Infectious, 3(2):43–58, July-December: 2026.
DOI: https://doi.org/10.58612/infectious325

Infectious
ISSN (Online): 3049-2513

Journal homepage: https://www.fpub.org/journal-details.php?journal-id=44



Review Article

Digital Epidemiology and Mathematical Modelling for HIV and Infectious-Disease Early Warning: Integrating AI, Genomics, Mobility, and Routine Surveillance

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Article Info

Keywords: *HIV, Digital epidemiology, Infectious diseases, Artificial intelligence, mathematical modelling, Genomic epidemiology, Mobility, Surveillance, Early warning, Epidemic intelligence.*

Received: *25.09.2026;*
Accepted: *26.10.2026;*
Published: *02.11.2026*

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Abstract

The growing availability of clinical, genomic, mobility, environmental, and digital data is expanding the capacity of infectious-disease surveillance beyond retrospective description toward earlier detection and prediction. However, greater data availability and increasingly sophisticated analytical methods do not automatically produce effective early warning. This narrative review critically examines the roles of artificial intelligence (AI), mathematical epidemiological modelling, genomic epidemiology, mobility data, digital signals, and routine surveillance in HIV and broader infectious-disease early warning. Across these domains, the evidence indicates that individual data streams provide complementary but incomplete views of epidemic dynamics. AI can identify complex patterns, mathematical models can represent transmission processes, genomics can reveal pathogen evolution and transmission relationships, and mobility data can characterize population connectivity; yet each remains constrained by data quality, representativeness, uncertainty, transportability, and implementation challenges. The central limitation of the field is therefore not simply predictive performance, but the difficulty of converting fragmented signals into validated intelligence that can support timely public-health decisions. To address this gap, this review proposes an Integrated Digital Epidemiology Early-Warning Framework that links heterogeneous data inputs with integration, analytical modelling, epidemic intelligence, validation, warning, public-health action, and continuous evaluation and learning. The framework adds an explicit validation gate between prediction and warning, rules for reconciling conflicting signals and propagating uncertainty, tiered criteria for progressing from signal to warning and action, and a staged pathway for implementation and prospective validation in resource-limited settings, including for HIV surveillance. Future systems should be evaluated not only by predictive accuracy but also by lead time, calibration, external validity, equity, actionability, and effects on population outcomes. The next frontier is to build integrated systems capable of transforming heterogeneous signals into timely, trustworthy, equitable, and actionable public-health intelligence.

How To Cite: I. Muhammed. Digital Epidemiology and Mathematical Modelling for HIV and Infectious-Disease Early Warning: Integrating AI, Genomics, Mobility, and Routine Surveillance. *Infectious*, 3(2):43–58, 2026. https://doi.org/10.58612/infectious325

1. Introduction

Infectious-disease surveillance has traditionally focused on documenting events that have already occurred: who has been diagnosed, where cases are concentrated, and whether incidence is increasing or declining. These functions remain essential, but they are often constrained by delays between infection, testing, diagnosis, laboratory confirmation, reporting, and analysis. As a result, surveillance systems may describe an epidemic accurately while still recognizing important changes too late for timely intervention [1].

This limitation is particularly important for HIV. Because infection may remain undiagnosed for a prolonged period, newly reported diagnoses do not necessarily represent recent transmission. Changes in diagnoses may also reflect testing patterns and case ascertainment rather than an immediate change in transmission [2]. Although treatment, viral-load monitoring, molecular surveillance, and prevention have strengthened the HIV response, transmission networks can still expand before conventional indicators reveal a clear epidemiological signal [3].

Similar challenges arise with emerging and re-emerging infectious diseases, particularly when transmission occurs rapidly across populations and geographic boundaries. By the time increases are evident in routine case reporting, opportunities for early containment may already have narrowed. The central challenge is therefore to move from surveillance that primarily describes past transmission toward epidemic intelligence that can recognize emerging risk early enough to influence what happens next. Earlier detection can provide valuable time for targeted testing, prevention, clinical preparedness, resource allocation, and outbreak response [4, 5].

1.1. The Digital Transformation of Epidemiology

The information available for infectious-disease surveillance has expanded considerably beyond conventional case reporting. Routine clinical and laboratory data can now be combined with pathogen genomic sequences, population mobility patterns, digital health signals, and other rapidly generated data streams [6]. At the same time, artificial intelligence (AI) and mathematical modelling provide increasingly sophisticated methods for identifying patterns, estimating transmission dynamics, detecting anomalies, and forecasting epidemic trajectories. Genomic epidemiology can reveal changes in pathogen populations and transmission clusters, while mobility data can help characterize the movement and connectivity through which infections may spread [7]. Together, these developments are shifting epidemiology from reliance on isolated surveillance indicators toward a more dynamic view of disease emergence and transmission.

1.2. The Central Challenge

Greater data availability, however, does not automatically produce better early warning. Different data streams measure different aspects of an epidemic, operate at different temporal and spatial scales, and carry distinct sources of bias and uncertainty [8]. A model may identify a statistical pattern without establishing its epidemiological significance, while an early signal may have little practical value if it cannot be validated or linked to a feasible intervention. The central challenge is therefore to convert heterogeneous information into intelligence that can support decisions. This requires progression from Data $\rightarrow$ Detection $\rightarrow$ Prediction $\rightarrow$ Warning $\rightarrow$ Action. Failure at any stage can leave technically sophisticated surveillance systems disconnected from meaningful public-health response.

1.3. Aim of the Review

This narrative review critically examines the evolving role of AI, mathematical modelling, genomic epidemiology, mobility data, digital signals, and routine surveillance in HIV and infectious-disease early warning. It evaluates the complementary strengths and limitations of these approaches, considers the challenges involved in integrating heterogeneous surveillance signals, and identifies important methodological, ethical, and implementation gaps. The review further proposes a multimodal early-warning framework for connecting diverse data sources with epidemiological inference, validated warning, and timely public-health action, and sets out how this framework differs from existing integrated surveillance approaches, how its components interact, how conflicting signals and uncertainty inform warning decisions, which criteria govern progression from prediction to warning and action, and how it could be implemented and prospectively validated in resource-limited settings.

2. From Conventional Surveillance to Digital Epidemic Intelligence

2.1. Conventional Surveillance

Conventional surveillance remains the foundation of infectious-disease intelligence. Case notifications provide information on diagnosed infections and their distribution across populations and locations, while laboratory surveillance adds diagnostic confirmation and information on pathogen characteristics. Sentinel systems can provide more detailed observations from selected populations or healthcare facilities, particularly where universal reporting is impractical. Hospitalization and mortality data capture severe disease and health-system burden, whereas routine clinical records provide information on testing, treatment, comorbidities, and patient outcomes. Together, these sources allow public-health agencies to monitor disease burden, identify changes in incidence, characterize affected populations, and evaluate interventions [1].

Their principal limitation is that most measure events after transmission has already occurred. Reporting delays, incomplete case ascertainment, differences in healthcare access, testing behaviour, and laboratory capacity can create substantial gaps between underlying transmission and the epidemic represented in surveillance databases [9]. Hospitalization and mortality are particularly delayed indicators because they occur relatively late in the disease process. Surveillance data therefore represent an observed portion of transmission rather than a complete or real-time account of epidemic activity.

HIV illustrates both the value and limitations of this model. Routine HIV surveillance extends beyond diagnosis counts to include CD4 and viral-load results, antiretroviral resistance, linkage and retention in care, treatment uptake, and viral suppression [3, 10]. These indicators provide a richer picture of the care continuum and can reveal where prevention and treatment systems are failing. Persistent losses across

this continuum are clinically consequential because delayed diagnosis, treatment interruption, and return to care with advanced disease can contribute to preventable HIV-related morbidity and mortality [11]. Molecular cluster surveillance adds another dimension by identifying genetically related infections and rapidly growing clusters that may indicate active transmission networks [12]. However, interpretation remains dependent on who is tested, diagnosed, sequenced, and successfully linked to surveillance systems. Conventional HIV surveillance is therefore indispensable, but its greatest value for early warning may increasingly come from serving as the epidemiological foundation against which faster and more diverse signals can be interpreted.

2.2. Digital Epidemiology

Digital epidemiology expands surveillance beyond information generated through formal reporting systems. Search-engine activity, social-media content, electronic health records, participatory surveillance platforms, wastewater monitoring, and environmental data can provide signals that emerge before confirmed case counts are fully available [13]. Search patterns may reflect changing public concern or symptom experience, while electronic health data can reveal shifts in clinical presentations, testing, or healthcare utilization. More broadly, the expansion of digitally enabled healthcare environments—including automated monitoring, connected clinical systems, and data-generating biomedical technologies—is increasing the volume and temporal resolution of health information potentially available for surveillance and population-health intelligence [14]. Participatory systems allow individuals to report symptoms directly, and wastewater surveillance can detect changes in pathogen circulation without depending on individual healthcare seeking or diagnosis [15].

The principal advantage of these sources is their potential speed, scale, and frequency. However, digital signals are not direct measures of transmission. Online behaviour may be influenced by media attention, public anxiety, or changes in information seeking, while electronic health data remain shaped by healthcare access and documentation practices [16]. Wastewater signals also depend on sampling coverage and analytical infrastructure. Digital epidemiology is therefore most valuable when these signals are interpreted alongside established epidemiological evidence rather than treated as substitutes for conventional surveillance [17].

2.3. Changing Surveillance Objectives

The expansion of available data has also changed what infectious-disease surveillance is expected to accomplish. Traditional systems were largely designed for retrospective description of disease burden and trends. More frequent data collection enabled monitoring, while increasingly timely analytical systems supported detection of unusual changes. These functions are now being extended toward nowcasting, forecasting, and ultimately early warning [5].

These terms describe different analytical tasks. Monitoring tracks an epidemic as observations accumulate, whereas detection identifies departures from expected patterns. Nowcasting estimates the current epidemiological situation when reporting is incomplete or delayed [18]. Forecasting estimates plausible future outcomes over a specified period [19]. Early warning goes further: it requires that a sufficiently credible signal or forecast be generated early enough to support a meaningful decision or intervention.

The progression can therefore be represented as Retrospective description → Monitoring → Detection → Nowcasting → Forecasting → Early warning, but it should not be interpreted as a simple technological hierarchy. A sophisticated forecasting model does not automatically constitute an effective early-warning system. Its public-health value depends on timeliness, reliability, interpretability, and whether the information can trigger an appropriate response [4]. This distinction shifts the focus from how rapidly data can be analysed to whether surveillance can provide useful intelligence before opportunities for prevention or control are lost. The growing diversity of surveillance data creates opportunities to observe different dimensions of infectious-disease emergence, but no single source provides a complete representation of transmission. As summarized in Table 1, these data streams differ in the signals they capture, their timeliness, population coverage, and their potential contribution to early warning.

3. AI and Mathematical Modelling for Prediction and Early Warning

3.1. Artificial Intelligence and Machine Learning

Artificial intelligence (AI) and machine learning are increasingly used to extract epidemiological signals from data that are too large, complex, or rapidly changing for conventional analytical approaches alone [21]. Their value in infectious-disease surveillance lies particularly in identifying patterns across multiple variables and data streams that may precede recognizable changes in reported disease burden. Rather than serving a single function, AI methods can support different stages of early warning, from detecting unusual activity to estimating where and when transmission risk may increase.

Supervised learning methods use labelled historical data to estimate outcomes such as infection risk, outbreak occurrence, case burden, or geographic hotspots. Unsupervised approaches can identify clusters and unusual patterns without requiring predefined outcomes, making them potentially useful for detecting unexpected changes in surveillance data. Anomaly-detection algorithms similarly seek departures from established baselines that may represent emerging outbreaks or changes in transmission [25]. Deep-learning approaches can model complex nonlinear relationships across high-dimensional datasets, while natural-language processing can extract epidemiologically relevant information from clinical records, public-health reports, news sources, and other text-based data [26].

Time-series methods are particularly relevant to epidemic forecasting because they use temporal patterns in previous observations to estimate current or future disease activity [27]. Graph and network-based approaches provide another important capability by representing relationships among individuals, locations, pathogens, or communities rather than treating observations as independent. This is especially relevant to HIV, where transmission occurs through interconnected networks and where molecular, clinical, behavioural, and geographic information may provide complementary evidence of emerging transmission patterns [28].

These methods have been applied to outbreak detection, hotspot identification, individual or population risk stratification, and forecasting of cases, hospital demand, and other epidemic outcomes [29]. Their attraction is therefore understandable: AI can potentially identify weak signals earlier, integrate heterogeneous information, and capture relationships that simpler models may overlook. Yet these capabilities should not be confused with epidemic understanding. An algorithm may predict where cases will increase without explaining the transmission

Table 1: Major data sources for infectious-disease early warning: signals, strengths, limitations, and potential applications

Data source	Signal captured	Key strengths	Key limitations	Potential early-warning application
Routine case surveillance	Diagnosed and reported infections	Established infrastructure; standardized reporting; population-level trends	Reporting delays; underdiagnosis; dependent on testing and healthcare access	Detecting changes in incidence and geographic or demographic patterns [1]
Laboratory surveillance	Confirmed infections and pathogen characteristics	High diagnostic specificity; supports pathogen characterization	Laboratory and reporting delays; unequal testing capacity	Detecting unusual positivity patterns, variants, resistance, or pathogen emergence [20]
Clinical and electronic health data	Symptoms, diagnoses, testing, treatment, and healthcare utilization	Rich clinical detail; potentially high temporal resolution	Incomplete interoperability; healthcare-access and documentation biases	Identifying changes in syndromic presentations, testing, or healthcare demand [21]
Genomic surveillance	Pathogen genetic variation and relatedness	Identifies variants, clusters, evolutionary change, and transmission patterns	Unequal sequencing coverage; sampling bias; privacy concerns	Detecting emerging variants and rapidly expanding transmission clusters [22]
HIV care-continuum data	Diagnosis, linkage, treatment, viral load, and viral suppression	Connects surveillance with treatment and transmission-related indicators	Delayed or incomplete clinical reporting; missing disengaged populations	Identifying geographic or population-level deterioration in care and viral suppression [3]
Mobility data	Population movement and connectivity	Captures movement patterns relevant to geographic spread	Privacy concerns; proprietary access; population representativeness	Estimating importation risk and potential pathways of spatial dissemination [23]
Search-engine data	Health-related information-seeking behaviour	Rapid, large-scale, and potentially sensitive to emerging public concern	Strongly influenced by media coverage and changing search behaviour	Detecting unusual increases in symptom- or disease-related searches [16]
Social-media data	Public discussion, self-reported symptoms, behaviours, and concerns	High volume and rapid availability	Noise, misinformation, demographic bias, platform-dependent populations	Identifying emerging health concerns or unusual disease-related activity [17]
Participatory surveillance	Directly reported symptoms or health experiences	Rapid collection; can capture illness outside formal healthcare systems	Self-selection and reporting biases; variable participation	Community-level detection of changing symptom patterns [6]
Wastewater surveillance	Population-level pathogen shedding	Does not require individual testing; can detect community circulation	Unequal sampling coverage; interpretation and standardization challenges	Detecting changes in pathogen circulation before clinical indicators rise [15]
Environmental data	Climatic, ecological, vector, and environmental conditions	Captures conditions associated with transmission risk	Associations may vary across pathogens, locations, and time	Anticipating conditions favourable to vector-borne, waterborne, or environmentally mediated transmission [24]

processes responsible for that increase. For early warning, predictive performance is valuable only when the resulting signal can be interpreted within the epidemiological context and used to support a decision [30].

3.2. Mathematical Epidemiological Modelling

Mathematical modelling provides a complementary approach by representing how infections arise, spread, and respond to changes in population behaviour or intervention, while increasingly incorporating real-time data and computational approaches to support responsive infectious-disease decision-making [31]. Compartmental models divide populations according to epidemiological states, such as susceptible, infected, treated, or recovered, and use transitions between these states to examine transmission dynamics [32]. For HIV, similar structures can represent diagnosis, treatment initiation, viral suppression, treatment interruption, and other stages relevant to transmission and care [33].

More detailed approaches relax assumptions of homogeneous populations. Network models represent connections through which transmission can occur, while spatial models examine geographic variation and movement between locations [28, 34]. Agent-based models simulate individuals with different characteristics and behaviours, allowing transmission to emerge from interactions among heterogeneous populations. Stochastic models incorporate random variation, which becomes particularly important when case numbers are small or transmission events are unpredictable. Bayesian approaches provide a formal means of combining prior knowledge with emerging observations while quantifying uncertainty.

These models also support nowcasting and forecasting. Nowcasting attempts to estimate the present state of an epidemic when current observations are incomplete or delayed, whereas forecasting estimates its likely future trajectory over a defined period [35]. Their value for early warning lies not only in projecting case numbers but also in examining how transmission may change under alternative assumptions, interventions, or patterns of population behaviour. Mathematical models therefore provide a bridge between observed surveillance data and the underlying epidemic processes that cannot be measured directly.

3.3. Mechanistic Versus Data-Driven Prediction

Mechanistic epidemiological models and machine-learning approaches differ fundamentally in how they generate predictions. Mechanistic models begin with assumptions about transmission processes and encode these relationships mathematically. Their structure can make it possible to examine why an epidemic trajectory changes, how particular parameters influence transmission, and how interventions might alter future outcomes. This interpretability is particularly valuable when public-health decisions require more than an estimate of what will happen [4].

Machine-learning models are generally less dependent on explicitly specifying transmission mechanisms. Instead, they learn predictive relationships from observed data and can accommodate large numbers of variables, nonlinear interactions, and complex data types. This flexibility may improve prediction where relationships are difficult to specify mechanistically, but it can also produce models whose predictions are difficult to explain or unstable when conditions differ from those represented in the training data [30].

The distinction should not be reduced to a competition between traditional modelling and AI. Mechanistic models can be transparent yet poorly specified, while highly flexible machine-learning models can achieve strong predictive performance without capturing the processes driving transmission. The appropriate approach therefore depends on the question being asked. For early warning, the strongest systems may require both: sufficient flexibility to recognize emerging patterns and sufficient epidemiological structure to determine whether those patterns are credible, interpretable, and relevant to intervention.

3.4. Hybrid AI–Epidemiological Models

The limitations of purely mechanistic and purely data-driven approaches have encouraged growing interest in hybrid models that combine epidemiological knowledge with machine learning. Rather than asking AI to infer epidemic dynamics entirely from historical observations, mechanistic structure can constrain learning to relationships that are epidemiologically plausible. Conversely, machine learning can assist conventional models by estimating difficult parameters, identifying nonlinear relationships, processing high-dimensional inputs, and updating predictions as new surveillance data become available [36].

Such integration is particularly relevant to multimodal surveillance. Mobility, genomic, clinical, environmental, and routine epidemiological data can be incorporated into models that retain an explicit representation of transmission while adapting to changing observations. Hybrid approaches may therefore provide a useful compromise between predictive flexibility and epidemiological interpretability. Their value, however, depends on whether integration produces meaningful improvements over simpler approaches rather than merely increasing model complexity [37].

3.5. Critical Limitations

Predictive models remain vulnerable to limitations that can substantially weaken their early-warning value. Overfitting can produce impressive performance on historical data that disappears when a model encounters new populations or epidemic conditions. Data leakage can further inflate apparent accuracy when information unavailable at the intended time of prediction inadvertently enters model development [38]. Poor external validation means that many models remain insufficiently tested beyond the settings in which they were created [39].

Infectious-disease prediction also operates in environments that continually change. New variants, interventions, population behaviour, testing practices, immunity, mobility, and healthcare access can alter relationships learned from previous data. This concept drift can rapidly reduce model performance [40]. Calibration is equally important: a model that ranks high-risk locations correctly may still systematically overestimate or underestimate the probability of an outbreak [41]. Uncertainty must therefore be quantified and communicated rather than concealed behind single-point predictions.

Interpretability and transportability create additional challenges. Public-health practitioners need to understand enough about a model's predictions to judge when action is warranted, while models developed in data-rich settings may perform poorly where surveillance infrastructure, population structure, or transmission patterns differ [42]. Ultimately, predictive accuracy is an intermediate outcome rather

than the endpoint of epidemic intelligence. The more consequential question is whether improved prediction provides sufficient lead time, confidence, and operational relevance to produce earlier and better public-health decisions.

4. Genomics, Mobility, and Multimodal Surveillance

4.1. Genomic Epidemiology

Genomic epidemiology has expanded infectious-disease surveillance by allowing pathogen evolution and transmission patterns to be examined alongside conventional epidemiological data. Sequencing identifies genetic variation, while phylogenetic and phylodynamic methods can characterize relationships among pathogens and changes in transmission over time. These approaches support variant detection, outbreak investigation, molecular cluster identification, and transmission-network inference [43]. Their value was particularly evident during COVID-19 and has also been demonstrated in influenza, mpox, tuberculosis, and antimicrobial-resistance surveillance [22].

HIV illustrates both the value and complexity of this approach. Sequences generated through routine testing can be compared to identify genetically related infections and rapidly growing molecular clusters that may indicate active transmission networks [12]. This information can help direct epidemiological investigation and prevention resources toward populations experiencing increased transmission. However, genetic similarity does not establish direct person-to-person transmission, and observed clusters are shaped by who is tested, diagnosed, sequenced, and represented in surveillance systems. Molecular evidence therefore requires interpretation alongside clinical, geographic, temporal, and behavioural information.

Genomic surveillance also faces important practical and ethical limitations. Delayed sequencing can reduce its early-warning value, while incomplete and geographically unequal sampling may create misleading pictures of pathogen circulation. Limited sequencing capacity can leave entire populations or regions poorly represented [44]. For HIV, molecular surveillance additionally raises concerns about privacy, stigma, confidentiality, and potential misuse of transmission-related information [45]. Genomics is therefore most useful not as an independent representation of an epidemic, but as a complementary biological signal that can strengthen early warning when interpreted alongside other surveillance evidence.

4.2. Mobility and Spatial Intelligence

Human movement shapes the geographic distribution of infectious diseases by connecting populations that would otherwise experience relatively separate transmission dynamics. Mobile-device data, transportation networks, migration patterns, commuting flows, and air-travel data can provide information on the intensity and direction of these connections. When combined with spatial epidemiological methods, mobility data can help identify locations vulnerable to disease importation, estimate pathways of geographic diffusion, and improve understanding of how local outbreaks may become regional or international threats [34, 46].

The epidemiological meaning of mobility, however, varies substantially across infections. For rapidly transmitted respiratory pathogens, short-term movement and travel may contribute directly to geographic spread. For HIV, mobility interacts with longer-term migration, sexual and social networks, healthcare access, and patterns of prevention and treatment [47]. A critical distinction is therefore necessary: movement is not equivalent to transmission. Mobility data indicate opportunities for epidemiological connectivity but rarely establish whether infectious contact occurred. Their interpretation is also constrained by unequal mobile-device use, proprietary datasets, privacy concerns, and the underrepresentation of populations whose movement is poorly captured digitally [23].

4.3. Why Individual Data Streams Are Insufficient

No individual surveillance source captures the complete state of an epidemic. Routine surveillance provides the strongest account of recognized disease burden but is constrained by diagnosis and reporting delays. Genomic data reveal pathogen evolution and relationships among infections but depend on who is sampled and sequenced. Mobility data identify potential connections between populations without demonstrating transmission, while digital signals may detect changes in health-seeking behaviour or population activity without establishing whether those changes represent actual disease occurrence.

Analytical technologies address some of these limitations but introduce others. AI can identify complex patterns across large datasets, yet those patterns may lack epidemiological meaning or fail when conditions change. Mathematical models can infer unobserved transmission processes and explore possible epidemic trajectories, but their conclusions depend on model structure, assumptions, and the quality of input data. These differences make the data streams complementary rather than interchangeable. The central opportunity for early warning therefore lies not in identifying a single superior source, but in determining how independent signals can be combined so that the weaknesses of one source are tested, contextualized, or partially compensated for by the strengths of another [8].

4.4. Multimodal Integration

Multimodal surveillance seeks to combine complementary data streams rather than relying on any single source to represent epidemic activity. Data fusion can integrate clinical, genomic, mobility, environmental, and digital information within a common analytical system, while triangulation asks whether independent sources point toward the same epidemiological change. Agreement across different signals can strengthen confidence in an emerging warning, whereas disagreement may reveal reporting delays, sampling bias, model error, or changes that require further investigation [48].

Effective integration, however, requires more than placing multiple datasets into the same model. Differences in data formats, geographic resolution, collection frequency, population coverage, and institutional ownership create substantial interoperability challenges. Dynamic data assimilation offers one way forward by allowing models to incorporate new observations as they become available and continuously update estimates of epidemic conditions and future risk [31, 35]. Such systems can potentially adapt more rapidly than models based on periodically updated datasets.

The objective of next-generation surveillance should therefore be integration rather than technological substitution. AI should not

simply replace epidemiological modelling, genomics should not replace case surveillance, and digital signals should not displace established public-health data. Their greater value lies in combination, where independent forms of evidence can reinforce, challenge, and contextualize one another. Multimodal surveillance consequently shifts the question from which technology is best to which combination of signals provides the earliest credible evidence of epidemiological change and the clearest basis for public-health action.

5. From Prediction to Public-Health Action

5.1. Detection Is Not Prediction

Early detection and prediction serve different epidemiological purposes. Detection identifies a change that appears unusual relative to an expected baseline, such as an increase in diagnoses, a rapidly expanding molecular cluster, an unexpected wastewater signal, or an abnormal pattern in digital data. Such signals can indicate that epidemic conditions are changing, but they do not by themselves establish what will happen next. A detected increase may persist, accelerate, stabilize, or disappear depending on transmission dynamics, population behaviour, interventions, and the reliability of the underlying data [20].

Prediction requires an additional inferential step. It uses available evidence to estimate a future epidemiological state, such as the probability of an outbreak, expected case burden, geographic spread, or changes in transmission intensity. This distinction matters because surveillance systems can become increasingly sensitive to unusual signals without becoming better at anticipating consequential events. Greater sensitivity may instead generate more false alerts or identify transient fluctuations with little public-health significance [25].

For early-warning systems, detection should therefore be treated as the beginning of an analytical process rather than its endpoint. An unusual signal must be evaluated against other evidence, interpreted within its epidemiological context, and assessed for its capacity to indicate future risk. The central question is not simply whether a system can detect change earlier, but whether the detected change contains reliable information about what is likely to follow.

5.2. Prediction Is Not Early Warning

Prediction extends surveillance from identifying change to estimating what may happen next, but predictive capability alone does not constitute early warning. A model may accurately forecast an increase in infections yet provide the information too late for meaningful intervention. Similarly, a prediction may have limited operational value if it cannot identify where risk is concentrated, which populations are affected, or how certain the estimate is. Effective early warning therefore requires more than statistical accuracy. It requires sufficient lead time, reliability, specificity, and interpretability for decision-makers to determine whether and how to respond [4].

This distinction is especially important when false alarms carry consequences. Repeated warnings that do not correspond to meaningful epidemiological events can consume limited resources and reduce confidence in surveillance systems. Conversely, overly conservative thresholds may fail to identify threats until intervention opportunities have narrowed. Early warning therefore represents a decision-oriented function: prediction becomes warning when information about future risk is sufficiently credible and timely to justify consideration of action.

5.3. Warning Is Not Action

Even a credible warning has little public-health value if it does not lead to an appropriate response. The pathway from surveillance to improved outcomes can be represented as Data → Signal → Detection → Prediction → Warning → Decision → Intervention → Outcome. Each stage represents a distinct transition at which information can be lost, delayed, misinterpreted, or disconnected from operational responsibility.

A warning must therefore be linked to decisions about what should happen, when action should begin, who is responsible, and which populations or locations should be prioritized. Depending on the disease, responses may include intensified testing, targeted prevention, treatment outreach, vaccination, genomic investigation, community engagement, or redistribution of healthcare resources; in HIV, rapidly detected transmission clusters may similarly trigger targeted investigation and prevention responses within affected networks [49]. The performance of an early-warning system should consequently not be judged solely by whether it predicts an event correctly. Its ultimate value lies in whether the warning arrives early enough to influence decisions, whether those decisions produce feasible interventions, and whether intervention measurably improves epidemiological or health outcomes [5].

5.4. Why Promising Systems Fail

Many early-warning systems perform well during model development but struggle when introduced into routine public-health practice. One reason is fragmentation. Clinical, laboratory, genomic, mobility, and administrative data are often maintained by different institutions, collected at different frequencies, and stored in incompatible formats. Poor interoperability can delay data exchange or prevent potentially complementary signals from being analysed together. Even when integration is technically possible, unclear institutional responsibility may leave uncertainty about who should verify an alert, authorize a response, or coordinate action across jurisdictions [24].

False alerts create another challenge. Highly sensitive systems may identify changes that are statistically unusual but epidemiologically unimportant, while intervention thresholds are often poorly defined. Without clear criteria for when predicted risk warrants action, public-health agencies may either respond unnecessarily or delay until conventional evidence confirms what an early-warning system was intended to identify sooner. Limited external validation compounds this problem because performance demonstrated in one population, pathogen, or epidemic period may not persist elsewhere [42].

Implementation also depends on people and workflows, not algorithms alone. Public-health agencies require personnel capable of interpreting model outputs, evaluating uncertainty, investigating signals, and translating warnings into interventions. Systems that operate outside established surveillance and decision-making processes can create additional work without changing practice. The failure of promising technologies therefore often reflects a mismatch between analytical capability and the institutional capacity required to act on it.

5.5. How Early-Warning Systems Should Be Evaluated

Evaluation must consequently extend beyond conventional measures of predictive discrimination such as accuracy or the area under the receiver operating characteristic curve (AUROC). These metrics indicate whether a model distinguishes outcomes under specified conditions, but they provide limited information about whether it functions effectively as an early-warning system. Calibration is necessary to determine whether predicted risks correspond to observed risks, while external validation establishes whether performance persists across populations, locations, and epidemic conditions [39, 41].

Lead time is particularly important because a correct prediction that arrives after practical response options have narrowed has little early-warning value. Interpretability affects whether decision-makers can understand and appropriately use an alert, while actionability concerns whether the warning is linked to a realistic intervention. Evaluation should also examine equity, including whether performance differs systematically across populations or regions because of unequal data availability [50]. Ultimately, outcome impact provides the strongest test: whether using the system leads to earlier intervention, more effective allocation of resources, reduced transmission, or improved health outcomes. Early-warning systems should therefore be assessed as public-health interventions rather than solely as predictive algorithms [51]. Because predictive performance alone does not establish public-health value, early-warning systems require evaluation across both technical and operational dimensions. Table 2 summarizes the principal criteria for determining whether a predictive system can progress from accurate forecasting to useful and equitable public-health action.

Table 2: From predictive accuracy to public-health utility: criteria for evaluating infectious-disease early-warning systems

Evaluation criterion	What it assesses	Why it matters for early warning
Accuracy	Agreement between predictions and observed outcomes	Establishes whether the system can correctly identify or predict epidemiological events [19]
Calibration	Agreement between predicted probabilities and observed risks	Prevents systematic overestimation or underestimation of epidemic risk [41]
Lead time	Time between the warning and the predicted event	Determines whether sufficient time exists to investigate and intervene [48]
External validity	Performance across different populations, locations, periods, and epidemic conditions	Establishes whether the system remains reliable beyond its development setting [42]
Interpretability	Extent to which predictions and their drivers can be understood	Supports appropriate interpretation of alerts and strengthens decision-making [30]
Actionability	Whether an alert can be linked to a feasible public-health response	Distinguishes informative predictions from warnings that can change practice [5]
Equity	Consistency of performance and benefit across populations and settings	Identifies whether data gaps or model bias systematically disadvantage particular groups [50]
Outcome impact	Effect of using the system on interventions, transmission, morbidity, mortality, or other relevant outcomes	Determines whether predictive performance translates into measurable public-health benefit [4]

6. Ethics, Equity, and Governance

6.1. Who Is Represented in Digital Surveillance?

Digital surveillance does not observe populations uniformly. The data available for early-warning systems are shaped by access to healthcare, diagnostic testing, internet connectivity, mobile devices, sequencing infrastructure, and participation in formal surveillance systems, with these limitations becoming particularly consequential in underserved communities where conventional HIV surveillance may incompletely capture epidemiological risk [52]. Populations with frequent contact with healthcare services may generate extensive clinical and laboratory data, while people facing financial, geographic, or social barriers to care may remain poorly represented. Similar inequalities affect digital data: mobile-phone and internet-derived signals may systematically underrepresent individuals with limited connectivity or different patterns of technology use [23].

Geographic inequalities create an additional problem. Sequencing and advanced surveillance capacity remain unevenly distributed, both within and between countries. Areas generating fewer diagnoses, sequences, or digital observations may consequently appear to have lower epidemiological activity even when transmission is substantial. This creates a fundamental interpretive problem: an absence of digital or surveillance signals may reflect an absence of surveillance capacity rather than an absence of disease transmission. Early-warning systems that ignore this distinction risk reproducing existing inequalities in where threats are detected and where resources are subsequently directed [44].

6.2. HIV-Specific Concerns

These concerns are particularly sensitive in HIV surveillance because the information collected may reveal details about health status, sexual or social networks, and potentially stigmatized populations. Molecular surveillance illustrates the tension clearly. Genetic relationships among HIV sequences can help identify rapidly growing clusters, but they can also create perceptions that surveillance reconstructs individual

transmission relationships. In settings where HIV exposure or transmission may have legal consequences, such information raises additional concerns about confidentiality and potential misuse [45].

Consent and community trust therefore cannot be treated as secondary implementation issues. Even technically secure systems may undermine surveillance if affected communities do not understand how their data are used or believe that public-health information could expose them to stigma, discrimination, or legal harm. Governance must clearly define permissible uses, access restrictions, data retention, and safeguards against inappropriate inference [53].

6.3. Algorithmic and Mobility-Data Governance

AI and mobility-based surveillance introduce further governance challenges. Highly granular mobility or linked health datasets may permit re-identification even after direct identifiers have been removed [54]. Many mobility datasets are also controlled by private companies, creating questions about ownership, access, commercial interests, and accountability [55]. Algorithmic systems can compound these problems when predictions are generated using datasets whose biases, exclusions, or processing decisions are poorly documented.

Transparency should therefore extend beyond explaining model architecture. Public-health agencies should be able to establish where data originate, which populations are missing, how predictions are validated, and who is accountable when model outputs influence decisions. These requirements are especially important in low- and middle-income countries, where limited digital, laboratory, and genomic infrastructure can create systematic surveillance blind spots [44]. Expanding digital epidemiology without addressing these structural inequalities could produce increasingly sophisticated early-warning systems while widening the gap between populations that are epidemiologically visible and those that remain unseen.

7. An Integrated Framework and Research Agenda for Next-Generation Early Warning

7.1. Proposed Integrated Digital Epidemiology Early-Warning Framework

The evidence considered in this review suggests that the central weakness of current early-warning approaches is not necessarily a shortage of data or analytical methods, but the absence of a coherent pathway connecting observation to public-health action. Routine surveillance, clinical data, genomics, mobility information, digital signals, AI, and mathematical models are often developed and evaluated as separate capabilities. Yet an epidemic does not present itself through a single data stream. Changes in transmission may first appear as a weak signal in one source and become credible only when interpreted alongside independent epidemiological evidence. This review therefore proposes an Integrated Digital Epidemiology Early-Warning Framework that connects heterogeneous data, analytical methods, validation, public-health action, and continuous learning within a single system Figure 1.

The framework begins with complementary data inputs, including routine surveillance, clinical records, genomic information, mobility patterns, and digital or environmental signals. These sources pass through an integration layer responsible for harmonization, interoperability, temporal and geographic alignment, and data-quality assessment. An analytical engine combining AI, mathematical modelling, and genomic epidemiology then supports detection, epidemiological inference, nowcasting, forecasting, and risk stratification. Importantly, integration does not mean that every available data stream should be included. Data sources should contribute because they provide epidemiologically relevant and incremental information, not simply because they are technologically available [8].

The framework then connects analysis to a broader prediction-to-action process: Observe $\rightarrow$ Detect $\rightarrow$ Infer $\rightarrow$ Predict $\rightarrow$ Validate $\rightarrow$ Warn $\rightarrow$ Act $\rightarrow$ Evaluate. This sequence makes an important distinction between generating a prediction and generating a warning that warrants public-health attention. Detected signals must first be interpreted epidemiologically, while predictions should be triangulated against independent evidence, assessed for uncertainty, and examined for plausible alternative explanations. Only when the resulting evidence is sufficiently credible, timely, and specific should it progress to warning and consideration of action. Depending on the threat, action may include targeted prevention, intensified testing, treatment outreach, resource allocation, genomic investigation, or outbreak response. Evaluation then determines whether the warning was accurate, whether it altered decision-making, and whether the resulting intervention improved relevant epidemiological or health outcomes [4].

The framework integrates routine surveillance, clinical, genomic, mobility, and digital or environmental data through harmonization and quality control; combines AI, mathematical modelling, and genomic epidemiology to generate epidemic intelligence; and subjects emerging predictions to validation before warning and public-health action. Evaluation of decisions and outcomes provides a feedback loop for continuous refinement of surveillance inputs, analytical models, and warning thresholds. The roles and interactions of each component are detailed in Table 3, and illustrative criteria for progressing from signal to warning and action are given in Table 4.

The framework is deliberately cyclical rather than a one-directional pipeline. Outcomes generated after intervention become new evidence for surveillance and model development. Successful warnings can identify useful combinations of indicators, whereas false alarms, missed events, and ineffective responses should prompt reassessment of data sources, model assumptions, decision thresholds, and intervention strategies. This learning function is essential because pathogens evolve, population behaviour changes, surveillance systems improve or deteriorate, and relationships learned from historical data may not remain stable [40]. The proposed framework therefore shifts the objective of digital epidemiology away from producing increasingly sophisticated predictions as an endpoint. Its purpose is to build an adaptive system in which heterogeneous signals are integrated, interpreted, validated, translated into proportionate action, and continuously evaluated against epidemiological reality.

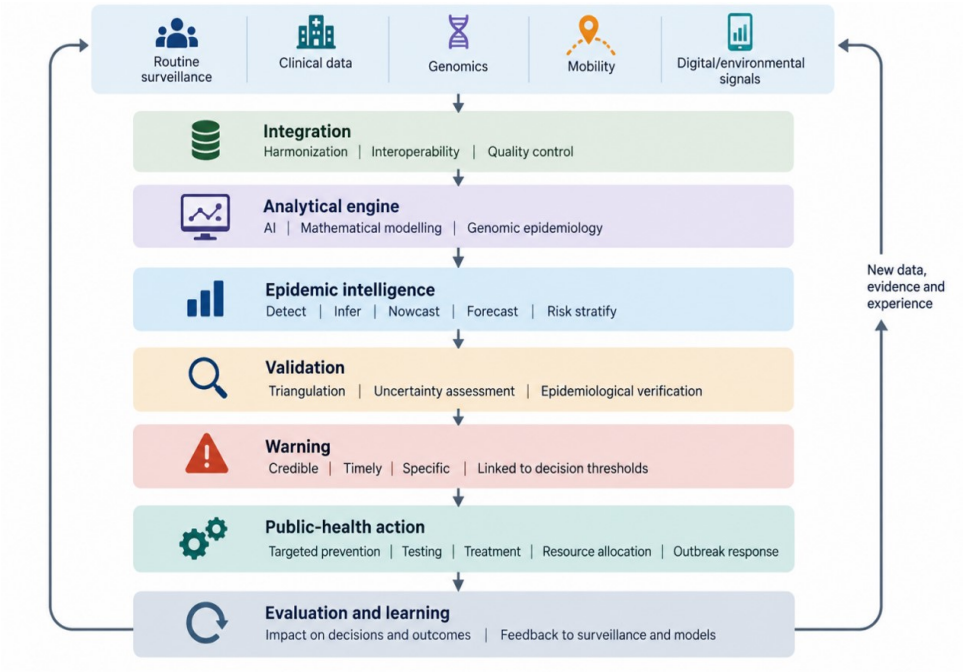


Figure 1: Integrated Digital Epidemiology Early-Warning Framework

7.2. Novelty Relative to Existing Early-Warning Approaches

Integrated surveillance and early-warning systems are not new. Indicator-based and event-based surveillance under the International Health Regulations, as set out in the World Health Organization's early warning and response guidance, combines routine reporting with the detection and verification of unstructured signals [56]. Integrated Disease Surveillance and Response (IDSR) has, for more than two decades, sought to consolidate disease-specific reporting systems in sub-Saharan Africa [57]. Digital disease-detection platforms such as HealthMap aggregate online and media reports [13, 26], multi-stream approaches have combined several digital traces to anticipate COVID-19 activity [48], and collaborative forecasting initiatives combine ensembles of models to produce probabilistic forecasts [19, 58]. For HIV, cluster detection and response programmes use routinely generated molecular data to prioritize rapidly growing clusters for public-health action [12, 59].

The proposed framework does not replace these systems; it builds on them. Its contribution lies in four features that existing approaches usually treat separately or leave implicit. First, it places an explicit validation stage between prediction and warning, so that model outputs become warnings only after triangulation, uncertainty assessment, and epidemiological verification (Sections 7.4 and 7.5). Existing systems typically either verify signals without a forecasting component [56] or produce forecasts without formal rules linking them to action [19]. Second, it combines mechanistic modelling, machine learning, and genomic epidemiology within one analytical engine and treats disagreement between data streams as information to be investigated rather than noise to be averaged away. Third, it links warnings to tiered, pre-specified decision criteria with named responsibilities and response options, addressing the poorly defined intervention thresholds identified in Section 5.4. Fourth, it closes the loop: warning outcomes, false alarms, missed events, and differences in performance across populations are fed back to recalibrate data inputs, models, and thresholds. Applied to HIV, the framework extends cluster detection and response by combining molecular signals with care-continuum, recent-infection, and programme data, and by building in the equity and governance safeguards discussed in Section 6.

7.3. Roles and Interactions of Framework Components

Figure 1 presents the framework as a sequence of layers, but each layer has a defined role, defined outputs, and specific interactions with the other layers Table 3. The integration layer does more than pass data forward. It attaches quality metadata to each stream, such as completeness, reporting delay, population coverage, and known changes in testing or sampling, and these metadata are used later to weight evidence and to interpret discordance. The analytical engine produces two kinds of output: signals, which are departures from expected baselines, and probabilistic estimates of current and future epidemic states with stated uncertainty. The validation layer acts as a gate. It compares these outputs across independent sources and returns one of three results: escalate to warning, maintain enhanced monitoring, or reject the signal as an artefact. Requests for further information, such as targeted sequencing or a data-quality audit, flow back from validation to the integration and analytical layers. The warning layer translates validated evidence into a graded alert level linked to pre-specified actions (Section 7.5). The action layer records which decisions were taken, by whom, and when, and the evaluation layer compares warnings, decisions, and outcomes to update data priorities, model parameters, and thresholds.

Table 3: Roles, outputs, and interactions of the components of the Integrated Digital Epidemiology Early-Warning Framework

Component	Primary role	Main outputs	Key interactions
Data inputs	Provide complementary observations of disease occurrence, transmission, pathogen characteristics, connectivity, and context	Routine, clinical, genomic, mobility, and digital or environmental data with dates and geographic units	Prioritized according to evaluation feedback; additional sampling (e.g., targeted sequencing) may be requested by validation
Integration	Harmonize, link, and align data in time and space; assess data quality	Analysis-ready datasets with quality metadata (completeness, delay, coverage, changes in testing or sampling)	Quality metadata used by the analytical engine to weight streams and by validation to interpret discordance
Analytical engine	Apply AI, mathematical models, and genomic epidemiology to detect anomalies, infer transmission, nowcast, forecast, and stratify risk	Signals; probabilistic nowcasts and forecasts with uncertainty intervals; cluster and risk rankings	Outputs passed to validation; model weights and parameters updated through evaluation
Validation	Triangulate across independent sources, quantify uncertainty, exclude artefacts, and verify epidemiologically	Decision to escalate, maintain enhanced monitoring, or reject; evidence summary with confidence rating	Requests additional data or reanalysis from integration and analytics; forwards validated evidence to warning
Warning	Convert validated evidence into graded alerts using pre-agreed criteria	Alert level, affected population and area, expected lead time, confidence statement, and response options	Applies thresholds agreed with decision-makers Table 4; thresholds revised through evaluation
Public-health action	Decide on and implement proportionate responses	Documented decisions, responsible units, timing, and interventions delivered	Reports decisions and timing to evaluation; generates new data (e.g., test results) for the inputs layer
Evaluation and learning	Assess accuracy, calibration, lead time, equity, actionability, and outcome impact Table 2	Performance reports; revised data priorities, models, and thresholds	Feeds back to all upstream components

7.4. Reconciling Conflicting Signals and Handling Uncertainty

Data streams will often disagree. Wastewater or digital signals may rise while case notifications remain stable, a molecular cluster may grow while aggregate diagnoses fall, and mobility may increase without any change in transmission. The framework treats such disagreement as an expected property of multimodal surveillance and reconciles it in four steps. First, each signal is assessed against its own quality metadata and known biases, so that changes caused by altered testing volume, reporting backlogs, media attention, or sampling changes can be identified before the signal is interpreted epidemiologically [9, 16]. Second, signals are aligned according to their expected lead–lag relationships. Wastewater, syndromic, and digital indicators are expected to change before confirmed diagnoses, and for HIV, recent-infection and molecular data reflect recent transmission more closely than new diagnoses do [15, 60]. Apparent disagreement may therefore reflect timing rather than contradiction. Third, the remaining evidence is combined formally rather than by informal judgement. Options include Bayesian evidence synthesis and data assimilation, in which each stream enters through its own observation model with its own error structure [35], and ensemble methods that weight models or streams according to their past out-of-sample performance [58]. Fourth, discordance that remains after these steps is not averaged away. It triggers targeted verification, such as field investigation, additional testing, or targeted sequencing, because unexplained disagreement may indicate an emerging change in a population that one data stream observes poorly.

Uncertainty enters warning decisions directly. Outputs are expressed as predictive distributions, or as the probability that a defined threshold will be exceeded within a defined horizon, rather than as single-point predictions, and these probabilities must be well calibrated [41, 51]. The appropriate response depends on both the probability of an event and the consequences of error. When the cost of a missed event is high relative to the cost of a false alarm, as for a rapidly growing HIV cluster in a population with low viral suppression, a lower probability may justify investigation; when a response is costly or potentially harmful, greater certainty is required [4]. High uncertainty therefore does not automatically prevent action. Instead, it changes the type of action, favouring low-cost and reversible steps such as verification, enhanced monitoring, or targeted testing over large-scale deployment of resources. Every warning should state its confidence level, its main sources of uncertainty, and the evidence that would confirm or refute it.

7.5. Decision Criteria for Progressing from Prediction to Warning and Action

To make the transition from prediction to warning and action transparent, the framework uses tiered alert levels with explicit entry criteria Table 4. The criteria combine three elements: statistical evidence of change, such as exceedance of a baseline prediction interval [25]; corroboration by independent evidence; and a calibrated probability that a pre-defined public-health threshold will be exceeded with enough lead time to intervene. The numerical values in Table 4 are illustrative. They should be agreed before deployment by analysts,

decision-makers, and affected communities, taking into account the relative costs of false alarms and missed events, the lead time each intervention requires, and the available response capacity, and they should then be recalibrated through the evaluation loop. The timelines shown assume a weekly reporting cycle and should be shortened for rapidly spreading pathogens. For HIV, an established operational example is the prioritization of molecular clusters showing rapid growth, such as five or more diagnoses within 12 months at a 0.5% genetic-distance threshold [12, 59]. Within the framework, such a cluster would enter at Level 2 and progress to Level 3 when corroborated by, for example, recent-infection testing results, low viral suppression among cluster members, or a concurrent increase in diagnoses in the same network or area.

Table 4: Illustrative tiered criteria for progressing from signal to warning and public-health action

Level	Entry criteria (illustrative)	Required validation	Response and responsibility	Indicative timeline
0: Routine monitoring	No stream exceeds its expected baseline; forecasts within the expected range	Routine data-quality checks	Scheduled surveillance and reporting (surveillance unit)	Ongoing
1: Signal	One stream exceeds its baseline (e.g., observed value above the upper 95% prediction limit) or a model flags an anomaly	Exclude artefacts (testing volume, reporting delay, sampling change)	Enhanced monitoring and data-quality review (surveillance analyst)	Review within 2-3 days
2: Alert	Signal persists or is corroborated by at least one independent stream; or an HIV molecular cluster meets priority growth criteria	Triangulation across sources; epidemiological review; uncertainty assessment	Investigation; targeted testing or sequencing; preparation of response options (epidemiology team)	Investigation within 1 week
3: Warning	Validated evidence and a calibrated probability above a pre-agreed level (e.g., ≥ 0.7) that an action threshold will be exceeded within the forecast horizon, with lead time at least equal to the time needed to implement the response	Independent verification completed; confidence and main uncertainties documented	Formal warning to decision-makers; pre-specified proportionate interventions (programme managers)	Decision within 1-2 weeks
4: Response	Warning confirmed by outcome data, or risk escalates	Continued monitoring of response effectiveness	Full response, cross-jurisdictional coordination, and resource reallocation (public-health authority)	As per response plan; evaluation after closure

7.6. Implementation and Prospective Validation in Resource-Limited Settings

The framework is not intended to be implemented in full from the outset. In resource-limited settings, a staged approach is more realistic. The first stage builds on infrastructure that already exists: aggregate routine reporting through national health information systems such as DHIS2 and IDSR structures [57], together with HIV programme data on testing yield, linkage, antiretroviral therapy initiation, retention, and viral suppression [3, 10]. At this stage, transparent and computationally light methods, such as baseline-exceedance algorithms and simple nowcasting to correct for reporting delays, are preferable to complex machine-learning models, which need larger and more stable training data [9, 25]. The second stage adds HIV-specific signals that are closer to recent transmission. These include recent-infection testing integrated into routine HIV testing services, which has been piloted within programme settings in Kenya and Zimbabwe [60], and molecular cluster analysis of pol sequences already generated for drug-resistance testing, supported by national or regional sequencing hubs where local capacity is limited [44]. Further streams, such as mobility or digital data, should be added only when they demonstrate incremental value. Governance arrangements, including data-protection rules, community advisory mechanisms, and clear limits on the use of molecular data, should be agreed before molecular or linked data are used [45], and staff at every stage need training in interpreting probabilistic outputs.

Prospective validation should also proceed in stages. In a silent or shadow phase, the system runs alongside routine surveillance for a pre-specified period: warnings are generated and time-stamped but not acted upon, and they are later compared with events identified by routine surveillance. This allows sensitivity, false-alarm rate, lead time, and calibration to be estimated without influencing practice, and it avoids the data leakage that can inflate retrospective performance [38]. The evaluation protocol, outcome definitions, and alert thresholds should be registered before this phase begins. In a second phase, the system is linked to decision-making and evaluated as a public-health intervention. Where resources allow, a stepped-wedge cluster randomized design, in which districts or facilities adopt the system in random order, offers a practical way to compare periods with and without the system when it is intended eventually to be rolled out everywhere [61]. For HIV, outcomes should include the time from first signal to response, the number of new diagnoses and linkages to care achieved through cluster-directed or area-directed testing, changes in viral suppression within affected networks, and, over longer periods, the proportion of recent infections or modelled incidence. Performance should be reported separately by population group and area so that the equity criterion in Table 2 can be assessed.

7.7. Priority Research Questions

The next phase of research should move beyond demonstrating that additional data or more complex models can improve retrospective predictive performance. A more consequential question is whether integrated systems identify epidemiologically important changes earlier

than well-functioning routine surveillance and whether the additional lead time is sufficient to alter public-health decisions. This requires direct comparison between multimodal systems and existing surveillance practice rather than evaluation against historical data alone [19]. Research should also determine which combinations of genomic, mobility, clinical, digital, and routine surveillance data provide meaningful incremental information. More data should not be assumed to be better; additional streams should justify their financial, computational, and governance costs by improving timeliness, reliability, or actionability.

A second priority is to establish the relationship between prediction and outcomes. The field needs evidence on how much lead time is actually required for different interventions and whether improved forecasts lead to earlier testing, prevention, treatment, resource deployment, or measurable reductions in transmission and morbidity. This also requires explicit consideration of error. Thresholds that maximize sensitivity may generate repeated false alarms, while conservative systems may miss the period in which intervention would have been most effective. Research should therefore examine acceptable trade-offs between missed events and unnecessary responses under different epidemiological conditions. Equally important is model robustness. Systems developed during one epidemic phase may deteriorate when new variants emerge, population behaviour changes, testing declines, interventions expand, or relationships between predictors and transmission shift [16]. Generalizability across pathogens, populations, geographic settings, and time should be demonstrated rather than assumed.

Finally, technical development must be matched by research on governance and implementation. For HIV, prospective work should examine how genomic early warning can be used without undermining privacy, community trust, or protections against inappropriate inference and legal misuse [45]. Low-resource settings require particular attention because weak diagnostic, genomic, and digital infrastructure can simultaneously reduce surveillance visibility and limit access to the technologies intended to improve it. International collaboration and cross-sector partnerships may help strengthen surveillance capacity, mobilize technical and financial resources, and support coordinated infectious-disease prevention and control in resource-constrained settings [62]. Future studies should therefore evaluate whether integrated systems reduce or reproduce existing surveillance inequalities. Most importantly, promising systems should move from retrospective validation toward prospective evaluation in real public-health settings, where their performance can be judged by whether warnings arrive earlier, trigger appropriate decisions, remain equitable across populations, and ultimately improve epidemiological outcomes [42].

8. Conclusion

Digital epidemiology is changing what can be observed, inferred, and anticipated during infectious-disease transmission. AI, mathematical modelling, genomic epidemiology, mobility data, and routine surveillance each provide a different view of epidemic dynamics. Their strengths are therefore complementary: routine surveillance establishes recognized disease burden, genomics reveals pathogen evolution and transmission relationships, mobility describes population connectivity, AI identifies complex patterns, and mathematical models help infer processes that cannot be observed directly. None, however, provides a complete representation of an evolving epidemic.

The central challenge is consequently not a lack of sophisticated analytical tools. It is the persistent gap between generating signals and converting them into intelligence that can support decisions. Prediction has limited value when it cannot be validated, interpreted, delivered with sufficient lead time, or connected to a feasible intervention. Future progress should therefore be judged not only by improvements in predictive accuracy, but also by calibration, timeliness, external validity, equity, actionability, and measurable effects on public-health outcomes.

Integrated surveillance offers a path forward, but integration should be purposeful rather than driven by technological availability. Data streams should be combined when they provide complementary information, reduce uncertainty, or improve decisions. The next frontier of digital epidemiology is not simply predicting infectious-disease threats more accurately, but building integrated systems capable of converting heterogeneous signals into timely, trustworthy, equitable, and actionable public-health intelligence.

Article Information

Ethics Approval: Not applicable.

Consent to Participate: This article is a narrative review based exclusively on previously published literature and did not involve the recruitment of human participants, collection of primary human data, or use of identifiable personal information.

Consent for Publication: Not applicable.

Data Availability: No new datasets were generated or analysed for this review. All information synthesized in this article was obtained from publicly available and previously published sources cited in the manuscript.

Funding: No external funding was received for this study.

Conflict of Interest: The authors declare that they have no conflict of interest.

Acknowledgements: The author acknowledges the contributions of the researchers whose published work formed the evidence base for this review.

AI Use Disclosure: No generative artificial intelligence tools were used in the preparation of this manuscript.

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