S, Shah P, Antony B, Hu J. Artificial intelligence for clinical trial design. Trends Pharmacol Sci. 2019;40(8):577-91. doi: 10.1016/j.tips.2019.05.005, PMID 31326235.
72. Khanbhai M, Anyadi P, Symons J, Flott K, Darzi A, Mayer E. Applying natural language processing and machine learning techniques to patient experience feedback: a systematic review. BMJ Health Care Inform. 2021;28(1):e100262. doi: 10.1136/bmjhci-2020-100262, PMID 33653690.
73. Ali M, Naeem F, Tariq M, Kaddoum G. Federated learning for privacy preservation in smart healthcare systems: a comprehensive survey. IEEE J Biomed Health Inform. 2023;27(2):778-89. doi: 10.1109/JBHI.2022.3181823, PMID 35696470.
74. Longo L, Goebel R, Lecue F, Kieseberg P, Holzinger A. Explainable artificial intelligence: concepts, applications research challenges and visions. In: Holzinger A, Kieseberg P, Tjoa AM, Weippl E, editors. Machine learning and knowledge extraction. Cham: Springer International Publishing; 2020. p. 1-16. doi: 10.1007/978-3-030-57321-8_1.
75. Holzinger A, Goebel R, Fong R, Moon T, Muller KR, Samek W, editors. Xx AI-beyond explainable AI. Berlin: Springer; 2022.
76. Char DS, Shah NH, Magnus D. Implementing machine learning in health care addressing ethical challenges. N Engl J Med. 2018;378(11):981-3. doi: 10.1056/NEJMp1714229, PMID 29539284.
77. Kokkotou E, Anagnostakis M, Evangelou G, Syrigos NK, Gkiozos I. Real world data and evidence in lung cancer: a review of recent developments. Cancers (Basel). 2024;16(7):1414. doi: 10.3390/cancers16071414, PMID 38611092.
78. Gichoya JW, Banerjee I, Bhimireddy AR, Burns JL, Celi LA, Chen LC. AI recognition of patient race in medical imaging: a modelling study. Lancet Digit Health. 2022;4(6):e406-14. doi: 10.1016/S2589-7500(22)00063-2, PMID 35568690.
79. Shah P, Kendall F, Khozin S, Goosen R, Hu J, Laramie J. Artificial intelligence and machine learning in clinical development: a translational perspective. NPJ Digit Med. 2019;2:69. doi: 10.1038/s41746-019-0148-3, PMID 31372505.
80. Nallamuthu M, Umadevi S, Anandan R. Artificial intelligence powered design of experiments: optimizing abiraterone acetate loaded gelatin nanoparticles for enhanced oral bioavailability of abiraterone acetate. IJAP. 2025;17(4):483-96. doi: 10.22159/ijap.2025v17i4.54437.