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Spillover Risk Is Created by Interfaces Rather Than Pathogens Alone: A Multilevel One Health Architecture Linking Wildlife, Livestock, Companion Animals, Humans, Environmental Persistence, Contact Networks, and Host Susceptibility

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ABSTRACT

Zoonotic spillover is often framed as a property of pathogens: host range, virulence, receptor use, environmental stability, or evolutionary potential. Yet pathogen hazard becomes epidemiologically consequential only when ecological, animal, environmental, behavioral, and host conditions create an interface through which exposure can occur and infection barriers can be crossed. This article develops an original non-empirical One Health architecture that treats the interface, rather than the pathogen alone, as the operational unit of spillover interpretation. The synthesis separates wildlife reservoir context, livestock and companion-animal interfaces, human behavior, food and water pathways, environmental persistence, contact intensity, contact-network structure, host susceptibility, and pathogen compatibility, then considers how these dimensions can combine to amplify or constrain risk. The proposed architecture does not assign a universal score or assume that detected pathogen, environmental persistence, molecular adaptation, or animal infection is equivalent to human transmission. Instead, it organizes heterogeneous signals around interface states, evidence boundaries, and reassessment needs. Contemporary highly pathogenic avian influenza A(H5N1) in dairy cattle provides a high-resolution example, while broader viral, bacterial, ecological, and network evidence prevents the model from becoming outbreak-specific. The architecture is intended to support surveillance design, intervention targeting, and cross-sector interpretation before and during emergence. Its propositions remain context-dependent and require prospective, multispecies, route-specific, and externally replicated validation before predictive or operational performance can be claimed. Risk is consequently treated as dynamic and revisable as interfaces change through movement, husbandry, behavior, environmental conditions, surveillance findings, or intervention.

Keywords: One health, Zoonotic spillover, Human–animal interface, Contact networks, Environmental persistence, Host susceptibility

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Introduction

Spillover is not a single event caused by the intrinsic properties of a pathogen. It is the outcome of sequential barriers involving reservoir infection, pathogen release, environmental or direct exposure, recipient-host entry, and within-host establishment; failure at any barrier can interrupt the pathway [1]. This multibarrier view makes the conditions surrounding contact central to interpretation.

One Health analysis further requires animal, human, and environmental observations to be represented together rather than as independent surveillance domains. Cross-sector integration can expose relationships that siloed datasets obscure, although integration itself does not guarantee better decisions or outcomes [2]. The preventive corollary is that ecological and interface conditions may be legitimate targets before recognized human cases occur, provided interventions are locally feasible and supported for the system concerned [3].

The 2024 emergence of highly pathogenic avian influenza A(H5N1) in U.S. dairy cattle illustrates why pathogen-centered expectations can be insufficient. Avian-origin virus infected a novel production host with marked mammary involvement, revealing an interface in which host tissue, animal management, and infectious product became simultaneously relevant [4]. This article therefore proposes an interface-centric architecture linking wildlife, livestock, companion animals, humans, food and water, environmental persistence, contact intensity and networks, host susceptibility, and pathogen compatibility. It is an organizing synthesis, not a validated risk score, and it preserves uncertainty about direction, mechanism, and transferability.

From pathogen-centric to interface-centric spillover

Pathogen properties define hazard, but hazard is not equivalent to realized spillover risk. A virus, bacterium, or other zoonotic agent must still encounter an ecologically available source, a route that delivers sufficient exposure, and a recipient host in which infection can establish [1]. An interface-centric view therefore asks not only what the pathogen can do, but where, how often, through which matrix or task, and in whom its opportunities are created.

Cross-sector interaction matters because the same event can be simultaneously biological, environmental, occupational, and organizational [2]. Ecological change can also alter those opportunities upstream, making prevention partly a problem of modifying contact-generating conditions rather than waiting for human infection to reveal them [3]. Neither proposition supplies a universal additive formula.

A multilevel interface framing is thus consistent with established multibarrier spillover theory, One Health integration, and ecological prevention, while remaining distinct from each of them [1–3]. The proposal developed here treats an interface as a conditional configuration of sources, recipients, routes, matrices, behaviors, networks, and susceptibility. Its purpose is adjudication: to distinguish pathogen detection from exposure opportunity, exposure opportunity from infection, and infection from onward transmission.

Wildlife reservoirs

Wildlife reservoir relevance depends on ecological context rather than wildlife presence alone. Across global assemblages, known zoonotic host species can become relatively more abundant or diverse in human-dominated ecosystems, indicating that land use can restructure the composition of interfaces where people and domestic animals encounter wildlife [5]. This association does not mean that biodiversity loss or wildlife proximity uniformly increases spillover; local contact and exposure remain necessary.

Wildlife interfaces are also temporally unstable. Climate-driven range shifts are projected to create novel mammalian encounters and opportunities for viral sharing, meaning that present-day reservoir maps may become progressively incomplete as species redistribute [6]. Modeled viral sharing, however, is not the same as observed zoonotic transmission, and projections depend on ecological and climatic assumptions.

Genomic surveillance adds another layer by revealing viral diversity and related lineages across wildlife, domestic, and managed-animal settings [7]. Such signals justify multispecies attention at shared interfaces, but phylogenetic relatedness alone cannot establish transmission direction, frequency, or human relevance. In the proposed architecture, wildlife therefore contributes reservoir pressure and changing encounter opportunity, not a self-sufficient risk designation.

Livestock interfaces

Livestock systems can transform an isolated host jump into a persistent epidemiological concern when susceptible tissues, animal aggregation, production practices, and infectious materials align. In dairy cattle affected by H5N1, field and laboratory investigation documented infection in a novel mammalian production context with prominent mammary involvement [4]. That evidence establishes host and production-system relevance without, by itself, resolving every within- or between-herd transmission route.

For interface analysis, “farm exposure” is therefore too coarse. This article proposes decomposing a livestock interface into animal-level infection, production procedures, animal products, movement, worker contact, and the

physical environment. The cattle evidence directly supports the coexistence of infected animals, susceptible tissue, and virus-rich milk; movement and occupational components require their own evidence rather than being inferred automatically from the farm label [4].

The same livestock setting may consequently contain several plausible exposure opportunities at once. Infected animals and infectious products can coexist, yet coexistence does not prove which route generated a specific subsequent infection [4]. Livestock interfaces should therefore be interpreted as layered systems whose components can amplify, constrain, or merely accompany transmission, with mechanism assigned only when the relevant evidence supports it.

Companion-animal interfaces

Companion animals can enter interfaces created by livestock outbreaks, households, veterinary care, food practices, or shared environments. During affected U.S. dairy outbreaks, domestic cats were infected alongside cattle, demonstrating that companion animals can become involved in a production-linked H5N1 setting [8]. Their epidemiological position remains conditional: infection may make them useful sentinels or potential bridges, but the available outbreak evidence does not establish cats as routine amplifiers or prove a single exposure route.

The companion-animal interface also extends beyond acute viral emergence. Genomic analysis of uropathogenic *Escherichia coli* from dogs and cats identified lineages similar to those associated with human urinary tract infection [9]. This supports attention to shared bacterial populations across human–animal settings, while genomic similarity alone cannot determine whether transfer was pet-to-human, human-to-pet, or from a common source.

Human behavior modifies these interfaces further. Among surveyed cat and dog owners in Bangladesh, zoonosis knowledge and preventive practices were heterogeneous [10]. Such evidence is geographically and behaviorally bounded, but it demonstrates that animal contact is mediated by what people know and do. Companion-animal risk should therefore be interpreted through both biological and behavioral context.

Human behavioral interfaces

Human behavior determines whether biological opportunity becomes meaningful exposure. Handling practices, hygiene, animal care, food choices, use of protective measures, and responses to animal illness can alter the circumstances in which contact occurs. Evidence from Bangladeshi pet owners shows measurable variation in zoonosis knowledge and preventive practice, supporting behavioral heterogeneity as an interface feature while not establishing that any reported deficit caused infection [10].

For spillover analysis, behavior should therefore be specified by task and plausible route rather than compressed into a binary statement that "animal contact" occurred. This task–route decomposition is proposed here: at this stage, the approved behavioral evidence supports heterogeneity of practices, not a universal ranking of biological efficiency across tasks [10]. The same reported animal contact may represent routine co-presence, direct handling, contact with excreta or products, or an incompletely characterized exposure; these categories should not be assumed equivalent.

Table 1 presents task, route, and source details required to resolve human animal-contact exposure.

Table 1. Task, route, and source details required to resolve human animal-contact exposure

Human activity context	Animal or source setting	Contact detail required	Exposure-pathway question	Classification outcome	Unknown route efficiency and reclassification
Routine companion-animal care with variable prevention	Animal illness; household setting; risk literacy	Handling, hygiene, prevention history	Behavior modifies exposure opportunity	Clarify practices before escalation	**Unknown:** Self-report; local context **Reclassify:** Update after practice or animal-status change **Basis:** Evidence-supported context; broader use proposed
Outbreak-linked farm–household overlap	Infected livestock; companion animals; products	Co-occurring infection plus task history	Multiple plausible exposures coexist	Separate source, task, and matrix	**Unknown:** Co-occurrence does not prove route **Reclassify:** Update with route-specific evidence **Basis:** Proposed adjudication state
Unspecified animal contact	Species; duration; task; material	Generic contact history	Exposure is insufficiently resolved	Obtain task- and route-specific detail	**Unknown:** No biological efficiency can be inferred **Reclassify:** Reclassify when

	resolved
	Basis: Proposed

Shared food and water interfaces

Food-production systems connect animal infection with environmental, occupational, processing, distribution, and consumer pathways. Their contribution to emergence is therefore multistage rather than reducible to a single "foodborne" route; food production can alter ecological conditions, husbandry, trade, animal density, and human exposure in pathogen- and commodity-specific ways [11]. The architecture proposed here separates production, processing, and consumption subinterfaces so that evidence from one stage is not automatically transferred to another.

Processing can materially modify an interface. Under controlled laboratory conditions, heating raw milk at defined temperatures reduced infectious H5N1, demonstrating thermal susceptibility of virus in that tested matrix [12]. These experiments do not constitute complete validation of every commercial pasteurization configuration, where scale, flow, equipment, and handling differ.

Matrices also differ in their capacity to preserve infectious material. Experimental work comparing milk, wastewater, and surfaces showed that H5N1 stability changes with matrix and temperature [13]. Persistence therefore modifies the duration of an exposure opportunity, but it does not establish that a contaminated food or water matrix caused transmission in the field. Product safety and spillover inference require the processing condition, matrix, route, and recipient to remain analytically separate.

Environmental persistence

Environmental persistence is best treated as a time-dependent modifier between pathogen release and effective exposure. In controlled experiments, infectious H5N1 showed different stability across milk, wastewater, surfaces, and temperatures [13]. This demonstrates that an environmental or product matrix can preserve or shorten opportunity for contact; it does not demonstrate that every persistent signal is epidemiologically capable of producing infection.

That distinction matters for surveillance. Detection of viable pathogen in a matrix can strengthen evidence that an exposure opportunity existed, whereas nucleic-acid detection may answer a different question; neither alone identifies the recipient, dose, route, or subsequent transmission chain. For the present architecture, persistence therefore occupies a boundary position between source and contact rather than serving as a surrogate outcome.

Field relevance also requires cautious transfer from controlled systems. Irradiated or experimentally inoculated matrices cannot reproduce all effects of dilution, sunlight, competing microorganisms, handling, or heterogeneous contamination [13]. Route-specific and multisource field evidence is consequently needed before laboratory stability is converted into a causal farm or community transmission explanation. Persistence extends the window in which an interface may operate; it does not complete the spillover pathway.

Contact intensity

Contact intensity should describe more than co-presence. Frequency, duration, route, material contacted, and ecological context can change the meaning of repeated human–animal encounters. At a Kenyan human–livestock–wildlife interface, exposure patterns and livestock serologic status were associated with human Crimean-Congo haemorrhagic fever virus serostatus [14]. Because vector exposure and cross-sectional timing provide credible alternatives, the finding supports a multidimensional contact construct rather than direct livestock-to-human causation.

Intensity must also be separated from network structure. Modeling of cattle movements showed that reorganizing who contacts whom can alter simulated epidemic spread even when the problem is not reduced to individual-level behavior [15]. Such results establish a network principle, not proven field effectiveness of a specific rewiring intervention across pathogens.

The 2024–2025 H5N1 cattle episode illustrates how local infection can become geographically consequential through connected production systems. Genomic and epidemiological reconstruction was consistent with cattle-associated interstate dissemination after a likely introduction, including movement occurring before infection was necessarily obvious [16]. In the proposed architecture, contact intensity therefore captures how much and under what conditions exposure occurs, whereas network structure captures how those contacts connect interfaces across animals, holdings, and places. Neither dimension substitutes for host susceptibility or route-specific evidence.

Contact-network structure

Contact-network structure determines how local interfaces become connected epidemiological systems. Similar contact intensity can produce different spread potential when holdings, movements, or bridge links differ. Cattle-movement modeling demonstrates that rewiring network connections can change simulated infection spread, supporting topology as a distinct determinant rather than a restatement of individual exposure [15].

The architecture therefore separates contact quantity from contact position. A frequent contact may have limited reach, whereas a bridge can connect farms, species, or sectors. Network-derived states should therefore remain measurement-dependent until temporal resolution, duration, proximity, and pathogen-relevant route are validated. **Table 2** presents local clusters, bridge connections, and sparse networks compared by spillover relevance.

Table 2. Local clusters, bridge connections, and sparse networks compared by spillover relevance

Network question	Repeated local clustering	Bridge-connected interfaces	Apparently sparse network
Spillover-relevant interpretation	Sustains opportunity within one interface	Links otherwise separated groups	Low observed connectivity, not necessarily low risk
Network measurement dependency	Group size; husbandry; persistence	Movement; shared personnel; premises	Sampling coverage; resolution
Connection pattern observed	Recurring within-group contacts	Cross-group contact or movement	Few recorded links
Priority node or link	Intensify local source/route investigation	Prioritize bridge investigation	Audit measurement before de-escalation
Failure mode of network data	Proximity may not equal effective contact	Direction and infectious timing may be unknown	Missed or short contacts possible
Temporal reconstruction needed	Reassess with pathogen-relevant contact definition	Update after temporal reconstruction	Repeat with validated resolution
Basis	Proposed	Proposed	Proposed

Host susceptibility

Host susceptibility is a barrier distinct from exposure and from onward transmissibility. Bovine H5N1 infected mammalian models while respiratory transmission among ferrets was inefficient under tested conditions [17]. Mammalian infection competence therefore cannot be treated as evidence of efficient human-to-human spread.

Compatibility can also change at a molecular level without determining the complete transmission phenotype. A Q226L substitution in bovine H5N1 haemagglutinin switched receptor specificity toward human-type receptors in the tested assays [18]. This identifies one barrier, not a sufficient cause of sustained transmission.

Interpretation must also accommodate conflicting or assay-dependent evidence. A subsequent reassessment found poor binding of bovine H5N1 to human-type sialic-acid receptors in the assays used [19]. Poor binding does not imply impossibility of human infection, just as a favorable receptor result does not establish population transmissibility. The proposed architecture therefore treats tissue availability, entry, replication competence, and host context as susceptibility layers, while onward spread remains a separate evidential state.

Pathogen adaptation and compatibility

"Adaptation" is too coarse when experiments measure different barriers. Bovine H5N1 pathogenicity and transmission experiments interrogate whole-virus behavior in animal models [17]. Receptor-switch experiments interrogate a narrower molecular component of host compatibility [18]. Tissue tropism, receptor use, replication, shedding, stability, and transmission competence can be related without being interchangeable.

Current bovine H5N1 evidence illustrates this non-equivalence particularly clearly. Receptor-binding observations and mammalian transmission phenotypes are partly discordant across experimental systems [17–19]. Each assay instead constrains a different component of the host–pathogen interface.

For this architecture, pathogen compatibility is consequently represented as a set of conditional barriers rather than a scalar "adaptation level." A change that lowers one barrier may leave others intact; conversely, successful infection in one tissue does not establish efficient exit, exposure of another host, or onward transmission. This proposed decomposition requires pathogen-specific adaptation.

Interface amplification

An interface becomes amplifying when conditions support more than an isolated cross-species event. Genomic epidemiology on mink farms demonstrated SARS-CoV-2 transmission from humans to mink and back to humans, providing proof that dense animal-production systems can support bidirectional animal–human transmission under some conditions [20]. Its magnitude and mechanism are not automatically generalizable.

Animal amplification may also occur without detected human infection. During an H5N1 outbreak in farmed mink in Spain, epidemiological and genomic findings were consistent with within-farm spread, while sampled workers tested negative [21]. Negative worker testing does not prove absence of human risk; it separates animal expansion from confirmed zoonotic spillover.

Observability further modifies apparent amplification. A mathematical model of H5N1 spread in U.S. dairy cattle showed that assumptions about cattle movement and under-ascertainment altered reconstructed epidemic dynamics [22]. The architecture therefore separates amplification from observability: surveillance gaps can hide transmission, while increased detection can mimic growth. Neither model output nor case counts establish mechanism alone.

A proposed spillover-interface architecture

The proposed architecture organizes six interacting, non-additive dimensions: source pressure, exposure interface, environmental persistence, contact structure, host susceptibility, and pathogen compatibility. The dimensions are deliberately separated because a strong observation in one domain cannot be assumed to compensate for absent evidence in another. Multibarrier spillover theory supports the requirement that several conditions align [1]; matrix-dependent persistence shows that exposure opportunity can be prolonged or shortened [13]; network evidence shows that connectivity changes spread potential [15]; and mammalian experiments demonstrate that infection competence is distinct from efficient transmissibility [17].

The architecture is noncompensatory. A highly connected interface cannot create infection if a necessary biological barrier is not crossed, while strong host compatibility cannot generate exposure where no viable route exists. Animal-production systems can nevertheless amplify successful transmission once barriers align, as demonstrated in mink, while amplification without observed human infection shows that progression between levels is not automatic [20].

Uncertainty is treated as a structural component rather than an afterthought. Assay discordance can alter interpretation of compatibility [19], and model results can depend on under-ascertainment and movement assumptions [22]. The figure separates evidence-supported conditions from proposed transitions, competing mechanisms, and reassessment feedback.

The architecture's scientific job is to show where converging evidence can justify escalation without falsely converting heterogeneous signals into one score.

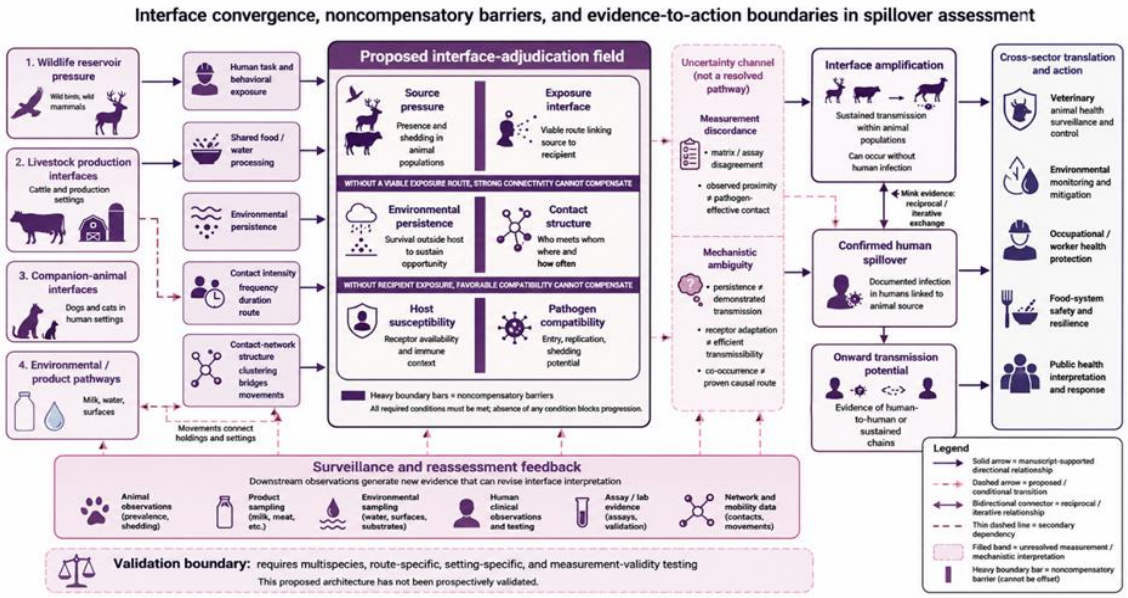

Figure 1. Interface convergence, noncompensatory barriers, and evidence-to-action boundaries in spillover assessment

High-risk interface states

A high-risk interface state should represent evidence that a barrier has actually been crossed, not merely that a hazardous pathogen is present. Confirmed H5N1 infection in a dairy farm worker after occupational exposure demonstrates zoonotic infection at an animal–human interface [23]. One case does not define incidence, severity distribution, or onward transmissibility.

Repeated zoonotic infections also remain distinct from self-sustaining human transmission. In the U.S. 2024 H5N1 case series, infections were predominantly associated with animal exposure and sustained person-to-person transmission was not identified during the observation period [24]. Ascertainment limitations prevent treating this as a permanent boundary.

Route matters within the state itself. Experimental work with a dairy-worker-associated H5N1 virus supported ocular infectivity and replication in tested in-vitro and ferret systems [25]. The architecture therefore proposes three nonnumeric states: unresolved exposure opportunity, recipient-host infection, and onward transmission. Route-specific portals, clinical findings, and network context modify interpretation within each state rather than generating interchangeable points.

Table 3 presents recipient-evidence thresholds separating exposure opportunity, spillover, repeated spillover, and onward transmission.

Table 3. Recipient-evidence thresholds separating exposure opportunity, spillover, repeated spillover, and onward transmission

Transmission boundary	Minimum recipient evidence	Epidemiological threshold crossed	Response focus	Next boundary to test
Exposure opportunity	**Observed:** Source plus route-specific contact **Conditions:** Task; matrix; duration; susceptibility	A plausible route exists	Target source and exposure investigation	**Not yet established:** Infection not established **Next test:** Seek recipient evidence **Basis:** Proposed
Confirmed zoonotic infection	**Observed:** Recipient infection linked to animal exposure **Conditions:** Portal; host factors; clinical context	A species barrier has been crossed	Escalate One Health investigation	**Not yet established:** Does not establish onward spread **Next test:** Assess contacts and transmission evidence **Basis:** Proposed hierarchy; case-supported distinction
Repeated animal-associated cases	**Observed:** Multiple animal-associated human infections **Conditions:** Ascertainment; shared exposures	Spillover may recur across interfaces	Intensify route and network analysis	**Not yet established:** Sustained human transmission not implied **Next test:** Reassess transmission chains **Basis:** Proposed state
Onward human transmission	**Observed:** Epidemiological and virological transmission evidence **Conditions:** Contact network; infectious period	Recipient becomes a source	Shift response toward human transmission control	**Not yet established:** Requires direct evidence **Next test:** Continuously update **Basis:** Proposed boundary

Intervention points

The interface framing permits intervention before, within, or after a documented species jump. Upstream measures can target ecological conditions that create encounters [3]. Within livestock systems, movement-network interventions can target connections that facilitate modeled spread [15]. After confirmed zoonotic infection, case investigation addresses a different barrier and decision problem [23]. These tiers are complementary, not an effectiveness ranking.

Process interventions require condition-specific validation. Heating raw milk reduced infectious H5N1 under specified experimental conditions [12], supporting control of a product-related interface while not establishing equivalence across every commercial processing system. Route-specific control should likewise follow the plausible portal rather than generic “farm contact.”

Ocular infectivity demonstrated in experimental systems provides mechanistic justification for considering eye exposure in task-specific control design [25], but it does not measure the effectiveness of any particular protective

device. The proposed principle is barrier matching: identify modifiable source, task, matrix, route, connectivity, and recipient conditions, then reassess the interface. Feasibility, animal health, livelihood, and implementation constraints remain system-specific.

Surveillance implications

Surveillance should target changing interfaces rather than sample all hosts and matrices uniformly. Adaptive risk-based surveillance at wildlife–livestock boundaries demonstrates that priorities can be updated as risk inputs change [26]. The architecture may structure such targeting but has not been shown to improve detection.

Different sampling streams interrogate different parts of the same interface. A One Health investigation on two H5N1-affected dairy farms found differing results across cattle, milk, and worker-related sampling [27]. California dairy-farm surveillance likewise found animal and environmental signals compatible with several pathways without resolving causal weights [28]. Milk-monitoring work further showed that assay choice, sampling coverage, and timing influence what surveillance can detect and how a result should be interpreted [29]. Surveillance should therefore represent discordance rather than erase it. Discordance can arise because matrices sample different compartments, assays have different analytical properties, or sampling occurs at different points in an evolving interface. A negative nasal sample need not negate a positive milk or environmental signal if the matrices address different biological questions; conversely, a positive environmental result does not prove recipient infection. The architecture proposes source, matrix, assay, timing, and coverage labels, followed by reassessment when streams disagree.

Cross-sector response

Cross-sector response should begin when converging evidence creates a consequential interface problem, not only after every sector reaches identical diagnostic certainty. One Health integration demonstrates the analytical value of connecting animal, human, and environmental information [2], while adaptive risk-based surveillance shows that attention can be reallocated under changing conditions [26]. This proposed trigger logic remains unvalidated operationally.

Farm investigations also show why sectors should reconcile, rather than rank, their observations as interchangeable tests. Multistream H5N1 surveillance demonstrates that animal, product, environmental, and human signals interrogate different components of the same interface [27–29]. Discordance may therefore identify a measurement or pathway question rather than simple surveillance failure.

Response should preserve sector-specific constraints while evidence is updated. Ecological intervention may be appropriate upstream [3]; human behavior can change exposure opportunity but is locally heterogeneous [10]; and farm investigations may reveal several plausible routes simultaneously [27]. The architecture proposes shared states, explicit uncertainty, assigned follow-up ownership, and reversible escalation. It does not establish that any governance arrangement is universally feasible, sufficient, or more effective than existing systems.

Transferability and validation

Transferability cannot be assumed from a global pattern, a single outbreak, or one measurement system. Validation must therefore examine not only discrimination but whether the same interface definitions remain interpretable across species, pathogens, husbandry systems, and surveillance intensities. Global modeling of emerging zoonotic disease hotspots showed that observed emergence reflects ecological correlates together with uneven reporting effort [30]. Local use therefore requires separating biological risk from observation intensity and external validation.

Interface priorities must also reflect local contact ecology. An ecologically founded framework for migratory wildlife–livestock contact demonstrated how prioritization can be built around actual opportunities for interspecies interaction rather than static species labels [31].

Network inputs require measurement validation. Real-time location data from confined feedlot cattle produced different inferred contact networks when temporal resolution and contact-duration definitions changed [32]. Proximity should not be assumed equivalent to pathogen-effective contact.

Finally, mechanisms must remain falsifiable. In controlled dairy-cow experiments, a low intramammary H5N1 dose produced infection, while transmission to sentinels through contaminated milking equipment or close contact was not demonstrated under the tested conditions [33]. This does not exclude those farm routes; plausible

mechanisms still require route-specific field and experimental testing. Prospective multisite validation should test state reproducibility, calibration, actionability, and failure across pathogens and production systems.

Conclusion

Spillover risk is better interpreted as a property of changing interfaces than as a fixed attribute of pathogens. The architecture proposed here separates source pressure, exposure routes and matrices, environmental persistence, contact intensity and topology, host susceptibility, pathogen compatibility, amplification, and surveillance observability so that evidence at one level is not mistaken for proof at another. Its central boundary is noncompensatory: strong signals cannot substitute automatically for a missing exposure or biological barrier. High-risk states therefore remain route-specific, evidence-bounded, and revisable. The framework offers a common language for veterinary, environmental, occupational, food-system, and public-health interpretation without assigning unsupported scores or universal thresholds. Its value remains hypothetical until prospective, multispecies, multisite, and route-specific validation establishes whether it improves risk discrimination, intervention targeting, or cross-sector decisions.

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