Review

A Systematic Review of Machine Learning Applications in Infectious Disease Prediction, Diagnosis, and Outbreak Forecasting

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Article

A Systematic Review of Machine Learning Applications in Infectious Disease Prediction, Diagnosis, and Outbreak Forecasting

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Abstract

Infectious diseases pose a significant global health burden, contributing to millions of deaths annually despite advancements in sanitation and healthcare access. This review systematically examines the role of machine learning in infectious disease prediction, diagnosis, and outbreak forecasting in the United States. We first categorize existing studies according to the type of disease and the ML methodology, highlighting key findings and emerging trends. We then examine the integration of hybrid and deep learning models, the application of natural language processing (NLP) in public health monitoring, and the use of generative models for medical image enhancement. In addition, we discuss the applications of machine learning in five diseases, including coronavirus disease 2019 (COVID-19), influenza (flu), human immunodeficiency virus (HIV), tuberculosis, and hepatitis, focusing on its role in diagnosis, outbreak prediction, and early detection. Our findings suggest that while machine learning has significantly improved disease detection and prediction, challenges remain in model generalizability, data quality, and interpretability.

Keywords: infectious disease; machine learning; outbreak prediction; disease diagnosis; systematic review

1. Introduction

Infectious diseases are considered a concerning global health burden for the millions of deaths out of it [1]. Despite improved sanitation and access to health care, recent global changes have greatly increased the risk and consequence of the outbreak of infectious diseases [2]. Infectious disease also remains a continued challenge on public health resources and individual health in the United States, where millions of people are affected by endemic diseases such as chronic hepatitis, HIV, and other sexually transmitted infections [3]. The increasing burden of infectious diseases highlights the importance of having predictive solutions, whether for estimating outbreak trends or diagnosing diseases [4].

Such solutions enable public health institutions to respond quickly and accurately at an early stage, reducing the risk and consequences of disease progression. This makes machine learning techniques a highly favorable tool in this field, with many studies and experiments demonstrating strong predictive performance [5]. In addition to traditional models, researchers have explored advanced techniques and hybrid approaches to enhance performance. Mishra et al. concluded that ensemble methods have significant potential to improve diagnostic accuracy in the early stages of disease detection [6]. To further enhance performance, Farooq et al. fine-tuned a pre-trained ResNet-50 model on chest X-ray images for early disease detection [7]. Islam et al. integrated a CNN-LSTM model, combining CNN with LSTM to enable automated disease diagnosis from X-ray images [8].

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Generative models have also shown promise in this domain. Ranolo et al. proposed a deep convolutional neural network integrated with an autoencoder (AE), referred to as CAE-COVIDX, for disease detection [9]. Similiarly, Mehta et al. utilized a conditional generative adversarial network (cGAN) combined with a fine-tuned deep transfer learning model to classify chest X-ray images, improving diagnostic accuracy [10]. Kalane et al. implemented a universal network (U-Net) architecture to develop an automated detection system for disease identification using insights from Computer Tomography (CT) images [11]. In parallel, large language models have also been applied to disease diagnosis and outbreak prediction. Agarwal et al. utilized a hierarchical multi-modal approach based on bidirectional encoder representations from transformers (BERT) to precisely predict patient outcomes [12].

Recognizing the significant potential of machine learning in infectious disease prediction, this review systematically explores the development and recent advancements in machine learning applications, with a particular focus on major infectious diseases prevalent in the United States. The Review design section outlines the search strategy and selection criteria employed to identify relevant studies. The Results section presents a detailed overview of machine learning applications across specific infectious diseases. Finally, the strengths and limitations of this review are discussed, followed by a concluding section that summarizes key findings and implications for future research.

2. Review Design

The primary objective of this review is to summarize and present the current development of machine learning applications in infectious diseases within the United States. All literature included was rigorously selected based on a predefined and systematic search strategy.

2.1. Search Strategy

We searched for the keywords "infectious disease" and "machine learning" together. The infectious diseases considered were COVID-19, Influenza (Flu), HIV/AIDS, syphilis, gonorrhea, chlamydia, sexually transmitted infections (STIs), hepatitis (A, B, C), and tuberculosis. These diseases were selected based on three factors: their widespread prevalence and impact (e.g., COVID-19 and influenza), their public health significance, and their continuing burden and relevance in the United States [13].

For the machine learning search, we used terms such as statistical learning, machine learning, deep learning, decision algorithms, clinical decision-making, artificial intelligence, neural networks, support vector machines, supervised learning, unsupervised learning, ensemble learning, Bayesian networks, random forests, natural language processing, clinical prediction, prognostic models, diagnostic analysis, and time-series analysis.

2.2. Search Selection

The topics of the selected articles include diagnosis, outbreak prediction, mortality and transmission forecasting and treatment. Several selection criteria were applied: (1) machine learning must be the primary technique used in the study; (2) only articles written in English were included; (3) studies involving humans were selected, while animal studies were excluded; (4) studies focusing on infectious diseases' genes, genomes, sequencing, or other non-machine learning analysis methods were excluded; (5) only studies with full-text availability were considered; and (6) studies related to public opinion or sentiment analysis were not included.

3. Results

In recent years, machine learning and deep learning techniques have gained significant traction in the medical domain, offering powerful tools for diagnosis, prognosis, and treatment optimization across various health conditions. Among the numerous applications, their role in understanding and managing infectious diseases has become particularly prominent. In this section, we highlight five carefully selected infectious diseases that illustrate the breadth and impact of these technologies in modern healthcare.

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3.1. Coronavirus Disease 2019 (COVID-19)

Coronavirus Disease 2019 (COVID-19) is a respiratory illness caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). [14]. It spreads primarily through direct human contact or respiratory droplets released when an infected person coughs or sneezes [15]. Approximately 14.9 million people lost their lives, directly or indirectly, due to the COVID-19 pandemic in 2020 and 2021 [16]. There have been approximately 103.4 million confirmed cases of COVID-19 and 1.2 million related deaths in the United States [17].

Forecasting the COVID-19 outbreak has become an increasingly critical challenge. Susceptible-Exposed-Infectious-Recovered (SEIR), Susceptible-Infectious-Recovered (SIR) models, agent-based models, curve-fitting models and traditional machine learning methods were widely applied [18]. Moulaei et al. predicted mortality in hospitalized patients with COVID-19 using machine learning methods, including Java 8 (J48) Decision Tree, EXtreme Gradient Boosting (XGBoost), Reinforcement Learning (RL), k-Nearest Neighbors (kNN), Random forest and Naive Bayes [19]. Arpaci et al. investigated various models, including BayesNet, Logistic, Instance-Based k-Nearest Neighbors (IBk), Classification Rule (CR), Partial Decision Tree (PART) and J48, for diagnosing COVID-19. Among these, CR demonstrated the best performance, achieving an accuracy of 84.21% [20].

Multilayer perceptron (MLP) and adaptive neuro-fuzzy inference system (ANFIS) playing a vital role. Ardabili et al. found MLP and ANFIS demonstrated strong generalization capabilities for long-term forecasting in their analysis of COVID-19 outbreak prediction [21]. The multilayered perceptron-imperialist competitive algorithm (MLP-ICA) and ANFIS are also applied to predict the number of infected individuals and the mortality rate in Hungary [22].

Various deep learning and hybrid models have also been utilized in this field. Dairi et al. used various machine learning and hybrid models, including LSTM-CNN (Long Short-Term Memory - Convolutional Neural Network) and GAN-GRU (Generative Adversarial Network - Gated Recurrent Unit), to forecast COVID-19 transmission, finding that LSTM-CNN achieved the best performance with a 3.718% error rate [23].

The application of machine learning (ML) and deep learning (DL) in COVID-19 forecasting has significantly evolved, demonstrating the potential of AI-driven models in epidemic prediction. Table 1 summarizes selected research papers in this domain. Early studies focused on statistical models such as SEIR and SIR, often integrated with ML techniques for enhanced accuracy. As the pandemic progressed, more advanced approaches, including hybrid deep learning models (LSTM-CNN, GAN-GRU), were introduced to improve predictive performance and adaptability to dynamic outbreak conditions.

Table 1. Summary of Selected Papers on COVID-19 Forecasting

Paper	Year	ML	DL	Algorithm	Complexity	Scalability
[18]	2020	✓	✗	SEIR, SIR, ABM, CF	Low–Med	High
[21]	2020	✓	✗	MLP, ANFIS	Medium	Medium
[22]	2020	✓	✗	MLP-ICA, ANFIS	Med–High	Medium
[20]	2021	✓	✗	BayesNet, IBk, J48	Low–Med	Medium
[23]	2021	✓	✓	LSTM-CNN, GAN-GRU	High	High
[19]	2022	✓	✗	J48, XGBoost, kNN, RF	Medium	Med–High

3.2. Influenza (Flu)

Influenza (flu) is a contagious respiratory illness resulting from influenza virus infection. There are four types of influenza viruses: A, B, C, and D. Influenza A is the only type that can lead to severe outbreaks [24]. From 2010 to 2024, the annual impact of the flu in the U.S. ranged from 9.3 million to 41 million illnesses, 120,000 to 710,000 hospital admissions, and 6,300 to 52,000 deaths [25].

Thus, forecasting flu outbreaks is crucial, and machine learning has been widely applied in recent studies. Alessa et al. compared FastText (FT) with six traditional machine learning algorithms,

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achieving an F-measure of 89.9%. They also combined FT with linear regression, resulting in a 96. 29% correlation to predict outbreaks [26]. Khan et al. used a feedforward propagation neural network (MSDII-FFNN) to predict outbreaks with 90% precision [27]. Zhang et al. first applied LSTM to predict influenza outbreaks, finding that a 5-layer LSTM model with regularization achieved the lowest root mean squared error (RMSE) of 0.002 [28].

Twitter data are widely utilized for predicting outbreaks using machine learning methods. Allen et al. applied geographic information science (GIS) and support vector machine (SVM) with Twitter data to track influenza outbreaks, finding a statistically significant correlation with national, regional, and local flu reports [29]. Amin et al. also use Twitter data to identify seasonal outbreaks early and found that Random Forest outperformed other methods [30].

Hemagglutinin Type 1 and Neuraminidase Type 1 (H1N1) is a subtype of the influenza virus that caused a global pandemic in 2009 [31]. Machine learning also plays a role in supporting H1N1 vaccine prevention. Inampudi et al. determined the probability that individuals would receive the H1N1 and seasonal flu vaccines, finding that the SVM model achieved 83. 97% precision for the prediction of H1N1, while the Artificial Neural Network (ANN) model reached 86. 10% precision for the prediction of seasonal flu [32]. Ayachit et al. used ensemble learning to predict the likelihood of vaccination for H1N1 and seasonal flu, with CatBoost achieving the best performance and an accuracy of 0.8617 [33].

Influenza forecasting is crucial for public health, with research evolving from traditional statistical models and basic machine learning (ML) techniques like SVM, LR, and Decision Trees to more advanced methods. Table 2 highlights studies applying ML and deep learning (DL) techniques, including LSTM networks, to improve flu prediction accuracy. Hybrid models combining ML and DL have also been explored. These methods, leveraging real-time data from sources like social media and health records, enhance forecasting precision. Models like Random Forest and CatBoost aid in feature selection and early outbreak detection, while LSTM and ANNs capture long-term flu transmission patterns.

Table 2. Summary of Selected Papers on Influenza Forecasting

Paper	Year	ML	DL	Algorithm	Complexity	Scalability
[29]	2016	✓	✗	SVM, GIS	Medium	Medium
[28]	2017	✗	✓	LSTM	High	Medium
[26]	2019	✓	✗	FastText, LR, SVM	Medium	Medium
[33]	2020	✓	✗	CatBoost, Ensemble	Medium	High
[27]	2020	✗	✓	FFNN	Medium	Medium
[30]	2021	✓	✗	RF, SVM, NB	Medium	High
[32]	2021	✓	✓	SVM, ANN	Medium	Medium

3.3. Human Immunodeficiency Virus (HIV) / Immunodeficiency Syndrome (AIDS)

Human immunodeficiency virus (HIV) weakens the body's immune system by targeting essential defense cells. When the infection progresses to its most severe stage, it leads to acquired immunodeficiency syndrome (AIDS) [34]. HIV continues to be a critical global health concern, resulting in an estimated 42.3 million deaths worldwide [35]. More than 38,000 individuals were diagnosed with HIV in the United States [36].

Machine learning is crucial in HIV prevention and behavior prediction. Wang et al. used SVM and Random Forest to predict high-risk HIV behaviors, with cost-sensitive SVM achieving an AUC of 0.86 for multiple sexual partners and Random Forest excelling in predicting sexual activity [37]. Pan et al. used Random Forest to identify key predictors of HIV testing uptake, highlighting condomless sex, self-efficacy, condom attitudes, and depression as significant factors [38]. Nisa et al. utilized the SMOTE technique to address classification bias and applied Random Forest, achieving an 82% accuracy in predicting the probability of future HIV acquisition in high-risk groups [39].

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Men who have sex with men (MSM) are disproportionately affected by HIV, accounting for 68% of new HIV diagnoses in the United States [40]. Researchers have also explored the application of machine learning methods in this field. Bao et al. used Gradient Boosting Machine (GBM) to achieve the highest Area Under the Curve (AUC) of 76.3% for predicting HIV in Australian men who have sex with men (MSM), finding that past syphilis infection was the top predictor, contributing 16.7% [41]. Chingombe et al. employed traditional machine learning algorithms, Bagging Classifier and RNNs, to predict HIV status among MSM and found that RNNs performed best, achieving an accuracy of 0.98 [42].

Deep learning has shown superior performance compared to traditional methods and machine learning techniques in both diagnosis and prediction. Turbe et al. used SVM and CNN to analyze field-based rapid diagnostic test (RDT) images for HIV, achieving 98.9% accuracy, significantly outperforming traditional visual interpretation methods [43]. Wang et al. found that LSTM outperformed Autoregressive Integrated Moving Average (ARIMA), Generalized Regression Neural Network (GRNN), and Exponential Smoothing (ES) models in forecasting HIV incidence, achieving the lowest Mean Squared Error (MSE) [44].

HIV prevention and prediction has been a critical area of research, with studies evolving from traditional statistical methods to more advanced machine learning (ML) and deep learning (DL) techniques. Table 3 highlights research applying both ML and DL methods, such as Random Forest (RF), Support Vector Machines (SVM), and Long Short-Term Memory (LSTM) networks, to enhance prediction accuracy. Hybrid models combining ML and DL approaches have been explored to improve predictive performance. These models, leveraging various data sources, such as electronic health records and social media, offer better precision in predicting HIV. Techniques like Gradient Boosting Machine (GBM) and Random Forest excel in feature selection, while deep learning models such as LSTM and Convolutional Neural Networks (CNN) capture complex patterns in HIV transmission.

Table 3. Summary of Selected Papers on HIV Prevention and Prediction

Paper	Year	ML	DL	Algorithm	Complexity	Scalability
[38]	2017	✓	✗	RF	Low–Med	Medium
[44]	2019	✗	✓	LSTM, ARIMA, GRNN	High	Medium
[43]	2021	✓	✓	SVM, CNN	High	High
[37]	2021	✓	✗	SVM, RF	Medium	Medium
[41]	2021	✓	✗	GBM	Medium	Medium
[42]	2022	✓	✓	Bagging, RNN	Medium	Medium
[39]	2023	✓	✗	RF, SMOTE	Medium	Medium

3.4. Tuberculosis

It has been known that early diagnosis of tuberculosis is favorable for disease management, and it is beneficial for both the patient and the public health to reduce the further transmission of the disease in society [45]. However, most of the conventional early detection techniques such as X-ray, conventional light microscopy, and other similar traditional techniques turn out to be very time-consuming and complex to operate [46]. There have been many immunoassay techniques developed to rapid diagnosis of TB, but they are financially costly and require more skilled staff to be involved [46]. Therefore, it will be very helpful if there can be reliable cost-effective techniques to diagnose TB at an early stage, and the ML-based techniques turn out to be promising toward this goal [47].

The early diagonis was firstly benefieted from the introduction of Artificial neural network(ANN) in 1990, which showed good performance in recognizing the structural patterns in the X-ray images [48]. In 1998, the first automated neural methods were developed to identify TB bacilli in sputum smears stained with auramine, realizing 93.5% sensitivity in diagnosing TB without too much involvement of the stuff. In 1999, the first ANN based early diagonisis method was developed, using general

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regression neural network (GRNN) to diagonize patients with active pulmonary TB [49]. This model used 21 different parameters to form input patterns and achieved a sensitivity of 100% (95% CI, 91 to 100%), significantly outperforming the clinical evaluation of physicians with respect to the precision of diagnosis [49]. Some other machine learning methods such as decision trees and random forest were also found very useful in predicting the diagnosis results [50].

However, there was a challenge of obtaining reliable and accurate prediction from these models, which led the researchers more to the deep learning and AI advancement that with better ability to understand images data [46]. Benefit from the introduction of genetic algorithm and fuzzy logic and single hidden layer feed-forward neural networks, the accuracy of the diagnosis of tuberculosis was further improved since 2010 [51]. Hooda et al. proposed a CNN architecture with 7 convolutional layers and 3 fully connected layers, reaching a validation accuracy of 82.09% with Adam optimizer [52]. In 2018, Kant and Srivastava presented another new neural network based TB diagnosis method which achieved a recall of 83.78%, providing great potential of evolution into an efficient and reliable TB early detection tool with its high sensitivity [53]. Hrizi et al. a comparisons study evaluating the diagonisis ability of different machine learning models such as KNN, CART, RF, NB, LDA and SVM, concluding SVM the best performing model with mean accuracy of 84% [54]. Hansun et al. further confirmed the high potential of ML and DL methods, with ML models showing a higher average precision (93.1 71%) and sensitivity (93.2 55%) and DL models showed greater average AUC(92.12%) and specificity(91.54%) [55].

Overall, tuberculosis diagnosis has greatly benefited from the evolution of machine learning and deep learning techniques. Early approaches relied on artificial neural networks and decision trees, while more recent models utilize convolutional neural networks (CNNs), genetic algorithms, and support vector machines (SVMs) to improve diagnostic accuracy and scalability. Comparative studies confirm that ML and DL models can achieve high sensitivity and specificity, making them promising tools for early and cost-effective TB detection in both clinical and remote settings.

Table 4. Summary of Selected Papers on Tuberculosis Diagnosis

Paper	Year	ML	DL	Algorithm	Complexity	Scalability
[48]	1990	✓	✗	ANN	Low	Low
[50]	1997	✓	✗	DT, RF	Low–Med	Medium
[49]	1999	✓	✗	GRNN	Low	Low
[51]	2011	✓	✗	Feed-Forward ANN	Medium	Medium
[52]	2017	✗	✓	CNN	High	High
[53]	2018	✗	✓	Deep NN	High	High
[54]	2022	✓	✗	KNN, RF, NB, LDA, SVM	Medium	Medium

3.5. Hepatitis

Hepatitis is a transmissible viral disease that has affected 350 million people in the world with only around 10% of them diagnosed [56]. Hepatitis virus A, B, C, D, and E are the five primary varities of the disease.The disease can be caused various factors such as excessive alcohol use, reactions to drugs, and viral or bacterial infections, and the chance of early detection greatly enhance the likelihood of a good recovery [57].

Different kinds of Artificial Intelligence techniques such as predictive analytics, Natural Language Processing and Machine Learning are found effective in the Hepatitis early detection, and ML is the most emphasized one for detection for its ease of use and excellent performance [58]. Bharathi et al. compared several classification techniques such as SVM, DT, LR and RF on detecting Hepatitis and without feature selection, concluding RF is the best one with an accuracy of 89% [59]. Yaganoglu employed machine learning methods for Hepatitis virus detection, achieving an accuracy of 99.31% by adding some new features and eliminating class imbalance with SMOTE [60]. Harabor et al. evaluated

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four machine learning models support vector machine (SVM), random forest (RF), naive Bayes, and K nearest neighbors for hepatitis screening based on a structured survery data from Romania, concluding the KNN the best model with excellent accuracy of 98.1% [61].

Deep learning models are also found very useful in Hepatitis early detection based on the works of past researchers. Wang et al. proposed a rapid screening method for hepatitis based on Long short-term memory(LSTM) neural network, realizing excellent results with an accuracy of 97.32% and AUC of 0.995 [62]. In 2022, Chen et al. proposed a Multilayer Perceptron (MLP)-based model that outperformed traditional machine learning techniques, such as LightGBM and XGBoost, in diagnosing Hepatitis [63]. Besides, deep learning models are also found to be effective in predicting the infection scale.Guo et al. adopted and compared ARIMA, SVM, and LSTM to predict case number and incidence of Hepatitis with the real data rom 2005 to 2017 in China, finding out the LSTM was the best-performing model [64].

In the case of hepatitis, both traditional ML methods and deep learning models have demonstrated strong predictive capabilities. Techniques such as Random Forest, SVM, and LSTM have been used successfully for early detection and outbreak forecasting. Recent advancements in deep learning, particularly with LSTM and multilayer perceptrons (MLP), have shown superior performance in diagnosis. These findings support the continued integration of AI-based tools into hepatitis screening programs, especially in resource-constrained healthcare environments.

Table 5. Summary of Selected Papers on Hepatitis Early Detection

Paper	Year	ML	DL	Algorithm	Complexity	Scalability
[62]	2020	✗	✓	LSTM	High	High
[64]	2020	✓	✓	ARIMA, SVM, LSTM	Medium	High
[60]	2022	✓	✗	SVM, SMOTE	Medium	Medium
[63]	2022	✗	✓	MLP	Medium	High
[61]	2023	✓	✗	SVM, RF, Naive Bayes, KNN	Medium	High
[58]	2024	✓	✗	Predictive Analytics, NLP, ML	High	High
[59]	2024	✓	✗	SVM, DT, LR, RF	Medium	Medium

4. Strength and Limitations

This review focuses on the application of machine learning in predicting infectious diseases specifically within the United States, providing targeted insights relevant to domestic healthcare settings. By organizing findings across five high-impact diseases—COVID-19, influenza, HIV, tuberculosis, and hepatitis—this review presents a clear picture of the developments and advancements in machine learning techniques for infectious disease estimation from a disease-specific perspective. Supported by a well-designed search strategy and a solid systematic review process, this work serves as a practical guideline for researchers, highlighting recent innovations such as hybrid models, deep learning, generative frameworks, and language models, which help to capture emerging directions in this rapidly evolving field.

Due to resource limitations, this review only includes publications written in English, which may have led to the exclusion of valuable studies published in other languages. In addition, while this review emphasizes a disease-specific approach to presenting and discussing findings, it does not provide a statistical comparison of model performance across studies from a model-specific perspective. Addressing this aspect in future work may offer additional insights into the comparative effectiveness of different machine learning techniques in infectious disease research.

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5. Discussion

Infectious diseases continue to pose a significant global health threat, with rising risks due to recent environmental and social changes. Traditional prediction and diagnostic methods have been increasingly supplemented by machine learning (ML) and deep learning (DL) techniques, which have shown strong potential in improving accuracy and early disease detection. This paper reviews the evolution of ML and DL approaches, including Random Forest, XGBoost, SVM, CNN, LSTM, and generative models like GANs and VAEs, emphasizing their contributions to predicting and diagnosing major infectious diseases such as HIV and chronic hepatitis. The trend in research is shifting towards hybrid models and advanced methods, which leverage complex data such as medical images and health records to provide more precise predictions.

The contribution of this review lies in its comprehensive examination of these technologies, identifying the strengths and limitations of different models, while exploring the potential of generative models and natural language processing for disease diagnosis and outbreak prediction. Future studies can build on this work by exploring the development of hybrid models that integrate multiple approaches, as well as leveraging emerging AI tools, such as ChatGPT, to further improve diagnostic speed and accuracy. The scalability of these models also suggests they can be adapted to both resource-rich and resource-limited settings, offering significant promise for improving public health responses worldwide.

6. Conclusions

Machine learning has become a valuable tool in the fight against infectious diseases, helping improve how we track, diagnose, and predict outbreaks. From COVID-19 and influenza to HIV, tuberculosis, and hepatitis, a wide range of ML techniques—such as ensemble models, deep learning, and natural language processing—have shown strong potential in making public health responses faster and more accurate. This review also highlights the growing interest in hybrid approaches and the increasing exploration of advanced models like transformers and generative networks.

That said, several important challenges remain. Many models still struggle with generalizability, interpretability, and practical deployment in real-world healthcare settings. Issues such as data imbalance, limited transparency in model decisions, and data privacy concerns must be addressed before broader adoption can take place. In addition, future research should expand beyond English-language literature and pay closer attention to infectious diseases that are more prevalent or impactful outside the United States. With continued progress, machine learning holds strong promise for making healthcare systems smarter, more proactive, and better equipped to handle future outbreaks.

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