

MEDICAL AND PHARMACEUTICAL RESEARCH USING ARTIFICIAL INTELLIGENCE

Abstract

A branch of computer science called artificial intelligence (AI) gives machines the ability to function well and understand complex data. Artificial intelligence research has significantly grown, and it is currently moving more quickly towards applications in education and healthcare. This study shows the potential and limitations of AI in terms of medical and pharmaceutical research. The literature was compiled using specific keywords and phrases such as "Artificial intelligence," "Pharmaceutical research," "drug discovery," "clinical trial," and "disease diagnosis" from sources like PubMed, Science Direct, and Google Scholar in order to choose the research and review articles published within the last five years. This article carefully considered the application of AI in disease diagnostics, digital therapy, individualized treatment, drug discovery, and pandemic or epidemic forecasting. While wearable technology and natural language processing are used to identify patients and monitor the progress of clinical trials, deep learning and neural networks are the most well-known AI technologies. Bayesian nonparametric models are a sensible choice for clinical trial design. Using deep learning and neural networks, the spread of COVID-19, Zika, Ebola, and seasonal flu might all be predicted. According to the scientific community, the development of AI technology may result in more effective and fairly cost pharmaceutical and medical research as well as better public services.

Keywords: This study shows the potential and limitations of AI in terms of medical and pharmaceutical research.

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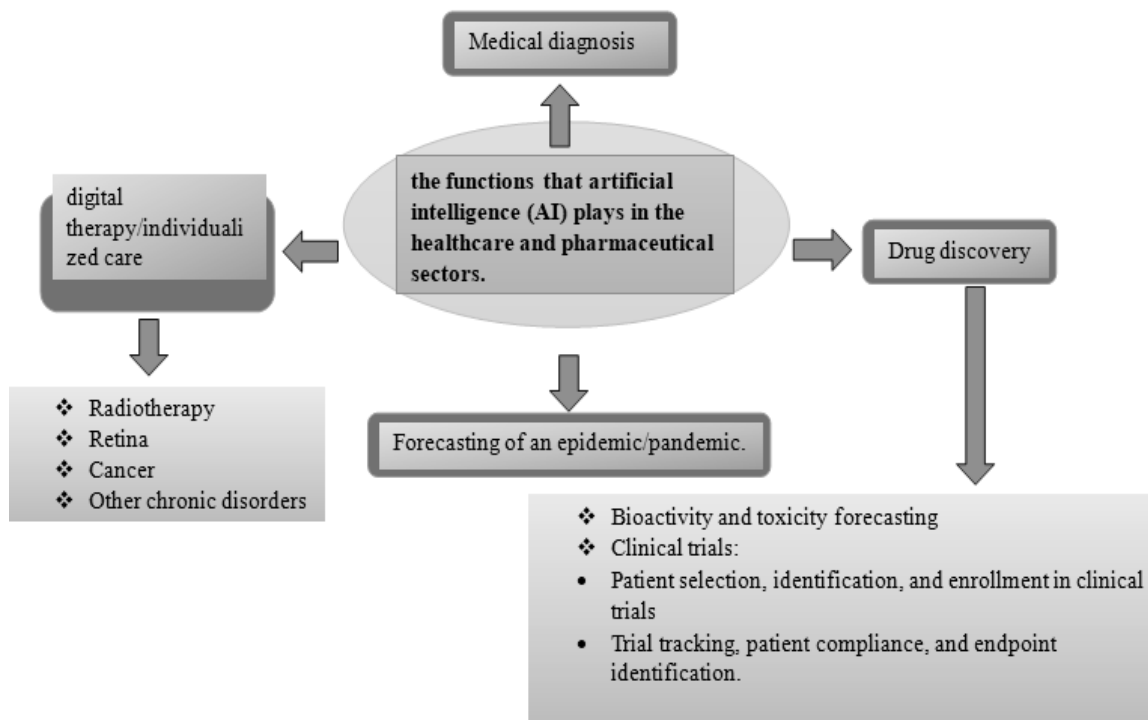
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I. INTRODUCTION

Artificial intelligence (AI) is the term used to describe a wide range of intelligent processes and behaviour that have been created using computer models, algorithms, or a set of rules that allow machines to mimic human cognitive abilities like learning and problem-solving, among others[1].Healthcare industry automation, disease detection, and clinical decision-making are all significantly impacted by AI's quick uptake[2].Because it can evaluate vast volumes of data from numerous modalities, artificial intelligence (AI) has the potential to be further researched in the field of pharmaceutical and healthcare research[3].A number of recent publications have extensively discussed the usage of AI in the corporate world and the healthcare industry. The healthcare sector uses robotic process automation (RPA), physical robots, natural language processing (NLP), and other AI-based technologies [4].As disruptive innovation continues, a route is opened for patients to receive speedy, accurate diagnoses and specialized therapeutic solutions [5].Platforms that may use a number of data types, including as patient-reported symptoms, biometrics, imaging, biomarkers, etc., have been identified as AI-based solutions. The development of AI has made it feasible to anticipate potential illnesses, increasing the likelihood that they can be prevented as a result of early detection. Several areas of healthcare, such as nursing, telemedicine, housekeeping, imaging, surgery, rehabilitation, etc., use physical robots [6,7].Robotic process automation makes use of technology that is low-cost, simple to programme, and capable of carrying out organised digital chores for administrative needs while acting as a semi-intelligent system user. Using this along with image recognition is another option. This technology can be used in the healthcare system for repetitive processes including prior authorization, patient record updating, and billing [8].

Due to its extensive applications across all phases, AI cannot be disregarded when focused on the pharmaceutical industry. It is clear that AI has an impact on pharmaceutical products at every level, from drug development to product management. These are just a few of the AI technologies used in drug discovery for both drug screening and drug design. Examples of machine learning and deep learning technologies include virtual screening (VS), support vector machines (SVMs), deep virtual screening, deep neural networks (DNNs), recurrent neural networks (RNNs), etc. Artificial intelligence (AI) neural networks are modelled after biological neural networks, which process input and produce an output in response. Multiple interconnected units make up artificial neural networks (ANN), which process information. When there are multiple layers of data processing units, DNNs are similar to ANNs. The output data from RNNs process one analysis as the input data for the subsequent analysis in a sequential way. SVMs are used for input data regression and categorization. In order to choose the best excipients, decide on the development process, and make sure that all requirements are met, AI is being employed in the production of pharmaceutical items. When creating pharmaceuticals, ANNs, model expert systems (MES), and other methods are employed. Manufacturing companies employ artificial intelligence (AI) to automate and tailor production while connecting manufacturing faults to predetermined restrictions. To deliver findings with the required quality, artificial intelligence (AI) tools like the meta classifier and tablet classifier are used. [9].Clinical trials that use AI benefit from improved subject selection and trial monitoring, which lowers dropout rates. The use of ML in clinical studies [10].

II. THE FOLLOWING ARE THE FUNCTIONS THAT ARTIFICIAL INTELLIGENCE (AI) PLAYS IN THE PHARMACEUTICAL AND HEALTHCARE INDUSTRIES.



1. AI in Medical Diagnosis: The creation of a compassionate treatment plan and the upkeep of the patient's general health depend on the accurate diagnosis of the patient's ailment. Human error becomes a barrier to accurate diagnosis, and the misinterpretation of the information produced results in a labor-intensive and complicated process. AI has a wide range of potential applications since it can ensure the right level of efficiency and accuracy. This article reports on the manner in which a variety of unique technologies and approaches have been used with the aim of disease detection after a thorough evaluation of the pertinent published material. As a result of the progression of the human population, there is always a continually growing need for the healthcare system, which varies depending on the manifestations of the many environmental factors [11].

In order to create a compassionate treatment plan and maintain the patient's general health, a patient's condition must be accurately diagnosed. Human error and incorrect information interpretation create a procedure that is complex and time-consuming, which makes it difficult to provide a thorough diagnosis. AI has a wide range of potential applications because it can provide the proper assurance in accuracy and efficiency. This article reports on how various technologies and approaches have been used to achieve the goal of disease detection after a thorough analysis of the pertinent published material. As a result of the progression of the human population, there is always a continually growing need for the healthcare system, which varies depending on the manifestations of the many environmental factors [12].

Numerous research were carried out for the purpose of predictive modeling, which proved to be significant in forecasting early stages of Parkinson's disease [13]. In order to assist in the detection of lung disorders, an algorithm for segmenting the ribs was devised using chest X-ray pictures [14]. Recently, researchers have processed the signals from electrocardiograms in order to identify and classify cardiac arrhythmia using algorithms and machine learning. This was done in order to determine the causes of cardiac arrhythmia [15]. In a different piece of research, tuberculosis was categorized and diagnosed with the help of an optimization genetic algorithm (GA) and a support vector machine (SVM) [16].

2. **Use of Artificial Intelligence in Digital Therapy/ Individualized Care:** Artificial intelligence has the capacity to unearth a significant association that is concealed in the raw datasheets and can then be used for illness diagnosis, treatment, and prevention. There are many contemporary techniques used for computational understanding in this developing area of computer science. Almost all other areas of medical science could benefit from using these techniques. The difficulty of compiling, analyzing, and applying vast amounts of knowledge must be met in order to address the challenging clinical problems that need to be solved. Clinical professionals now have help in solving challenging clinical problems thanks to the development of medical artificial intelligence. Healthcare professionals can benefit from the use of systems like artificial neural networks (ANNs), evolutionary computational systems, fuzzy expert systems, and hybrid intelligent systems for data manipulation [17]. Neurons are a type of interconnected computer processor that create a network that is capable of doing simultaneous calculations for the purpose of data processing. A binary threshold function was utilized in the development of the very first artificial neuron [18]. The most prevalent model with multiple layers was the multilayer feed-forward perceptron. An input layer, a middle layer, and an output layer were among these layers. There are connections between each neuron that have a specific numerical weight [19].

The model with the most multilayer layers was the multilayer feed-forward perceptron. A middle layer, an output layer, and an input layer made up these layers. Each neuron is joined to the others via connections that have a weight in numbers [20]. The genetic algorithm is currently the most common type of algorithm. It generates a large number of potentially useful solutions to the issue at hand, narrows the field down to one that is optimal, and discards others that are less desirable [21].

3. Digital Therapy/Individualized Care

- **Radiotherapy:** Planning automated radiation therapy with new technology is advantageous. The accuracy rate, consistency, and quality of treatment plans are all improving with automated treatment planning. The therapy process is divided into three steps: Logic modeling of prior knowledge in clinical practises, automated rule implementation, and multi-criteria optimization [22]. Clinical guidelines can be implemented by a basic structured computer program. The patient's anatomy and physiology can be examined by the treatment planning system, which can also simulate the thought process involved in manual therapy planning. The potential of 3D dose distribution and spatial dosage models is high [23]. Radiomics can provide

detailed tumor information using imaging biomarkers. Individual radiation therapy outcomes and toxicity can be predicted using radiationomics [24].

- **Retina:** Retinal imaging with great resolution has made it significantly easier to evaluate people's health. With the help of high-definition medications, an ophthalmologist or retinal specialist can define a personal therapy and create an ever-improving learning healthcare system from a single image of the retina [25].
 - **AI in Cancer:** AI is essential in the diagnosis and management of cancer due to its wide range of applications. With the aid of gene expression data from a multilayer perceptron neural network, the non-Hodgkin lymphoma subtypes were identified. By combining 20,863 genes, the neural network generates several forms of lymphoma. MCL, follicular, DLBCL, marginal zone, and Burkitt are among the subtypes of lymphoma. Successful AI neural network predictions of lymphoma subtypes [26]. An artificial neural network discovered new MCL prognostic indicators using data on gene expression. 5 genes were associated with good survival, 10 genes with bad survival, and 58 genes accurately predicted survival. [27]. AI diagnoses cancer quickly and accurately. AI-based PET imaging of lymphoma evaluates tumour load, characterizes tumours, quantifies heterogeneity, and predicts therapy response [28]. Colorectal cancer (CRC) screening technology and visual nocturne prediction of Helicobacter pylori infection help predict gastric cancer development in gastrointestinal cancer patients. Blood testing, endoscopic imaging, and AI can slow cancer growth [29]. It is helpful to employ AI for screening and early diagnosis of lung cancer. Because they can properly define pulmonary nodules and store enormous volumes of data, deep learning and machine learning AI approaches enhance the diagnosis of lung cancer. [30].
- 4. AI in other Chronic Diseases:** Depending on a person's aptitude for computer programming, a variety of computerized therapies are accessible. Treatment is the main objective of the behavioural and cognitive strategy, which makes use of multiple-choice questions or joysticks[31]. On the basis of the patient's own biopsies, AI can be used to adopt n-of-1 pharmacological suggestions and create a combination therapy. Recently, intelligent computer-assisted learning has been developed, with the ability to use additional AI technologies like expert systems and natural language processing. Artificial intelligence may enable virtual medical assistants to carry out the continual monitoring required for chronic diseases. This form of support has been popular among businesses; it typically uses mobile applications to give text-based virtual coaching and makes use of artificial intelligence (AI) to generate nutrition recommendations that are precisely based on gut flora. It is possible to predict arterial fibrillation using a system that integrates data from an accelerometer, a smart watch, and a deep learning single-lead ECG sensor. AI-developed case-based reasoning is a method that is frequently used to treat diabetes[32].

The autonomous system can recognize problems and remember the best treatment for each patient. At the moment, it is used to improve insulin therapy. Different approaches, such as the vector regression method, are frequently used to treat diabetes. Machine learning-based methods, such as clinical decision support, can also predict the short- and long-term HbA1c response following the injection of insulin in patients with type 2 diabetes mellitus. The likelihood that a person will get a particular disease can also

be determined using AI techniques. A wide range of severe diseases can be treated using advanced molecular-level AI techniques, such as molecular phenotyping, genomics, epigenetic alterations, and the development of digital biomarkers. Thanks to cutting-edge technology, patients can now control their diabetes using web-based applications on their cellphones and other mobile devices.

- 5. AI in Drug Discovery:** Due to a lack of adequate technology, it is more difficult to generate several medicinal molecules from a chemical space. This issue can be resolved by incorporating artificial intelligence into the process of creating new medications[33].The forecasting activities of various parameters, such as log P or log D, which can predict and generate predictions through computations and can justify the biological safety, efficacy, and side effects, including the pharmacokinetics of the significant molecule, are affected by the relationship between the quantitative structure and activity[34].The enormous space requires a delocalization of molecules due to the dispersion of molecules and their three-dimensional properties. It is advisable to obtain all past information regarding the selectivity and placement of the molecules for the goal of proving the bioactivity using a range of domains, such as PubChem, ChemBank, DrugBank, and ChemDB. Many in silico techniques are employed for virtual screening, and they frequently provide a better analysis, faster exclusion, and variety [33].

QSAR is focused for the potential application of the drug candidate using AI-based QSAR algorithms. Controlling newly discovered and created biological activity could take ten years if traditional approaches are employed to achieve statistical differences. When a novel medication is being developed, the drug's solubility, partition coefficient, level of ionisation, and intrinsic permeability are all factors that affect target receptor binding. Algorithms employ molecular descriptors like Simplified Molecular Input Line Entry System (SMILES) to predict the binding properties [35].The six physicochemical properties are often calculated using the Estimation Programme Interface Suite, which includes a quantitative structure-property relationship (QSPR). The lipophilicity and solubility of a range of chemicals have been predicted using the ADMET predictor, neural networks, and ALGOPS program-based deep learning. The solubility is predicted by a large number of undirected graphs. Surface area, mass, hydrogen count, refractivity, volume, log P, surface area, sum of the indices, solubility index, and rotatable bonds are all included in the prediction of a new chemical entity[36].

- 6. AI in Prediction of Bioactivity and Toxicity:** A protein's or receptor's affinities determine efficiency. The medicine and target are expected to interact because of how similar they are to one another. To forecast how the medicine and the target will interact, Chem Mapper and the similarity ensemble technique are utilized [37].Additionally, connection, substructure, or a combination of these may be taken into account. Deep learning has shown enhanced performance since it is independent of the three-dimensional protein structure. Deep affinity, protein, and drug molecule interaction prediction are some of the techniques[38].

The forecast is crucial for preventing dangerous repercussions. Following in vitro testing, preclinical investigations are typically carried out to identify the timeliness and areas that still want improvement. Numerous Web-based options are available to cut costs. The Tox21 Data Challenge was hosted by the US Food and Drug Administration, the Environmental Protection Agency, and the National Institutes of Health to assess

computational approaches for drug toxicity estimation[39].When it came to identifying static and dynamic properties inside chemical descriptors, an algorithm by the name of Deep Tox outperformed all other methods; the eToxPred was used to determine the toxicity of tiny compounds. The guilt-by-association theory is applied by TargeTox, a biological target-based drug toxicity prediction tool [40].The properties of the novel compounds can be predicted with the use of a scoring function. ProCTOR could predict with ease if a drug's toxicity would cause it to fail in clinical trials. It also recognized negative medication interactions [41].

7. AI in Clinical Trials: The most time- and money-consuming phase of drug development is clinical trials. Clinical studies that are approved by the Food and Drug Administration (FDA) have a relatively low success rate despite the time and money invested in them [42].Clinical studies frequently experience bottlenecks, and those can result in study failure. These bottlenecks include a lack of participants, trial dropouts, adverse effects from the test substance, or conflicting data. Sponsor must bear a tremendous financial cost if such failure occurs in late stages of clinical trials, such as in phase-III and phase-IV [43].The high expense of clinical trials has an effect on the price of patient treatment. Because of this, biopharmaceutical companies include the expenses of R&D for unsuccessful trials in the price of approved medicines in order to maintain a profit[44].Design, patient recruitment and selection, site selection, monitoring, data collection, and analysis are just a few of the numerous procedures that go into a clinical trial. Patient recruitment and selection, the most difficult of these steps, causes 30% of phase-III trials to finish early and 80% of trials to go past the permitted number of participants. In a multicentered, international investigation, trial monitoring is an incredibly expensive and time-consuming task. The amount of time it takes from the "last subject last visit" to data submission to regulatory agencies, which necessitates extensive data gathering and processing procedures, is another issue in clinical research. These difficulties in clinical trials are changing as a result of artificial intelligence and digitization[45].

8. Clinical Trial Design, Patient Identification, Recruitment and Enrolment: The FDA asserts that using AI models can raise the bar for trial design and patient selection by decreasing population heterogeneity and prognostic and predictive enrichment[46].Bayesian nonparametric models (BNMs), in addition to its many other uses, have shown to be a helpful tool for clinical trial planning. This model is adaptable and employs a nonparametric methodology. By using a finite subset of limited parameters, this paradigm enables the use of infinite-dimensional parameter sets. Clustering and trial design take less time using this method. Dirichlet process mixture models and Markov Chain Monte Carlo (MCMC) methods are two BNMs that are frequently employed. These BNMs can be used for a number of clinical trial design-related activities, such as cancer patient dose selection studies, immuno-oncology, and cell therapy. The variety of patients makes dose selection difficult and poses the risk of choosing the wrong dose or target populations in the future. Because they consider all the characteristics and variability of the research subjects, BNMs are an efficient and useful tool for dose selection in these people[45].Using Bayesian nonparametric design, adaptive dose selection is applied to many populations. This facilitates information sharing among diverse groups while taking into account their differences. These devices offer accurate dose selection, lowering the possibility of error [47].Other designs, such modified toxicity probability interval (mTPI) designs, employ the Dirichlet process. This technology

automatically groups patients into comparable clusters and determines the dose by learning from the incoming data [48]. The selection of participants is the most important stage of a study, and the health records of the patients or participants include important information for evaluating whether they meet inclusion or exclusion criteria. Putting together the patient's information, history, or fresh test results would require time and money. With the use of artificial intelligence (AI), it is possible to connect patient data from the electronic medical record (EMR) with additional patient data that is spread across many locations, owners, and formats. Utilising optical character recognition (OCR) and natural language processing (NLP), two computer vision techniques, patients can be quickly identified and categorized in these examinations [46].

- 9. Monitoring Trial, Patient Adherence and Endpoint Detection:** Another difficulty in the clinical trial is keeping track of the participants, but wearable technology with AI capabilities can handle this. Real-time, individualized, and power-saving, such monitoring. RBM, a methodology enabled by AI, has recently come to replace traditional monitoring as the most effective and economical method. The cost of data monitoring at the trial site may be decreased, and its effectiveness and quality could be improved with an upgraded version of RBM. Predictive analysis and data visualization are two tools that AI-assisted "smart monitoring" might utilize to enhance trial site performance and data quality checks. To acquire accurate data and ensure the trial's success, patients must comply to the trial's adherence guidelines. The experiment is effective in monitoring patient adherence because to wearable sensors and video surveillance, which automatically and continuously collect patient data. When compared to manual reading, AI-enabled medical image-based endpoint and illness identification is considerably simpler and faster [46]. According to recent breakthroughs, AI may be able to change the conventional clinical trial process into one that is less expensive, safer, and quicker.
- 10. AI IN Forecasting of an Epidemic/Pandemic:** The scope of a pandemic is limitless, and it can result in morbidity and mortality. Black Death, Spanish flu, cholera, influenza, AIDS, and COVID-19 are just a few of the pandemic epidemics that have occurred globally and have the potential to disrupt social and economic life [50]. Active surveillance requires a significant amount of money, labour, and time. It might be difficult to forecast epidemics and pandemics in real life. However, thanks to recent developments, it is now possible to analyze the spread of terrible diseases. The best choice for achieving surveillance with effective resource use is AI. ML and deep learning are being used in a variety of healthcare sectors since they are more efficient than human resources [51]. In pandemics and epidemics, AI is utilized for detection, prevention, reaction, and recovery. Prediction, surveillance, and information are all being used more and more frequently in prevention, especially in light of the recent COVID-19 outbreak [52]. The shifting epidemic peak, repeated peaking, and other factors make influenza epidemic forecast extremely difficult. Even in regions with variable seasonal influenza, a reliable forecast is attainable with the use of the SAAIM (self-adaptive AI model) [53]. In Taiwan, for example, seasonal influenza predictions have been made using machine learning and ensemble methods, and the predictions and forecasts have proven to be accurate [54]. Machine learning anonymised mobility map (AMM) has been used to predict influenza in Australia and the USA. AMM collects information from smartphones and can anticipate epidemics based on human movement, even between states [55]. Big Data and the AI model (Enerpol) are integrated in Switzerland to anticipate COVID-19 [56]. A number of statistics and deep learning systems, including the feed-forward neural

network (FNN), multilayer perception (MLP), autoregressive integrated moving average (ARIMA), and long short-term memory (LSTM), were used to explore the dynamical behavior of COVID-19. The generated data may serve as a helpful guide for the COVID-19 forecast [57].

III. DISCUSSION AND CONCLUSIONS

Recent advances in AI have scientists enthralled, especially when it comes to how they are being used to services and research in the pharmaceutical and healthcare industries. The future of healthcare will be shaped by intelligent hospitals and healthcare facilities that integrate AI, ML, and Big Data. Table 1 presents some limitations and difficulties associated with the use of these technologies.

Artificial intelligence (AI) will have the ability to reduce the price and time of medical research in the pharmaceutical industry, given how swiftly technology is growing. It's incredibly impressive to see how deep learning, neural networking, and unsupervised learning can be used to use AI to identify diseases.

These artificial intelligence (AI) tools can manage unstructured data and compare it to learnt data to accurately predict a result, making them valuable in providing a diagnosis of a specific condition. Intelligent computer-assisted instruction (ICAI), case-based reasoning, vector regression approach, and clinical decision support are a few examples of how AI has been shown to be a crucial tool for chronic disease monitoring and therapy optimization. It can be crucial to comprehend the connections between different factors while attempting to evoke a thoughtful reaction from patients. Clinical decision support gives the medical staff patient-specific data to improve illness monitoring and treatment, whilst case-based reasoning speeds up problem-solving by drawing on prior, comparable experiences. These tools help the difficult process of creating a customized treatment.

Additional methods, such as high-resolution retinal imaging and radiomics, which predicts the results and toxicity of a patient's radiation therapy, enable the study of human health. The main goals of pharmaceutical research and development, which is a time-consuming and expensive process, are to discover new treatments and bring them to market. From target identification to clinical trials, artificial intelligence has the ability to automate every stage of the procedure.

The first stage in creating a novel drug is to identify the biological molecules that interfere with the condition. Thousands of synthetic compounds are created during the process of creating a novel pharmaceutical in an effort to bind to a target and change that target's behaviour in order to treat a particular condition. The physicochemical and pharmacokinetic properties are determined using computer-aided drug design and quantitative structure-activity relationships (QSAR) or quantitative structure-property relationships (QSPR). The lipophilicity and solubility of an NCE are predicted using deep learning and neural networks constructed using the ADMET predictor and ALGOPS software. Artificial intelligence (AI) approaches that anticipate drug-target interactions include the similarity ensemble approach and Chem Mapper. The technologies Deep Tox, eToxPred, TargeTox, and ProCTOR are used to forecast the toxicity of a small chemical. Such forecasts can assist the business in saving time and money by keeping potentially harmful compounds out of preclinical or clinical trials. The majority of the time and money

spent on the pharmaceutical development process is spent on clinical trials for new molecules. The standard for trial design, patient selection, dose selection, patient adherence, trial monitoring, and endpoint analysis has increased as a result of the usage of AI. In contrast to OCR and NLP, which are effective tools for patient identification and characterisation, BNMs can be employed in clinical trial design and dose selection. Patients can be monitored and their adherence to treatment programmes verified by using RBM, video surveillance, and wearable sensors. The time and expense involved in bringing a medicine to market could be considerably reduced with the use of artificial intelligence (AI). Epidemic and pandemic outbreaks are common and frequently fatal over the world, causing a great deal of misery for people. Almost six million people have died as a result of the COVID19 sickness, which is currently causing devastation on the entire planet. Cholera, Spanish Flu, AIDS, and other illness epidemics in the past have all been fatal.

AI can be used to recognize, stop, respond to, and recover from pandemics or epidemics. Deep learning has been found to be more efficient at tracking pandemics and epidemics. More significant AI tools for predicting pandemics or epidemics include neural networks, AMM, and the machine learning algorithm SVR. AI has a number of uses, and it has a number of advantages over more traditional methods; yet, it also has significant limitations and obstacles. The most significant obstacles include the demand of enormous volumes of data to feed the system for training, the logistical problems in putting the system into place, the expense, and the reliance on the hardware or computational facilities. Due to epistemic uncertainty, inaccuracies, and a lack of flexibility, artificial intelligence systems like QSPR and Chem Mapper can, at times, be inaccurate. The pharmaceutical and healthcare sectors will have more opportunities for research as a result of AI-enabled methodologies, which may have an impact on how future studies are carried out.

Table 1: The AI Applications and Some Limitations of AI in Healthcare and Pharmaceutical Research.

Sectors	AI Technologies	Applications	Limitations/Challenges
Disease diagnosis	Deep learning Neuronal networking Unsupervised learning	Cancer, Dementia, Dermatological disorders, Atrial fibrillation	<ul style="list-style-type: none"> • Development takes longer and is more complicated. • Requires more data than typical ML algorithms. • Expensive computationally compared to traditional algorithms.
Digital therapy and personalized treatment	In short: ANN Computational evolution Fuzzy expert systems Intelligent hybrid system Automation of treatment planning	Analysis of images, interpretation of data Administration of anaesthesia and vasodilator	<ul style="list-style-type: none"> • Hardware-dependent. • Network functioning is unclear. • Challenges in determining the best network structure. • Challenge in communicating the issue to the network. • Values do not yield optimal results.

Drug discovery	QSPR (Estimation programme interface suite)	Physical and chemical properties of tiny molecules are determined.	<ul style="list-style-type: none"> • Aleatoric error and epistemic uncertainty. • Extensive data and computing resources needed.
	Chem Mapper Deep learning	Target-drug interaction	<ul style="list-style-type: none"> • Lack of adaptability and model generalization.
Forecasting epidemic/pandemic	DNN	Zika prediction	<ul style="list-style-type: none"> • It requires a very large amount of data in order to perform better than other techniques. • Expensive. • No standard theory to guide in selecting deep learning tools
	ARIMA	Explore the COVID-19 dynamic pattern.	<ul style="list-style-type: none"> • Hard to anticipate turning moments. • High computational cost. • Poor results for long-term projections. • Seasonal time series cannot be used. • More difficult to explain than exponential smoothing.

REFERENCES

- [1] Chen, M.; Decary, M. Artificial intelligence in healthcare: An essential guide for health leaders. In Healthcare Management Forum; SAGE Publications: Los Angeles, CA, USA, 2020.
- [2] Sunarti, S.; Rahman, F.F.; Naufal, M.; Risky, M.; Febriyanto, K.; Masnina, R. Artificial intelligence in healthcare: Opportunities and risk for future. *Gac. Sanit.* 2021, 35, S67–S70
- [3] Toepper, M. Dissociating Normal Aging from Alzheimer’s Disease: A View from Cognitive Neuroscience. *J. Alzheimer’s Dis.* 2017, 57, 331–352
- [4] Davenport, T.; Kalakota, R. The potential for artificial intelligence in healthcare. *Futur. Healthc. J.* 2019, 6, 94–98.
- [5] Horgan, D.; Romao, M.; Morré, S.A.; Kalra, D. Artificial Intelligence: Power for Civilisation—And for Better Healthcare. *PublicHealth Genom.* 2019, 22, 145–161.
- [6] Khan, Z.H.; Siddique, A.; Lee, C.W. Robotics Utilization for Healthcare Digitization in Global COVID-19 Management. *Int. J. Environ. Res. Public Health* 2020, 17, 3819.
- [7] Ribeiro, J.; Lima, R.; Eckhardt, T.; Paiva, S. Robotic Process Automation and Artificial Intelligence in Industry 4.0—A Literature Review. *Procedia Comput. Sci.* 2021, 181, 51–58.
- [8] Ribeiro, J.; Lima, R.; Eckhardt, T.; Paiva, S. Robotic Process Automation and Artificial Intelligence in Industry 4.0—A Literature Review. *Procedia Comput. Sci.* 2021, 181, 51–58.
- [9] Paul, D.; Sanap, G.; Shenoy, S.; Kalyane, D.; Kalia, K.; Tekade, R.K. Artificial intelligence in drug discovery and development. *Drug Discov. Today* 2021, 26, 80–93
- [10] Bhatt, A. Artificial intelligence in managing clinical trial design and conduct: Man and machine still on the learning curve? *Perspect. Clin. Res.* 2021, 12, 1.
- [11] Menschner, P.; Prinz, A.; Koene, P.; Köbler, F.; Altmann, M.; Krcmar, H.; Leimeister, J.M. Reaching into patients’ homes Participatory designed AAL services: The case of a patient-centered nutrition tracking service. *Electron. Mark.* 2011, 21, 63–76.
- [12] Obeng, O.; Paul, S. Understanding HIPAA compliance practice in healthcare organizations in a cultural context. In Proceedings of the 25th Americas Conference on Information Systems 2019, Cancún, Mexico, 15–17 August 2019.

- [13] Prashanth, R.; Roy, S.D.; Mandal, P.K.; Ghosh, S. High-Accuracy Detection of Early Parkinson's Disease through Multimodal Features and Machine Learning. *Int. J. Med. Inform.* 2016, 90, 13–21.
- [14] Wang, H.; Zhang, D.; Ding, S.; Gao, Z.; Feng, J.; Wan, S. Rib segmentation algorithm for X-ray image based on unpaired sample augmentation and multi-scale network. *Neural Comput. Appl.* 2021, 1–15.
- [15] Qaisar, S.M.; Khan, S.I.; Srinivasan, K.; Krichen, M. Arrhythmia classification using multirate processing metaheuristic optimization and variational mode decomposition. *J. King Saud Univ.—Comput. Inf. Sci.* 2022; in press.
- [16] Hrizi, O.; Gasmi, K.; Ben Ltaifa, I.; Alshammari, H.; Karamti, H.; Krichen, M.; Ben Ammar, L.; Mahmood, M.A. Tuberculosis Disease Diagnosis Based on an Optimized Machine Learning Model. *J. Heal. Eng.* 2022, 2022, 8950243.
- [17] Ramesh, A.N.; Kambhampati, C.; Monson, J.R.; Drew, P.J. Artificial intelligence in medicine. *Ann. R. Coll. Surg. Engl.* 2004, 86, 334.
- [18] Jain, A.; Mao, J.; Mohiuddin, K. Artificial neural networks: A tutorial. *Computer* 1996, 29, 31–44.
- [19] Hopfield, J.J. Artificial neural networks. *IEEE Circuits Syst. Mag.* 1988, 4, 3–10.
- [20] Hanson III, C.W.; Marshall, B.E. Artificial intelligence applications in the intensive care unit. *Crit. Care Med.* 2001, 29, 427–435.
- [21] Whitley, D. A genetic algorithm tutorial. *Stat. Comput.* 1994, 4, 65–85.
- [22] Moore, K.L. Automated radiotherapy treatment planning. In *Seminars in Radiation Oncology*; WB Saunders: Philadelphia, PA, USA, 2019; Volume 29, pp. 209–218.
- [23] Troulis, M.; Everett, P.; Seldin, E.; Kikinis, R.; Kaban, L. Development of a three-dimensional treatment planning system based on computed tomographic data. *Int. J. Oral Maxillofac. Surg.* 2002, 31, 349–357.
- [24] Arimura, H.; Soufi, M.; Kamezawa, H.; Ninomiya, K.; Yamada, M. Radiomics with artificial intelligence for precision medicine in radiation therapy. *J. Radiat. Res.* 2019, 60, 150–157.
- [25] Schmidt-Erfurth, U.; Sadeghipour, A.; Gerendas, B.S.; Waldstein, S.M.; Bogunovi'c, H. Artificial intelligence in retina. *Prog. Retin. Eye Res.* 2018, 67, 1–29.
- [26] Carreras, J.; Hamoudi, R. Artificial Neural Network Analysis of Gene Expression Data Predicted Non-Hodgkin Lymphoma Subtypes with High Accuracy. *Mach. Learn. Knowl. Extr.* 2021, 3, 720–739.
- [27] Carreras, J.; Nakamura, N.; Hamoudi, R. Artificial Intelligence Analysis of Gene Expression Predicted the Overall Survival of Mantle Cell Lymphoma and a Large Pan-Cancer Series. *Healthcare* 2022, 10, 155.
- [28] Hasani, N.; Paravastu, S.S.; Farhadi, F.; Yousefirizi, F.; Morris, M.A.; Rahmim, A.; Roschewski, M.; Summers, R.M.; Saboury, B. Artificial Intelligence in Lymphoma PET Imaging: A Scoping Review (Current Trends and Future Directions). *PET Clin.* 2022, 17, 145–174.
- [29] Mitsala, A.; Tsalikidis, C.; Pitiakoudis, M.; Simopoulos, C.; Tsaroucha, A. Artificial Intelligence in Colorectal Cancer Screening, Diagnosis and Treatment. *A New Era. Curr. Oncol.* 2021, 28, 1581–1607.
- [30] Joy Mathew, C.; David, A.M.; Joy Mathew, C.M. Artificial Intelligence and its future potential in lung cancer screening. *EXCLI J.* 2020, 19, 1552–1562.
- [31] Posner, M.I.; Rothbart, M.K. Research on Attention Networks as a Model for the Integration of Psychological Science. *Annu. Rev. Psychol.* 2007, 58, 1–23.
- [32] Ellahham, S. Artificial Intelligence: The Future for Diabetes Care. *Am. J. Med.* 2020, 133, 895–900.
- [33] Mak, K.K.; Pichika, M.R. Artificial intelligence in drug development: Present status and future prospects. *Drug Discov. Today* 2019, 24, 773–780.
- [34] Zhu, H. Big Data and Artificial Intelligence Modeling for Drug Discovery. *Annu. Rev. Pharmacol. Toxicol.* 2020, 60, 573–589.
- [35] Hessler, G.; Baringhaus, K.-H. Artificial Intelligence in Drug Design. *Molecules* 2018, 23, 2520.
- [36] Chai, S.; Liu, Q.; Liang, X.; Guo, Y.; Zhang, S.; Xu, C.; Du, J.; Yuan, Z.; Zhang, L.; Gani, R. A grand product design model for crystallization solvent design. *Comput. Chem. Eng.* 2020, 135, 106764.
- [37] Lounkine, E.; Keiser, M.J.; Whitebread, S.; Mikhailov, D.; Hamon, J.; Jenkins, J.L.; Lavan, P.; Weber, E.; Doak, A.K.; Côté, S.; et al. Large-scale prediction and testing of drug activity on side-effect targets. *Nature* 2012, 486, 361–367.
- [38] Feng, Q.; Dueva, E.; Cherkasov, A.; Ester, M. Padme: A deep learning-based framework for drug-target interaction prediction. *arXiv* 2018, arXiv:1807.09741.
- [39] Yang, X.; Wang, Y.; Byrne, R.; Schneider, G.; Yang, S. Concepts of Artificial Intelligence for Computer-Assisted Drug Discovery. *Chem. Rev.* 2019, 119, 10520–10594.
- [40] Lysenko, A.; Sharma, A.; Boroevich, K.; Tsunoda, T. An integrative machine learning approach for prediction of toxicity-related drug safety. *Life Sci. Alliance* 2018, 1, e201800098.
- [41] Gayvert, K.M.; Madhukar, N.S.; Elemento, O. A Data-Driven Approach to Predicting Successes and Failures of Clinical Trials. *Cell Chem. Biol.* 2016, 23, 1294–1301.

- [42] Thorlund, K.; Haggstrom, J.; Park, J.J.; Mills, E.J. Key design considerations for adaptive clinical trials: A primer for clinicians. *BMJ* 2018, 360, k698.
- [43] Goldsack, J. Synthetic Control Arms Can Save Time and Money in Clinical Trials. 2019. Available online: <https://www.statnews.com/2019/02/05/synthetic-control-arms-clinicaltrials/> (accessed on 5 November 2021).
- [44] Unger, J.M.; Vaidya, R.; Hershman, D.L.; Minasian, L.M.; E Fleury, M. Systematic Review and Meta-Analysis of the Magnitude of Structural, Clinical, and Physician and Patient Barriers to Cancer Clinical Trial Participation. *Gynecol. Oncol.* 2019, 111, 245–255.
- [45] Kolluri, S.; Lin, J.; Liu, R.; Zhang, Y.; Zhang, W. Machine Learning and Artificial Intelligence in Pharmaceutical Research and Development: A Review. *AAPS J.* 2022, 24, 19.
- [46] Harrer, S.; Shah, P.; Antony, B.; Hu, J. Artificial Intelligence for Clinical Trial Design. *Trends Pharmacol. Sci.* 2019, 40, 577–591.
- [47] Li, M.; Liu, R.; Lin, J.; Bunn, V.; Zhao, H. Bayesian Semi-parametric Design (BSD) for adaptive dose-finding with multiple strata. *J. Biopharm. Stat.* 2020, 30, 806–820.
- [48] Liu, R.; Lin, J.; Li, P. Design considerations for phase I/II dose finding clinical trials in Immuno-oncology and cell therapy. *Contemp. Clin. Trials* 2020, 96, 106083.
- [49] Madhav, N.; Oppenheim, B.; Gallivan, M.; Mulembakani, P.; Rubin, E.; Wolfe, N. Pandemics: Risks, Impacts, and Mitigation. *Disease Control Priorities: Improving Health and Reducing Poverty*, 3rd ed.; The International Bank for Reconstruction and Development/The World Bank: Washington, DC, USA, 2017; Volume 9, pp. 315–345.
- [50] Gopinath, N. Artificial intelligence: Potential tool to subside SARS-CoV-2 pandemic. *Process Biochem.* 2021, 110, 94–99.
- [51] OECD. Artificial Intelligence in Society; OECD: Paris, France, 2019.
- [52] Su, K.; Xu, L.; Li, G.; Ruan, X.; Li, X.; Deng, P.; Li, X.; Li, Q.; Chen, X.; Xiong, Y.; et al. Forecasting influenza activity using self-adaptive AI model and multi-source data in Chongqing, China. *Ebiomedicine* 2019, 47, 284–292.
- [53] Cheng, H.-Y.; Wu, Y.-C.; Lin, M.-H.; Liu, Y.-L.; Tsai, Y.-Y.; Wu, J.-H.; Pan, K.-H.; Ke, C.-J.; Chen, C.-M.; Liu, D.-P.; et al. Applying Machine Learning Models with An Ensemble Approach for Accurate Real-Time Influenza Forecasting in Taiwan: Development and Validation Study. *J. Med. Internet Res.* 2020, 22, e15394.
- [54] Venkatramanan, S.; Sadilek, A.; Fadikar, A.; Barrett, C.L.; Biggerstaff, M.; Chen, J.; Dotiwala, X.; Eastham, P.; Gipson, B.; Higdon, D.; et al. Forecasting Influenza Activity Using Machine-Learned Mobility Map. *Nat. Commun.* 2021, 12, 726.
- [55] Marini, M.; Chokani, N.; Abhari, R.S. COVID-19 Epidemic in Switzerland: Growth Prediction and Containment Strategy Using Artificial Intelligence and Big Data. *medRxiv* 2020. medRxiv:2020.03.30.20047472
- [56] Yu, C.S.; Chang, S.S.; Chang, T.H.; Wu, J.L.; Lin, Y.J.; Chien, H.F.; Chen, R.J. A COVID-19 Pandemic Artificial Intelligence-Based System with Deep Learning Forecasting and Automatic Statistical Data Acquisition: Development and Implementation Study. *J. Med. Internet Res.* 2021, 23, e27806.