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Adaptive Hybrid Models for Disease Outbreak Prediction Using Clinical and Genomic Data: A Systematic Review of Artificial Intelligence-Driven Early Warning Systems

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Abstract
Artificial intelligence (AI) is now a crucial breakthrough technology for disease outbreak prediction that can process complex healthcare data in real-time and help take proactive public health action. The aim of this systematic review is to give a critical overview of the recent scientific progress in the field of adaptive hybrid AI models for intelligent disease surveillance and AI-enabled disease outbreak early warning systems, such as clinical, genomic, environmental and epidemiological data. Following the PRISMA 2020 guidelines, a comprehensive literature search has been performed in all major scientific databases with the final selection of 67 relevant peer-reviewed articles published in 2021-2026. The review analyzes the recent progress made in Machine Learning (ML), Deep Learning (DL), ensemble learning, transformer models, Graph Neural Networks (GNN), explainable AI, Federated Learning (FL), and multimodal data fusion for disease outbreak prediction. Moreover, it assesses the adaptive learning approach, clinical-genomic data integration, and AI-powered early warning system design with identification of research gaps and challenges. While previous review studies tend to analyze individual AI approaches or specific applications for disease surveillance, the present review offers a new perspective on this problem by introducing a novel taxonomy of AI-based disease outbreak prediction systems, an adaptive hybrid framework, and a research gap matrix for multimodal healthcare data and adaptive AI.

Keywords: Adaptive Hybrid Models; Disease Outbreak Prediction; Artificial Intelligence; Clinical and Genomic Data; Early Warning Systems

1. Introduction

Due to the increased occurrence of infectious disease outbreaks such as COVID-19, flu, Ebola, dengue, and others, the demand for accurate and reliable disease surveillance systems that help in making informed public health decisions has been realized. Traditional epidemiological surveillance approaches mainly use retrospective analyses of clinical records and laboratory tests. Therefore, they usually provide delayed identification of disease outbreaks and limited prediction abilities. The advancements made in artificial intelligence (AI), big data analysis, and genomic sequencing have helped transform disease surveillance by providing the ability to monitor diseases in real time, predict outbreaks, and plan for interventions based on evidence (Sharma et al., 2026; Kraemer et al., 2025). The recent developments in machine learning, deep learning, transformers, graph neural networks, and explainable AI have enabled healthcare systems to analyze complex datasets and detect disease outbreaks early (Miranda et al., 2025; Rudwan et al., 2026). On the other hand, the combination of next-generation sequencing, electronic health records, mobility data, and environmental data has led to precision public health through better predictions of the dynamics of disease spread and pathogen evolution. Nevertheless, the studies done so far have been quite scattered, as there is a lot of focus on AI algorithms individually, data types separately, or particular diseases alone without a hybrid learning approach.

This review aims to fill this knowledge gap by presenting an updated synthesis of recent evidence regarding the adaptive hybrid AI techniques for prediction of disease outbreaks using multimodal healthcare data. In particular, the systematic review covers AI approaches, methods of fusing genomic with clinical data, adaptive

learning approaches, and intelligent early warning systems architecture, as well as the challenges observed in these areas and the future directions. The strength of this review is the integration of these technologies in a holistic approach, including adaptive hybrid learning, multimodal fusion of clinical-genomic information, AI-based intelligent early warning systems architecture and adaptive learning. In addition to reviewing the literature, a new taxonomy, adaptive hybrid framework and research gap matrix are developed which offer a more holistic view than other literature reviews focusing on distinct parts of AI applications or surveillance itself.

2. Review Methodology

2.1 Review Design and Methodological Framework

The current study was carried out using a Systematic Literature Review (SLR) to conduct a critical evaluation of the recent advancements in adaptive hybrid artificial intelligence (AI) for predicting the disease outbreak based on clinical and genomic data. The SLR has been conducted following the guidelines for Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) to assure that the method of research would be clear and reproducible as well as comprehensive enough. PRISMA is one of the most popular frameworks for carrying out the systematic reviews used in the health care, biomedical informatics, and AI-related research due to the minimal selection bias and structure that helps identify, screen, and synthesize the appropriate literature (El Morr et al., 2024; Miranda et al., 2025). The research will include peer-reviewed publications released within the time span from January 2021 to June 2026 since this is a period of fast development of disease surveillance through AI after the COVID-19 pandemic. The period was characterized by numerous advancements in machine learning, deep learning, genomic surveillance, explainable AI, federated learning, and real-time epidemiological intelligence that made the disease prediction and outbreak (Sharma et al., 2026; Kraemer et al., 2025; Rudwan et al., 2026).

The methodological process involved six stages: (i) formulation of objectives and research questions, (ii) systematic literature search, (iii) study selection and eligibility criteria, (iv) quality appraisal, (v) data extraction, and (vi) qualitative evidence synthesis. Instead of carrying out a statistical meta-analysis, this review uses a narrative and comparative synthesis, which is justified by the presence of significant diversity in the datasets, algorithms, evaluation metrics, disease areas and healthcare environments presented in the existing literature (Babanejaddehaki et al., 2025; Towfek and Elkanzi, 2024). The review specifically focuses on how adaptive hybrid AI models utilize diverse healthcare data such as EHRs, lab results, genomic sequencing, environmental factors, climatic data, mobility data, and epidemiological surveillance data for improving the accuracy of outbreak prediction. In addition, the review evaluates new techniques such as transformers, graph neural network, continual learning, transfer learning, federated learning, explainable AI, and foundation models in the design of future disease surveillance systems (Yang et al., 2026; Kaur and Butt, 2025). To maintain consistency of methodology, all duplicate articles, incomplete methodological conference abstracts, editorials, opinion papers, and studies with insufficient validation were removed from the revie. The resulting dataset included high-quality papers that together provided an exhaustive analysis of AI-based disease outbreak prediction and early warning systems.

2.2 Literature Search Strategy

A detailed and thorough literature search was performed for finding studies related to artificial intelligence applications in disease outbreak prediction, adaptive hybrid learning, integration of clinical-genomic data, and AI-based early warning systems. Various international scientific databases were searched in order to ensure a maximum scope of literature and minimize the bias towards publication. Databases used for literature search included Scopus, Web of Science, PubMed, IEEE Xplore, ScienceDirect, SpringerLink, ACM Digital Library, Wiley Online Library, MDPI, Frontiers, Nature Portfolio, and Google Scholar. Overall, these databases cover research from various fields including medicine, public health, computer science, artificial intelligence, bioinformatics, and epidemiology. Grey literature and preprints were considered only if there was some valuable methodology in the paper; however, preference was given to peer-reviewed journal publications. Search strategy was based on the combination of controlled vocabulary and free-text keywords. Keywords were chosen on the basis of preliminary literature review and consultations of recent reviews on AI-based disease surveillance (El Morr et al., 2024; Miranda et al., 2025; Sharma et al., 2026). Boolean operators (AND, OR, and NOT) were used to make the search more precise and find studies covering multiple aspects of AI-driven outbreak prediction.

Table 1. Literature Search Strategy

Component	**Description**
Publication	January 2021 – June 2026

period	
Language	English
Document type	Peer-reviewed journal articles and high-quality review papers
Research domains	Artificial Intelligence, Healthcare, Epidemiology, Bioinformatics, Public Health
Databases	Scopus, PubMed, Web of Science, IEEE Xplore, ScienceDirect, SpringerLink, ACM Digital Library, Wiley, Nature, Frontiers, Google Scholar

The principal search keywords included:

- Artificial Intelligence
- Machine Learning
- Deep Learning
- Disease Outbreak Prediction
- Infectious Disease Surveillance
- Early Warning System
- Epidemic Prediction
- Pandemic Forecasting
- Clinical Data
- Genomic Data
- Multi-omics
- Disease Surveillance
- Hybrid AI Models
- Explainable AI
- Federated Learning
- Transfer Learning
- Continual Learning
- Transformer Models
- Graph Neural Networks
- Epidemiological Modeling
- Precision Public Health

The primary Boolean search string used during database searching was:

("Artificial Intelligence" OR "Machine Learning" OR "Deep Learning" OR "Hybrid AI") AND ("Disease Outbreak Prediction" OR "Infectious Disease Surveillance" OR "Early Warning System") AND ("Clinical Data" OR "Genomic Data" OR "Electronic Health Records") AND ("Epidemiology" OR "Public Health" OR "Disease Surveillance")

Additional database-specific search strings were developed by incorporating controlled indexing terms such as MeSH, subject headings, and database-specific descriptors to improve retrieval efficiency. The initial search identified 642 records across all databases. Following duplicate removal, 518unique publications remained for title and abstract screening. In light of the application of predefined criteria, 167 articles underwent full-text screening. Sixty-seven articles met all inclusion criteria and thus became the body of evidence used in this systematic review. They constitute the latest advancements in AI-powered disease surveillance, adaptive hybrid learning, predictive genomics, explainable AI, epidemiological forecasting, and clinical decision support system that have been published within the scope of this review. There is an observable acceleration in AI-driven studies aimed at predicting outbreaks since the emergence of the COVID-19 pandemic, with a focus on multimodal healthcare data integration, real-time disease surveillance, federated learning, and trustworthy AI. All these studies form the basis for next-generation adaptive hybrid disease outbreak prediction systems.

2.3 Inclusion and Exclusion Criteria

In order to guarantee that the systematic review is credible, relevant, and scientifically sound, specific inclusion and exclusion criteria were set beforehand prior to the commencement of the search process. This was done using the PRISMA 2020 recommendations and was intended to include quality research articles on the topic of artificial intelligence usage in predicting and detecting disease outbreaks, epidemiological surveillance, clinical decision support and genomics. The inclusion criteria allowed including only those studies that were recent and

reflected the latest technologies in terms of machine learning, deep learning, explainable AI, federated learning, and adaptive hybrid learning. Those peer-reviewed journal articles published from 2021 to 2026 in English language, dealing with AI-based disease surveillance, outbreak prediction, genomic epidemiology, or healthcare analytics were included into the study. Research conducted using clinical data, genomics sequencing data, epidemiological surveillance systems, environmental factors, mobility data, or other health care data sources were considered eligible. Furthermore, studies proposing novel machine learning algorithms, deep learning architectures, hybrid prediction frameworks, explainable AI models, or intelligent early warning systems were prioritized because these directly aligned with the objectives of this review (Sharma et al., 2026; Miranda et al., 2025; Kraemer et al., 2025). Conversely, studies were excluded if they were conference abstracts, editorials, opinion papers, letters, book reviews, or publications lacking sufficient methodological descriptions. Research that is only centered on applications of artificial intelligence other than healthcare, as well as research that lacks any experimentation, testing, and comparative analysis, was also ruled out. Full-text articles as well as articles written in languages other than English were not included in the review.

Table 2. Inclusion and Exclusion Criteria

Criteria	**Inclusion**	**Exclusion**
Publication Period	2021 - 2026	Before 2021
Language	English	Non-English
Publication Type	Peer-reviewed journal articles and systematic reviews	Editorials, conference abstracts, letters, opinions
Research Area	AI, Machine Learning, Disease Surveillance, Epidemiology, Genomics	Unrelated AI domains
Data Sources	Clinical, genomic, environmental, epidemiological, multimodal healthcare data	Studies without healthcare datasets
AI Techniques	ML, DL, Hybrid Models, Explainable AI, Federated Learning	Studies without AI implementation
Methodology	Experimental evaluation with performance metrics	Conceptual papers without validation
Accessibility	Full-text available	Incomplete publications

The inclusion/exclusion criteria were strict, greatly enhancing the consistency of studies selected and reducing the publication bias, but also ensuring only scientifically sound investigations contributed to the evidence synthesis. This method improved the confidence in the review results.

2.4 Study Selection Process

The study selection process followed the four sequential stages recommended in the PRISMA 2020 framework, namely Identification**,** Screening**,** Eligibility, and Final Inclusion. The above procedure guaranteed clarity during the entire process of literature review while limiting any form of bias. The identification process involved extensive searches of the scientific database which resulted in 642 publications. After excluding duplicates in the database through reference management software, only 518 papers remained for the first level of screening. In the second phase, where the title and abstract of each publication was independently evaluated to determine the suitability, publications not related to disease outbreaks prediction, infectious diseases surveillance, applications of artificial intelligence in the medical field or genomic analysis were eliminate. Studies focusing on unrelated biomedical domains, healthcare management without predictive analytics, or purely theoretical AI discussions were also removed. This process reduced the number of potentially relevant articles to 167 full-text publications. Eligibility assessment entailed critical analysis of all full texts against the established inclusion and exclusion criteria. Those that did not present transparency in the methodology, validation datasets, comparative experiments, or evaluation metrics were excluded. The same applied to duplicate data, preliminary findings, and those that had insufficient technical information to maintain consistency in methodological approach. After conducting quality assessment and full text analysis, 67 studies were found eligible and incorporated in the synthesis. These studies collectively represent current developments in adaptive hybrid AI models, disease

surveillance systems, genomic prediction, epidemiological intelligence, explainable artificial intelligence, and intelligent early warning frameworks published between 2021 and 2026.

Table 3. PRISMA Study Selection Summary

PRISMA Stage	Number of Studies
Records identified through database searching	642
Duplicate records removed	124
Records screened	518
Full-text articles assessed	167
Articles excluded after eligibility assessment	100
Final studies included	**67**

The PRISMA workflow demonstrates a systematic and reproducible methodology for identifying relevant literature while ensuring methodological transparency.

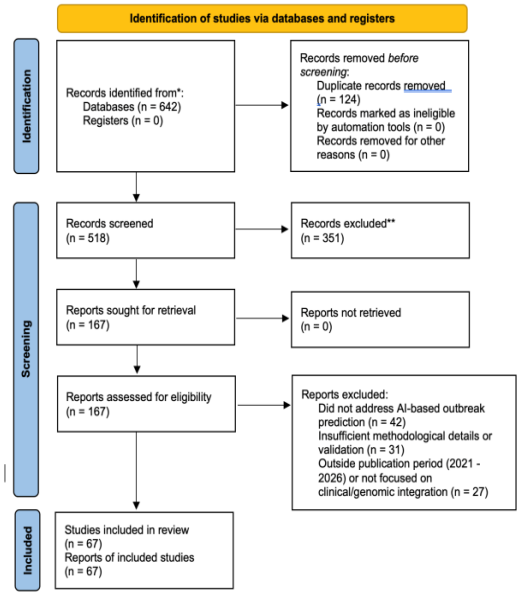

Figure 1. PRISMA 2020 Flow Diagram of the Systematic Literature Review Process

Identification → Screening → Eligibility → Final Inclusion (67 Studies)

Figure 1 shows the study selection process used in this systematic review based on the PRISMA 2020 protocol. A total of 642 citations were obtained from an extensive literature search, out of which 67 citations fulfilled the pre-established inclusion and quality standards and were selected for the review. This clear and formal identification, screening, eligibility and inclusion process reduced selection bias and enhanced methodological rigour of evidence synthesis.

2.5 Quality Assessment of Selected Studies

To assess the quality of the studies, their scientific accuracy, credibility, and rigor were determined through a quality assessment approach. The quality appraisal process was carried out based on PRISMA 2020 guideline and systematic review practice in the field of health informatics. Independent quality assessment was carried out for each of the identified studies in several dimensions such as research aims, dataset used, AI methodology employed, validation procedure, reproducibility, performance assessment, and practicality. It was important to determine whether studies provided clear description of the data sets used, algorithms for AI application, evaluation criteria, baseline comparison, and validation processes (El Morr et al., 2024; Babanejaddehaki et al., 2025; Rudwan et al., 2026). High, moderate, and low quality categories were established depending on

methodological completeness of the studies. The majority of the articles revealed good methodological quality due to the use of reliable data sets, well-designed experiments and thorough performance measurements. Nevertheless, some studies exhibited poor external validation, explainability or ethical and privacy issues discussions.

Table 4. Quality Assessment Criteria

Assessment Criterion	Evaluation Focus
Research objective	Clearly defined study aims
Dataset quality	Availability and diversity of healthcare datasets
AI methodology	Algorithm description and implementation
Validation strategy	Cross-validation, external testing, benchmarking
Performance metrics	Accuracy, Precision, Recall, F1-score, AUC
Explainability	Model interpretability and transparency
Reproducibility	Methodological clarity and implementation details
Practical relevance	Clinical and public health applicability

To ensure a more uniform quality assessment, each study included was assessed on eight criteria presented in Table 2.4: clarity of the research objective, quality of the data, description of the AI methodology, validation strategy, reporting of performance metrics, explainability, reproducibility, and practical relevance. The criteria were evaluated on a scale of 0 (criterion not addressed at all), 1 (criterion partially addressed), and 2 (criterion clearly and adequately addressed) with a maximum possible total quality score of 16 per study. The studies were classified as high quality (13–16), moderate (9 - 12) and low quality (0–8). The scoring model was adopted in the main to facilitate the structured methodological appraisal, but in no sense to suggest that studies with different designs were, themselves, directly equivalent. The validation strategy, transparency of the datasets, reproducibility, and the practical relevance were given special consideration as they directly impact the reliability and transferability of the AI models used for disease surveillance. During full-text eligibility assessment, studies with significant methodological flaws or missing information for meaningful appraisal were excluded. This systematic review allowed for the identification of evidence from relatively well-validated studies and evidence that required more careful interpretation. The quality assessment identified most selected studies to have credible data on AI-based disease surveillance, prediction analytics and adaptive hybrid learning. Current challenges such as incomplete datasets, inadequate multimodality, and real-world application are the barriers to the scaling up of existing outbreak prediction systems.

2.6 Data Extraction and Synthesis Process

After the quality assessment of the studies, information from each study was extracted in a systematic way by means of a consistent data extraction format. Information extracted included among others publication details, domain of the diseases being investigated, geography of the studies, sources of healthcare data, AI algorithms, methods of integration of genomics into AI, methods of validation, evaluation metrics, results, limitations of the study and future research areas. Other information extracted included information on adaptability learning processes, explainable AI implementations, federated learning, multimodal data fusion, and architecture of the early warning systems.

Table 5. Data Extraction Framework

Data Category	Extracted Information
Bibliographic information	Author(s), year, journal
Disease application	COVID-19, Influenza, Tuberculosis, Vector-borne diseases, etc.
Data sources	Clinical, genomic, environmental, epidemiological

AI methods	Machine Learning, Deep Learning, Hybrid Models
Learning strategy	Transfer Learning, Continual Learning, Federated Learning
Validation	Internal, external, cross-validation
Performance metrics	Accuracy, F1-score, AUC, Sensitivity, Specificity
Key findings	Major contributions
Limitations	Research gaps and future work

A qualitative narrative synthesis approach was adopted because of the diversity of AI methodologies, disease types, datasets, and evaluation strategies reported in the selected studies. The results from this paper have been analyzed using the thematic categorization method rather than carrying out the meta-analysis because it is possible to compare different AI methods used, integration of healthcare data, hybrid adaptive learning models, and disease surveillance systems intelligently. These analyses lay the groundwork for the analysis that will be carried out in the next sections on future trends in AI-based disease outbreak prediction.

3. Artificial Intelligence for Disease Outbreak Prediction: Current Landscape

3.1 Evolution of Disease Surveillance Systems

Disease surveillance has evolved from conventional manual reporting systems to intelligent, AI-driven platforms capable of supporting real-time outbreak prediction and public health decision-making. Conventional surveillance was based on hospital records, laboratory diagnosis, physician reporting, and government reporting systems to track the presence of any disease in a given area. Even though the traditional methods were quite effective in terms of registering confirmed cases, these methods had problems with delayed reporting, poor health care information, incomplete geographical coverage, and lack of predictive power that made the detection of outbreaks difficult. The current pandemic showed these deficiencies of traditional methods and increased the popularity of the usage of artificial intelligence, big data, and computational epidemiology in disease surveillance (Sharma et al., 2026; El Morr et al., 2024; Miranda et al., 2025). Disease surveillance could be divided into four generations. The first generation is passive surveillance that is based on the confirmation of cases, and the second generation is active surveillance using laboratory testing, field studies, and monitoring of the community to improve the accuracy of the report. The third generation included EHRs, laboratory information system, and digital reporting tool. Nevertheless, these types of models were largely descriptive as opposed to being predictive. In contrast, fourth-generation models incorporate AI-powered surveillance ecosystems that utilize machine learning, deep learning, graph neural networks, transformers, and explainable AI to analyze clinical, genomic, environmental, demographic, mobility, and social data for learning and prediction of outbreaks (Kraemer et al., 2025; Yang et al., 2026; Rudwan et al., 2026).

Modern developments in genomic surveillance using next-generation sequencing (NGS) technologies have also helped improve the capability of disease intelligence by making it possible to detect early pathogens' mutation, antimicrobial resistance, and variants (Katiyar et al., 2025; Shahin et al., 2026). Equally important, environmental factors, mobility, climate data, and behavioral data have become integral parts of AI-powered surveillance tools used for predicting climate-sensitive and zoonotic diseases (Abi and Adetunji, 2023; Inam, 2025). Real-time epidemic intelligence tools and federated learning have made it possible to keep machine learning models up to date without compromising on the issues of data privacy and collaboration between healthcare institutions (Kaur and Butt, 2025; Lawal et al., 2025). Although challenges of data heterogeneity, interoperability, privacy, and explainability persist, AI-powered surveillance has changed disease surveillance from being a mere reactive reporting process to an adaptive predictive process that can make global public health more prepared (Babanejaddehaki et al., 2025; Akanbi et al., 2026).

Table 6. Evolution of Disease Surveillance Systems

Generation	**Characteristics**	**Primary Data Sources**	**Limitations**	**Representative Technologies**
First Generation (Passive Surveillance)	Manual reporting of confirmed cases	Hospital reports, physician notifications	Delayed reporting, under-reporting	Paper-based surveillance

Second Generation (Active Surveillance)	Targeted investigation and laboratory monitoring	Laboratory tests, field investigations	Resource intensive, limited scalability	Public health surveys
Third Generation (Digital Surveillance)	Electronic collection and sharing of healthcare information	Electronic Health Records, laboratory information systems	Limited predictive capability	EHR platforms, digital reporting systems
Fourth Generation (AI-Driven Intelligent Surveillance)	Predictive analytics, adaptive learning, real-time monitoring	Clinical, genomic, environmental, epidemiological, mobility and multimodal healthcare data	Data interoperability, explainability, privacy and governance challenges	Machine Learning, Deep Learning, Graph Neural Networks, Transformer Models, Explainable AI, Federated Learning

3.2 Healthcare Data Sources for Disease Prediction

The effectiveness of artificial intelligence (AI)-based disease outbreak prediction depends on the quality, diversity, and integration of healthcare data from multiple sources. Contrary to classical models of epidemiology, which mainly depend on historic records of the cases, contemporary AI systems utilize clinical, genetic, environmental, and epidemiological data in order to detect complicated patterns of diseases and increase the accuracy of predictions. Multimodal healthcare data allow for gaining complementary information about patients' condition, pathogens' evolution, environmental risks, and population dynamics and thus help to perform interventions at an appropriate time and implement precision disease surveillance (Sharma et al., 2026; Kraemer et al., 2025; Babanejaddehaki et al., 2025). Clinical data involve electronic health records (EHRs), laboratory reports, medical images, medication, vital signs, and hospital admissions. These datasets allow for identifying the symptoms of the diseases, assessing their severity, stratifying the patients by risk, and planning healthcare resources. AI models analyze temporal clinical indicators in order to enhance diagnostics and predictions of outbreaks, but certain difficulties associated with missing data, interoperability, and privacy protection still persist (Dong et al., 2025; Li et al., 2025; Mairi et al., 2025; Badidi, 2023). Genetic data, gathered by next-generation sequencing (NGS), contain useful information on mutations, antimicrobial resistance, and evolution of pathogens. AI-supported genomic surveillance allows for detecting emerging variants, transmission paths, and vaccine development through analyzing complicated genomic (Al-Amran et al., 2023; Katiyar et al., 2025; Shahin et al., 2026). However, the use of genomics analytics is computationally intensive and requires standard infrastructure for genome sequencing. Environmental and epidemiological factors like climate factors, travel behaviors, demography, vaccination coverage, and surveillance play an important role in disease transmission. AI models can model the non-linear relationship between the environment and the spread of infectious disease effectively to predict climate-sensitive and vector-borne diseases and help identify hotspots. Multi-source healthcare data integration involves using clinical, genomic, environmental, and epidemiological data in adaptive AI models to improve the prediction of diseases (Abi and Adetunji, 2023; Inam, 2025; Egbuna et al., 2025). The use of advanced data fusion techniques allows the system to learn continuously and predicts accurately. However, although there are many benefits of multimodal systems, they have some drawbacks concerning interoperability, heterogeneity of the data, governance, and privacy issues. However, technologies such as federated learning and explainable AI provide promising approaches for disease surveillance (Yang et al., 2026; Kebeba and Agyei, 2026; Kaur and Butt, 2025).

3.3 AI Techniques for Disease Outbreak Prediction

AI has changed disease outbreak forecasting by providing the opportunity to analyze big data to detect transmission dynamics, predict disease outbreaks, and inform decision-making for public health measures. Unlike traditional models that use pre-defined assumptions, AI models continue learning through historical and current data and thus are much flexible when predicting the dynamics of disease transmission (Sharma et al., 2026; Kraemer et al., 2025; Rudwan et al., 2026). Selection of an AI technique is influenced by the nature of data used, computation costs, interpretability, and goals of forecasting, hence, the increasing popularity of hybrid models. Machine Learning (ML) models such as Random Forest (RF), Support Vector Machine (SVM), Decision Tree (DT), Logistic Regression (LR), Gradient Boosting, and XGBoost are commonly used in disease classifications, disease outbreak forecasting, and risk evaluation. Such models provide efficient analysis of the electronic health records, laboratory results, environment factors, and mobility data in order to find high-risk groups and predict disease transmission. However, ML models require extensive feature engineering and may fail with very complex temporal data sets (Towfek and Elkanzi, 2024; Adeoye et al., 2025; Lawal et al., 2025).

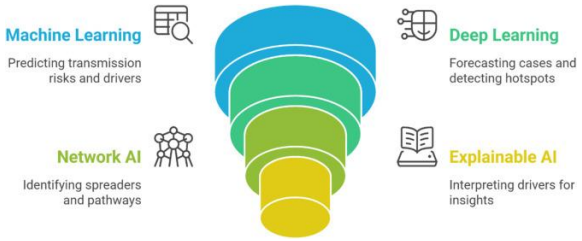

Fig 2. AI approaches for analysing disease

The Deep Learning (DL) approach has advanced prediction further through automatic extraction of complex features from clinical, imaging, genomic, and time series data. CNNs, LSTM, RNNs, GNNs, and Transformers models have proven more effective in modeling disease progression, pathogen evolution, and transmission dynamics (Dong et al., 2025; Yang et al., 2026; Shahin et al., 2026). However, these models need huge data and computing capacity. The Ensemble Learning approach involves use of several machine learning and deep learning models including Random Forest, AdaBoost, XGBoost, and Stacking to achieve better predictive performance and robustness. Hybrid ensemble models overcome the challenge of overfitting and improve prediction performance of diseases such as COVID-19, influenza, tuberculosis, and malaria by combining clinical, genomic, environmental, and epidemiological data (Oluwafemi et al., 2024; Gawande et al., 2025; Akanbi et al., 2026). For better transparency, explainable AI approaches such as SHAP, LIME, attention models, and feature importance methods are used to give explanations of AI outcomes. XAI improves clinicians' trust, helps meet regulatory requirements, and facilitates better decision-making processes, especially in the genomic surveillance and clinical diagnostics domains (Awotunde et al., 2022; Kaur and Butt, 2025; Fahim et al., 2025). In conclusion, an integration of ML, DL, ensemble learning, and XAI provides the foundation of adaptive hybrid AI solutions which are capable of predicting disease outbreaks effectively.

Table 7. Comparative Analysis of AI Techniques for Disease Outbreak Prediction

AI Technique	Representative Algorithms	Primary Applications	Major Advantages	Limitations
Machine Learning	Random Forest, SVM, Decision Tree, Logistic Regression, XGBoost	Disease classification, outbreak prediction, patient risk assessment	High accuracy, interpretable, efficient with structured data	Requires feature engineering, limited temporal modelling
Deep Learning	CNN, RNN, LSTM, GRU, Transformer, Graph Neural Network	Time-series forecasting, genomic analysis, medical imaging, multimodal prediction	Automatic feature extraction, superior performance on complex datasets	High computational cost, large data requirements, limited interpretability
Ensemble Learning	Random Forest, AdaBoost, XGBoost, LightGBM, Stacking	Hybrid prediction, multimodal data integration, early warning systems	Improved robustness, reduced overfitting, enhanced predictive accuracy	Increased computational complexity and implementation difficulty
Explainable AI (XAI)	SHAP, LIME, Attention Maps, Feature Importance, Counterfactual Explanations	Clinical decision support, trustworthy AI, model interpretation	Improves transparency, clinician trust, regulatory acceptance	Additional computational overhead and implementation complexity

Such integrated approaches combine high predictive accuracy with transparency and scalability, providing a robust foundation for intelligent early warning systems capable of supporting real-time public health surveillance and precision healthcare decision-making.

3.4 Clinical - Genomic Data Integration Strategies

The integration of clinical and genomic data is the key approach that will enhance the accuracy, flexibility, and efficiency of AI-based disease outbreak prediction. The clinical data that include the EHRs, laboratory results, medical imaging, demographics, and history offer useful details about the onset and progress of a disease. On the other hand, the genomic data obtained through NGS shed light on how pathogens evolve, mutate, become resistant to antibiotics and how they are transmitted. The two data sources individually are informative but together they allow the development of disease dynamics understanding by the AI model (Al-Amran et al., 2023; Katiyar et al., 2025; Nwokedi et al., 2026).

Current research trends have seen an increase in the use of multimodal artificial intelligence approaches that integrate clinical findings and genomic monitoring for improved outbreak prediction and precision public health care (Raza et al., 2026; Shahin et al., 2026). Machine learning and deep learning models can extract complementary attributes from varied data sources, thus increasing prediction accuracy and facilitating early identification of infectious diseases. Models such as transformers, graph neural networks, and multimodal learning models have been found to be very effective in combining structured clinical notes and unstructured genomic sequences while considering the interactions between patients, pathogens, and the environment (Yang et al., 2026; Kraemer et al., 2025). Data fusion techniques include early fusion, which entails combining data sets before modeling; intermediate fusion, which involves extracting attributes from each dataset independently and merging them at the hidden layers of the model; and late fusion, which combines the output of separate model. Of these methods, those that use intermediate or hybrid fusion strategies have been found to perform better as they retain the features of each individual domain while using complementary information of other modalities effectively (Babanejaddehaki et al., 2025; Kebeba and Agyei, 2026). Although much work has been done in this area, the use of both clinical and genomic data is still difficult owing to various issues such as differences in the format of data, missing information, lack of interoperability, computational complexity, and data protection laws (Awotunde et al., 2022; Kaur and Butt, 2025).

3.5 Challenges in AI-Based Disease Prediction

While there have been improvements in disease outbreaks forecasting because of artificial intelligence, several technological, clinical, and logistical obstacles still prevent its adoption on a large scale. The first and foremost problem that needs to be addressed is the availability of good healthcare data sets. Data collected from the clinical, genomics, and epidemiological domains are inconsistent, non-interoperable and are often collected using different standards (Miranda et al., 2025; Rudwan et al., 2026). Secondly, interoperability in the context of healthcare information systems continues to remain an important challenge. Information gathered by hospitals, laboratories, public health departments, and genomic sequencing centers is often in non-interoperable formats and thereby restricts timely information exchanges, ultimately rendering the entire process of AI-based surveillance less effective (Lawal et al., 2025). In a related information systems context, Murugapandian (2026) examined nonlinear modelling of secure internet service dynamics in academic library and research data systems, highlighting a relevant application of nonlinear approaches to distributed information infrastructures. Additionally, legal and ethical concerns over patient data make it difficult to collaborate and share information between countries and different healthcare institutions. Lastly, model interpretability is another challenge that persists. The deep learning algorithms used in AI work like black boxes and are not easily interpretable by doctors and public health officials. Such a lack of transparency negatively impacts clinical confidence and could potentially impact regulatory acceptance of AI-enabled healthcare applications. In light of the foregoing, Explainable Artificial Intelligence (XAI) methods like SHAP and LIME are progressively included to enhance the transparency of AI models to allow for evidence-based decision making (Awotunde et al., 2022; Fahim et al., 2025). Computationally, state-of-the-art deep learning and hybrid AI models need considerable computing resources, large amounts of annotated data, and model revisions to adapt to changes in diseases characteristics. New pathogens, virus mutations, and environmental changes can drastically reduce the performance of such models when there is no adaptive learning in place (Sharma et al., 2026; Yang et al., 2026). Future AI-based disease prediction systems must focus on adaptive learning, federated AI, explainability, standardization of healthcare data interoperability, and multimodal surveillance of real-time data.

4. Adaptive Hybrid Models and AI-Driven Early Warning Systems

4.1 Concept and Characteristics of Adaptive Hybrid Models

Adaptive hybrid approaches signify the future of AI-based disease outbreak prediction systems by using various artificial intelligence methods along with heterogeneous sources of healthcare data. As opposed to conventional machine learning models that utilize a particular algorithm and a unique data source, adaptive hybrid models employ a combination of machine learning (ML), deep learning (DL), epidemiological modeling, genomics, and real-time monitoring for enhancing prediction performance and adapting to new circumstances (Sharma et al., 2026; Kraemer et al., 2025). Such models are capable of constantly learning based on newly gathered clinical,

genomics, environmental, and epidemiological data in order to provide up-to-date disease predictions. Key features of adaptive hybrid models include multimodal data integration, learning adaptability, real-time predictions, interpretability, scalability, and interoperability within health systems. Recent research findings prove that hybrid structures are superior to conventional AI models due to their ability to account for nonlinear relationships between various healthcare parameters (Miranda et al., 2025; Babanejaddehaki et al., 2025).

4.2 Taxonomy of AI-Based Disease Outbreak Prediction Systems

The current review highlights a new taxonomy framework to categorize AI-based disease outbreak prediction systems as follows:

(i) Data sources (clinical, genomic, environmental, and epidemiological data)

(ii) AI algorithms (machine learning, deep learning, ensemble learning, graph learning, and transformers)

(iii) Adaptive learning approaches (online learning, transfer learning, continual learning, and federated learning)

(iv) Intelligent decision support (risk prediction, hotspot detection, genomic surveillance, and resource optimization)

(v) Public health outcomes (early warning, precision public health, and outbreak preparedness).

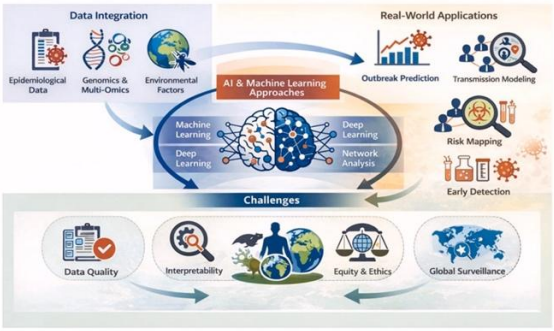

Fig 3. Proposed Taxonomy of AI-Based Disease Outbreak Prediction Systems

4.3 Hybrid Learning Architectures

New studies have developed several hybrid learning frameworks that can be applied in intelligent disease surveillance systems. The ML - DL framework combines conventional machine learning and deep learning models to enhance the robustness of predictions and minimize overfitting problems. Clinical-genomic framework utilizes both electronic health records and pathogen sequencing data to detect the emergence of diseases and new variants (Raza et al., 2026; Shahin et al., 2026). Graph-based framework studies the interaction between patients, pathogens and mobility networks, while transformer-based framework can efficiently learn long-term temporal dependencies and multimodal health care data (Yang et al., 2026).

4.4 Adaptive Learning Mechanisms

This approach makes AI systems maintain their efficiency amid the changing nature of disease dynamics. Online learning is capable of updating predictive models based on continuous flow of health care data, while transfer learning takes advantage of the learned disease patterns in order to develop solutions for new diseases. Continual learning avoids catastrophic forgetting amid sequential model updating, while federated learning allows collaborating in model building without disclosing sensitive patient data (Kaur and Butt, 2025; Lawal et al., 2025).

4.5 AI-Based Early Warning System Architectures

Current AI-enabled early warning systems combine hospitals, labs, genomic sequencing centers, environmental monitoring systems, and public health agencies to form an integrated surveillance system. With real-time data capture, predictive analysis, explainable AI, and dashboard decision support, they provide instant recognition of hot spots for diseases, their transmission channels, and required healthcare resources (El Morr et al., 2024; Rudwan et al., 2026). This type of intelligent system allows proactive action rather than reactive treatment of disease.

4.6 Comparative Analysis of Existing Adaptive Hybrid Models

Table 8. Comparative analysis of models and its strengths and limitations

Model Type	Strengths	Limitations
ML Models	Interpretable, efficient	Limited temporal learning
Deep Learning	High predictive accuracy	Large data and computational requirements
Hybrid ML–DL Models	Improved robustness and multimodal learning	Higher implementation complexity
Clinical–Genomic Models	Early mutation detection and precision prediction	Data integration challenges
Transformer & Graph Models	Superior temporal and relational modelling	High computational cost

Novel Contribution: Unlike previous reviews focusing mainly on either AI techniques or surveillance approaches (El Morr et al., 2024; Miranda et al., 2025), this review attempts to put together all those components such as adaptive hybrid architecture, clinical-genomic fusion approach, adaptive learning processes, and intelligent early warning systems to provide a holistic conceptual framework for future prediction of outbreaks.

5. Comparative Review, Research Gaps and Critical Analysis

5.1 Comparative Positioning Against Existing Reviews

There have been some recent reviews on the use of AI in infectious disease surveillance and forecasting, but they have addressed different aspects than the present review. For instance, El Morr et al. (2024) systematically reviewed early warning systems for epidemics and pandemics that utilize artificial intelligence, and explored the attributes and uses of current approaches to early warning. In parallel, Miranda et al. (2025) investigated the use of AI in infectious disease early warning systems, offering valuable insights into the increasing significance of intelligent surveillance. Towfek and Elkanzi (2024) narrowed their scope down to machine learning techniques for forecasting the spread of infectious diseases; Babanejaddehaki et al. (2025) gave a more comprehensive examination of methods for detecting and predicting outbreaks of infectious diseases and the data sources used. Kraemer et al. (2025) also showed that AI is rapidly becoming a crucial tool for modelling infectious disease epidemics and offered chances to combine cutting-edge computational methods with information about infectious diseases.

Unlike previous review articles, the present review looks at outbreak prediction from an integrated adaptive and multimodal angle, instead of individual AI techniques and surveillance functions separately. Especially, it merges the five related dimensions of clinical data integration, multimodal data analysis, adaptive learning mechanisms, explainable and privacy-preserving AI, and intelligent early warning systems. This greater distance on the methodological front shows that there is a significant disconnect in the current literature: better predictive algorithms do not automatically lead to accurate outbreak surveillance in the real world. In addition, data quality, temporal adaptability, interoperability, external validation, interpretability and the capacity of models to maintain their predictive performance when epidemiological conditions evolve are also essential for predictive performance. Another important note to take: The benefits that have been reported as a result of the application of hybrid and deep learning techniques should be taken with a grain of salt. Some of the studies cited reported better prediction performance when using multiple algorithms or data modalities; however, it is challenging to compare the results of different studies directly due to the very different datasets, diseases, geographical settings, prediction time horizons, validation strategies, and evaluation metrics used across studies. For now, none of the AI models can be considered the ultimate solution for outbreak forecasting. Instead, the evidence indicates that, in fact, model suitability is context-specific and that hybrid architectures can offer specific benefits in the presence of complementary data modalities and relevant validation procedures.

Table 9. Comparative Positioning of the Present Review against Existing Reviews

Review	Primary emphasis	Adaptive learning	Clinical-genomic integration	Hybrid AI	Early warning systems	Distinctive difference from present review
El Morr et al. (2024)	AI epidemic/pandemic early warning systems	Limited	Limited	Partial	Strong	Primarily examines early warning systems
Towfek and Elkanzi (2024)	ML for infectious disease spread	Limited	Limited	Limited	Partial	Primarily ML-focused
Miranda et al. (2025)	AI in infectious disease early warning	Partial	Limited	Partial	Strong	Focuses mainly on AI-enabled surveillance/EWS
Babanejaddehaki et al. (2025)	Outbreak detection, forecasting methods and data	Partial	Partial	Partial	Partial	Broad methods/data-source review
Kraemer et al. (2025)	AI modelling of infectious disease epidemics	Partial	Partial	Strong	Partial	Focuses primarily on epidemic modelling
Present review	Adaptive multimodal AI for outbreak prediction	Core focus	Core focus	Core focus	Core focus	Integrates adaptive learning, clinical-genomic fusion, hybrid AI, XAI/federated learning and EWS within one conceptual synthesis

The unique value of this review is thus not only in its capability to identify successful approaches to AI but also in its ability to draw on the factors needed to make them effective tools for adaptive disease monitoring. The proposed taxonomy provides a structure that shows how data sources are linked to AI algorithms, adaptive learning strategies, decision-support functions, and public health outcomes; the research gap matrix highlights areas where there is lacking evidence. Together, these contributions provide a structured basis for moving research from isolated predictive models toward clinically relevant, adaptive, explainable, privacy-aware, and multimodal early warning systems. Nevertheless, these contributions represent a synthesis of the reviewed evidence and require empirical validation before their effectiveness in operational public health environments can be established.

5.2 Research Gap Analysis

Review articles have continuously illustrated the efficiency of AI technology for disease surveillance purposes, although most of the literature focuses on the independent application of such technologies as machine learning, genome analytics, or epidemiological modeling (Towfek and Elkanzi, 2024; Sharma et al., 2026). Hybrid models of AI have proven to be more efficient for predicting due to the fact that these models use complementary data from various sources of health care (Kraemer et al., 2025). Clinical data include valuable patient-related data while genomic surveillance allows detecting pathogens' evolution. The combination of both types of data results in better predictions of an outbreak than the usage of only one source (Katiyar et al., 2025; Nwokedi et al., 2026). Still, the existing research faces a number of challenges (Awotunde et al., 2022; Badidi, 2023).

Table 9. Research Gap Matrix

Existing Limitation	Research Opportunity
Single-source datasets	Multimodal data fusion

Static prediction models	Adaptive hybrid learning
Limited explainability	Explainable AI frameworks
Centralized data sharing	Federated learning
Limited genomic integration	Multi-omics prediction
Lack of real-time surveillance	Intelligent early warning systems

This current review is different from existing literature reviews in terms of analyzing aspects like adaptive hybrid learning, integrating clinicogenomics, federated intelligence, and explainable artificial intelligence under one umbrella. The proposed taxonomy and conceptual framework relate to artificial intelligence techniques, multiple healthcare data modalities, and public health decision-making.

6. Proposed Conceptual Framework and Future Research Directions

6.1 Proposed Adaptive Hybrid Framework for Disease Outbreak Prediction

The framework proposed in this literature review comprises six components arranged sequentially: (1) multimodal healthcare data acquisition, (2) data preprocessing, (3) hybrid adaptive AI modeling, (4) continuous learning, (5) explainable decision making support, and (6) AI-based early warning. The framework utilizes clinical, genomic, environmental, and epidemiological data in hybrid machine learning and deep learning frameworks by means of federated learning and explainable AI.

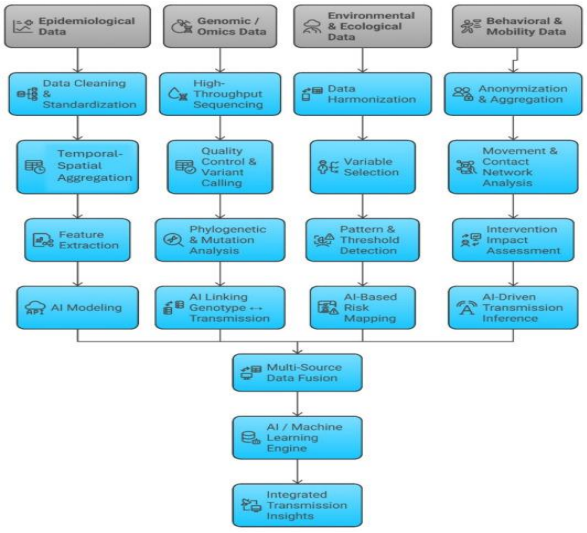

Fig 4. Proposed Adaptive Hybrid Framework for Disease Outbreak Prediction

The Adaptive Hybrid Framework proposed in this review is a conceptual framework synthesized from the patterns, methodological advances, limitations, and research opportunities identified across the reviewed literature. It should therefore not be interpreted as an empirically validated prediction model or a currently deployed clinical surveillance system. Rather, the framework integrates recurring evidence concerning multimodal data fusion, hybrid AI modelling, adaptive learning, explainability, federated intelligence, and early warning mechanisms into a unified architecture that may serve as a foundation for future system development, implementation, and validation. The conceptual framework comprises six interconnected components: (1) multimodal healthcare data acquisition, (2) data preprocessing and harmonization, (3) hybrid adaptive AI modelling, (4) continuous and adaptive learning, (5) explainable decision support, and (6) AI-enabled early warning and public health response. Clinical, genomic, environmental, and epidemiological information can potentially be integrated through multimodal fusion strategies and analyzed using complementary machine learning and deep learning architectures. Adaptive mechanisms such as continual, transfer, online, and federated learning may further enable models to respond to changing epidemiological patterns while supporting privacy-preserving collaboration. However, the comparative effectiveness, scalability, interoperability, clinical utility, and generalizability of the proposed architecture require prospective evaluation using geographically and epidemiologically diverse real-world datasets before operational adoption can be recommended.

6.2 Integration Framework for Clinical and Genomic Data

This model uses EHRs, lab reports, genomics sequencing, environment factors and epidemiology surveillance through multimodal feature fusion to make predictions about diseases and enable precise decisions for public health.

6.3 Implications for Artificial Intelligence Early Warning System

The presented model can provide timely outbreak detection, better resource allocation in healthcare, genomic surveillance, intervention planning and policy-making based on facts. The integration of adaptive AI with surveillance systems can greatly improve epidemic preparedness worldwide.

6.4 Future Research Directions

Future studies must focus on Explainable AI for improved transparency and clinical acceptance, Federated Learning for secure collaborative work between institutions, Foundation Models that can learn generalized representations of diseases, Multi-Omics Integration for combining genomics, proteomics and metabolomics information, Digital Twins for modeling disease development and designing interventions, Real-Time Disease Surveillance with streaming healthcare and Internet-of-Things data, and Privacy-Preserving Healthcare AI with secure computing and differential privacy methods. Together, these technologies have the power to revolutionize intelligent disease surveillance from a reactionary monitoring system into a proactive one.

7. Discussion

7.1 Summary of Major Findings

In this systematic review, we have considered the most recent research articles (67 peer-reviewed studies) published between 2021 and 2026 to evaluate the potential of adaptive hybrid artificial intelligence (AI) models in the prediction of disease outbreaks by leveraging clinical and genomic data. This evidence suggests that the use of intelligent models based on AI is gradually replacing the traditional statistical approach for outbreak surveillance, where AI-driven intelligent models help make decisions through the integration of diverse healthcare datasets. It was observed that across all the articles, machine learning, deep learning, ensemble learning, transformers, graph neural network, and explainable AI outperform traditional epidemiology-based approaches for prediction (Sharma et al., 2026; Kraemer et al., 2025; Miranda et al., 2025; Rudwan et al., 2026).

7.2 Theoretical Contributions

The present literature review enriches the current body of literature through an exhaustive analysis of adaptive hybrid AI architecture, adaptive learning approaches, and the integration of clinical-genomic data. While prior literature reviews mostly concentrated either on AI algorithms, disease surveillance tools, or genomic analysis (El Morr et al., 2024; Babanejaddehaki et al., 2025; Towfek and Elkanzi, 2024), this literature review proposes a new taxonomy of AI-based disease outbreak forecasting systems and an innovative adaptive hybrid framework that connects multimodal health care data with intelligent learning and AI-based early warning systems. Moreover, the gap analysis framework proposed in this review reveals new directions for the future research, such as the areas of explainable AI, federated learning, foundation models, multi-omics analysis, digital twins, and privacy-preserving health care AI.

7.3 Practical and Clinical Implications

These results hold great significance for the field of health care organizations, researchers, and public health organizations. The incorporation of the adaptive hybrid AI models into disease surveillance systems will lead to earlier outbreak detection, better resource allocation, fast recognition of mutations in pathogens, and evidence-based intervention strategies. The integration of genomics and clinical data leads to precision public health through personal risk assessment and disease control interventions, while explainable AI and federated learning provide for better clarity, physician confidence, compliance with regulations, and collaboration between different health care institutions (Kaur and Butt, 2025; Yang et al., 2026; Lawal et al., 2025).

7.4 Limitations of This Review

A few limitations in the interpretation of the results of this systematic review should be taken into account. First, the review included only publications in English, which could have resulted in the exclusion of relevant evidence that was published in other languages and could have introduced language-related selection bias. Secondly, the publication period was restricted to 2021-2026 for the reporting period to reflect more recent advances in AI-driven disease surveillance. This gives a modern look, but other significant methodological works might be underrepresented. Third, there was significant variation in the disease types, geographic context,

dataset characteristics, AI architecture, prediction time horizon, validation method and performance metrics reported by the included studies. Therefore, a quantitative meta-analysis was seen as inappropriate, and the results were synthesized qualitatively and narratively, and also by comparing them.

Furthermore, publication bias cannot be ruled out as a complete cause as studies with positive predictive results are more likely to be published than studies with negative or inconclusive results. This effect may be exacerbated by the requirement for mainly peer-reviewed literature, while increasing the methodological validity of the evidence base. Moreover, direct comparisons of model accuracy or AUC should be taken with a pinch of salt as the apparent accuracy or AUC could be different across various datasets, class distributions, evaluation protocols, or validation settings, potentially masking the inherent strength of a specific AI architecture. Lastly, the Adaptive Hybrid Framework that was constructed in this review is a conceptual synthesis of all the evidence available and not a system that has been experimentally validated. However, future studies should consider evaluating its individual components and integrated architecture with external, multicenter, geographically diverse data and real-world surveillance.

8. Conclusion

The PRISMA 2020 systematic review, this review focused upon the recent developments of adaptive hybrid artificial intelligence in relation to disease outbreak prediction and intelligent early warning systems by collecting evidence from 67 studies published between 2021 and 2026. Based on the evidence reviewed, machine learning, deep learning, ensemble methods, transformers, graph-based methods, explainable AI, and adaptive learning methods show great promise in bolstering infectious disease surveillance. The combination of clinical, genomic, environmental, epidemiological and mobility data can, in particular, allow for a comprehensive picture of the dynamics of diseases than the use of individual data sources. The relative merits of hybrid approaches are however, still subject to the quality of the datasets, the disease situation, model architecture, validation strategy and implementation environment, and cannot be assumed to be superior to individual models in general. The main novelty of this review lies in the comprehensive and integrated synthesis of the concepts of adaptive hybrid learning, clinical-genomic data fusion, intelligent early warning architectures, adaptive learning mechanisms, and trustworthy AI considerations. Based on this synthesis, taxonomy is presented, a research gap matrix, and a conceptual Adaptive Hybrid Framework that aims to structure the existing knowledge and to lay the groundwork for future research and not to be an operational system already validated. Several critical issues need to be addressed, such as multimodal data interoperability, external validation, model explainability, privacy, algorithmic bias, computational demands, and integration into the public health system. Future research should thus strive for prospective, multicenter and real-world validation of models in different populations, pathogens, healthcare systems, and geographical settings. This will be crucial to assessing how much potential adaptive hybrid AI frameworks have for becoming viable, equitable, clinically interpretable, and operationally useful early warning systems for public health practice.

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