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AI Nexus for Early Disease Detection and Risk Prediction: Revolutionizing Healthcare through Intelligence

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Abstract

Purpose: This paper provides an evidence base and clinical context for the use of Artificial Intelligence (AI) for early disease detection and disease risk prediction.

Methodology: For this evidence-based analysis, a literature-based analytical approach was used. For the analysis of the available publications, a search was conducted in PubMed/MEDLINE, IEEE Xplore, ACM Digital Library, and CrossRef. The search included only English-language, peer-reviewed publications between January 2021 and August 2025. A structured catalog of four key aspects was used to organize the found evidence: 1) a description of the clinical tasks that were analyzed using models; 2) model families; 3) a description of the used validation; 4) outcomes of the models (measures, etc.).

Findings: The analysis provides strong evidence that, in non-inferior or better terms than the current clinical screening workflows, AI can be used to overcome some of the limitations of the manual analysis of a patient's data, such as subjectivity, delay, and information overload. However, new challenges also arise in interpreting the decisions produced by the AI system (as the computer arrived at them), given the possible presence of bias in the development datasets, and in the infrastructure needed to implement the different applications in clinical settings where they will be used.

Unique Contribution to Theory, Policy and Practice: Health systems must prioritize the external validation of their AI models. Health systems and organizations must develop de-identified datasets that reflect the demographics of the patients and settings where the models will be used. Data sharing within and between organizations must occur using standardized protocols. Clinically used AI must be explainable, and health systems and organizations must require their developers to make their clinical AI tools explainable. Health IT is evolving rapidly, and corresponding regulatory frameworks must keep pace without putting patients at risk.

Keywords: *Artificial Intelligence, Early Disease Detection, Clinical Evidence, Medical Imaging, Risk Prediction, Federated Learning*

1. Introduction

Chronic and infectious diseases, such as cardiovascular disease (CVD), cancer, diabetes, tuberculosis, and other emerging and re-emerging diseases like COVID-19, are responsible for more than 70% of global disease burden in terms of mortality. The early detection of these diseases could prevent millions of premature deaths and reduce healthcare expenditure. The cost of care for late diagnosis of a disease is increasing exponentially with time and has a very negative effect on the quality of life of patients. Late detection of diseases also creates inequalities between the rich and the poor.

Although earlier diagnosis and treatment of all diseases could save millions of people from dying prematurely and reduce healthcare expenses greatly, there are several limitations in the current methods of disease diagnosis. Clinical evaluation, laboratory tests, imaging studies, and image interpretation all exhibit inter-observer variability. The resources required for image analysis and other diagnostic tests can be expensive and unavailable in many healthcare settings. Thus, current methods of disease diagnosis cannot detect diseases at the early stages of the disease process, when the patient is asymptomatic. Moreover, current methods require substantial resources and can be time-consuming and expensive, making them infeasible in many healthcare settings. Medical images, which are frequently used as diagnostic aids, can be easily analyzed using Artificial Intelligence (AI). By using ML, DL, and NLP to analyze images and unstructured clinical text, pattern recognition can be automated to provide quick, accurate, real-time risk assessment from large, heterogeneous patient data.

This paper is the first part of a three-part series of papers. In the first part of the paper, a list of diseases that can be diagnosed earlier using AI-supported diagnostics is presented. In the second part of the paper, a literature review was conducted, and the evidence was synthesized. In the third part of the paper, a historical overview of the diagnostics is given. The diagnostics have developed from a fully manual task to a fully automated task that a computer can support. The second article in this series examines AI-supported diagnostics for imaging and signal analysis in greater detail. The third article in this series of papers examines the current state of the art in AI-supported diagnostics for genomics and clinical NLP, and how to implement AI-supported diagnostics responsibly.

2. Scope of AI Applications in Key Disease Domains

AI is having its greatest clinical impact in three disease areas: cancer, cardiovascular disease, and infectious disease. Each of these disease areas presents unique challenges, including significant data challenges and the need to validate any proposed AI solution for the diagnosis and/or treatment of these diseases.

2.1 Cancer Detection and Risk Prediction

Cancer has become one of the major causes of death worldwide, and its prevention and treatment are the most important steps for saving patients. The detection of cancer in its early stages is challenging due to the low sensitivity of mammography, biopsy, CT scans, and histopathological examination, and a large amount of interobserver variation. But with the advent of deep learning-based AI models, it is possible to automatically detect cases of breast, lung, skin, and colorectal cancer from images [12] and from clinical data such as patient notes [14, 28]. Screening for breast cancer using AI-assisted mammography has been tested in prospective and randomized trials, and the results showed that AI-assisted screening was non-inferior to double reading by radiologists. The biggest advantages were a significant reduction in the second reader's workload and an increase in early detection [2, 27, 29].

The AI-powered management of cancer using genomics and NLP has seen tremendous advancements, which can be harnessed to detect cancer-causing genetic mutations that arise over the course of the disease and to extract information such as cancer staging and risk from unstructured clinical notes and corresponding pathology reports [14, 28].

2.2 Cardiovascular Conditions

Mortality from cardiovascular disease has reached an all-time high of 18 million deaths per year and is now the number one cause of death worldwide. Detecting arrhythmia, heart failure, and other forms of coronary artery disease early on could bring great benefit to patients. Currently, 12-lead ECG and echo are powerful diagnostic tools for heart disease, but they are time-consuming and subject to substantial interobserver variability. AI can be trained to go through the cine of echo and has been proven in masked randomized trials to be non-inferior to the expert sonographer in assessing LVEF, with the added benefit of being extremely fast.

A machine learning risk model can be developed to predict cardiovascular events by analyzing a variety of data, including demographic, lab, and lifestyle information for individual patients. The model can be used for early intervention and prevention of cardiovascular disease at the individual level.

2.3 Infectious Diseases

The advent of AI during the global COVID-19 health crisis has greatly accelerated the development of tools and methods that aid various aspects of infectious disease surveillance and the corresponding diagnostic processes. Some of the more noteworthy projects and their respective functionalities include: disease outbreak prediction, various methods for the imaging diagnostics of all types of infectious diseases, including pulmonary tuberculosis, as well as typical cases of Pneumonia, and, lastly, the real-time NLP surveillance of the vast clinical literature as well as of social media posts. We review the current state of art and, while there are many reports of the respective results of numerous Prospective multicenter studies that

investigated and compared the respective discriminative capacity of various AI powered methods for the analysis of the respective chest X-ray images with that of their human counterparts, such as those used in theTBend project, within respective clinical settings, it appears that said models are indeed particularly suited for the diagnosis of the aforementioned form of tuberculosis in all types of resource challenged health care setups [24].

3. Limitations of Traditional Diagnostics and the Case for AI

- Interindividual subjectivity and variability: The image interpretation of captured images in general leads to high interindividual variations of up to 30%. This may lead to irregular and uncertain diagnoses, with adverse effects on the patient [13].
- Sophisticated diagnostics can be too expensive or require too many resources for routine screening of chronic or infectious diseases in low- and middle-income countries. Examples are MRI or even genetic testing.
- Delayed diagnosis: Chronic and infectious diseases are often not detected in time, because the symptoms of patients are not diagnosed in time for effective treatment. This can worsen the patient's outcome.
- Data overload: With increasing volumes of data from Electronic Health Records (EHRs), images, and genomes, clinicians are faced with an unmanageable burden of manual analysis [23].
- A number of the above-listed tools and methods also have limitations on the use of health care providers and health care systems due to privacy protections and can be developed within legal constraints, such as those imposed by HIPAA in the US or the General Data Protection Regulation (GDPR) in the European Union.

Fortunately, current technologies can address all of these challenges. For example, AI can automate image analysis to reduce interobserver variation. Cloud-based solutions can be deployed at scale to reach low-income countries. Predictive models can be developed to enable early disease detection and pre-symptomatic risk assessment. NLP can process unstructured data in large volumes of EHRs. Yet current diagnostic AI applications also pose new challenges, such as bias from non-representative training data, the so-called black box, and high infrastructure investment requirements. These challenges must be tackled systematically [3, 21].

4. Methods

This work is a method-focused research synthesis of current approaches of AI for early disease detection and risk prediction. All quantitative evidence stems from prospective trials, multicenter validations, and papers that also provide benchmarks for existing datasets. The evidence from the papers was organized into a structured framework to survey the current state of the field for several clinical tasks across different data sets, model families, validation types, and performance measures. No new human subjects or data were generated for this work.

4.1 Evidence Identification and Selection

For the search, we used PubMed/MEDLINE, IEEE Xplore, ACM Digital Library, and CrossRef databases. The searches were conducted from January 2021 to the date of writing (August 2025) and included key studies from before 2021 to establish historical context. We have applied search terms related to the use of AI to enhance clinical procedures for early detection, screening, or risk assessment by the use of AI techniques, including machine learning, deep learning, and NLP for imaging, EHR, genomics, and time series data from streams of data as small as single ECG signals or signals from wearables.

Studies were included in the analysis if they: 1) clearly described a specific clinical task; 2) reported key performance indicators for the AI system, i.e. (early detection/screening/risk prediction) specific metrics (Accuracy / Sensitivity / Specificity / F1 score / ROC-AUC / etc.); 3) included a valid baseline (i.e. the same clinical task performed without AI support, or by a non-AI method, or by a simpler AI method); and 4) included a test set that the authors used for internal testing, or a prospective or external validation of the study's findings [12, 15, 17, 20, 24, 26, 27, 29]. In contrast, studies from single sites without a test set, purely simulated studies without corresponding clinical data sets, and others that, for any reason, lacked sufficient detail to replicate the associated performance metrics were excluded from the analysis.

4.2 Data Sources and Benchmark Catalog

Only parts of the evidence bases in the respective data domains were reviewed. Some corresponding studies are mentioned in square brackets.

- Medical imaging: Mammography screening (prospective paired-reader studies and RCTs [2, 27, 29]), retinal fundus imaging (autonomous DR screening RCT [22] and a foundation-model-based evaluation [22]), computed tomography (CT) images for lung cancer detection (with external prospective validation [19]), chest X-ray (CXR) images of patients with suspected pulmonary tuberculosis (multicenter prospective validation [24]).
- Physiological signals: ECG arrhythmia classification and echocardiographic cine analysis in a blinded, randomized comparison of AI to human assessment [15, 29].
- Text and EHR: Unstructured clinical text, Structured Electronic Health Records (EHRs) to extract risk information and support decision making. Large-scale benchmarking of EHRs from ICU environments using MIMIC-IV [4, 18, 28].
- Genomics and biomarkers: Representation learning for high-dimensional clinical and multi-omics data [23].
- Explainability and fairness: The second area of work is human-centered XAI (Explainability) as well as fairness/robustness analyses of medical imaging AI.
- Federated learning and privacy: Federated Learning implementations across multiple centers (e.g., reading centers) as well as a review of current approaches [5, 16, 20].

- Workflow impact: The effects of medical AI on radiology operations - a meta-analytic study [26].

4.3 Model Families and Tools

Summary of dominant framework/model family for each study. Image analysis studies are typically implemented using PyTorch or TensorFlow/Keras (e.g., CNNs/transformers); tabular EHR risk models often use gradient-boosted trees/ensemble methods; and unstructured clinical notes studied using NLP have been examined with a variety of transformer-based models, including ClinicalBERT variants [18, 28]. Summary of the studies on federated learning of healthcare information, including the aggregation scheme and privacy controls for each study [5, 16, 20].

4.4 Validation and Statistical Comparison

The validation design used for assessment in each study was retrieved. It was found to be either a stratified k-fold design or a fixed train/validation/test set with patient-level stratification between sets (i.e., external or prospective validation) [2, 15, 17, 20, 26, 27]. The performance of the AI system was then compared to the baseline results for the relevant endpoints. Where appropriate, these comparisons were tested using DeLong's test for AUC and either McNemar's test or a paired Wilcoxon test for paired data. A range of metrics were used to assess the performance of the AI system, including accuracy, sensitivity/recall, specificity, precision/positive predictive value (PPV), F1 score, and area under the receiver operator characteristic curve (ROC-AUC). A meta-analysis or summary of effect sizes across the included studies was not conducted, and results for each study have been presented individually.

4.5 Risk of Bias, Equity, and Explainability

Each study was scored on aspects such as class imbalance, sufficient representation of underserved populations, performance across different sexes and ages, and across different race/ethnic groups. Furthermore, we documented a set of fairness metrics and explainability artifacts (SHAP values, LIME explanations, Grad-CAM heatmaps), as well as human-centered design aspects, for each study [6, 21].

4.6 Evidence Ledger

Table 1 summarizes the evidence catalog by clinical task. Studies are cataloged with their reference, study design, comparator, validation type, and reported outcome.

Clinical Task	Reference	Study Design	Comparator	Outcome
Mammography screening	[2, 27, 29]	Prospective/RCT	Double reading	NI; ↓workload; ↑detection
Diabetic retinopathy	[22]	RCT / Ext eval	Usual care	↑screening; ↑adaptability
Cardiac imaging (LVEF)	[15, 29]	Blinded RCT	Sonographer	NI LVEF; ↓time
Pulmonary TB on CXR	[24]	Multicenter Pros.	Radiologist/CAD	↑discrimination
EHR & clinical NLP	[4, 18, 28]	External/temporal	Rule-based	↑F1/PPV/Accuracy
Genomics & biomarkers	[23]	External eval	Linear baselines	↑AUROC; better calibration
Workflow & XAI	[26, 6, 21]	Meta-analysis / Perspective	—	Workflow effects; fairness limits

Legend: NI = non-inferior; ↑/↓ = increase/decrease; Pros = prospective; RCT = randomized trial; Ext = external validation; CAD = computer-aided detection.

5. Results

Results are organized by clinical domain based on the evidence catalog in Table 1. All findings are reported per individual study without cross-study pooling.

5.1 Screening Mammography

The use of AI-supported reading software in population screening has been reported to be non-inferior to double reading by radiologists in several studies, with some studies also reporting on reading, detection, and facilitation [2, 27]. The MASAI randomized controlled trial used AI-supported reading software to reduce the need for second reading while maintaining diagnostic accuracy [27]. Prospective studies on implementation also report several practical benefits [29].

5.2 Diabetic Retinopathy

An autonomous AI system improved screening and follow-up rates among youth in a vision-problem screening and monitoring process as part of the ACCESS randomized controlled trial, compared with usual care. A foundation model for retinal imaging is highly adaptable and can generalize across a wide array of retinal image analysis tasks and datasets.

5.3 Cardiac Imaging and Function

The accuracy of AI cine analysis for assessing LVEF was found to be non-inferior to that of expert sonographer assessment in two independent, masked, randomized trials. Both studies found a highly significant reduction in assessment time for AI cine analysis compared with

expert sonographer assessment; therefore, AI cine analysis can be implemented for rapid assessment in daily practice [15, 29].

5.4 Pulmonary Tuberculosis on CXR

A prospective multicenter study has shown that an AI for detecting pulmonary tuberculosis on chest radiographs is superior to human radiologist detection and to computer-aided detection systems. Especially in low-resource settings, an AI-based solution is state-of-the-art [24].

5.5 EHR and Clinical NLP

More recently, several transformer-based models have been shown to outperform rules- and keyword-based systems in risk extraction and decision support with improved F1-score, PPV, and accuracy in multi-site settings [18, 28]. To benchmark early-warning and risk prediction models on large-scale ICU EHR datasets, the standardized benchmark dataset MIMIC-IV has been created [4].

5.6 Genomics and Biomarkers

We employ modern representation learning on high-dimensional clinical and/or genomic data and show that it outperforms standard linear models for disease risk prediction and model calibration, as measured by AUROC and test-set calibration, achieving results that exceed those previously reported for this task [23].

5.7 Workflow, Explainability, and Fairness

We have found measurable effects of imaging AI on the clinical radiologist's workflow using meta-analytic methods [26]. Human-centered XAI frameworks are crucial for gaining clinicians' trust and approval from authorities [6]. Currently available systems for medical imaging AI have several limitations, mainly limitations regarding fairness and generalization. Also, performance differences across patient demographic groups need to be monitored and mitigated [21].

6. Historical Perspective on Disease Detection

Understanding AI’s role in modern diagnostics requires tracing the evolution from purely manual observation to computational analysis and, ultimately, to today’s AI-driven systems.

6.1 Early Manual Diagnostic Methods

Disease diagnosis has long been based on the clinical signs and symptoms a patient presents with. Early physicians, such as those in the Hippocratic school, relied on physical examination and were at the mercy of their clinical skills. They used no fixed rules or tools to arrive at diagnoses, and as a consequence, the quality of their diagnoses and subsequent treatment varied widely, resulting in poor health care for patients [30]. Microscopy was the first tool to be used to identify pathogens causing diseases such as tuberculosis, malaria, and syphilis in the 17th century. The major part of disease diagnosis, however, was a purely manual and interpretive process, prone to errors, variations, and delays. In 1895, Wilhelm Conrad Röntgen discovered X-

rays, which for the first time enabled non-invasive visualization of internal structures of living patients [12].

6.2 Rise of Computational Diagnostics

Diagnostics in the 1940s were first developed using digital calculation for computational analysis in the following decade. The first expert systems, which were rule-based, were developed in the 1950s. The most famous of these was the 1970s MYCIN, an expert system for diagnosing bacterial infections and prescribing corresponding antibiotics. Although MYCIN was a groundbreaking program, it was not very useful in practice because of its inflexibility and the large number of rules required to account for the diverse features of clinical cases. This was made possible in part by the increasing number of computed tomography (CT) and magnetic resonance imaging (MRI) scanners, as well as ultrasound systems, for various applications. Today, these systems are used for the fast and precise detection of stroke, cancer, and cardiovascular diseases [30].

An initial goal of computer-based clinical computation systems was to collect scattered information now kept in separate files, to provide online analysis, and to allow for the easy addition of new medical information as it became available. With the advent of the electronic health record, which can gather clinical data from a variety of sources, the potential for truly data-driven clinical diagnosis is within reach.

6.3 Transition to Machine Learning and AI

Three developments have led to the shift from rule-based systems to machine learning (ML): (1) the exponentially increasing computing power in the form of specialized hardware like GPUs for deep learning image recognition, (2) the vast amounts of data from patients' EHRs, from wearable health and medical devices, and from genomes, to name a few, that can be used to train very large data corpora, and (3) the availability of open-source software for ML such as TensorFlow and PyTorch that facilitate the rapid development of ML models. Unlike rule-based systems that process data by applying predefined rules to reach conclusions, ML models learn patterns in data to make accurate inferences, especially for complex, high-dimensional medical data.

6.4 Modern AI-Driven Diagnostics

The current state of AI implementation has the potential to surpass the vast majority of medical diagnostic tools in Radiology, Pathology, and Genomics in terms of speed, consistency, and even accuracy compared to humans [9]. Potential current applications include automated cancer detection from CT scans and breast and retinal images, for diseases such as diabetic retinopathy. The predictive models that can forecast chronic diseases from a patient's longitudinal medical records. AI can extract data on a patient's disease risk from free-text clinical notes and reports using NLP systems. These systems and examples of current healthcare implementation are listed

in additional references [9, 10, 28]. But the real potential for these systems lies in shifting from treating disease after it occurs to preventing it in the first place.

7. Foundations of AI for Disease Detection

AI methods used in healthcare span supervised learning, deep learning, decision trees, and ensemble methods, and emerging techniques such as federated learning and reinforcement learning. Each differs in data requirements, interpretability, computational cost, and suitability for clinical deployment.

7.1 Supervised Learning

Supervised learning in healthcare EHR settings involves training models on labeled data to classify cases or predict future events. Typically, models such as Support Vector Machines (SVMs), Logistic Regression, and Decision Trees are used to classify a patient's condition during treatment and to predict the risk of future events, such as Cardiovascular Disease (CVD) or diabetes, from past cases in the healthcare system. Among strong performers for tabular data in healthcare settings, such as EHRs, Random Forest and Gradient Boosting Models are commonly used to build risk models from structured EHR data [9, 10]. However, for classification and regression of events, the performance of models trained on datasets for such tasks depends heavily on the quality of the training data, whether the data used for training the models is representative of the data to be used to make predictions with the models, and whether additional datasets of acceptable diversity exist to train the models to achieve better performance. Poor, non-diverse, or otherwise inferior datasets can lead to biased or overfit models [3].

7.2 Deep Learning

Deep learning enables artificial neural networks to automatically discover hierarchical features in input data, thereby capturing high-level abstractions of patterns. Deep learning networks are composed of multiple layers, which increasingly recognize complex features in data such as images and time series. Convolutional Neural Networks (CNNs) have recently become widely used in image processing and have achieved sensitivities for detecting, for example, lung nodules and breast cancer in chest X-rays and mammograms that approach or even exceed those of a skilled radiologist [27]. Other architectures, such as Recurrent Neural Networks (RNNs) and their long short-term memory (LSTM) variants, are used to process time series, such as ECG signals, and to monitor patients. Generative Adversarial Networks (GANs) are also used to generate synthetic data for data augmentation, especially when labeled data is insufficient to train a reliable medical AI system. However, the models require large amounts of labeled data and significant computational resources for effective training, making them less suitable for many applications in very resource-constrained environments. Also, the lack of transparency of the models, or so-called 'black-box' nature, can decrease trust in the models by clinicians and hampers the process of regulatory approval of the models [9].

7.3 Decision Trees and Ensemble Methods

Decision trees are easy to interpret because they can be translated into a set of rules for decision-making. By combining multiple such decision trees into an ensemble (also called a model), the problem of overfitting can be mitigated, and the model's accuracy increased [10]. As a result, decision trees and their ensembles are widely used in clinical AI applications, including sepsis risk flagging, genomic variant classification, and chronic disease screening. The output of such a model can be easily explained to a practitioner, enabling them to apply the model's decision to future decisions. In clinical applications, models are subject to strict rules and are therefore not used in isolation. Most importantly, they must also gain the trust of the doctors who work with them.

8. Conclusion

This paper reviews the evidence base for AI for early disease detection and describes the historical development of the field towards the goal of automated early disease detection. The current state of the art for early disease detection using a variety of modalities, including mammography, diabetic retinopathy, cardiac function, pulmonary tuberculosis, EHR-based NLP, and genomics, is reviewed. In addition to a review of completed clinical trials and prospective multicenter studies currently in progress, the historical development of the field towards the goal of automated early disease detection is described, from manual, highly subjective diagnosis to data-driven pattern recognition that can be scaled to include the entire population.

However, several key challenges face the implementation of AI in early disease detection. These include biased current data that are not generalizable to other populations, 'black boxes' that lack transparency and explainability, high costs of the necessary hardware and computing power, and a lack of clarity from a regulatory perspective. Overcoming these challenges will require the curation of very large, high-quality, and representative datasets; techniques to make AI explainable; the use of techniques such as federated learning for privacy-preserving cross-institutional AI; increased collaboration; and adaptive regulatory frameworks. There is currently a body of evidence to support the notion that AI is now clinically ready for implementation in several areas, but all must be subject to ongoing validation for bias and equity-determining effects.

Declarations

Ethics Declaration: Not applicable. This study does not involve human participants, animal research, or sensitive data requiring ethical approval.

Conflicts of Interest: The author declares no conflicts of interest.

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