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THE ROLE OF MACHINE LEARNING IN CLINICAL RESEARCH: TRANSFORMING THE FUTURE OF EVIDENCE GENERATION

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ABSTRACT

The main purpose of this paper is to explore how machine learning is revolutionizing clinical research. A huge transition is about to occur in clinical development, thanks to the confluence of vast new digital data sources, computer capacity to discover clinically important trends in the data employing efficient artificial intelligence and machine-learning algorithms, and policymakers who are welcoming this transformation through new partnerships. There are different perspectives presented in this article, including those from academia, the biotechnology industry, non-profits, regulators, and technology firms on how to incorporate relevant computational data into clinical research and health care [1]. The use of machine learning (ML) in clinical trial design, conduct, and analysis has gained interest, but the evidence base has not been reviewed. Traditional randomized, controlled trials have become exponentially more difficult and expensive over time, and this is now threatening to hinder the development of novel treatments and technology in the future. Clinical trials may be transformed to be more pragmatic and efficient by using electronic health records, mobile apps, and wearable technologies, which are all on the rise [1]. Before these improvements can be widely deployed in randomized, controlled trials, several obstacles must be addressed.

Keywords: Machine learning, clinical research, clinical trials, biotechnology, Biomedical innovation

INTRODUCTION

We're in the midst of a digital revolution, ushered in by a steady stream of ground-breaking technical developments. Clinical research is no exception, and technology has been progressively embraced in recent years to allow more efficient, more accurate, and more creative trial management [1,2]. Clinical research is no exception. Many technological advances have made this possible, but one in particular – Machine Learning (ML) – is playing an increasingly important role in driving transformation throughout the whole business. The clinical trial is a cornerstone of the drug development process in the pharmaceutical industry. Clinical trials are research investigations conducted to examine whether a medical therapy or gadget is both safe and effective in people. This is the essence of clinical trials. Despite occasional volatility, the pharmaceutical medication sector is still a lucrative one. Predicting clinical trial results using machine learning technology may lead to quicker medication approval timeframes, reduced costs, and more financing for the development of novel medicines.

Precision medicine (also referred to as stratified medicine or personalized medicine) is now possible thanks to modern medical big data. Precision medicine involves evaluating and coordinating health care for patient characteristics based on their disease susceptibility, predictive and therapeutic details, and treatment response [2]. Modern statistical technologies, like machine learning and artificial intelligence, are opening up previously untapped and fast-rising data sources for the benefit of patients. Many interesting studies are being carried out right now, notably in imaging, but the literature as a whole lack openness, clear reporting to promote replication, investigation of possible ethical considerations, and unequivocal evidence of efficacy [2,3]. A major cause for these issues (for which we provide a tentative solution here) is the existing dearth of best practice recommendations for machine learning and artificial intelligence. When working on health-

related machine learning and artificial intelligence projects, we think multidisciplinary teams would benefit from addressing issues such as openness, reproducibility, ethics, and efficacy.

PROBLEM STATEMENT

The main problem that this paper will address is to explore what prole machine learning plays in clinical research. Many stakeholders, from regulators to biopharmaceutical industry executives to individual patients and their loved ones, face significant challenges during randomized clinical trials. The possibility of a medication failing in clinical trials affects everyone. We intend to attract additional investment at this critical juncture in biomedicine by providing more precise evaluations of the risk associated with new medication and device development [4]. Biomedical innovation has become more difficult due to the growth of medical advances including immunotherapies, gene treatments, and gene editing methods. Novel medicines are created as a result of these advances, and each one will need several years of translational research and clinical testing, at a cost of hundreds of millions to billions of dollars. Despite advances in science and technology, productivity in drug research — the number of new pharmaceuticals permitted to R&D investment each year — has decreased substantially over the last 50 years [5].

LITERATURE REVIEW

A. Challenges in Clinical Research

As a major investment in the pharmaceutical medication or healthcare development process, clinical trials may be extremely expensive. Studies that test medical equipment, medicines, or therapy approach on people to see whether they're safe and effective are called clinical trials. Low success rates and high expenditures are major obstacles for clinical trial designers. The complexity and amount of clinical trial data are expanding constantly as it is gathered in a variety of forms and from various sources [6]. To find the next big medical discovery, Contract research organizations and Trial sponsors must cope with larger and more sophisticated treatment regimens to conduct their study effectively. To reach a broader patient population, research is being conducted in more nations and at more locations.

B. Machine learning in Clinical trials

With machine learning, researchers can identify, forecast, and avoid dangers linked with clinical research. As a result of the information it generates during clinical trial monitoring and decision-making, machine learning may help enhance clinical trial dependability, quality, and safety. The involvement of patients in clinical trials is impacted by adherence, site management, and illness or therapy effect [6]. The agile platform can evaluate and utilize data from a variety of sources such as e-Consent and e-Source technological advances, central lab data or safety information, electronic clinical outcomes or reviews, electronic data acquisition infrastructures, and smartwatches data, as well as electronic trial master files, electronic medical, electronic patient care outcomes or reports. That means no more costly data warehouse upgrades or maintenance hassles for this platform which leverages visualized data or format to control risk in clinical studies [7]. Clinical trial management solutions like this utilize a variety of machine learning algorithms to assist users in making sense of the data and making timely suggestions about hazards that are both common and particular. It is possible to tailor the user interface algorithms so that they run on-demand or according to a timetable and adhere to tight or timely recommendation criteria as needed. By applying statistical computing and predictive machine learning, challenges and hazards that are invisible to humans may be identified and mitigated for the better [8]. Using a computer application, clinical trial personnel may analyze in near real-time and be notified as a result.

Clinical Trial Design, Patient Recruitment, and Clinical Trial Optimization are the three most common uses for machine learning and new clinical trial technology. During the initial few years of business, most firms' applications are focused on attracting patients with the most traction. Some of the newest uses of machine learning are inpatient optimization and engagement. The demands of participants from all around the world will be met through international studies with different language choices for thousands of patients [9,10]. Clinical trial processes and the pharmaceutical drug business may benefit from machine learning technologies that analyze complicated and large amounts of clinical data [10,11].

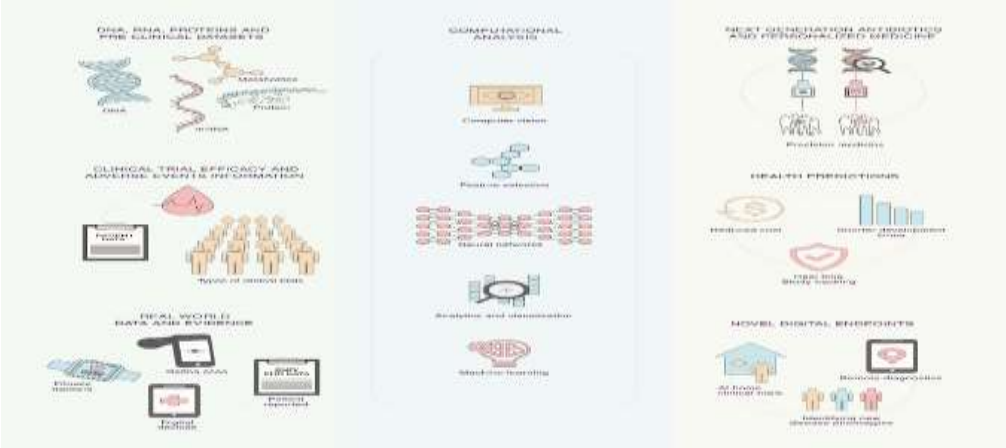

Fig i: Clinical development

C. The role of ML in preclinical drug discovery and development research

Before beginning a clinical trial, researchers must do extensive preclinical research to identify interesting compounds and targets, as well as determine the best investigative method for getting regulatory clearance for the study's findings. Mistakes made during this phase might cause clinical studies to be terminated prematurely or postpone the discovery of potential medications. Researchers may use ML to make use of prior and continuing research to make the preclinical process more efficient [11].

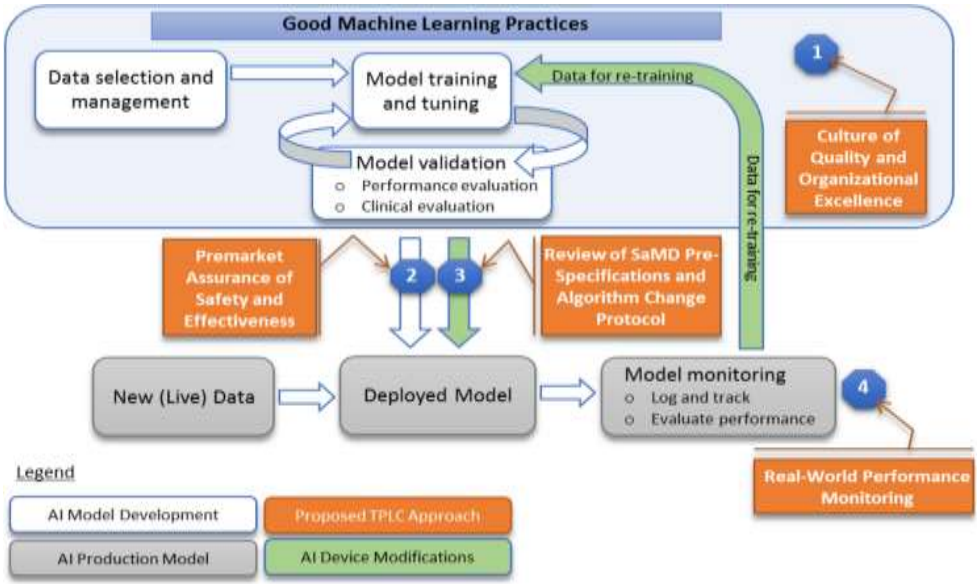

Fig ii: Good ML Practices

D. Drug target identification, candidate molecule generation, and mechanism elucidation

By synthesizing vast volumes of the previously conducted research, clarifying pharmacological mechanisms, and projecting protein structure and future drug-target interactions into the model, ML can simplify the process and boost drug target identification and candidate molecule generation likelihood of success [11]. A machine-

learning approach may find certain kinds of gene-disease correlations from big datasets even when relevant data points are scarce [11], whereas Jia et al has extracted drug-gene mutation interactions from scientific articles [11,12]. These initiatives [14] assist researchers to utilize and avoid repeating previous work to target more promising areas for additional exploration, as well as other attempts to make extraordinarily huge volumes of biological data interpretable by humans. To generate potential candidate compounds, ML uses a gated graph neural network to optimize molecules within the limits of a target biological system after relevant research topics have been discovered.

When a therapeutic candidate does not behave as predicted in vivo, machine learning may synthesize and analyze massive volumes of data to better understand the drug's mechanism of action as demonstrated by using a Bayesian technique to an anti-cancer molecule [12]. Increasing the likelihood that pharmaceuticals will be tested on those who will benefit the most from them is made possible by work like this. Greater knowledge of the mechanism of the medication studied by scholars permitted fresh clinical studies in a cancer kind (pheochromocytoma) that we're more likely to react to the therapy. To choose which next steps to take, in vitro translational researchers must assess enormous volumes of highly dimensional data collected during benchtop biological, chemical, and biochemical investigations. Experimental data may be used as feedback for autonomously ML-powered labs, which integrate ML into pharmaceutical development's preparation, analysis, and synthesis stages. Products of ML-enabled medication development are now being tested on humans for the first time. The first phase I trials of an OCD medicine allegedly created utilizing AI-based technologies will begin this year, for example. Only 250 candidates were considered for development, and the medicine was produced in about 12 months, as opposed to the 2000+ candidates and over five years of development time generally needed for new drugs [12]. Because there are no peer-reviewed publications on the development of this medicine, it is impossible to validate or use the information of its development in future research.

E. Optimization of the protocol for a clinical trial

A role for machine learning (ML) is emerging as medicinal compounds approach human trials, with simulation methods used to massive volumes of earlier trial data to help build trial protocols. This will contribute to the success and productivity of tests during the planning stage. For example, reinforcement learning methods to Alzheimer's disease and non-small cell lung cancer [12] have demonstrated that research modeling may maximize products are target selections for trials. Trials is a new start-up firm. Using artificial intelligence, researchers may upload procedures and utilize natural language processing to detect possible stumbling blocks and roadblocks to completing a successful experiment [13]. Nevertheless, the efficacy of these models has not been assessed in a consensus set, and as a result, they can only provide a theoretical assurance that using machine learning in research design might assist in guaranteeing that a particular trial design is ideally matched to the demands of the stakeholders. Preclinical research and clinical trial design may both be made more efficient and more productive by using machine learning. However, the majority of peer-reviewed publications describing the use of machine learning in this capacity concentrate on preclinical research and innovation instead of clinical research preparation [13]. This might be because huge, highly dimensional datasets are more readily available in translational contexts, and there are also more potential costs, dangers, and regulatory difficulties involved with the use of ML in clinical trial settings. To get past these stumbling blocks, we'll need peer-reviewed proof that machine learning can be used in clinical trial design.

F. The use of machine learning in the management of clinical trial participants

Recruiting participants for clinical trials, as well as keeping them engaged, is part of clinical trial participant management. Patient drop-out and non-adherence sometimes lead trials to go over budget or take longer than

expected, or they fail to provide useful data despite extensive resources being spent on participant management, including time, preparation, and trial coordinator effort. Phase 1–3 clinical trials supporting drug development fail at a rate between 33.6% and 52.4%, resulting in a 13.8% total likelihood that a medicine evaluated in phase I will be approved [14]. Approaches based on machine learning (ML) may help identify, attract, and retain participants more efficiently and fairly.

G. The process of selecting which individuals to study

Smaller sample size may be necessary to detect a meaningful impact if certain patient groups are better selected for studies. A better selection of the patient group may result in fewer people receiving treatments from which they will not benefit. This area continues to be tough, as past research has shown that for everyone planned response, there are between three and twenty-four non-responders for the most commonly used drugs, resulting in a high proportion of patients receiving undesirable side effects in addition to the intended impact [15]. Along with making it easier to pick patients by rapidly analyzing huge previous research datasets (as stated above), unsupervised ML of clinical groups may identify trends in patient attributes that can be utilized for selecting patients who would most gain from the therapeutic process or intervention [15]. Unstructured data is key to phenotyping and selecting target groups, showing that collecting more data from patients is important [15]. According to the information from 11,210 individuals, there are 3 subgroups of diabetes mellitus type II, each with specific phenotypic manifestations and treatment needs [15,16]. Founded in 2016, Bullfrog AI aims to leverage the potential of targeted clinical setting screening by examining clinical research data sources "to anticipate which patients would react to a specific medicine under development, hence enhancing inclusion/exclusion parameters and verifying main study results are achieved"[16]. It's an enticing argument in theory, but it's based on unsubstantiated assumptions and confuses result projection (which is unlikely to work and goes against the objective of clinical tests). As a result, trials may overlook subgroups that might benefit from the intervention but which the ML model did not detect. Underserved patient populations in rural areas, distant locations, and those who get little treatment may be more vulnerable to these potential dangers. These two flaws may have ramifications for drug/device research federal approval and distribution, since crucial trials in more carefully chosen and less representative clinical populations may necessitate weighing the significance of increased trial breakthroughs against the disadvantages of increased restricted drug/device indications.

H. Finding and recruiting potential participants

Patients that fulfill the needed phenotype once a certain cohort has been discovered may be identified using natural language processing (NLP), which otherwise requires a lot of manual work. It links patients with clinical studies effectively using Electronic health records by combining textual and tabular data from both sources into a shared latent space. No peer-reviewed evidence exists to support the development or success measurements used by Mendel.AI and Deep6AI, which raises questions regarding the efficacy of these approaches [16]. Trialists should avoid relying on structured data fields to precisely identify participants by using this method, which has been shown to have a significant impact on the outcomes of clinical trials [16]. EHR biases may hinder the effectiveness of novel machine learning approaches for patient registration because they rely on them. As a consequence, one element of bias (underpinning correctness of data structure) may be replaced with another cause of bias (underlying the generation of EHR documentation).

I. Participants' retention, progress tracking, and procedure adherence

To increase participant retention and procedure adherence, ML-assisted approaches may be employed in one of two different ways: as a reminder or as a reward. To detect study non-compliance risk individuals and

intervene, the first step is to collect and evaluate massive amounts of data using machine learning. Machine learning (ML) is the second technique, which is intended to minimize participant study load while simultaneously improving participant experiences. Patient medication compliance is monitored by AiCure, which uses image recognition technologies to optimize that patients receive their prescribed medications per protocol. [16] AiCure outperformed a modified directly observed therapy strategy when it comes to detecting and boosting patient adherence in schizophrenia studies, as well as in an anticoagulation study in stroke patients. It has been shown in other computer vision disciplines that different patient subgroups perform differently when utilizing AiCure's model building and validation technique [17] provided the AiCure model creation and validation approach is used. These techniques have the potential to be successful in the future; yet, they may be hampered from being completely applied because of the perceived infringement on privacy that may not be acceptable to all study participants. Furthermore, choosing patients who have access to and are comfortable with the appropriate instruments and technologies may add bias to the study. Encouraging participants to stay in the study by reducing trial load and collecting additional information from existing data acquired during clinical practice and/or study activities is another possibility. Clinical data collected during routine treatment may be processed using machine learning techniques to give information for the study. The use of standard clinical hematoxylin-and-eosin staining procedures may identify individuals who need more intensive and costly multiplexed imaging while placing everybody in danger [17]. By leveraging the Unified Medical Language System to auto-populate study case report forms, it may be possible to make repurposing clinical material for research more straightforward using NLP [17]. Examples include patients employing machine learning to convert social media posts into research data, such as by using natural language analysis of posts to detect adverse drug reactions with high fidelity [18]. Participants in the experiment will have less work to do as a result of this reduction in data gathering. Patient data gathered by the International Parkinson and Movement Disorders Society (IPMDS) via the use of wearable devices reveals a relationship between participant activity and the IPMDS. It's yet unclear how ML/NLP applications will affect clinical trial performance and participant satisfaction, even though ML and NLP have shown potential in a broad range of activities related to better participant supervision in clinical studies. Investigations on participant management practices are needed to determine the most successful approaches.

J. Data collection and management

Data collection, management, and analysis procedures that are required in clinical trials may be altered as a result of the use of machine learning (ML). ML techniques may help with missing data and the collecting of real-world data, which can be difficult to deal with in certain cases. In certain circumstances, mobile/electronic devices that collect health data from patients might supplement or even completely replace traditional research visits and the data gathering that goes along with them. Novel patient-centered biomarkers may be validated and put to use as a consequence of the usage of wearables and other devices. As a consequence, the development of new "digital biomarkers" necessitates the analysis of data acquired by mobile devices' numerous sensors to generate meaningful insights from it (such as camera sensors, audio recorders, accelerometers, and photoplethysmography). This is since the data supplied by these devices is scarce and varied in terms of quality, availability, and timeliness, among other characteristics.

A large and sophisticated quantity of data is generated by wearables and other devices, necessitating the employment of specialized methodologies for data collection, storage, validation, and analysis [18]. To handle neural network input, for example, an ECG mobile platform was utilized [18]; the audio output of Parkinson's disease patients was processed using a random forest model [18], and accelerometer data from patients with the condition were processed using a neural network [18]. However, although the use of these new digital indicators may make clinical trials operate more easily and with a greater focus on patients, there are hazards

associated with doing so. The findings of ML processing of wearable sensor output may be tainted if the models are compromised by purposefully or inadvertently manipulated sensor data, according to an electrocardiogram classification model (even though this risk remains irrespective of processing technique) [18]. To show this, researchers used an electrocardiogram classification model. Due to the general inherent difficulties of software meant to identify, assess, or cure medical conditions, regulatory techniques and guidelines for biomarker validity and verification have been put in place.

K. Impact of machine learning on clinical trials in the future

Predictions are tough to come by in such a sophisticated industry. Machine learning will almost certainly have ever-increasing applicability in clinical trials, as evidenced by recent significant breakthroughs in healthcare, in particular the use of natural language processing [18] in the mining of free text healthcare data, which are almost certain to continue. Several processes that are now conducted nearly completely manually [18] may be automated with the use of machine learning in the context of clinical trials data management [18]. Because of the large amount of data involved, these activities are highly costly. There will be a slew of big difficulties to solve [9] as the potential of machine learning grows. These problems include assuring model robustness while also safeguarding privacy, understanding models, and resolving ethical considerations. These are only a few examples. Though these concerns are common to all machine learning applications, the healthcare sector and clinical trials, in particular, are especially troubled by them.

Machine learning can shape and lead clinical trial research, and it offers a wide range of important prospective applications. When employing sophisticated predictive analytics to find clinical trial candidates, it would be feasible to leverage a considerably broader variety of data than is now possible, such as social media and medical visits, as well as genetic information when attempting to target certain demographics. Overall, this would result in smaller, quicker, and less costly clinical trials. Remote monitoring and real-time data access enabled by machine learning may improve safety, for example, by keeping a watch on biological and other signals for any indication of harm or death amongst the participants. According to McKinsey, the application of machine learning may be able to increase the efficiency of clinical trial processes [18]. Consider the following examples: identifying ideal sample sizes, addressing and reacting to changes in patient recruiting sites, and using electronic medical records to avoid data inconsistencies (duplicate entry, for example).

FUTURE IN THE U.S

The future of machine learning in clinical research in the United States is about to undergo a sea shift as a result of the convergence of vast new digital datasets, the availability of computing capacity to discover clinically important patterns in the data employing efficient artificial intelligence and machine-learning technologies, and regulatory authorities welcoming this transition via new partnerships. Because of the confluence of massive new digital data sources, computer capacity to discover clinically important patterns in data utilizing efficient artificial intelligence and machine-learning techniques, policymakers welcoming this transition via new partnerships, the future of clinical research is on the brink of a dramatic revolution. Machine learning may aid in not only improving the quality of goods and services but also in providing clients with more tailored items and a wider range of options. Furthermore, new entrants to the market can gauge client demand for specific items with incredible accuracy. Big data will be used to forecast the future. Machine learning algorithms will sift through tens of thousands of terabytes of data to determine the most likely conclusion or trend. It will no longer be reliant on "reading tea leaves," thus we should anticipate it to be much more accurate [18]. And, as previously said, incorporating machine learning in economics and econometrics may lead to significantly more accurate models by combining the capacity to evaluate massive volumes of data with conventional modeling.

ECONOMIC BENEFITS IN THE UNITED STATES

In the United States, the application of machine learning for clinical research is helpful to health economics, particularly for pharmaceutical corporations. Machine learning is a driving force behind increased productivity. Many of today's professions and duties will be done entirely or in part by machine learning and AI algorithms in the near future. McKinsey forecasts that big data and machine learning in pharma and medicine may provide up to $100 billion in yearly value via enhanced decision-making, streamlined innovation, increased research/clinical trial efficiency, and the development of new tools for doctors, consumers, insurers, and policymakers. Increased usage of tiny biosensors and devices, as well as mobile applications with more advanced health measurement and remote monitoring capabilities, will generate another flood of data that may be utilized to aid R&D and treatment effectiveness during the next decade [18]. This form of individualized therapy has significant consequences not just for the individual's health, but also for lowering total healthcare expenses. If more patients take their prescribed medications or follow their treatment programs, for example, healthcare expenses will fall and (hopefully) return to normal. Pharmaceutical firms are eager to invest in potential AI startups that will provide them a competitive advantage in drug development and other R&D procedures. Emerj AI Opportunity Landscapes are used to rate AI providers in pharma and life sciences based on their likelihood of delivering a significant ROI in a range of business sectors. According to another research, there were around 3000 persons with Artificial Intelligence abilities and backgrounds in 2018, and there was a need for more than 9000 professionals in the United States.

CONCLUSION

The purpose of this work was to investigate how machine learning may be used in clinical research. The number and complexity of healthcare data are quickly increasing, necessitating the adoption of ML for analysis. To promote peer review and evaluation by the general audience, ML techniques and analysis findings should be provided in a short, standardized, and accessible manner to help in repeatability as well as greater knowledge and application of ML within the clinical research community. Many topics significant in traditional statistics reporting are equally relevant in ML, with a few crucial enhancements. Access to software details and analytic code, preferably in a working, publicly accessible workspace, is an essential complement to a paper to assure transparency and encourage repeatability. We believe that by using these principles, the research community will be able to properly assess these beneficial studies as ML becomes more widely understood. Conventional clinical trials with blinding and randomization that are closely monitored by statisticians are still the gold standard for generating scientific data, but using machine learning methods may help clinical research be more successful and efficient while also boosting the benefits it provides to all stakeholders. Human lives and agony may be saved and reduced if ML-enabled medical studies can increase the efficiency and quality of biological evidence. This creates an ethical duty to investigate this potential. Overcoming challenges with data format and access, outcome definitions, the openness of development/validation procedures and the risk of bias will be required to realize this potential. Due to a lack of prospective studies on the efficacy of ML compared to conventional ways and the fact that change takes time, energy, and collaboration, ML's potential uses in clinical research now outweigh its actual usage. Stakeholder readiness to incorporate ML into clinical research is influenced by strong answers to challenges of data provenance, bias, and validation, as well as trust in the regulatory system around ML in clinical research.

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