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From Detection to Action: Building Next-Generation HIV Cluster Detection and Rapid-Response Systems in the United States

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Abstract

Background: Despite major advances in HIV treatment and prevention, rapid HIV transmission within specific networks and communities remains an important challenge in the United States. Cluster detection and response (CDR), including molecular and time-space surveillance, is now central to identifying networks experiencing accelerated transmission. However, detecting a cluster is not equivalent to interrupting transmission.

Objective: To examine the evolution and current architecture of U.S. HIV CDR, with particular attention to the pathway from surveillance signal to public-health intervention.

Methods: Critical narrative review of epidemiological and implementation studies, cluster and outbreak investigations, surveillance evaluations, methodological literature, and authoritative public-health guidance.

Findings: Molecular, time-space, epidemiological, clinical, partner-services, and community-informed evidence provide complementary but individually incomplete intelligence. Detected clusters are partial observations of networks that may be several times larger. Persistent weaknesses between signal generation and intervention include incomplete and delayed data, fragmented systems, multijurisdictional coordination, workforce and resource constraints, structural barriers, and concerns about trust, privacy, and equity. Published responses have coincided with improvements in testing, prevention, care, and transmission, but the contribution of detection itself is rarely separable from the multicomponent responses it triggers.

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Conclusions: A Detection-to-Action Framework is proposed—Detect, Interpret, Prioritize, Mobilize, Intervene, Evaluate, and Adapt—with equity, community partnership, and data stewardship as cross-cutting principles. Next-generation CDR should be judged not by the number or speed of clusters detected, but by its capacity to convert actionable signals into timely, equitable, community-informed interventions with measurable improvements in HIV prevention and care. Time-to-action should become a core performance metric.

Keywords: HIV, Cluster Detection and Response, Molecular Surveillance, Rapid Response, Transmission Networks, Public Health Surveillance, Outbreak Response, Ending the HIV Epidemic, Health Equity, Data Governance

Key Messages

- HIV cluster detection in the United States has evolved into a multimodal system combining molecular, time-space, partner-services, clinical, and community signals; no single stream fully represents a transmission network.
- Detected molecular clusters are partial observations: modelled full networks are estimated to be 3-9 times larger, so response must extend beyond the detected cluster.
- As analytical capacity grows, the limiting step is shifting from finding clusters to acting on them—the detection-to-action gap.
- The proposed Detection-to-Action Framework (Detect, Interpret, Prioritize, Mobilize, Intervene, Evaluate, Adapt) makes mobilization and evaluation explicit and introduces time-to-action as a core performance metric.
- Trust is part of CDR infrastructure: privacy protection, restrictions on secondary use, attention to surveillance-visibility bias, and community governance are preconditions for effective response.

1. INTRODUCTION

Despite major advances in antiretroviral therapy (ART), pre-exposure prophylaxis (PrEP), HIV testing, and treatment as prevention, HIV transmission remains an important public-health challenge in the United States. In 2024, 38,793 HIV diagnoses were reported among people aged 13 years and older in the United States and 7 territories and freely associated states, with the burden unevenly distributed across populations and regions [1]. Among people with diagnosed HIV at the end of 2024, 77% received HIV medical care, 56% were retained in care, and 69% were virally suppressed [2]—breakdowns along the care continuum that sustain onward transmission and undermine national control efforts [3]. Such aggregate measures are essential for tracking progress toward Ending the HIV Epidemic targets [4,5], but they can obscure localised periods of accelerated transmission within particular sexual, social, geographic, or drug-use networks [6,7]. By the time these become apparent through conventional trends, opportunities for earlier intervention may have been lost, as the 2014-2015 outbreak among people who inject drugs in Scott County, Indiana, demonstrated [8].

Cluster detection and response (CDR) has consequently become a core component of U.S. HIV prevention and part of the Respond pillar of the Ending the HIV Epidemic initiative [4]. Recognition of outbreaks through increases in diagnoses, provider reports, and partner-services investigation has been complemented by time-space analyses and by molecular cluster detection using sequences generated through routine drug-resistance testing [9]. Guidance from the Centers for Disease Control and Prevention (CDC) now recommends that health departments routinely analyse surveillance data using these complementary approaches while incorporating signals from providers, partner-services staff, and affected

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communities [10]. CDC initiated molecular cluster detection with data from 27 jurisdictions in 2016; during 2018-2023 it identified 404 molecular clusters of rapid transmission, 325 (80%) of which involved multiple jurisdictions [11].

Yet greater capacity to detect rapid transmission does not guarantee greater capacity to interrupt it. A signal must be interpreted, prioritised, investigated, connected to the broader network, and translated into an appropriate response, and delay at any stage can erode the value of timely detection [12,13]. As surveillance becomes more sophisticated, the limiting step may increasingly shift from identifying signals to acting on them [14]. This review examines the evolution and architecture of U.S. HIV CDR with particular attention to this pathway from signal to intervention; evaluates technical, operational, and ethical barriers along it; assesses what existing evidence can establish about CDR effectiveness; and proposes a Detection-to-Action Framework. The central argument is that CDR should be judged not only by its ability to identify rapid transmission, but by its capacity to convert actionable intelligence into timely, equitable, community-informed interventions with measurable impact.

2. REVIEW APPROACH

A critical narrative review was conducted, an approach suited to integrating heterogeneous literature and developing a framework rather than estimating a pooled effect [15], designed and reported with reference to the Scale for the Assessment of Narrative Review Articles (SANRA) [16]. PubMed/MEDLINE, Embase, Scopus, and Web of Science were searched for English-language articles published between January 2010 and August 2026 (final search 31 August 2026), combining terms for HIV with terms for cluster detection and response (e.g., “HIV” AND (“cluster detection” OR “molecular surveillance” OR “time-space” OR “outbreak” OR “transmission network”) AND (“response” OR “intervention” OR “ethics” OR “evaluation”)). Searches were supplemented with CDC and U.S. Department of Health and Human Services guidance, published outbreak investigations, and backward citation searching. Evidence from epidemiological and implementation studies, outbreak investigations, surveillance evaluations, methodological literature, and ethical and community-perspective studies was synthesised thematically around the operational pathway from detection to evaluation. Both authors independently screened the retrieved records for relevance, and disagreements were resolved by discussion. No formal risk-of-bias assessment or meta-analysis was conducted.

3. HOW HIV CLUSTER DETECTION EVOLVED IN THE UNITED STATES

3.1 Epidemiological and time-space recognition

HIV cluster detection did not begin with molecular surveillance. Unusual transmission has long been recognised through increases in diagnoses, provider notifications, partner-services investigations, and observations from frontline organisations and communities; several major outbreaks among people who inject drugs in Indiana, Massachusetts, Washington, and West Virginia were first recognised this way [8,17-19]. Partner services remain particularly valuable because information about sexual and injection networks reveals connections invisible in aggregate data, and providers and communities may recognise changes in transmission circumstances before they produce a statistical signal [10]. The limitation is that recognition depends on visible increases in diagnoses or on information reaching health departments; networks that cross boundaries, involve undiagnosed people, or are weakly connected to healthcare can expand unnoticed [12].

Time-space analysis, now recommended for routine use, strengthened this architecture by comparing observed with expected diagnoses within defined populations, areas, and periods [10]. Its signals require careful interpretation: an increase in diagnoses is not synonymous with an increase in recent transmission.

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Intensified testing can identify infections acquired years earlier—sometimes at an advanced stage with risk of preventable mortality [20] and changes in access, reporting, migration, or population composition can alter observed patterns. A geographically defined cluster may also capture only part of the relevant network. Time-space detection therefore identifies an anomaly requiring investigation rather than proof of a discrete transmission network.

3.2 Molecular cluster detection

Comparison of HIV sequences reported to surveillance identifies groups of highly similar viral sequences; among recently diagnosed people, such groups can indicate rapid transmission in ways that diagnosis counts cannot [6,9]. From 2018, CDC supported all health departments to collect sequence data and conduct routine molecular cluster detection using Secure HIV-TRACE, the secure implementation of the HIV TRAnsmission Cluster Engine [21]. CDC analyses national data quarterly and health departments analyse local data monthly; during 2020-2023, health departments themselves first detected most of the clusters they reported [11].

Analytical precision should not be confused with certainty about person-to-person transmission. Sequence similarity cannot establish that two people transmitted HIV directly to one another or the direction of transmission [10,22], and network members are absent from a detected cluster if they are undiagnosed, untested for resistance, lack a usable sequence, or have no sequence reported [10]. Molecular clusters are therefore partial observations of broader networks, not reconstructions of them.

3.3 Toward multimodal cluster intelligence

The evolution of CDR is better understood as a movement toward multimodal cluster intelligence than as replacement of traditional epidemiology. Each source reveals a different dimension of rapid transmission and has distinct limitations (Table 1), and CDC treats them as complementary rather than interchangeable [10]. The investigation of rapidly growing molecular clusters among Hispanic or Latino gay, bisexual, and other men who have sex with men in metropolitan Atlanta illustrates this integration: combining molecular data with partner-services information, medical-record review, and interviews with providers and community members identified language, immigration-related, and stigma-related barriers that sequences alone could not reveal, and informed culturally tailored prevention and navigation [23]. The advance is therefore not only greater technical precision but the ability to assemble evidence on where transmission is occurring, who is connected, which gaps sustain it, and what response is required. As signals become more granular, however, interpretation becomes more not less important.

Table 1. Complementary sources of HIV cluster intelligence: what each contributes and its principal limitations

Signal source	What it detects	Principal strengths	Principal limitations
Time-space analysis	Unusual increases in diagnoses within a defined population, area, and period	Uses routine case surveillance; available in all jurisdictions; captures people without sequences	Diagnoses ≠ recent transmission; sensitive to testing intensity, reporting changes, migration; geographically bounded
Molecular analysis (e.g., Secure HIV-TRACE)	Groups of closely related viral sequences	Identifies networks invisible to case counts; detects multijurisdictional	Requires diagnosis, resistance testing, and reported sequence; cannot establish direct or

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Signal source	What it detects	Principal strengths	Principal limitations
	indicating rapid transmission	clusters; standardised national criteria	directional transmission; misses HIV-negative network members
Partner services	Sexual and drug-use partners and network connections	Reaches undiagnosed and HIV-negative people; links directly to testing and prevention	Anonymous or undisclosed partners; workforce-intensive; dependent on trust
Clinical and care-continuum data	Care engagement, viral suppression, coinfections, service use	Identifies modifiable care gaps (e.g., viral non-suppression) sustaining transmission	Fragmented across systems; reporting delays; incomplete for people outside care
Provider and community signals	Changes in transmission circumstances, service access, or network vulnerability	Early, contextual, and explanatory; identifies structural barriers	Unsystematic; depends on relationships and on information reaching health departments

Note. Adapted from current CDC cluster detection and response guidance and the literature reviewed. No single source fully represents a transmission network; signals are complementary rather than interchangeable.

4. AFTER DETECTION: THE DETECTION-TO-ACTION GAP

Detecting a cluster initiates rather than completes the response. CDC positions cluster review as a multidisciplinary process combining surveillance with epidemiological, clinical, partner-services, and contextual evidence to determine the level of concern and response [10]. The pathway can be represented as data → signal → intelligence → decision → action; each transition adds information but also creates opportunities for delay or loss. The detection-to-action gap is the cumulative distance between recognising a signal and delivering an intervention that addresses the conditions sustaining transmission. It rarely results from a single failure.

4.1 Interpretation, prioritisation, and network characterisation

Verification is iterative rather than binary: time-space increases may reflect testing or reporting changes, and molecular signals must be interpreted against sequence completeness, growth, diagnosis timing, and local epidemiology [10]. Not every cluster requires the same response. Prioritisation weighs rapid growth, recent infections, high viral load or non-suppression, injection drug use, STI or hepatitis coinfection, large or poorly characterised sexual networks, service gaps, and structural conditions such as unstable housing, incarceration, and discrimination [10]. Because a technically similar signal can carry different implications in different settings, prioritisation is a contextual public-health judgement, not an algorithmic ranking.

The detected cluster is also not the network. CDC defines the network as cluster members plus sexual or drug-use partners who may or may not have HIV [10]. A nationally representative simulation estimated that full networks underlying priority molecular clusters are 3-9 times larger than detected clusters, with around one-third of infections in new priority networks undiagnosed [24]. Investigation must therefore move outward toward the larger network and its prevention and care environment.

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4.2 Constraints along the pathway

Data incompleteness and latency. Molecular detection depends on diagnosis, resistance testing, sequencing, and reporting; undiagnosed people are absent by definition, and completeness varies [10,24]. Gaps are often greatest in underserved communities with limited testing and weaker reporting infrastructure [25]. Partner information may be incomplete, and reporting delays mean that information may arrive after the network has expanded. An apparently small cluster may reflect limited observation rather than limited transmission, so uncertainty propagates into prioritisation and resource allocation.

Fragmentation. A valid signal does not specify whether the principal need is testing, re-engagement in care, PrEP, partner services, syringe services, housing support, or a combination. That knowledge is distributed across surveillance, clinical, prevention, STI, substance-use, community, and social-service systems, which is why CDC recommends multidisciplinary CDR leadership and coordination groups [10].

Multijurisdictional networks. With 80% of molecular clusters of rapid transmission spanning more than one jurisdiction [11], people may live, receive care, and have partners in different jurisdictions. Recognising such clusters is easier than coordinating a response across health departments that differ in staffing, infrastructure, services, legal environments, and data-sharing arrangements. CDC recommends that all relevant jurisdictions participate and notes that formal secure data-sharing arrangements may be needed [10]; experience across infectious-disease control shows that formalised partnership structures are central to coordinated action across institutional boundaries [26]. Multijurisdictionality is thus a governance challenge, not merely a descriptive feature.

Workforce and resources. Automated surveillance can monitor many clusters, but each signal may require epidemiological review, partner-services investigation, community engagement, and expanded services. CDC recommends surge planning and dedicated response staff where feasible [10], and large outbreak responses have required substantial federal, state, and local surge support [12,19]. More surveillance can generate more actionable signals without generating capacity to act, shifting the bottleneck from finding clusters to deciding which can receive intensive response.

Trust and structural determinants. Molecular surveillance raises concerns where stigma, criminalisation, and prior experiences of institutional surveillance shape trust [27]. In King County, Washington, community members and providers raised concerns about confidentiality, stigma, legal uses of molecular information, and disengagement from services [28]. Meanwhile, the poverty, unstable housing, discrimination, incarceration, and inadequate harm-reduction and healthcare access that contribute to rapid transmission also constrain the response [10,18]. Identifying people who could benefit from care or PrEP has limited effect if services are inaccessible, unaffordable, or culturally unacceptable.

These mechanisms are interconnected rather than additive, and together they make CDR increasingly an implementation problem. Further gains in detection sensitivity will not yield proportional gains in prevention unless the systems receiving those signals become equally capable of acting on them.

5. FROM SIGNAL TO INTERVENTION

Because a detected cluster represents only part of the network, effective response must operate simultaneously at individual, network, and systems levels, matched to the epidemiological characteristics of the network and the service failures revealed by investigation rather than applied as a standard package [10,14].

At the *individual level*, priorities are rapid linkage or relinkage to care, timely ART, and support for sustained viral suppression [10]. Because viral suppression prevents sexual transmission [29,30], treatment engagement serves both health and prevention. Yet referral is not success: where housing, transport,

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stigma, insurance, or substance use prevent sustained engagement a recurring failure point along the care cascade [3] nominal linkage has little durable effect, so outcomes should be measured as service uptake and continuity. At the *network level*, response extends to undiagnosed and HIV-negative network members [24] through intensified testing, partner services, social-network strategies, PrEP and post-exposure prophylaxis, STI services, and harm reduction [10]; intervention should follow the network rather than the boundaries of the original dataset. At the *systems level*, clusters can expose failures that cannot be corrected one person at a time insufficient testing, limited PrEP prescribing, weak retention, or inadequate harm-reduction services [12,17]. Expanding services, partnerships, and culturally and linguistically appropriate care, or revising impeding policies, may require substantial investment but can produce broader and more durable effects [10]. In this role, CDR acts as a diagnostic instrument for the prevention system itself.

A review of 30 cluster and outbreak responses in North America during 2000-2020 documented increased testing, greater uptake of prevention, improved care and viral suppression, and reductions in transmission or new diagnoses, as well as new collaborations and corrected service deficiencies [13,19]. These findings support responding to rapid transmission but require careful interpretation. Responses are multicomponent, so declining cluster growth cannot be attributed to detection itself. Detection is best understood as an enabling intervention whose effect is mediated by the prevention, treatment, and structural actions it triggers. The relevant question is which components work, for whom, under what conditions, and how much benefit earlier detection and action add.

6. MEASURING WHAT MATTERS

Counts of clusters detected or investigated are implementation indicators, not evidence of impact: a system could detect clusters rapidly while response takes months, or improve services without an immediately measurable effect on transmission. Evaluation therefore needs to span detection performance, operational performance, service outcomes, and population and systems outcomes, with equity as a cross-cutting dimension (Table 2); CDC's evaluation guidance already incorporates several service and policy measures [10]. One metric deserves particular emphasis: time-to-action. Early detection has limited value if delay follows the signal. Measuring signal-to-review, review-to-prioritisation, prioritisation-to-response, and overall signal-to-intervention intervals would show where delays accumulate and whether better surveillance technology yields faster action. The relevant endpoint is whether earlier and better intelligence produces earlier and better action, and whether that action improves prevention, care, and transmission outcomes.

Table 2. Proposed performance domains and illustrative metrics for evaluating HIV cluster detection and response across the detection-to-action pathway

Domain	Core question	Illustrative metrics
Detection performance	Does surveillance generate complete, accurate, and timely signals?	Sequence completeness; diagnosis-to-sequence-report interval; analysis frequency; time to detect cluster growth
Operational performance (time-to-action)	How quickly does a signal become a decision and a mobilised response?	Signal-to-review; review-to-prioritisation; prioritisation-to-response initiation; overall signal-to-intervention interval

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Domain	Core question	Illustrative metrics
Service outcomes	Did the response change access to and uptake of interventions?	Partner-services completion; HIV testing; PrEP initiation; linkage or relinkage to care; ART engagement; viral suppression among cluster and network members
Population and systems outcomes	Did transmission and the service environment change?	Cluster growth and new diagnoses; sustained viral suppression; persistence of service expansions or policy changes
Equity and legitimacy (cross-cutting)	Were benefits equitable and was trust maintained?	Outcomes stratified by population; data completeness by group; community-reported acceptability and perceived harms

Note. ART = antiretroviral therapy; PrEP = pre-exposure prophylaxis. Time-to-action metrics are proposed and would require standardised definitions.

7. BUILDING NEXT-GENERATION CDR SYSTEMS

Multimodal, near-real-time surveillance. Next-generation systems should formalise the complementarity of data streams (Table 1) so that together they answer whether transmission is accelerating, who is affected, what gaps exist, and what interventions are possible. CDC identifies automated analysis, integration of data from HIV and related programmes, and dashboards for visualisation and secure sharing as enhancements [10]. Automated updating could flag meaningful changes for multidisciplinary review, but automation should accelerate information flow, not replace epidemiological judgement.

Decision support. The more consequential transition is from systems that identify clusters to systems that support decisions on which cluster requires action, what intervention, at what level, and how urgently. Decision support should integrate growth, recent diagnoses, viral suppression, network characteristics, service availability, and structural conditions, while supporting rather than replacing deliberation and documenting why responses are initiated, modified, or stopped.

Predictive analytics without hype. Statewide surveillance data have been used to predict cluster growth [31], and mathematical modelling is increasingly positioned to inform adaptive public-health decisions [32]. But identifying a cluster that has already grown is not forecasting which network will accelerate next. Before influencing resource allocation, models require external and prospective validation, assessment of calibration and transportability [33], transparent reporting [34], and evidence that model-informed decisions improve outcomes. Because surveillance completeness is socially patterned, models may also reproduce existing inequities [25,35].

Pre-positioned capacity and learning. A system cannot be rapid if response infrastructure is assembled only after detection. Predefined escalation protocols, standing multidisciplinary teams, established community and provider partnerships, cross-jurisdictional data-sharing agreements, surge mechanisms, and dedicated funding all recommended by CDC [10] shift CDR from reactive mobilisation to response readiness [14,26]. Outcomes should then feed back into detection and decision-making, so that CDR operates as a learning system in which action generates evidence that improves subsequent response [36].

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8. ETHICS, PRIVACY, EQUITY, AND COMMUNITY GOVERNANCE

Molecular surveillance is particularly sensitive because sequences generated for clinical care are reused for public-health cluster detection [27,37]. Sequence similarity should not be interpreted as establishing direct or directional transmission [22]; CDC cautions against both interpretations, recommends strong protections for sequence and cluster data, advises against releasing surveillance-derived sequences to public databases, and limits sharing to what is necessary for public-health purposes [10]. Privacy protection must therefore extend beyond cybersecurity to decisions about collection, access, sharing during investigations, retention, and handling of non-public-health requests.

Concerns about criminalisation and secondary use matter because perceived misuse can deter engagement; state laws criminalising HIV exposure have not been associated with lower diagnosis rates [38]. Community members and providers in King County voiced such concerns [28], and a 2023 survey of practitioners and researchers in HIV molecular epidemiology ranked legal prosecution, group stigma, and individual harm as the most pressing ethical issues [39]. The perceived consequences of data use thus matter independently of the technical limits of the analysis, making legal protections, transparent governance, and explicit restrictions on non-public-health use integral to legitimacy [27].

CDR also raises a less visible equity problem. Populations with more complete testing, sequencing, and healthcare engagement are more observable to molecular surveillance than those with substantial undiagnosed infection or weak access [25], creating a surveillance-visibility bias in which the best-documented communities are easiest to prioritise. Data completeness should therefore be treated as a potential determinant of resource allocation, not merely a data-quality issue. Similarly, CDC recommends community participation in CDR planning, implementation, communication, evaluation, and data protection [10], but informing communities after practices are set differs from sharing influence over them. A stronger governance model would let affected communities shape terminology, priorities, acceptable data uses, safeguards, and evaluation criteria.

These considerations reveal a surveillance-trust paradox: CDR depends on complete, timely information, yet that information depends on people testing, engaging in care, and participating in partner services behaviours that opaque, stigmatising, or coercive surveillance can undermine. Trust is therefore part of CDR infrastructure. Systems must be informative enough to support rapid action, protected enough to minimise misuse, equitable enough to avoid reproducing surveillance disparities, and participatory enough to retain legitimacy.

9. A PROPOSED DETECTION-TO-ACTION FRAMEWORK

Existing CDR processes contain many of the elements needed to convert intelligence into action, but they are usually described as separate surveillance, investigation, and response activities rather than as a single pathway in which failure at one stage diminishes all subsequent stages. This review therefore proposes a Detection-to-Action Framework comprising seven interconnected functions (Figure 1). *Detect* identifies potential rapid transmission through complementary signals. *Interpret* tests whether patterns plausibly represent accelerated transmission, considers alternative explanations, characterises uncertainty, and extends investigation to the broader network. *Prioritize* sets urgency and intensity through contextual judgement. *Mobilize* the bridge between knowing and doing activates personnel, funding, partners, providers, and data-sharing mechanisms; separating it from intervention exposes a stage where delays otherwise remain hidden. *Intervene* delivers coordinated individual-, network-, and systems-level action. *Evaluate* asks whether the response produced meaningful change, including time-to-action, service uptake, and cluster trajectory, rather than whether activities were completed. *Adapt* feeds this evidence into thresholds, criteria, preparedness plans, and partnerships. Equity, community partnership, and data

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stewardship operate across all seven functions as conditions for legitimate and effective CDR.

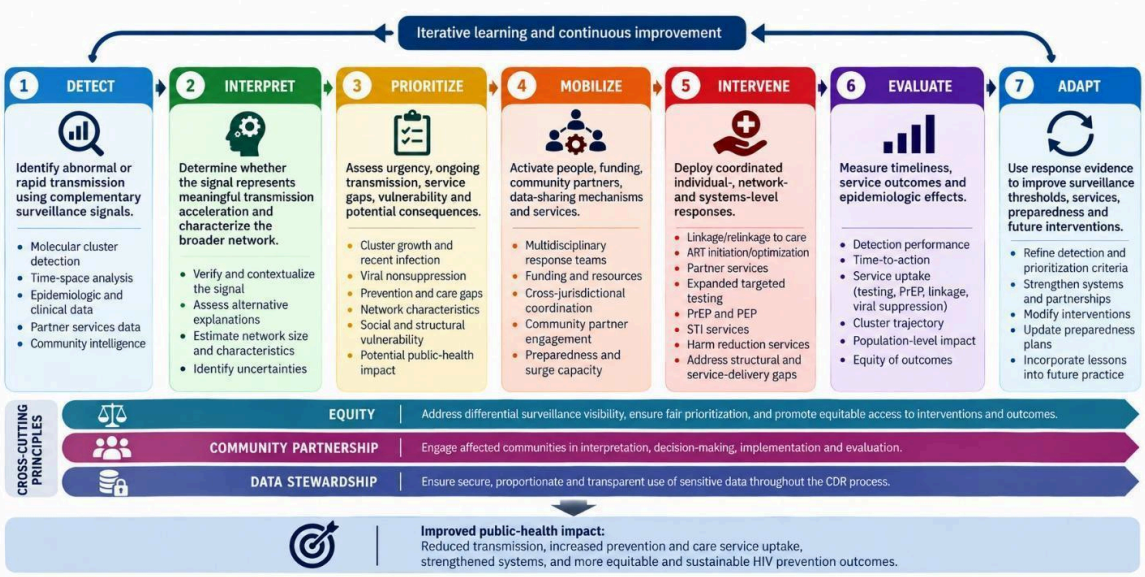


Figure 1. Detection-to-Action Framework for next-generation HIV cluster detection and rapid response. The framework links complementary surveillance signals to interpretation, prioritisation, resource mobilisation, multilevel intervention, evaluation, and adaptation. Equity, community partnership, and data stewardship operate across all stages, while feedback from evaluation and adaptation informs subsequent detection and response cycles.

The framework also makes visible where public-health value can be lost between detection and impact: delayed reporting weakens detection, missing context impairs interpretation, competing priorities delay decisions, insufficient resources impede mobilisation, fragmented services weaken intervention, and inadequate evaluation prevents learning. These cumulative losses are conceptualised here as the detection-to-action gap (Figure 2). Together, the figures distinguish CDR capability (the functions a system has) from CDR performance (whether those functions produce timely, equitable impact).

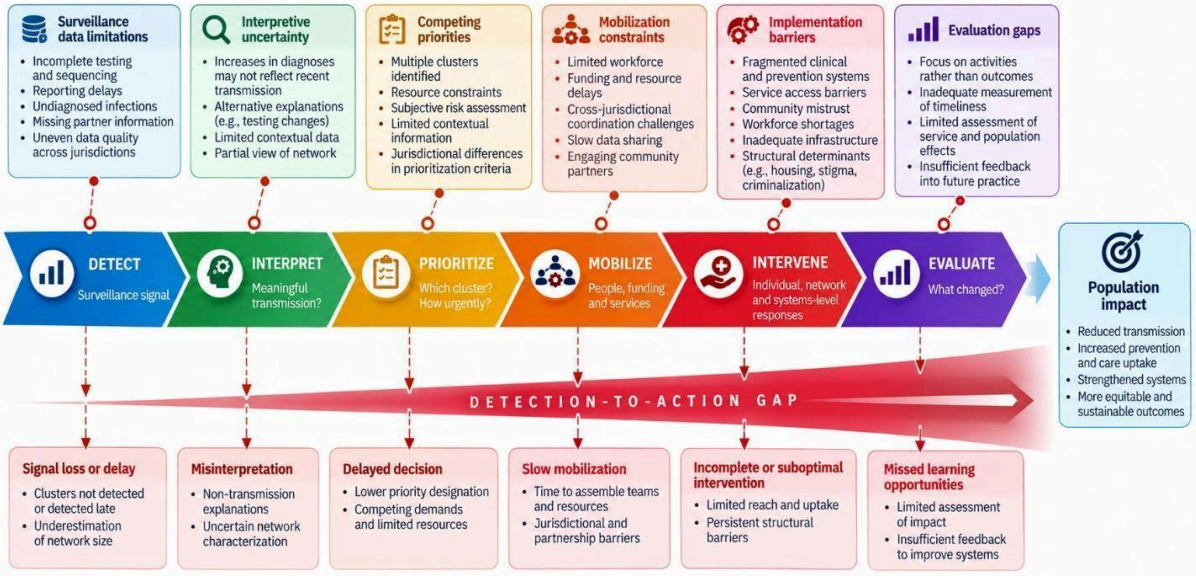


Figure 2. The detection-to-action gap in HIV cluster detection and response. The figure illustrates potential points of delay, information loss, coordination failure, or insufficient capacity between surveillance signal generation and measurable population impact. Widening of these gaps can progressively reduce the public-health value of otherwise timely cluster detection.

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10. RESEARCH PRIORITIES AND POLICY IMPLICATIONS

The most fundamental research question is whether earlier detection changes transmission trajectories that is, whether it shortens time to intervention and whether that improves prevention, care, and transmission outcomes. Studies should measure where delay accumulates and identify which combinations of molecular, time-space, clinical, partner-services, and network indicators best distinguish clusters needing intensive response from those suited to monitoring [31]. Because responses are multicomponent, attribution requires comparative implementation studies, natural experiments, interrupted time-series analyses, and modelling of counterfactual trajectories [24,32]. Research should also examine how workforce, infrastructure, funding, and partnerships shape effectiveness; which governance and data-sharing models minimise delay in multijurisdictional clusters [11]; and community trust, acceptability, perceived harms, and surveillance-visibility bias alongside epidemiological outcomes [28,39].

For policy, investment in detection technology is insufficient unless response capacity advances alongside it; otherwise the bottleneck simply moves from detection to implementation [14]. Four priorities follow. First, surveillance modernisation should emphasise interoperability and timeliness, with predefined cross-jurisdictional protocols for communication, leadership, data exchange, and responsibilities. Second, workforce and financing should treat response readiness as part of preparedness, with flexible surge resources directed toward underserved jurisdictions where surveillance and service gaps are greatest [25]. Third, affected communities should be treated as components of CDR infrastructure rather than recipients of interventions. Fourth, accountability should move beyond counts of clusters to time-to-action, service uptake, viral suppression, prevention access, cluster trajectory, equity, and sustained systems improvement [5]. The strongest system is one in which cluster detection both triggers a response and corrects the weaknesses that would otherwise permit future transmission.

11. STRENGTHS AND LIMITATIONS

This review integrates molecular epidemiology, outbreak investigation, implementation science, predictive analytics, and ethics into an operationally specific framework. As a narrative review, it may be subject to selection bias and provides no pooled estimates. The evidence is predominantly from the United States and draws heavily on CDC guidance and CDC-affiliated analyses, limiting transferability, and published outbreak reports may over-represent successful responses. The framework and time-to-action metrics are conceptual and have not been prospectively evaluated.

12. CONCLUSION

U.S. HIV cluster detection has evolved from conventional epidemiological recognition to a multimodal architecture incorporating molecular, time-space, clinical, partner-services, and community-derived information. This has strengthened the capacity to identify rapid transmission, but detection is only the beginning of the public-health pathway. The Detection-to-Action Framework Detect, Interpret, Prioritize, Mobilize, Intervene, Evaluate, and Adapt, underpinned by equity, community partnership, and data stewardship reframes CDR around the full pathway and exposes how the benefits of early detection can be lost through delayed decisions, fragmented systems, inadequate resources, structural barriers, or insufficient trust. The defining question should no longer be only “How quickly can we detect rapid transmission?” but “How quickly and effectively can detection be converted into action?” The next advance in HIV cluster response will depend on building public-health systems capable of acting on signals rapidly, equitably, and responsibly.

Declarations

Author contributions: Jane Ifeyinwa Anatuanya: conceptualisation, methodology, literature search,

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synthesis, visualisation, and writing of the original draft. Blessing Nwakaego Enenmoh and John Akor : literature search, synthesis, validation, and critical review and editing of the manuscript. Both authors read and approved the final version and agree to be accountable for all aspects of the work.

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Ethics approval: Not applicable; this review did not involve human participants or identifiable data.

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