INTEGRATING ARTIFICIAL INTELLIGENCE IN DISEASE DIAGNOSIS, TREATMENT, AND FORMULATION DEVELOPMENT: A REVIEW

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ABSTRACT

Artificial intelligence (AI) is rapidly advancing and significantly impacting clinical care and treatment. Machine learning and deep learning, as core digital AI technologies, are being extensively applied to support diagnosis and treatment. With the progress of digital health-care technologies such as AI, bioprinting, robotics, and nanotechnology, the health-care landscape is transforming. Digitization in health-care offers various opportunities, including reducing human error rates, improving clinical outcomes, and monitoring longitudinal data. AI techniques, ranging from learning algorithms to deep learning, play a critical role in several health-care domains, such as the development of new health-care systems, improvement of patient information and records, and treatment of various ailments. AI has emerged as a powerful scientific tool, capable of processing and analyzing vast amounts of data to support decision-making. Numerous studies have demonstrated that AI can perform on par with or outperform humans in crucial medical tasks, including disease detection. However, despite its potential to revolutionize health care, ethical considerations must be carefully addressed before implementing AI systems and making informed decisions about their usage. Researchers have utilized various AI-based approaches, including deep and machine learning models, to identify diseases that require early diagnosis, such as skin, liver, heart, and Alzheimer’s diseases. Consequently, related work presents different methods for disease diagnosis along with their respective levels of accuracy, including the Boltzmann machine, K nearest neighbor, support vector machine, decision tree, logistic regression, fuzzy logic, and artificial neural network. While AI holds immense promise, it is likely to take decades before it completely replaces humans in various medical operations.

Keywords: Artificial intelligence, Disease diagnosis, Health-care digitization, Machine learning.

INTRODUCTION

The advancements in digital health-care technologies such as artificial intelligence (AI), 3D printing, robots, and nanotechnology have immense potential to shape the future of health care by reducing human errors, improving therapeutic outcomes, and facilitating long-term data monitoring. The integration of AI techniques, including machine and deep learning, has played a significant role in improving medical systems, patient information management, and the treatment of various ailments [1,2]. The use of AI approaches in disease diagnosis has shown promising results, with researchers employing deep learning models to identify early signs of diseases such as skin, liver, heart, and Alzheimer’s [3,4]. AI has also been used to identify high-risk demographics or environmental regions associated with specific illnesses. The incorporation of AI in the existing technical infrastructure of the health-care industry facilitates the quick identification of relevant medical data suitable for patient needs and therapy. Moreover, AI enables the sharing of knowledge across departmental boundaries, breaking down silo thinking, and providing equivalent findings based on a wider population [5,6]. Various AI-based approaches, such as the Boltzmann machine, K nearest neighbor, support vector machine (SVM), decision tree, logistic regression, fuzzy logic, and artificial neural network, have been employed to achieve accurate diagnoses of diseases [7]. Researchers have also utilized a backpropagation neural network to diagnose skin diseases and developed a five-phase machine learning pipeline with multiple sublevels for each stage to restore data patterns and improve decision methods [8]. The effect of digital breast tomosynthesis on time and cancer detection in residents has also been investigated. A self-determining dual analysis test was performed on women aged 50–69, comparing full-field digital mammography with and without a data creation tool [9]. To meet the established criteria, a secure health-care system based on the Internet of things called “body sensor network care” was proposed, utilizing a body sensor network consisting of networks, microcontrollers, cloud databases, and analog-to-digital converters [10]. Personal health-care gadgets that detect and evaluate an individual’s biological signals were also used as a health-care monitoring system for diabetic and hypertension patients at home. This technology can promptly notify medical personnel in real-time in case of emergencies [11]. An administered AI approach was used to conduct a pre-determined TB discovery examination, aimed at improving a knowledgeable, adaptable, and powerful master. The portable stage of the TB antigen-specific antibody identification showed an accuracy of 98.4% in the test [12].

History of AI in health care

In 1950, the emergence of turning tests marked the beginning of AI in health care. The significance of AI in medicine was further emphasized in 1975 with the development of the first research tool on computers in medicine and the first central AIM workshop at the NIH. The application of AI in health care continued to expand with the introduction of deep learning in the 2000s and the development of deep in 2007. In 2010, CAD was first used in endoscopy, followed by the creation of the first Pharmbot in 2015 [13]. The introduction of AI in the medical field was further solidified with the release of the first cloud-based DL application with the Food and Drug Administration (FDA) approval in 2017 [14]. Numerous experiments exploring the use of AI in gastroenterology were conducted between 2018 and 2020, as shown in Fig. 1.

TYPES OF AI ARE USEFUL IN HEALTH CARE

AI is not a singular technology but rather a collection of technologies. These technologies are being rapidly adopted in the health-care
Machine learning and deep learning

Amidst deep learning and emotional networks, machine learning is a mathematical framework that incorporates data models and training models to “learn” from data [16,17]. In a 2018 Deloitte survey of 1,100 US managers whose organizations were already exploring AI, 63% of the surveyed companies were using machine learning in their operations [18]. The most prevalent application of machine learning technology in healthcare is precision medicine, which predicts treatment strategies likely to benefit a patient based on their numerous features and treatment settings [19]. Supervised learning is typically required for most machine learning and precision medicine applications, which involves training a database with known variables, such as disease onset. The neural network, the most advanced type of machine learning accessible since the 1960s, has been well-established in health-care research for several decades [20]. It is employed for isolated applications, such as predicting whether a patient will contract a particular disease, by detecting issues with inputs, outputs, and changeable weights or “features” that link outputs and inputs. While it has been compared to how neurons process impulses, the parallel to brain function is not as robust. One of the most intricate techniques for machine learning is deep learning, which involves neural network models with numerous degrees of variability or complexity that predict outcomes. Modern image processing units and cloud architectures enable thousands of hidden elements to be uncovered in such models. A frequent research program in health care using deep learning involves identifying probable malignant tumors in radiology imaging [21]. Radiomics, which discovers crucial clinical aspects in imaging data beyond the human eye’s purview, is increasingly used in deep learning studies [22]. In oncology-focused image analysis, both radiomics and deep learning are often used together, and their combination offers better diagnostic precision than the previous generation of image analysis technologies known as computer-assisted detection. Deep learning is also gaining popularity for speech recognition and is thus a type of natural language processing (NLP), which is discussed further below. In contrast to previous forms of mathematical analysis, each element in a deep learning model usually has little meaning for the observer. As a result, interpreting the model results may be too difficult or impossible. Recently, machine learning algorithms have been extensively explored in medical and public health diseases [23]. Machine learning algorithms are essential in analyzing multiple and complex variables in clinical datasets [24]. A wide range of machine learning algorithms with different characteristics and design goals are available. Some advanced machine learning algorithms, such as deep neural networks (DNN) and SVM, utilize complex non-linear transformations to achieve superior prediction accuracy [25]. However, it is not possible to determine how these algorithms make predictions due to their complex non-linear transformations. On the other hand, some machine learning algorithms, such as decision trees (DT) and naive Bayesian classifiers (NBC), follow highly interpretable decision processes to achieve predictions [26]. DT and NBC offer inferior prediction accuracy compared to DNN and SVM algorithms due to the absence of complex non-linear transformations [27]. All of these algorithms are useful in predicting accuracy in various infectious diseases, and several prediction models have been developed for identifying new COVID-19-infected patients [28].

NLP

Since the 1950s, AI research has aimed to understand human language. NLP is an example of this research and includes speech recognition, text analysis, translation, and other language-related programs. There are two types of NLP: Mathematical and semantic [15]. Mathematical NLP relies on machine learning, especially in-depth studies of neural networks, which has led to recent improvements in visual accuracy. To use mathematical NLP, a substantial corpus or language course is required for learning. The most common application of NLP in the health-care industry is the generation, comprehension, and classification of published research and clinical literature. NLP systems are capable of conducting AI discussions, creating reports (e.g., based on radiological tests), recording patient contacts, and evaluating randomized clinical notes on patients [29].

Robotic process automation (RPA)

Digital control operations are carried out by these technologies in an ordered manner, similar to how human users would follow a manual or set of instructions. This is achieved through the use of automation, which may be performed by computers running on servers or through RPA rather than robots. Compared to other forms of AI, RPA is less costly, easier to configure, and more transparent in
its actions. RPA utilizes workflow, business rules, and a combination of the “presentation layer” and information system to perform tasks that a less intelligent programmer could accomplish. In the health-care industry, RPA is used to automate routine tasks such as billing, prior authorization, and updating patients’ information. RPA can also be integrated with other technologies such as image recognition to extract information from faxed images and incorporate them into transaction systems. While these technologies were previously distinct, they are increasingly becoming more integrated, with robots gaining powerful AI “brains” and RPA and image recognition merging. The feasibility of integrated solutions will depend on future developments in these technologies [17].

**Explainable and interpretable AI**

Although explainability and interpretability are sometimes used interchangeably, they have distinct meanings [30,31]. While they lack a formal mathematical definition, efforts have been made to differentiate these two concepts [32,33]. Explainability refers to the ability to communicate with humans in understandable terms [34], whereas interpretability concerns the ability to comprehend the reasoning behind a model’s outputs [35]. Explainable AI (XAI) is used in health care to communicate transparent and understandable automated decision-making to impacted patients [36]. XAI is linked to the fundamental logic and functioning of a machine learning system, which may help us understand human illnesses better using simpler models. However, the fundamental logic or supporting mechanisms of an interpretable model may not be understandable to humans [37,38]. Therefore, interpretability does not necessarily imply explainability, and vice versa, when it comes to machine learning systems. It has been suggested that both explainability and interpretability are necessary for a complete understanding of XAI, and a range of models is available [39-41]. Health-care systems also use participatory machine-learning modeling techniques that involve both experts and machine-learning specialists to enhance interpretability and transparency [40,42].

**AI in disease diagnosis**

Infectious diseases are challenging to avoid, and their spread necessitates persistent research and data gathering. Therefore, timely and precise responses to information have a significant impact on people’s lives worldwide, both financially and socially [43]. The advantage of using AI in health care is its potential to revolutionize everything from data collection and processing to programming surgical robots. This section outlines the techniques and applications of AI in health care, as well as disease symptoms, diagnostic hurdles, and a framework for disease detection modeling that employs learning models and AI [44].

**Framework for AI in disease detection modeling**

AI is the ability of a machine to imitate human learning mechanisms, including the recognition of patterns in complex situations and the identification of images. In the health-care industry, AI has transformed how patient care information is generated, assessed, and produced [45]. The fundamental conceptual structure of the system is referred to as systems planning, which consists of framework functions with specific constraints. By understanding its design, the user can become aware of the framework’s limitations and boundaries. Fig. 3 illustrates a visual representation of the disease recognition model using practical machines and deep learning classification techniques. Real-world data is often plagued with errors in the used metrics, which are justifiable but cannot be ignored. Therefore, before processing by computers, real-world information requires upkeep and pre-preparing to enhance accuracy [46]. Information pre-processing involves a sequence of procedures to clean, combine, and correct data from various sources, such as filling in missing values or removing irrelevant characters [47]. The next step is to standardize data using different methods [42], which is crucial for accurate information mining algorithms. Information diminution is then performed to reduce data to more beneficial levels. Subsequently, data gathering and testing information are performed, where the information collected is divided into sections, and indexes are created and tested [48]. Experimental data is frequently copied from a comparable informative index to evaluate the real data sample. The correctness of the framework is verified after pre-handling the model. Analytical displaying methodologies are particularly effective in predicting disease when logical models are used to quantify the likelihood of a given incidence given commitment parameters and the person’s condition [48,49].

**Medical imaging for disease diagnosis**

Clinical imaging refers to a series of procedures that generate images of internal organs. These procedures are employed for therapeutic purposes, such as locating, examining, or studying injuries, fractures, or diseases, to obtain images of the human body [50]. The imaging results from CT scans are a noteworthy example of valuable suggestive imaging that facilitates precise diagnoses, interventions, and evaluations of injuries and dysfunctions that health-care providers routinely encounter [51]. Furthermore, advanced imaging techniques such as X-rays or magnetic resonance imaging are utilized for demanding and intricate tasks, as outlined in Table 1.

**Symptoms of diseases and challenges to diagnostics**

The severity of an illness can range from mild to severe, chronic, or even fatal. The term “fatal” implies that there is a risk of death, while “persistent” and “severe” refer to the duration of the condition. It is also possible for seemingly insignificant symptoms to be warning signs of a more serious illness that requires more intensive treatment. Here are some examples of illnesses, along with their symptoms and warning signs:

- **Heart attack symptoms** include pain, anxiety, tightness, or a sense of width in the center of the chest that lasts for more than a few seconds, as well as pain or anxiety in other areas of the chest, shortness of breath, cold sweat, heaving, or dizziness.
- **Stroke symptoms** include facial listing, arm weakness, difficulty speaking, sudden happiness or equalization, unexpected weakness or lack of feeling, loss of vision, confusion, or excruciating pain.

![Fig. 3: A framework for the disease detection system](image-url)
Reproductive health takes care of symptoms such as blood loss or spotting between periods, tingling, copying, and disturbance at the genital area, pain or unease during sexual activity, real or painful feminine death, extreme pelvic/stomach pain, strange vaginal release, feeling of totality in the reduced mild-region, and regular urinate or renal weight.

Skin condition symptoms include changes in skin moles, persistent flushing and redness of the face and neck, jaundice, skin wounds that do not heal or go away, new skin growths or moles, and thick, red skin with brilliant patches.

Emotional problems include anxiety, melancholy, fatigue, feeling tense, flashbacks and nightmares, skipping daily exercise, having self-destructive thoughts, mental arguments, and having fancies.

Headache symptoms (apart from common tension headaches) include migraines that strike suddenly, "than most visibly dreadful migraine of your life," and headaches accompanied by tremendous vigor, heaviness, nausea, and immobility [52].

**Health-care applications**

The health-care industry has a longstanding history of embracing technological advancements. Currently, machine learning and deep learning, which are subsets of AI, are rapidly gaining traction as essential components of the health-care system, performing various tasks such as health check-ups, patient data management, and account management. The efficient organization and completion of administrative tasks represent one of the most significant challenges facing health-care offices today [53]. The implementation of automation can assist health-care organizations in resolving this issue, allowing physicians to focus on patient care. Table 2 provides an overview of the AI techniques employed in health-care applications [54-56].

**AI TRANSFORMS DRUG DESIGN: REVOLUTIONIZING COMPUTATIONAL APPROACHES**

For an extended period, computational tools have played a crucial role in drug discovery and design, altering the entire drug design process. Nonetheless, traditional computational approaches suffer from a few significant drawbacks, such as reliability, time consumption, few significant drawbacks, such as reliability, time consumption,
and computational costs. These computational barriers in drug design can be overcome using AI, and computational methods can become more prominent in drug discovery [57-59]. Furthermore, the emergence of machine learning (ML) based methods has made it relatively easier to determine the three-dimensional structure of a target protein, a crucial step in the drug discovery process, as new drugs are designed on the tri-ligand binding environment of a protein. AlphaFold is a recently developed AI-based tool from Google’s deep mind (https://github.com/deepmind), which predicts the 3D structure of proteins given their amino acid sequences. AlphaFold, a deep learning model, was trained on structural data from the Protein Data Bank to predict the 3D structures of proteins [60,61]. The prediction process involves two steps: First, the amino acid sequence of the protein is transformed into a distance and torsion angle matrix using Convolutional neural networks. Then, a gradient optimization approach is utilized to convert these two matrices into the tertiary structure of the protein. Similarly, Torrisi et al. have created a DL-based program that uses the amino acid sequence of a protein as input to produce the three-dimensional structure of the protein. To determine the three-dimensional form of a particular protein, the recurrent geometric network model (https://github.com/aqlaboratory/rgn) employs a single neural network to calculate bond angles and angles of spin of chemical bonds joining distinct amino acids. Another drug design has furthermore recently found support from AI [62,63]. For instance, molaical (https://molaical.github.io/), a program developed by Bai et al. in 2020, may build three-dimensional pharmaceuticals for three-dimensional protein pockets. Two factors work together to create 3D medicines in molaical for de novo drug design, the first component employs DL and genetic algorithms trained on medications authorized by the US FDA, whereas the second component mixes molecular docking and DL models trained on the ZINC database [64]. Similar to this Popova et al. 2018 developed release, a deep reinforcement learning-based system for de novo drug creation (https://github.com/isayev/release) by combining the two DNNs, referred to as generative and predictive, release is able to deliver the necessary results. The generative model creates novel compounds, whereas the predictive model forecasts the attributes of the molecule. In addition, AI has recently been applied to improve the method of synthesis planning, which is used to find the best strategy to synthesize a certain molecule [65]. DT-based software called Chematica is a computer program that creates new ways to make molecules. It does this by using decision trees. Aizynthfinder is another computer program that does similar work. It helps chemists find new ways to make molecules. Aizynthfinder uses a neural network and a method called Monte Carlo tree search. To make new ways to make molecules, Aizynthfinder combines the results of three different neural networks with Monte Carlo tree search. Another tool that may develop innovative chemical synthesis routes utilizing a set of chemical rules produced by ML models in ICSYNTH (https://www.deepmatter.io/products/icsynth/) [66]. Various text mining-based techniques have been created, which can help the conventional drug discovery process. NLP techniques are used in text mining to convert unstructured texts from various databases and works of literature into structured data that can then be properly evaluated to produce fresh insight. NLP is a subfield of AI that uses AI-based techniques to let computers process and interpret human languages such as voice and text. A number of text mining-based tools have been created using these AI-driven methodologies [67]. For example, Albalawi et al. 2019 developed a tool called DT-APRON. This tool integrates NLP and topic modeling to predict pharmacological side effects and drug indications [68]. Similar to this, disgenet (https://disgenet.org/) is a word mining-driven database with a wealth of data on the links between genes and diseases and variations and diseases. Dignet data may be used to examine a variety of biological processes, including drug responses, disease-related molecular pathways, and medication impact on targets. Another text mining-driven database that has a wealth of data on protein-protein interactions for many animals is STRING (https://string-db.org/). In addition, STITCH (https://stitch-embl.de/) is a text mining-driven database that has details on how proteins interact with other chemicals and tiny molecules. Drug-target associations and drug-binding affinities may both be determined using information from STITCH [13].

**DISCUSSION AND FUTURE DIRECTIONS**

The selected papers were carefully assessed, considering both their strengths and weaknesses. We aimed to identify potential areas for future research based on the recommendations for Clinical Research Support. Our findings were categorized under relevant topics that address similar or interconnected issues. This approach helps to consolidate the results and make them more accessible for further analysis or comparison.

**Advancements and explicity**

Recent research has focused on developing specialized algorithms for disease identification. However, certain algorithms have received more attention than others. Future investigations should explore the potential benefits of merging multiple existing algorithms to improve diagnostic outcomes [69]. We strongly advocate for more research on deep learning for disease diagnosis, which can accelerate the processing of large medical datasets and improve diagnostic accuracy. Nonetheless, one major technical limitation of deep learning systems is their lack of interpretability, making it difficult for humans to understand the reasoning behind AI-generated outcomes [70]. To address this issue, future studies should focus on increasing the interpretability and explainability of AI-generated findings. An open and trustworthy prediction-making process can facilitate a reliable partnership between AI and medical experts [71]. Thus, we propose RPI: Conducting further studies on AI applications for improving diagnostic outcomes, while ensuring that the outcomes are understandable and explainable and that the process is open and trustworthy [72].

**Corroboration and portability**

In recent years, AI algorithms supporting diagnosis have been developed, with a focus on textual input from a single dataset. While studies have demonstrated positive outcomes, it is important to note that the effectiveness of these algorithms may be limited to specific applications and may not be generalizable to other areas [74]. AI is also being used in COVID-19 detection and treatment of various medical imaging modalities, such as X-ray, computed tomography, and ultrasound (US), which have played a significant role in mitigating the COVID-19 outbreak through the application of AI techniques. These advances have proven instrumental in facilitating early diagnosis and detection [75-77]. Therefore, further investigation is necessary to evaluate their efficacy in diverse patient populations. This may be done by employing heterogeneous and bigger datasets (i.e., with N>1,000 samples) using a variety of formats, including currently underutilized X-ray pictures and USs [78]. Furthermore, to improve the reliability of the results, it is recommended to use a larger dataset that is divided using cross-validation to simulate external validity. The findings should also be applied to various clinical applications and illnesses, including different types of cancers [79-82]. Moreover, it is essential to contemplate why disease diagnoses performed in clinical settings have not been extensively integrated with scientific evidence. The durability of AI strategies in practical settings is still uncertain, and it will significantly impact the future of AI in disease diagnosis. Hence, we propose the following statement:

RPI: We suggest further investigation on how AI in diagnostics might be applied in real-world settings and validated using bigger datasets with improved validity. In addition, we recommend testing AI for illness diagnosis in a real-world setting to determine its applicability [70,83].
Integration and collaboration
The diagnosis of various diseases is a highly individualized procedure that depends on the clinicians' particular experience and varies depending on the clinician's outcomes emotions and mental state. It is also a cognitively demanding activity. Medical professionals are supported by AI when it is used in the diagnosis process, perhaps producing better outcomes [84,85]. Instead of focusing on how AI may be incorporated into the already-existing technical infrastructure, present research on AI in illness diagnostics has only focused on technical implementations [86,87]. Recent advances in AI may provide adequate findings for illness diagnosis; however, it is yet unclear how data is presented to medical professionals. Diagnostics still require human and AI cooperation. This necessitates the increased study of integration techniques, particularly the creation of user-friendly interfaces for various devices [88,89]. To improve patient outcomes, researchers and health-care professionals should collaborate to create AI. By creating a system that might aid in the complete diagnostic process rather than only concentrating on detecting specific ailments, scientific initiatives may move even further [90]. In addition, we stated before that cooperation between humans and AI can provide better outcomes. Further research has to pay more attention to the collaborative features that occur when humans and AI work together in the diagnostic process, but there are not many real-world instances of this yet. It is possible that virtual human-AI teams do better than individuals working alone [91]. This leads us to our last suggestion.

RP3: We suggest further investigation into how AI may be included in the current technical infrastructure to aid in the diagnostic procedure utilizing appropriate interfaces operating on various devices. Researchers also need to look at whether medical teams or lone experts can diagnose illnesses more effectively than virtual teams made up of humans and AI [92].

Strengths and Limitations
To help with the diagnostic process utilizing appropriate interfaces operating on many devices, we suggest more studies on how AI may be incorporated into the current technical infrastructure [93,94]. Researchers also need to investigate if medical teams or lone experts do better at illness diagnosis than virtual teams made up of humans and AI. There are, however, certain restrictions on this study. First, we only looked for, gathered, and assessed SRS that was published in English or Chinese during a certain calendar year (2020). As a result, we could have overlooked studies that were published in other languages and were unable to evaluate historical changes in the methodological quality of SRS. The results are limited to an average estimate of the AI performance of various AI approaches [95].

CONCLUSION
In summary, our analysis revealed numerous systematic reviews that employed AI as one of the diagnostic or treatment methodologies for various disorders. Specifically, in the context of digestive system disorders, AI has demonstrated high sensitivity for detecting certain conditions. However, there is a need to enhance the overall methodological rigor of systematic reviews on AI technologies in disease diagnosis and treatment. Notably, this involves addressing issues such as publication bias and assessing the scientific quality of the included studies. Improved data quality from robust primary research could facilitate the practical application of AI in clinical settings.

CONSENT TO PARTICIPATE
Not Applicable.

CONSENT FOR PUBLICATION
Not Applicable.

AUTHOR CONTRIBUTION
D.K., and P.K. conducted the literature search, extracted and organized data, and wrote the main manuscript text. M.I.A., and S.S. drafted the paper, organizing references, critically revising the article, and editing for the English language. D.K., M.I.A., and S.S. created the tables and figures. All authors reviewed the manuscript.

CONFLICT OF INTEREST
Not Applicable.

FUNDING
Not Applicable.

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