Magna Scientia Advanced Research and Reviews
eISSN: 2582-9394
Cross Ref DOI: 10.30574/msarr
Journal homepage: https://magnascientiapub.com/journals/msarr/

(REVIEW ARTICLE)

Challenges and innovations in real-time infectious disease surveillance: A U.S. public health infrastructure perspective

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Magna Scientia Advanced Research and Reviews, 2026, 16(02), 204-219

Publication history: Received on 06 March 2026; revised on 15 April 2026; accepted on 17 April 2026

Article DOI: https://doi.org/10.30574/msarr.2026.16.2.0056

Abstract

The U.S. public health infrastructure includes real-time infectious disease surveillance as one of its pillars, but its effectiveness is conditioned by a complicated interaction between structural fragmentation, workforce shortages, data lapses, and technological advancement. This narrative review summarizes the existing literature on national surveillance systems, such as NSSP/ESSENCE, NNDSS, wastewater monitoring, genomic sequencing networks, and immunization registries, and how they can be used and in what ways they are limited in a decentralized context. Although the modernization efforts like the CDC data modernization Initiative and electronic expansion of case reporting have enhanced interoperability and timeliness, the fact that the systems of the states differ, some datasets are still missing, and reporting delays still occur, hinder prompt identification. Other constraints to the capacity of health departments to utilize advanced analytics are workforce shortages and low informatics capacity. Recent developments, such as the use of digital epidemiology, machine learning-based forecasts, and extended genomic and wastewater surveillance have high potential in detecting the outbreak earlier and providing better situational awareness. Nonetheless, biased coverage, artificial preferences, privacy issues, and governmental restrictions constrain the fair usage of these tools. The development of the future needs to be based on the integration of the models of analysis, long-term financing, enhanced human resources, and the coordinated system of sharing data. Combined, these results indicate the potential transformations and challenging issues that define real-time surveillance of infectious diseases in the United States.

Keywords: Infectious Disease Surveillance; Real Time Modeling; Data Modernization

1. Introduction

Real-time infectious disease surveillance represents a critical component of public health infrastructure in the U.S., allowing for the early detection of disease outbreaks and subsequent response measures to be taken to protect public health (Ali, 2024). Systems such as National Syndromic Surveillance Program (NSSP) aggregate data regarding emergencies treated in thousands of healthcare facilities across the nation using near-real-time analytics for anomaly detection for influenza-like disease cases, respiratory disease cases, and surveillance for novel pathogens (Haenchen et al., 2024). The Electronic Surveillance System for the Early Notification of Community-Based Epidemics (ESSENCE) tool used in the NSSP (Burkom et al., 2021) uses statistical methods for syndromic data analysis to detect spatial-temporal clusters (Savory et al., 2010). Additionally, National Notifiable Diseases Surveillance System (NNDSS) serves uniform reporting for more than 120 infectious disease cases nationwide. Since 2020, surveillance capacity has expanded through the National Wastewater Surveillance System (Kirby, 2021) and the U.S. SARS-CoV-2 genomic sequencing consortium (Paul, 2021), both of which strengthened early detection and variant tracking during the COVID-19 pandemic (Fontenele et al., 2021; Lambrou, 2023).

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Modernization endeavors for decades have helped to build a better level of interoperability and analytic capability among surveillance systems. The Center for Disease Control and Prevention (CDC)'s Data Modernization Initiative, launched in 2021, accelerated the shift to modern data systems including cloud-based analytics, standardized formats for health data exchange, and automated electronic case reporting (eCR) substantially reducing reporting delays and improving workflows across state and local health departments (Ivanovic et al., 2023; Knicely et al., 2024; Ross & Baker, 2023). By late 2024, more than 45 states had begun eCR, with a marked improvement in reporting time for cases to go from several weeks to a matter of days (Knicely et al., 2024). The use of wastewater surveillance had proven its effectiveness during a COVID-19 pandemic response and had a distinct advantage of predicting cases 1-3 weeks before clinical lab cases were reported in a community (Cheung et al., 2021; Hasing et al., 2023; Piggott et al., 2023). These advancements contributed to improved outbreak forecasting, enhanced local decision-making, and more equitable detection in areas with limited testing access.

The COVID-19 pandemic exposed major structural gaps in public health data sharing while accelerating innovation in syndromic surveillance (Hartnett et al., 2020). The National Syndromic Surveillance Program (NSSP) now ingests over 100 million emergency department (ED) visits annually in near real time and expanded during the pandemic to cover approximately 75% of all U.S. ED visits, making syndromic data a key indicator for real-time COVID-19 situational awareness (Ageron et al., 2022; Hartnett et al., 2020; Lange et al., 2020). Rapid innovation took place for AI-powered predictive models for genomic surveillance systems (Ray et al., 2020) which enhanced situation awareness. Public investments totaling about $7.4 billion were made via pandemic relief acts (Maani & Galea, 2020). This aided modernization in data systems, genomic sequencing infrastructure, and health departments.

Nevertheless, existing gaps undermine the full effectiveness of real-time surveillance. A patchworked electronic health record infrastructure, data-sharing agreements that vary in effectiveness, and state reporting capabilities have continued to exist as barriers for more effective real-time surveillance (Bosco et al., 2021; Holmgren et al., 2020). Delays in NNDSS reporting of 7 to 14 days continue to be prevalent for early surveillance potential in rapidly evolving outbreaks (McGough et al., 2020). Variability for data completeness and timeliness continues to exist regionally. Data completeness and timeliness vary significantly by region, with rural and underfunded health departments experiencing disproportionately slower reporting and weaker analytic capacity (Zavuga et al., 2023).

Workforce shortages are widespread across U.S. local health departments, with nationally representative surveys documenting persistent staffing gaps and high turnover risk among epidemiology, informatics, and related data science roles essential for real-time public health analysis (Rajamani et al., 2025). Certain state and privacy laws for conditions such as Health Insurance Portability and Accountability Act (HIPAA) continue to hamper effective data transfer between jurisdictions for real-time surveillance needs (Schmit et al., 2023). Certain false positives continue to occur for syndromic surveillance data management for similar symptoms for surveillance trends for reaffirmed respiratory viruses for a particular time (Morbey et al., 2017).

Finally, wastewater genomic surveillance continues to face impromptu scalability and representational barriers for surveillance needs (Machtinger et al., 2025; Munteanu et al., 2023). Such gaps have profound implications for healthcare security. This delay leads to unnecessary morbidity and mortality and economic losses that were estimated to be $16 trillion for a single pandemic event in COVID-19 (Cutler & Summers, 2020). There exist critical unknowns about how best to interconnect and leverage data streams for syndromic data, genomic data, lab data, wastewater data, and digital data. This narrative review examines the current challenges and emerging innovations shaping real-time infectious disease surveillance within the U.S. public health infrastructure, and identifies strategies to strengthen the resilience, equity, and effectiveness of future surveillance systems.

2. Literature Review

2.1. Current Landscape of U.S. Real-Time Infectious Disease Surveillance

The United States of America has a complex multi-tiered system for real-time disease surveillance that has undergone a lot of changes especially following the COVID-19 pandemic. This surveillance environment consists of several interlinked state, national, and local systems. All of these systems are designed to collect a specific category of data (Hamilton et al., 2021).

At the same time, the state of real-time surveillance in the U.S. is often described as a collaborative effort in which the leading integrator for syndromic surveillance, disease notification systems, and new data sources for quick detection of outbreaks is the Centers for Disease Control and Prevention (CDC) (Silk, 2023). Such systems are assumed to have developed significantly beyond 2020 in response to requirements posed by pandemics with a focus on near-real-time analytics for emerging threats such as antibiotic resistance and new infectious agents (Guralnik, 2024). Effective stewardship and antibiotic use are further supported by robust policy frameworks and advocacy strategies, which have shown promise in reducing unnecessary antibiotic prescribing and improving surveillance at both local and national levels (Amofah et al., 2024). Nevertheless, despite descriptions of a unified and increasingly streamlined national surveillance system, participation and capacity across states remain highly uneven. Although most states contribute to coordinated national data flows, the underlying infrastructure continues to vary widely in adoption of modern technologies, interoperability, and data-sharing practices. Effective stewardship and antibiotic use are further supported by robust policy frameworks and advocacy strategies, which have shown promise in reducing unnecessary antibiotic prescribing and improving surveillance at both local and national levels (Amofah et al., 2024). Thus, while the U.S. surveillance system is often portrayed as both highly integrated and rapidly modernizing, it simultaneously retains fragmentation and inconsistencies that challenge the goal of true real-time, nationwide infectious disease monitoring (Zaoli & Grilli, 2022).

2.1.1. Overview of National Systems

ESSENCE serves as a core component for syndromic surveillance in the United States (Moreland et al., 2024). Operating within the National Syndromic Surveillance Program (NSSP) and using BioSense Platform infrastructure, ESSENCE facilitates real-time surveillance of data for emergency department chief complaints, over-the-counter medication sales data, clinical lab data, and other syndromic data for several jurisdictions (Wiedeman, 2017). This flexibility has also been shown with its adaptability to track several health threats such as heat-related illness, drug overdoses, and firearm injuries. Thus, providing state and local health departments with near real-time situational awareness critical for planning response action for outbreaks (Moreland et al., 2024). For example, during the COVID-19 pandemic response, more than 100 million visits were tracked using ESSENCE with 85 to 90% specificity when validated with confirmed cases for respiratory surges; however, varying levels of involvement and data quality exist among jurisdictions affecting national levels of coverage and comparison (Romano et al., 2022).

The National Notifiable Disease Surveillance System (NNDSS) has remained a critical backbone of disease surveillance in the United States for tracking case data for reportable infectious conditions submitted by healthcare providers, laboratories, and public health departments across the United States (Ren et al., 2019). Traditionally, NNDSS has aided nationwide epidemic surveillance for conditions where data for cases are submitted for aggregation from county and state departments to CDC. Though this tool has been critical for longitudinal surveillance for disease incidence, current assessments of this surveillance system in recent years for a condition such as the 2022-2023 mpox epidemic have made it clear that this tool NNDSS is not optimized for real-time situational awareness (Rainey et al., 2024). This remains a problematic cause for concern regarding current surveillance capabilities.

Wastewater surveillance and genomic surveillance represent innovative additions to the surveillance architecture in the U.S., especially considering the ongoing COVID-19 pandemic. The National Wastewater Surveillance System (NWSS), launched by the CDC in 2020, has evolved to become a critical tool in population-scale surveillance for SARS-CoV-2 and other pathogens (Kirby, 2021; Lorenzo-Redondo et al., 2023). This innovation offers a community-wide unbiased measure of disease presence that does not rely on healthcare-seeking behavior (Schneider et al., 2025). This genomic surveillance effort has grown also to encompass a real-time whole genome SARS-CoV-2 genomic surveillance capability for use in surveillance and investigation of cases (Struelens et al., 2024). This program marks a major innovation in genomic surveillance capacities for public health in the U.S., providing integration with molecular and environmental surveillance approaches for a more integrated surveillance architecture.

Immunization Information Systems (IIS) and registry programs such as California Immunization Registry (CAIR) form a distinct but rapidly blurring tool used for real-time surveillance (Groom et al., 2022). They track vaccination administration events in healthcare facilities (Trotter et al., 2021). They help in carrying out real-time surveillance for immunization coverage and vaccine safety for effective data used in managing immunization programs as well as surveillance for vaccine-prevented disease outbreaks (Derrough et al., 2017).

2.1.2. Data Flow, Fragmentation, and Timeliness

The data system for public health in the US is decentralized in that data for a region initially would be compiled before being transferred to a federally operated system (Weber-Fares et al., 2024). This has contributed to discrepancies in data format and timeliness (Rigby et al., 2024). Evaluation of data completeness and timeliness for surveillance during and following the occurrence of this pandemic have indicated improvements but with variable data completeness and time delays (Nansikombi et al., 2023). The CDC's Data Modernization Initiative (DMI) directly addresses such deficiencies in interoperability and data pipelines in promoting standards such as FHIR/HL7 adoption, automated electronic lab and clinical reporting, and cloud architecture (Kadakia & Desalvo, 2023; Michaels et al., 2025). There appears to be a great amount of investment being made in data modernization by the federal government.

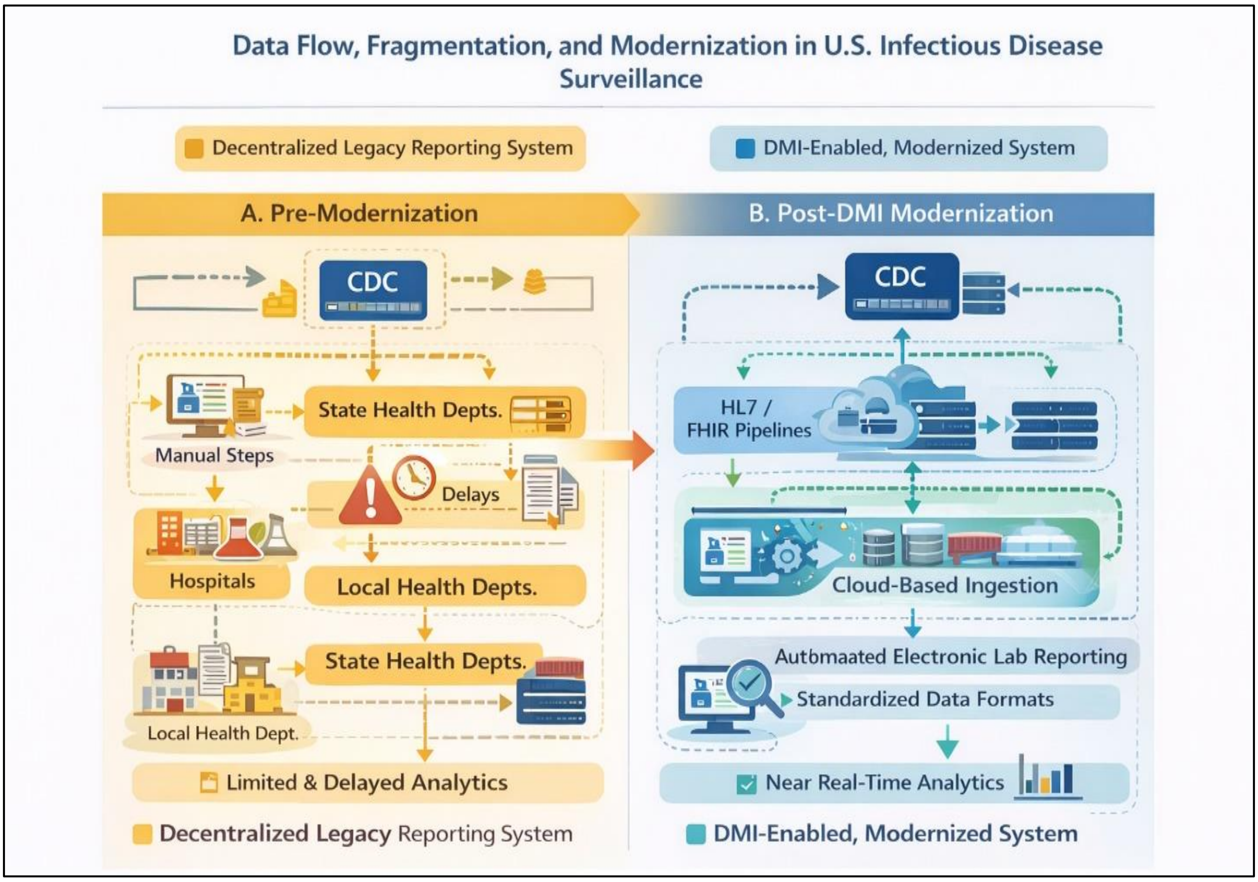

Figure 1 The contract between legacy decentralized reporting and the DMI-enabled system, highlighting the transition from manual, delayed, and fragmented data flow to automated, standard (HL7/FHIR), cloud-based pipelines that support near real-time surveillance analytics

3. Challenges In Real-Time Infectious Disease Surveillance

3.1. Fragmented Surveillance Architecture

Real-time infectious disease surveillance within the United States built on a public health infrastructure that is inherently decentralized (Rigby et al., 2024). This means that power is distributed among federal, state, territorial, local, and/or tribal jurisdictions with varying statutory authorities and capacities (Clark et al., 2024). This decentralized surveillance infrastructure results in several benefits for decentralized data but also leads to diverse reporting standards and data-sharing practices among surveillance systems. Assessments of data streaming for syndromic and other forms of surveillance data in and out of a pandemic environment for COVID-19 have shown that state and local health agencies often face legal, bureaucratic, and political barriers when sharing data with federal agencies to compile a nationwide trend (Rigby et al., 2024).

This fragmentation is compounded by a legacy of siloed information systems. This has involved a series of disease-surveillance programs such as tuberculosis, sexually transmitted infections, vaccine-preventable diseases, foodborne diseases, each of which has built its own information systems, user interface designs, and data reporting structures (Lee & Thacker, 2011). The Centers for Disease Control and Prevention's Data Modernization Initiative (DMI) and later Public Health Data Strategy (PHDS) series clearly point out that a major barrier to a more inclusive vision of population health data remains: 'Siloed information across disconnected and/or proprietary disease systems (Jernigan, 2022). Because many of these systems are tied to categorical, program-specific funding streams, they have been developed independently, often without a shared data model, common terminology, or standardized metadata. This generates a situation where data generally associated with surveillance but critical for consideration within real-time surveillance today resides in a number of incompatible systems for laboratories, healthcare providers, and public health agencies that cannot be integrated via a contemporary national vision (Zeba et al., 2025).

Technical interoperability between healthcare and public health remains a particular pain point. While federal incentives have spurred a great amount of adoption of electronic health records (EHRs) in healthcare delivery, public health agencies were for the most part left out of this first wave of investment and standards development in healthcare information technology (Jernigan, 2022). As a result, many state and local health departments have outdated data repositories, often homegrown systems that cannot easily interact with more contemporary EHR systems. A recent assessment of data modernization efforts across this nation indicates that variations in data format, methods of transport, and interface designs among jurisdictions today form a continued barrier to electronic case reporting and automated reporting of lab results (Richwine et al., 2021).

These technical and structural issues directly affect time and gaps in surveillance data. In most countries, reporting cases of certain infectious conditions remains partly dependent on manual methods such as fax, secure email, and Web forms that require manual data entry. In cases where a large number of cases are reported for a particular disease, such as a COVID-19 outbreak, manual data entry causes delays of a few days to a few weeks (Clark et al., 2024). The implications of this patchy architecture for real-time surveillance are far-reaching. Structural variability across jurisdictions produces uneven visibility (Zeba et al., 2025). Also, inconsistent data flows complicate the use of advanced analytics such as nowcasting or early-warning models, which rely on assumptions about the stability of reporting delays and the completeness of inputs; when those assumptions are violated, model outputs can become misleading exactly when they are most needed (Clark et al., 2024). Furthermore, this patchy level of data would also affect equity in that those in rural communities with lower socioeconomic healthcare standards would likely be those with the least capable data input architecture. This would lead to a limiting visibility of data concerning those communities and would thus lead to sustaining a level of health inequity (Simoes & Jackson-Thompson, 2023).

3.2. Workforce, Staffing, and Informatics Capacity

Real-time infectious disease surveillance in the United States is inherently challenged regarding the staff involved in managing surveillance systems. Even when data infrastructure and analytics capabilities are available, a shortage of epidemiologists among staff and a lack of training for more sophisticated analytics techniques with continued manual reporting processes may limit the overall potential for producing quality intelligence (Drehobl et al., 2012).

Over the course of a decade, a body of evidence has accrued regarding a severe reduction in the public health workforce available to the government. Between the 2009 Great Recession and the start of the COVID-19 pandemic, state and local health departments lost roughly 40,000 positions, including many core epidemiology roles (Leider, Yeager, et al., 2023). Subsequent analyses show ongoing turnover during and after the pandemic, with large proportions of staff leaving or intending to leave (Leider, Castrucci, et al., 2023; Weiss et al., 2024). This places a severe surge burden on a remarkably small number of staff with sufficient capacities for ongoing real-time analytics when surveillance exceeds mere reporting requirements for enhanced ongoing analytics for surveillance beyond simple reporting requirements.

Simultaneously, however, the skill set demanded of epidemiologists and surveillance professionals has grown more quickly than has the underlying structure for building a skilled workforce. Contemporary surveillance systems now consistently use electronic case reporting (eCR), automated lab notifications, and data sourced directly from electronic health records (EHRs); and this necessitates a skill set in data management and analysis, informatics, and advanced analytics (Aliabadi et al., 2020). Patient adherence to prescribed treatment regimens, a critical factor in controlling infectious disease spread, can be improved through digital health tools and personalized education programs, as demonstrated in recent reviews (Amofah et al., 2024). Nevertheless, several studies have shown that a lack of training in such areas may be a common characteristic among public health professionals.

Training gaps are compounded by an entrenched reliance on manual reporting workflows. Despite standards-based eCR and electronic laboratory reporting being in use, a great proportion of disease surveillance in the United States still depends on manual reporting mechanisms such as paper forms submitted via fax or email with subsequent re-entry (Dixon et al., 2020; Revere et al., 2017). As indicated in a series of studies concerning reporting of notifiable conditions, problems such as manual data entry requirements, unavailability of data for reporting, and competing clinical demands have always ranked among major factors leading to poor timeliness of reports (Revere et al., 2017). However, more recent studies have indicated that a satisfactory enhancement of timeliness and data completeness can be achieved with eCR only when public health organizations possess the capability to configure and manage electronic interfaces for eCR and overcome dependence altogether on manual reporting pipelines (Dixon et al., 2020; Knicely et al., 2024).

Layered atop this are increasing volumes of data regarding burnout and mental health effects of public health staff during major outbreaks. Early in the COVID-19 pandemic response, data indicated that fully two-thirds of public health staff in the United States reported burnout symptoms and had strong desires to quit their work (Stone et al., 2023). Longitudinal studies indicate that public health staff continued to meet high levels of anxiety, depression, and burnout during later waves of this pandemic (Scales et al., 2024; Stone et al., 2023). Global estimates regarding burnout levels among public health staff indicate a marked increase in burnout prevalence-many methods more-than doubled between 2017 and 2021, with over half of public health staff experiencing a symptom of burnout in 2021(Nagarajan et al., 2024). Together, these independent problems constitute a central bottleneck in real-time infectious disease surveillance.

3.3. Data Gaps, Reporting Delays, and Equity Challenges

Persistent data gaps and the resulting reporting lag has been hindering the effectiveness of infectious disease surveillance in the United States in terms of the completeness, validity, and timeliness of the information available to those who need it for decision-making (Silk, 2023). The pandemic has made the shortcomings in the quality and timeliness of the data available to be starkly apparent, with an apparent pattern of missing data regarding the key variables of race/ethnicity, co-morbidities, occupation, and social determinants of health in many data streams (Millett et al., 2020). The pattern of this missing data is certainly not random but instead reflects a tendency to lack the data concerning high-risk and marginalized communities, making it difficult to understand the nature of disparities and population-level risks in those groups and communities (Adekugbe & Ibeh, 2024).

The delayed reporting of cases additionally widens this gap, and in countries with older surveillance transmission networks and traditional disease investigation processes, this gap is worse. The COVID-19 pandemic has shown the existence of delays of two to three days in the reporting of positive test results to public health officials due to a lack of standardized reporting formats and the inability to adequately electronically report to the public health networks due to the unavailability of capacities in the local health facilities (Holmgren et al., 2020; Torres et al., 2021). Geographic variation and the corresponding disparity in test reporting networks add to the gap in near-real-time reporting, and in rural, frontier, and tribal areas where the quality and availability of testing facilities and broadband networks are less and the availability of human expertise is missing, the delay in test reporting and the availability of missing demographic data are higher (Lipsitch et al., 2023).

These inequities extend to genomic and wastewater surveillance, where coverage remains uneven and resource-constrained jurisdictions face substantial barriers to participation (Brito et al., 2022; Shrestha et al., 2021). The low sequencing capacity in the first emergence of the new variants of SARS-CoV-2 resulted in a geographic blind spot in the monitoring of variants (Harsha et al., 2022), while the networks in the area of wastewater monitoring were developed mostly in urban and rich areas, with little to no access for the rural and tribes (Polo et al., 2020). This means that a population disproportionally affected by structural vulnerabilities has little to no visibility in the monitoring results.

3.4. Privacy, Ethical, and Governance Constraints

The legal and ethical rules, such as the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and state privacy laws, set the limits of infectious disease surveillance in the United States, while also hindering the exchange of data needed to facilitate a timely response to the outbreak (Van Panhuis et al., 2014). The HIPAA Privacy Rule was put in place to protect individually identifiable health information while allowing the disclosure of certain information to report notifiable diseases and conditions to health departments (US Department of Health and Human Services, 2025). Nonetheless, in applying the HIPAA rules and obligations, health care facilities and organizations, and even public health facilities, too often view HIPAA in a proximately conservative manner to avoid risks associated with data exchange and utilization. The issue of hindrance in data exchange in public health due to legal and ethical complexities has been systematically examined in a review article of public health data exchange barriers by Van Panhuis et al., highlighting that legal and ethics difficulties such as the threat of breaches in confidentiality, unclear policies, and the ambiguity of data ownership consistently hamper data exchange even if the rule allows the exchange in the context of surveillance (Van Panhuis et al., 2014). The hindrance in the exchange of information across a number of systems in the United States has been described in a similar manner by a current publication by Worobiec et al. (2023) asserting that the interlocking federal and state laws concerning privacy and the aversive attitude of the organizations to risks thwart the exchange of data across a number of systems in the United States, even if the objectives in this instance are very compelling from the perspective of public health (Worobiec et al., 2023). All the above issues are worsened by the current global shift to increase the level of data privacy. According to Conduah et al. (2025), the existence of laws and regulations such as HIPAA, GDPR, CCPA, and other country regulations is important for securing patients but has resulted in a patchwork environment that allows fast flow across jurisdictions but is difficult to accomplish (Conduah et al., 2025).

Governance and infrastructure issues add to the disconnections in the process of real-time interoperability within the clinical and public health domains. The current environment in the United States utilizes redundant portals, discordant reporting structures, and traditional methods of manually interfacing and delaying the process of data exchange in the face of emergency events such as the COVID-19 pandemic (Jiang et al., 2024). The structure and functioning of the Health Information Exchanges Organizations (HIOs) in the United States offer wide variations in their partnering levels and experiences with public health organizations regarding the complexities and issues of stability in infrastructure and governance, causing challenges to the enhanced utilization of electronic health record messages, electronic laboratory reporting, and the admission, discharge, and transfer notification messages and syndromic data (Rosenthal et al., 2024). Despite initiatives and efforts by the CDC in the form of the Public Health Data Strategy to enhance the regulations and processes associated with data exchange and interoperability in the United States, the processes and operations associated with the interface for the public and clinical domains are unidirectional and batch processing-based and do not enhance the current processes of real-time monitoring and, in turn, the associated analytics and incentives for enhanced quality and efficiency in the interface and exchange processes of clinical and public health domains (CDC, 2025).

The current processes and facilities in the exchange and interface domains provide little to no analytics and incentives in terms of quality public trust, and privacy issues factor into the viability and efficacy regarding the implementation of digital tools for enhanced surveillance and real-time analytics. Studies point to the implementation of digital contact tracing platforms depending on privacy guarantees and trust in institutions (Fox et al., 2024; Pigera et al., 2025). Initial assessments related to the early stages of the COVID-19 pandemic emphasized the need to avoid privacy-threatening digital surveillance architecture to encourage system utilization, proposing privacy-friendly and decentralized architecture approaches instead (Bengio et al., 2020; Berman et al., 2020). Despite the availability of solutions facilitated by encryption and privacy-by-design approaches to enhance the security of shared data (Shojaei et al., 2024), these solutions will have to coexist in governance architecture conducive to accountability and transparency to gain the approval and trust of the public for the successful implementation of enhanced real-time surveillance capabilities across communities based on shared data at faster rates than ever before.

4. Innovations Transforming Real-Time Surveillance

4.1. Digital Epidemiology and Non-Traditional Data Streams

Digital epidemiology extends the reach of classic surveillance by analyzing data that is not collected within the traditional frameworks of public health but is instead generated elsewhere, such as the digital traces of clinical activity, wearables, mobility patterns, and the pursuit of online health-related information (Fallatah & Adekola, 2024; Tarkoma et al., 2020). The detection and response to infectious disease outbreaks have been significantly enhanced by integrating innovative technological tools such as artificial intelligence, machine learning, and genomic surveillance, as shown in recent outbreak management reviews (Doreen Ugwu et al., 2025). Such digital exhausts do not merely substitute for laboratory results and notifiable disease cases, but they can provide precursors for the situation awareness that already exists when properly validated and incorporated into existing infrastructure (Mavragani & Ochoa, 2019). This shift is visible in the United State in the growth of national syndromic platforms, the increasing feasibility of physiological monitoring at scale, and the widespread use of mobility and web-search data for real-time epidemic assessment.

Syndromic surveillance is at the cutting-edge nexus between conventional and digital approaches. The ESSENCE system, developed and operated by the CDC's National Syndromic Surveillance Program (NSSP), processes millions of emergency department and urgent care data per day, using automated aberration detection for near real-time alerts for respiratory, gastrointestinal, and febrile illness (Burkom et al., 2021). During the COVID-19 era, the ESSENCE system was widely leveraged for the monitoring of COVID-like illness and mental health crises, and for facilitating the rapid development of state and local situational awareness. To add data from the healthcare setting, wearables offer population-scale physiological data. Radin et al. (2020) illustrated the effectiveness of using Fitbit data for the detection of irregularities in aspects of sleep and rest heart rate, which, when incorporated, bolstered state-based predictions for influenza-like illness (Radin et al., 2020), and the existing literature suggests that monitoring heart rate, respiration rate, and body temperature continuously offers the underlying dynamics for the modeling of pre-symptomatic infections (Ming et al., 2020).

Mobilities and online information-seeking patterns are other high-speed digital data sources, which have revolutionized epidemic intelligence (Grantz et al., 2020). Also, county-level analyses carried out during the initial COVID-19 phase showed that decreased mobile phone mobility strongly predicted decreased numbers of new cases, providing new estimates of transmission intensity and the effects of non-pharmaceutical measures (Badr et al., 2020). Similarly, web search and social media data patterns offer promising early warnings: global and U.S. search volumes for coronavirus peaked 11–12 days before case peaks (Effenberger et al., 2020), while social media data, along with Google Trends, offered early warnings of the initial and secondary peaks of COVID-19 in the USA and Canada (Yousefinaghani et al., 2021). However, cases like Google Flu Trends also highlight the problem of overfitting digital data patterns for media-related behavior, and hence the importance of using digital data patterns for interactive ensemble modeling with epidemic surveillance data collected through the traditional surveillance system (Santillana et al., 2015). Through these, the problem of representation, algorithmic privacy, and the issue of data governance, among other challenges, retain relevance, emphasizing the central idea that digital epidemiology must support, not substitute public-health infrastructure (Mavragani, 2020; Rovetta, 2021).

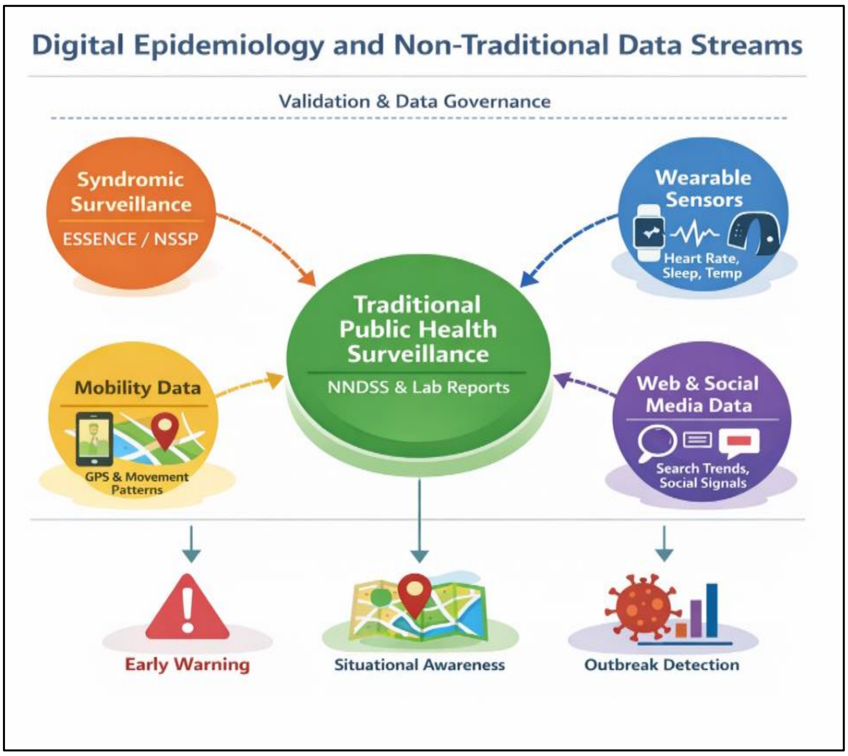

Figure 2 How non-traditional digital data streams integrate with traditional public health surveillance to support early warning, situational awareness, and outbreak detection

4.2. Machine Learning, Nowcasting, and AI-Enhanced Early Warning

Machine learning (ML) and artificial intelligence (AI) have greatly improved the areas of outbreak identification, nowcasting, and early warning systems for the analysis of large-scale, multi-source data, along with the identification of complex patterns not previously recognized by surveillance efforts (Biu et al., 2024; El Morr et al., 2024; Rahman et al., 2023). Initiatives to promote responsible antibiotic use and stimulate the development of new antimicrobial agents have played a crucial role in combating antimicrobial resistance and improving public health outcomes in the United States (Gyasi-Darko et al., 2024). In contemporary efforts, the increasing use of long short-term memory (LSTM) networks, Random Forests, Bayesian models, LightGBM, Gated Recurrent Units (GRU), and other approaches for the accurate prediction, at rates of 88-95%, of the dynamics of outbreaks (Dhanda et al., 2025; Villanueva-Miranda et al., 2025) demonstrates the increasing practical relevance of these sophisticated approaches. Furthermore, the use of Explainable AI improves the efficiency of early warning systems, converting complex outputs into useful data for effortless interpretation, hence boosting the trust of public health professionals (Balogun et al., 2023). However, the use of geographic information systems for the integration of geographic data with other sophisticated ML-based approaches not only develops sound geospatial modeling for the spread of diseases, guaranteeing advanced awareness and precise outputs (Babanejaddehaki et al., 2025; Olawade et al., 2023), but also develops a sound platform for the timely implementation of intervention measures, hence increasing the reliability of diagnostic and treatment processes (Chen et al., 2024; Dhanda et al., 2025; Ijeh et al., 2024).

Leveraging these, cloud-based AI frameworks have enabled the development of scalable, real-time nowcasting platforms that can automatically incorporate data from electronic healthcare records, social media platforms, weather datasets, and mobility data obtained from mobile phones for the purpose of discovering initial indications of new disease outbreaks (Kareem & Quazi, 2024; Raza et al., 2024). Apart from these forecasting engines, AI-based systems also enhance the readiness of the public healthcare system by optimizing the allocation of facilities, healthcare supplies, and personnel, according to predicted geographic locations of new disease outbreaks (Adedayo Adefemi et al., 2023). Apart from optimizing the allocation of facilities, healthcare supplies, and personnel, AI-based predictive frameworks model the societal and economic effects of new disease management policies, rendering well-informed decision-making for the improvement of readiness and responses for new disease threats (Anjaria et al., 2023; McKee et al., 2025).

4.3. Genomic Epidemiology and Wastewater Surveillance

4.3.1. SARS-CoV-2 wastewater monitoring expansion

Wastewater-based epidemiology (WBE) quickly became a revolutionary part of public health surveillance in the U.S. in the SARS-CoV-2 pandemic, offering a non-invasive means of viral population-level monitoring even in situations where test capacities were limited. Early studies showed that SARS-CoV-2 viral RNA in wastewater preceded reported cases by a number of days, offering a precursor signal for transmission trends themselves (Peccia et al., 2020). This method of surveillance proved especially useful for detecting asymptomatic and missed cases, and it spurred a rapid expansion in the U.S. through a coordinated effort of the Centers for Disease Control-associated National Wastewater Surveillance System (NWSS)(Peccia et al., 2020). The results of a year evaluation of community-level performance of NWSS showed that community infection patterns were reliably ascertained by this method in a wide range of sewershed areas, and that this data also preceded noted hospitalizations over a period as reported by (Kirby, 2021). As coverage broadened to include universities, correctional facilities, and small communities, wastewater surveillance demonstrated its utility as a resilient, cost-effective early-warning platform that complements clinical reporting in a real-time surveillance ecosystem.

4.3.2. Rapid sequencing for variant detection

Genomic epidemiology became a priority in U.S. surveillance as SARS-CoV-2 variants of concern arose, highlighting the utility of rapid, high throughput sequencing. The utility of SARS-CoV-2 genome data for tracing chains of transmission and regional spread was explored in early studies; for example, SARS-CoV-2 genome data enabled visualization of epidemic patterns in near real-time, as done by Du Plessis et al. (2021) in which the authors showed how SARS-CoV-2 genome data analysis allowed discrimination between importation events and community transmission (Du Plessis et al., 2021). To address this, expanding SARS-CoV-2 genomic surveillance in the United States has been important for early detection and tracking of SARS-CoV-2 variants, such as Alpha, Delta, and Omicron. Sustainable pharmaceutical practices, including eco-friendly manufacturing, distribution, and disposal, are essential for long-term public health and environmental protection, as highlighted in recent studies (Misszento & Amofah, 2024). The early detection and rapid expansion of B.1.1.7 SARS-CoV-2, Alpha, using SARS-CoV-2 genome data integrated with epidemiologic data has been reported in early studies by Galloway et al. (2021).

5. Future Directions and Research Gaps

To advance with real-time infectious disease surveillance in the USA, it is imperative to make substantial strides in analytical innovation, with a focus on developing predictive models that provide a means for putting together disparate data sets into a comprehensive, meaningful message. The current state of surveillance capabilities operates in a vacuum. While there are rich sources of data from healthcare surveillance, wastewater sources, genomic analysis, digital signals, and mobility patterns, very little has been done using modeling that brings all this data together in a comprehensive, predictive manner in real-time. There needs to be a pressing effort invested in developing analytical models that are transparent and aware of their own potential for bias, which can then be used to synthesize a wide range of data sources. There are common issues with machine learning models, including concerns of generalizability, particularly in areas of low representation, where there are concerns of overfitting.

These technical needs are inextricably linked with those of infrastructure and personnel. There are many public health departments, even now, especially locally, which lack sufficient personnel and informatic support for using advanced surveillance tools, let alone support sufficient for processing large volumes of data in real-time. Without a scheme for developing and maintaining a pool of epidemiologists, data scientists, informaticians, and genome experts, advancements would be limited to richer countries. Also, a viable business model for sustaining costs has been emphasized as essential, in that, projects like a cloud-based infrastructure, a common interoperability standard like HL7/FHIR, an expansion of wastewater and genome networks, and automated reporting systems would never be sustained solely by emergency allocations. Studies that estimate, for example, the long-term effects of data upgrade projects on costs and functionality would help leaders make their cases for sustained support.

Finally, it must be noted that equity and governance issues must also be remedied in future research to avoid vulnerable groups being left behind. There are inequalities in data availability for real-time data streams. On one side, wearables and mobility data sources are prone to over-representation of wealthier individuals. At the same time, wastewater surveillance requires a sewerage network that may not be available in rural and/or tribal areas. Finally, digital surveillance technology requires access to broadband internet, which may not be ubiquitous. Therefore, in the absence of proper design, it merely creates a structural blind spot that worsens equity issues. There needs to be further research to ascertain the nature of this potential discrepancy and find a method to correct it. Together, it has become imperative for a governance overhaul that aims to standardize data sharing laws, develop country-level norms for sharing emergency data, and provide ethical bounds for using digital bio-surveillance technology.

6. Conclusion

The real-time surveillance of infectious diseases in the United States has been experiencing a major overhaul; despite this, many major impediments still exist. With a fragmented environment among the traditional structures, lack of personnel, data gaps, and a situation where technology in environmental surveillance has not been taken full advantage of, what has been experienced in this field has been a situation where early response has been difficult. At the same time, with major advancements in genome analysis, environmental surveillance, cloud capabilities, and epidemiology, unprecedented opportunities now exist that could improve early response capacities in ways that were unimaginable in the past. These opportunities, however, will never be maximized without major investments in data reform, a standard in interoperability, development of a public health workforce, and development of structures that would support effective data sharing without undermining public trust.

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