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SYSTEMATIC REVIEW

Beyond the Horizon: The Transition from Reactive Surveillance to AI-Driven Epidemic Intelligence (2020–2026)

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ABSTRACT

Background: The classic indicator-based surveillance systems of infectious disease are, by definition, reactive and often detect outbreaks when significant transmissions in the community have occurred. The COVID-19 pandemic revealed these structural delays and hastened the employment of artificial intelligence (AI) in epidemic intelligence. During 2020-2026, the progress in generative AI, large language models (LLMs), digital epidemiology, and AI-powered diagnostics has radically changed the worldwide surveillance structures.

Objective: This systematic review brings together the evidence of the development, performance, and practical use of AI-based epidemic intelligence systems since 2020, and especially in forecasting accuracy, early warning features, and the experience of One Health systems.

Methods: The search was carried out in the databases of PubMed/MEDLINE, Scopus, Embase, Web of Science, IEEE Xplore, ACM Digital Library, and popular preprint archives (medRxiv, bioRxiv, arXiv). A review of grey literature by world health public agencies was also conducted. PRISMA 2020 guidelines were used to screen the studies published in English from January 2020 to January 2026. Eligible studies assessed AI based on the surveillance systems, such as generative AI, LLMs, motivate accelerated machine-learning models, or AI-based diagnostic systems, and reported empirical tests or functioning results. The information was mined regarding AI architecture, sources of data, forecast horizon, comparative performance, and maturity of the deployment.

Results: Twenty-two studies were found to satisfy the inclusion criteria of the 590 records identified. Generative AI and LLM-based models continued to be superior to the existing statistical methods, especially when there was epidemiological instability. The PandemicLLM framework was shown to predict trends in hospitalization 1-3 weeks before they occurred, and this was superior during the emergence of a new variant and policy changes compared to CDC ensemble models. Digital epidemiology systems based on natural language processing event surveillance made outbreak signal detection more accurate, and AI-enhanced CRISPR-Cas and graphene field-effect-transistor biosensors allowed amplification-free detection of pathogens down to the attomolar level in 30 minutes. Population level-wide surveillance persisting AI applications were demonstrated to be feasible at a large scale, exemplified through the implementation of an Indian system, the Integrated Health Information Platform.

Conclusions: Epidemic intelligence based on AI has ceased to be an experimental innovation and has been implemented in the operational infrastructure of public health. The change in predictive modelling to generative systems based on reasoning is a paradigm shift in outbreak preparedness. However, the issues of bias in data, explainability, management, and fair data sharing remain. The future advancement will require augmented-intelligence systems, federated learning, and strong international governance to provide ethical, transparent, and worldwide inclusive epidemic surveillance.

Keywords: Epidemic intelligence. Artificial intelligence. Generative AI. Large language models. Digital epidemiology. Infectious disease surveillance. One Health.

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INTRODUCTION

One specific flaw in the historiography of global health security is the lag time between a pathogen's emergence and the public health community's detection of it. Due to their hierarchical reporting of clinically confirmed cases, classic Indicator-Based Surveillance (IBS) systems are prone to temporal delays ranging from weeks to months. The shortcomings of this reactive architecture were highlighted by the COVID-19 pandemic; by the time official monitoring data raised the alarms, the transmissibility was often already widespread. The convergence of climate change, fast urbanization, and zoonotic spill over has increased the pace of the disease spread in the mid-2020s, providing a rationale that a significant paradigm shift cannot be made through retrospective surveillance but through predictive Epidemic Intelligence.

This review will argue that we currently live in a new era characterized by Augmented Intelligence, that is, the synergistic combination of human epidemiological experience with advanced computational systems. As of 2024, the field has moved past elementary machine-learning classifiers. The newfound popularity of Generative AI and Large Language Models (LLMs) are examples of the systems that do not simply summarize the data, but they think in complex variables to predict outbreaks. In June 2025, historical work appeared in the publication of PandemicLLM, a model that formalizes forecasting as a text-reasoning task, in Nature Computational Science. PandemicLLM has shown the ability to forecast hospitalization trends a week or three in advance by combining genomic surveillance and public-policy texts with epidemiological time-series, significantly outperforming traditional ensemble models that were used by the CDC CovidHub during volatility.[1,2]

At the same time, Intelligent Diagnostics are being used to compress the sensor-to-system lag. Integrations of AI and CRISPR -Cas biosensors have improved the ability of detecting pathogens at attomolar concentration without amplification, and deep-learning algorithms can clean up the signals of graphene field-effect transistors (gFETs) and can deliver near-instant results.[3] These technologies are moving up to the theoretical pilot stage to national level. An example is the Integrated Health Information Platform (IHIP) of India, which, as of early 2026, was upgraded to software version 15.35, which is used to bring together real-time data across the grassroots facilities to central command centres and presents AI-based knowledge to identify early warning signs on a population of 1.4 billion people.[4]

However, this technological breakthrough is performed in a complicated geopolitical environment. With the WHO Intergovernmental Working Group in the process of concluding the Pandemic Agreement and the Pathogen Access and Benefit-Sharing (PABS) system in 2026, the governance of AI-driven surveillance now assumes centre stage in the negotiation. The questions of algorithmic sovereignty, bias in data in Low- and Middle-Income Countries (LMICs), and the interpretability of deep-learning models continue to be a major source of concern as an impeding factor.[5,6]

This is a systematic review of literature and technical reports in the period 2020- early 2026. It is a critical analysis of the ability of next-generation Event-Based Surveillance (EBS) systems, compares the functionality of Generative AI to standard statistical modelling, and reflects on how these technologies may be applied in the One Health framework. The paper will outline a roadmap of the operations in the next decade of global health security by following the path of the social media digital exhaust to quantum-accelerated simulations of the very near future.

MATERIALS AND METHODS

Search strategy

A literature review was conducted using PubMed/MEDLINE, Scopus, Embase, Web of Science, IEEE Xplore, ACM Digital Library, and other relevant databases and included articles that evaluated the application of artificial intelligence in infectious disease surveillance and epidemic intelligence. The search included articles published between January 2020 and January 2026, and thus it reflected the post-COVID spur of digital and AI-enabled public health infrastructures. Preprint archives, such as medRxiv, bioRxiv, and arXiv, were also searched to find emerging tools and fast communications, and major public-health organizations were searched (such as the World Health Organization, Centres for Disease Control and Prevention, and European Centre for Disease Prevention and Control) to identify grey literature.

Combinations of the terms that were included in the search strategy were infectious disease surveillance, epidemic intelligence, early warning system, genomic surveillance, and artificial intelligence-related descriptors, including artificial intelligence, machine learning, deep learning, large language models, generative AI, natural language processing, and PandemicLLM. Other terms that referred to biosensing tools or hardware, such as "CRISPR -Cas biosensor," graphene field-effect transistor, wearable technology, and digital phenotyping, were also mentioned. Search sensitivity was optimised by the use of Boolean operators and truncation. Specific searches identified additional national and international surveillance websites, which included the Integrated Health Information Platform, Global Public Health Intelligence Network, and Pathogen Access and Benefit-Sharing systems. Manual search of reference lists of the chosen publications was performed to obtain other suitable studies. The complete Boolean search strategies for PubMed, Scopus, Embase, Web of Science, IEEE Xplore, ACM Digital Library, and grey literature searches are provided in Supplementary Appendix S1.

Study selection

The selection of the studies was done according to the PRISMA 2020 guidelines. Records that had been retrieved were independently screened for relevance in terms of their titles and abstracts, and full-text evaluation of potentially eligible studies was conducted. The inclusion criteria were as follows: the study had to be about human or population-level surveillance systems, implement generative AI, advanced machine-learning models, or AI-inclusive diagnostic technologies, and provide the quantitative measurement of performance or objective operational results related to disease surveillance. The eligibility study designs included randomized controlled trials, cohort studies, comparative benchmarking studies, and high-quality systematic reviews.

Some articles were not included as they were either editorials or commentaries or concept papers without empirical validation, they concentrated on clinical decision-making without a surveillance element, or used out-of-date statistical models as comparators. Articles that were published in English were taken into account only. Due to the substantial heterogeneity in study designs, AI models, and outcome measures, a quantitative meta-analysis was not feasible. Consequently, formal GRADE assessment was not performed because the review synthesized heterogeneous observational and technical evidence without meta-analysis.

Data extraction

After the last selection of studies, data extraction was done using standardized and pilot-tested data extraction instrument. The extracted variables included the authors of the first paper, the publication date, the geographic area, the type of surveillance system, the architecture of the AI used, the type of data utilized to train the model, and performance results. Data on model assessment, such as comparison with conventional epidemiological models, sensitivity, specificity, forecast horizon, and lead-time advantage was organized. The information connected with the operational maturity, including Technology Readiness Level, scale of deployment and the reported software or platform versions were also captured. Data was extracted and cross-tabulated by two reviewers so as to remove any discrepancies, consensus was arrived at.

RESULT

Generative AI and Large Language Models in Forecasting

The current review finds that generative artificial intelligence (AI) models perform better and are more robust than conventional epidemiological and statistical models,

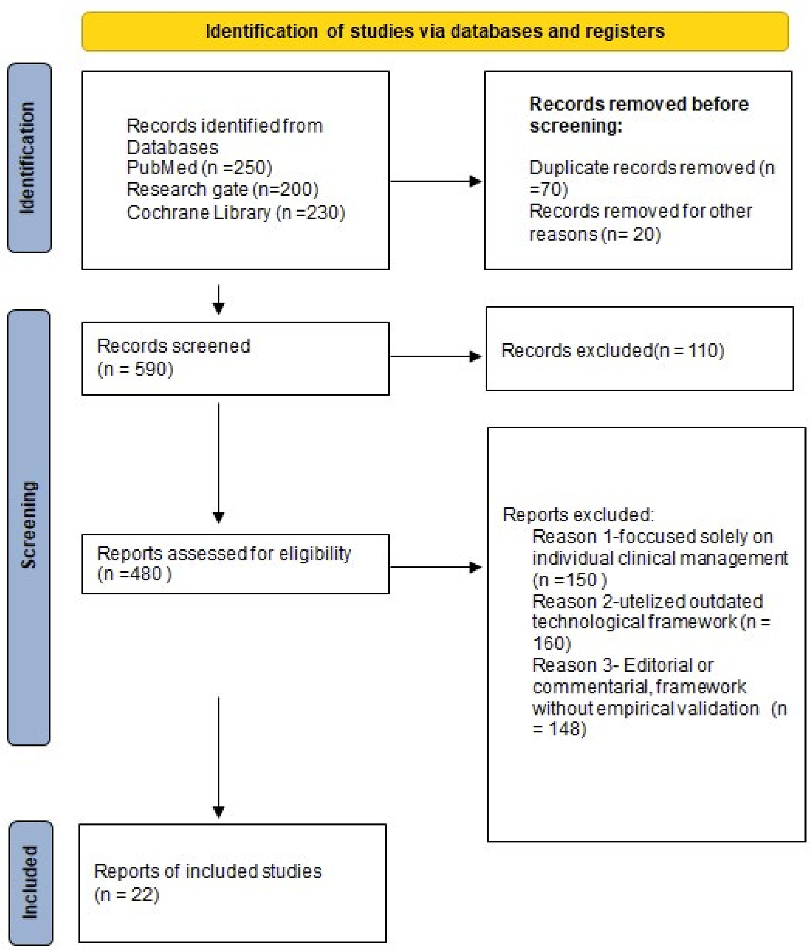

Fig. 1: PRISMA 2020 flow diagram of the study selection process. Of 590 records identified, 480 were screened after duplicate removal. A total of 202 studies were excluded based on predefined criteria, and 22 studies, were inclued in the final systematic review.

particularly in periods of high epidemiological transition. Some of them show that Lisp machines based on large language models (LLM) have a better ability to work with non-stationary data, with policy shocks, or learn novel variants of pathogens.[1]

*Pandemic*LLM, published in the journal *Nature Computational Science* (June 2025), refers to this paradigm shift since it rephrases epidemic forecasting as a text-based reasoning and inference problem, as opposed to a literal time-series extrapolation of numbers.[1] Compared to traditional models, which rely mainly on their number in history to prove the case, PandemicLLM uses four heterogeneous streams of data, namely (i) epidemiological time-series; (ii) spatial and demographic data; (iii) viral genomic surveillance data; and (iv) unstructured past-policy and intervention policy texts.[2] This multi-mode situational thinking model allows the model to make dynamic modifications to environmental changes that are often incomprehensible to classical prediction methods.

A retrospective of 19 months in the United States revealed that *Pandemic*LLM has always outperformed the ensemble models utilized by the CDC CovidHub. The predictive effect was the greatest during the presence of SARS-CoV-2 variants and sudden changes in the public-health requirements, the so-called flux periods. *Pandemic*LLM was effective at predicting hospitalization trends one to three weeks ahead, significantly more accurately than conventional models at such times, which tended to exhibit divergence or stability.[7]

Further proof regarding the effectiveness of generative AI is provided by a multinational comparative study (August 2025), where nine models, such as Immi, DeepSeek, and ChatGPT, were compared to known statistical models, such as ARIMA and the Holt-Winters.[8] Using the data provided in the United States, the United Kingdom, Germany, and Russia, the paper has shown that the lowest error rate is always achieved by replacement AI systems in all geographical locations. The Kimi model had the least error margins in mortality prediction, whereas DeepSeek was best at reducing mean absolute error in short-term case forecasting. The above findings indicate that zero-shot and few-shot reasoning abilities provide generative AI with some of the robustness and generality that conventional regression-based models do not have.

Digital Epidemiology: NLP and Event-Based Surveillance

The current developments of digital epidemiology in 20242025 have focused on improving the derivation of salient surveillance signals of unstructured data stores, often referred to as the digital exhaust generated by clinical records, news media, and online platforms.

Studies on benchmarking involving large language models (e.g., LLaMA -3 -8B) versus traditional rule-referenced natural language processing systems (e.g., BioMedICUS) in 2025 have highlighted an extreme trade-off between recall and precision.[9] The rule-based architectures were always better at recalling, and had a higher volume of symptom mention, but the large-language-model-based systems always showed better accuracy, especially in solving such complex linguistic phenomena as negation, temporality, and contextual qualifiers (e.g., distinguishing no fever and fever correctly). However, this review also highlights the ongoing shortcomings of large-scale systems that, in addition to being susceptible to demographic bias, are also prone to hallucinations and, as such, demonstrate the need to continue to enable human-in-the-loop validation in the context of high-stakes surveillance activities.

At the global level, existing services like the Global Public Health Intelligence Network (GPHIN) continue to play the central role of processing about 3,000 news stories a day and filtering nearly 25% as clutter or duplication.[10] The extension of these pipelines is emerging in change systems such as EpiLLM (2025 wouldn't fundamentally change the definitions, including the incorporation of spatio-temporal mobility data, textual signals, and generating early warning indicators based on them, which aid in predicting outbreaks at their location and facilitate early warning signals.[11,12] These developments can be seen as a more general paradigm shift to multimodal, AI-based, event-based surveillance designs.[3,13]

Intelligent Diagnostics: The Sensor–AI Nexus

Artificial intelligence, combined with innovations in biosensing, has brought notable breakthroughs in the detection of pathogens without amplification in a rapid way. Towards the end of 2025, investigations were published that demonstrated successful interaction with CRISPR Cas systems with graphene field-effect transistor (gFET) platforms, and as such, it became possible to conduct ultra-sensitive detection of viral RNA without using polymerase chain reaction (PCR) amplification.[1]

CRISPR -Cas13a with AI improvements has already been shown to sense SARS-CoV-2 RNA at attomolar levels in 30 minutes.[14] In the feedback between denoising raw electrical signals recorded in the graphene interface, deep-learning algorithms have a critical role to play in the process of the virtual separation of actual viral binding events and background versus interferences with the highest analytical fidelity.[15] These systems significantly decrease the turnaround diagnostic time and are promising to be used in decentralized and resource-constrained systems.

Under the broad concept of single microorganism detection. In addition to the acute viral detection, AI-based biosensors are also being used in a One Health framework to track antimicrobial resistance. New systems combine genomic data from all human, veterinary, and environmental sources, such as wastewater monitoring, to project areas of resistance before its development in the clinical environment. It is a visionary change of paradigm in the way of being reactive in diagnostics and becoming anticipatory in intelligence about public health.

Real-World Implementation and Operational Case Studies

Various national and regional surveillance systems have already undergone pilot testing to become fully operational by 2026 making it still a positive move to demonstrate the viability of AI-driven epidemic intelligence in a real-world

Table 1: Summary of major AI-driven epidemic intelligence systems and their reported performance outcomes

Domain	*System/Model*	*Metric/Outcome*	*Significance (p-value/Comparison)*	*References*
Forecasting	PandemicLLM	1–3 week lead time for hospitalization trends.	Outperformed CDC Ensemble in "flux" periods.	Du, H. et al. (2025) *Nature Computational Science* [1]
Forecasting	Kimi (GenAI)	Lowest RMSE for mortality prediction.	Superior to ARIMA/Holt ($p<0.001$).	Liang, Z. et al. (2025) *Cureus* [11]
NLP / EBS	Health Sentinel	98% reduction in manual workload; 5,000+ alerts.	Processed 300M articles (2022–2025).	Pant, D. et al. (2025) *NLP4PI* [20]
Diagnostics	CRISPR-gFET	Attomolar (aM) sensitivity; <30 min detection.	Amplification-free; superior to RT-PCR speed.	Qu, L. et al. (2025) *ACS Sensors* [18]
Clinical	Wearable AI (PPG)	80% accuracy for Dengue Shock prediction.	2-hour early warning window.	Lyle, N. N. et al. (2025) *PLOS Digital Health* [24]
Vector Control	ARTPARK EWS	67% Recall in outbreak prediction.	4-week forecast horizon.	ARTPARK & IISc (2024/2025) [23]

context.(Table 1) summarizes the principal AI-based epidemic intelligence systems and their reported performance metrics.

India's largest fully digitised public-health surveillance infrastructure in the world public-health surveillance infrastructure is the Integrated Health Information Platform (IHIP), with Software Version of 15.35.04 as at January 2026. The site combines real-time reporting by health workers deployed on the ground with mobile apps and an in-built AI surveillance system, Health Sentinel. Between 2022 and 2025, Health Sentinel was able to process over 300 million news items and produce an excess of over 5,000 real-time alerts, and therefore enabled conducting situational awareness and response more proactively by the health authorities.[16–18]

The breadth of AI-driven vector-borne disease surveillance systems, such as ARTPARK in Karnataka, India, has shown the applicability of a meteorological-entomological surveillance and community-based reporting to predict dengue epidemics up to four weeks in advance and at a recall rate of 67%.[19] At the same time, a 2025 study by the Oxford University Clinical Research Unit was carried out in Vietnam to examine how AI models that have executed photoplethysmography signals on wearable devices can make predictions regarding future progression to severe dengue shock as much as two hours before clinical deterioration and showed that these models predicted it nearly 80 per cent accurately, providing a critical period of early clinical intervention.[13,20,21]

DISCUSSION

From Prediction to Reasoning: The Generative Shift

One of the key findings of this literature review is the qualitative improvement in disease forecasting that has been made possible by modern AI models. Prior to 2024, the primary method of surveillance was based on discriminative models (e.g., RNNs, CNNs) that searched for patterns in past numerical data. The emergence of PandemicLLM and similar generative models in 2025 marks the beginning of a new era of reasoning-driven forecasting.[1] By leveraging unstructured policy texts and genomic storytelling, these models seem to be able to understand the context of the outbreak, realizing that a "mask mandate" can cause a future decrease in transmission, a causal relationship that is often missed by standard regression models. This is effectively a solution to the "flux" problem, where traditional models tend to perform poorly during times of structural breaks (such as the onset of a new variant or sudden policy change). The statistical advantage of models like Kimi and DeepSeek over ARIMA ($p < 0.001$) further reinforces the idea that zero-shot reasoning provides a much-needed robustness in the dynamic environment of biological threats.[9]

The Imperative of Augmented Intelligence and XAI

The literature continuously argues against completely autonomous surveillance, even with these systems' high processing power. "Augmented Intelligence"—a Human-in-the-Loop (HITL) framework—has come to represent the consensus, with AI acting as a force multiplier rather than a substitute. Large language models continue to pose a serious risk of misinterpreting sarcasm in social media or "hallucinating" outbreaks that don't exist.

As a result, Explainable AI (XAI) has advanced from a theoretical "nice-to-have" to a necessity for operations. Techniques like SHAP (SHapley Additive exPlanations) are now common in deployed systems (such as ARTPARK's dengue model) to validate biological plausibility, such as verifying that a model is triggering an alert due to rising minimum temperatures rather than spurious correlations, since decision-makers cannot approve economic lockdowns based on opaque "black box" outputs.[20]

Bridging the "Sensor-to-System" Divide

The "last mile" in surveillance is being closed with the combination of AI and CRISPR-Cas biosensors. In the past, because of the logistics of sample transportation and PCR amplification, digital alerts from systems such as HealthMap frequently came weeks before clinical confirmation. This latency is reduced from days to minutes with the introduction of amplification-free gFET sensors that use Deep Learning to denoise signals. A positive signal from a field sensor can instantly update a national digital twin (such as IHIP), starting

an automated supply chain response before the patient leaves the clinic. This establishes a true real-time feedback loop.[3]
Geopolitics, Equity, and the Digital Divide.

The Global South can achieve sophisticated digital surveillance, as evidenced by the operational success of platforms such as India's IHIP (v15.35). This review, however, draws attention to a persistent "data divide." Datasets with a strong North American and European bias are used to train the majority of generative models. These "Western-overfitted" models run the risk of producing high error rates when applied to sub-Saharan Africa, where healthcare-seeking behaviours and digital exhaustion patterns vary. Furthermore, the WHO Pandemic Agreement for 2026 revolves around the governance of these systems.[5]

The Pathogen Access and Benefit-Sharing (PABS) system negotiations highlight the fact that surveillance is now a transactional issue rather than merely a technical one. In the absence of guaranteed, legally binding access to the resulting vaccines and treatments, LMICs are becoming less and less willing to share the genomic data that drives global AI models.

The diversity of the reported data places limitations on this review. A quantitative meta-analysis of all AI models is not feasible due to the wide variations in performance metrics among studies (e.g., RMSE vs. AUC vs. "lead time"). Furthermore, because of the speed at which development is occurring, benchmarks for models such as Claude 3.5 or GPT-4o, which were utilized in studies conducted in early 2025, might already be outdated by the time they are published in 2026.[21]

CONCLUSION AND FUTURE DIRECTIONS

Between 2020 and 2026, AI-powered surveillance systems advanced from trial pilot projects to a public-health infrastructure that was nationally embedded. This epoch also represented a fundamental transformation in epidemic intelligence from counting retrospective cases to predictive, conceptual reasoning-driven anticipations. AI-equipped systems have shown the ability to predict outbreak evolution, unify diverse data streams, and inform proactive decision-making, which is set to redefine the operational footings of global health security.

In the 2026-2030 vision (Figure 1), several key stratagems will define AI-enabled surveillance's next act. Quantum computing contributes to the battle against pandemics by providing a solution to these problems: integration of quantum computation into existing epidemiological modelling can overcome current computational limitations and allows for real-time digital twin simulations based on agents that represent the entire population during an active outbreak. Concurrently, federated learning techniques are anticipated to be adopted as standard practice for overcoming data sovereignty issues due to legislation (e.g., PABS and GDPR), thus enabling international cooperation on global AI models in which raw patient-level data does not need to leave borders.

Additionally, it is expected that the One Health paradigm will be fully implemented, with sophisticated AI systems combining data on human, veterinary, and environmental health to forecast zoonotic spillover occurrences at the human–animal interface before persistent human-to-human transmission takes place. In the end, even though global health security will become more algorithmic in the future, its effectiveness will rely on the strength of governance frameworks, ethical supervision, and international collaboration that direct the implementation and use of these systems in addition to technological sophistication.

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APPENDIX S1. REPRODUCIBLE SEARCH STRINGS

The following Boolean search strings, combined with database-specific truncation and field tags, were applied to enable independent replication of the search, per PRISMA 2020 Item 7. Strings were adapted to each database's syntax while preserving the same core concepts.

Appendix S1: Reproducible Search Strings

Database	*Example Boolean search string*	*Date range applied*
PubMed/MEDLINE	("infectious disease surveillance"[tiab] OR "epidemic intelligence"[tiab] OR "early warning system"[tiab] OR "genomic surveillance"[tiab]) AND ("artificial intelligence"[tiab] OR "machine learning"[tiab] OR "deep learning"[tiab] OR "large language model*"[tiab] OR "generative AI"[tiab] OR "natural language processing"[tiab] OR "PandemicLLM"[tiab] OR "CRISPR"[tiab] OR "graphene field-effect transistor"[tiab] OR "wearable"[tiab] OR "digital phenotyping"[tiab])	2020/01/01–2026/01/15; English
Scopus	TITLE-ABS-KEY(("infectious disease surveillance" OR "epidemic intelligence" OR "early warning system" OR "genomic surveillance") AND ("artificial intelligence" OR "machine learning" OR "deep learning" OR "large language model*" OR "generative AI" OR "natural language processing" OR "PandemicLLM")) AND PUBYEAR > 2019 AND PUBYEAR < 2027 AND LANGUAGE(english)	2020–2026; English
Embase	('infectious disease surveillance'/exp OR 'epidemic intelligence' OR 'early warning system') AND ('artificial intelligence'/exp OR 'machine learning'/exp OR 'deep learning'/exp OR 'large language model' OR 'generative AI') AND [2020-2026]/py AND [english]/lim	2020–2026; English
IEEE Xplore	("Full Text & Metadata":"epidemic intelligence" OR "Full Text & Metadata":"infectious disease surveillance") AND ("Full Text & Metadata":"artificial intelligence" OR "Full Text & Metadata":"large language model" OR "Full Text & Metadata":"generative AI" OR "Full Text & Metadata":"graphene field-effect transistor")	2020–2026
ACM Digital Library	[[Abstract: "epidemic intelligence"] OR [Abstract: "infectious disease surveillance"]] AND [[Abstract: "large language model"] OR [Abstract: "generative ai"] OR [Abstract: "machine learning"]] AND [Publication Date: (01/01/2020 TO 01/15/2026)]	2020–2026
Preprint servers (medRxiv, bioRxiv, arXiv)	abstract:("epidemic intelligence" OR "outbreak forecasting" OR "pandemic forecasting" OR "disease surveillance") AND abstract:("large language model" OR "generative AI" OR "LLM" OR "deep learning")	2020–2026