

LEVERAGING SYSTEMS-OF-SYSTEMS ANALYSIS TO STRENGTHEN EPIDEMIC INTELLIGENCE FOR PREPAREDNESS AND RESPONSE

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The COVID-19 pandemic exposed significant gaps in the coordination and integration of efforts required to effectively manage large-scale infectious disease outbreaks. A successful response to such crises demands the swift and ongoing synthesis of information and activities across multiple sectors, including government, healthcare, and private industry. However, these systems are often managed in isolation, leading to misaligned policies, fragmented communications, and inefficiencies that hinder pandemic response efforts. To address these challenges, we propose adopting a systems-of-systems (SOS) paradigm to enhance epidemic intelligence and improve preparedness and response during infectious disease emergencies. The SOS approach, widely used in engineering, offers a framework for integrating diverse fields such as virology, ecology, psychology, and policy. We illustrate the potential of this approach using highly pathogenic avian influenza (HPAI) as a case study and discuss key considerations for implementing SOS thinking in the context of global epidemic intelligence systems.

Keywords: Epidemic preparedness, Infectious disease intelligence, Interdisciplinary integration, Pandemic response framework, Systems-of-systems (SOS)

INTRODUCTION

THE COVID-19 PANDEMIC illustrated and surfaced much about how emerging pathogens, particularly ones with the ability to cause widespread and severe illness, can quickly stress our public and private healthcare systems, economies, and social structures. An effective sustained response to a large-scale infectious disease outbreak

is one that reduces and prevents premature deaths, severe illness and hospitalizations, and social and economic disruption. Achieving such a response requires fast, extensive, and ongoing integration of the information and activities of multiple entities. Significant and visible policies, actions, and communications need to be consistently aligned among elected leaders, federal government agencies and ministries, state and local public health departments, private sector

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health and medical care providers, health care payors (eg, insurance and managed care), pharmaceutical and biotechnology firms, and a host of businesses and industries. However, as the COVID-19 pandemic demonstrated, while these entities and their efforts are highly interconnected with multiple codependencies, they are typically managed in isolation. During the COVID-19 pandemic, for example, poor and inconsistent policies and communications,¹ along with manufacturing and supply chain challenges,² impeded government and healthcare providers' ability to respond, limited the availability and use of medical care, and reduced public and patient confidence in the pandemic response.³

We propose adapting a systems-of-systems (SOS) paradigm for information synthesis and decision support to advance outbreak preparedness and response. An SOS approach, commonly used to solve complex engineering problems, holds particular promise in addressing challenges at the intersection of fields from virology to ecology, human psychology to policy, and governance. Accommodating such wide-ranging interdisciplinarity is a key requirement of any effort to build epidemic intelligence systems at national or global scales.

PANDEMIC COMPLEXITY

The imperative for developing a systematic approach to epidemic and pandemic response is underscored by several factors, starting with the significant cost and frequency of novel zoonotic events.⁴ These events wreak havoc not only in terms of public health but also through economic and societal dimensions. The impacts of epidemics and pandemics are manifold, encompassing nearly every sector of society,⁵ and disproportionately affect vulnerable communities⁶ by exacerbating existing inequalities. Supply chains may be disrupted,⁷ leading to shortages of essential goods and services. Business closures contribute to a domino effect of economic decline, resulting in unemployment and social dislocation. Health impacts extend beyond immediate mild and severe illnesses and fatalities to include adverse impacts on mental wellbeing⁸ and stress on healthcare systems⁹ disrupting services (eg, cancer treatment) and routine care (eg, vaccination against other infectious diseases).¹⁰

The principal obstacle to the needed advances in our pandemic response system is that existing paradigms are ineffective when it comes to delivering reliable predictions and decision support. Pandemics are complex, influenced by a multitude of variables that range from virus characteristics to local human behaviors to global travel patterns.¹¹ Furthermore, they are relatively rare events, which makes past experiences an unreliable basis for modeling or anticipating future occurrences.¹² Each pandemic also comes with its own set of unique, often idiosyncratic properties that are crucial for understanding disease spread and

impact. For example, the asymptomatic transmission of SARS-CoV-2¹³ presented an unprecedented challenge for containment, as infectious disease response plans were based on individuals knowing they were infected as the basis of behavior modification.¹⁴ Similarly, culturally significant but biomedically unsafe practices, such as those involving burial, contributed significantly to virus transmission during the 2014–2016 West Africa Ebola epidemic.

Further complicating pandemic planning and response is the fact that an effective response to a pandemic requires a multifaceted strategy tailored to a wide variety of stakeholders.¹⁵ Different stakeholders, ranging from public health officials to businesses and local communities, require different kinds of information for effective decisionmaking. Moreover, these stakeholders often have access to different information to which they respond differently, perhaps due to competing interests. One analysis of feedback between global supply chain disruption and COVID-19 dynamics showed that better sharing of information between sectors would have significantly improved pandemic containment.¹⁶

Modeling is integral to infectious disease intelligence, but as practiced, it remains disjointed. As the COVID-19 pandemic unequivocally demonstrated, models of transmission, behavior, environment, mobility, or molecular evolution can each provide insights about a pandemic but are an incomplete approach on their own. While many validated models address aspects of epidemic progression,¹⁷ a critical question for scalable infectious disease intelligence is how to synthesize information from disparate sources in a rigorous yet timely fashion.¹⁸ As a consequence, scientific and medical experts, decisionmakers, and other stakeholders must informally balance the competing and sometimes incommensurable findings that result from the fractured and pluralistic practices of modeling and data analysis. This contributes to a lack of unified public messaging, potentially exacerbates the spread of misinformation and inconsistent guidance, and limits the effectiveness of biomedical and nonpharmaceutical interventions that are necessary for control and long-term management.

Dynamical modeling is essential to managing epidemics because there are no alternative purely data-driven approaches for generating the full range of intelligence needed.^{19,20} Of course, we can and must learn from past outbreaks²¹ (and “near misses”), but each epidemic is sufficiently different from previous ones that prior experience is an inadequate guide for future decisionmaking. Similarly, unlike severe weather events, pandemics are sufficiently infrequent that it is challenging to establish robust and definitive insights through statistical generalization. Dynamical modeling is also necessary for simulating counterfactual scenarios that are used to assess the potential effectiveness of different control strategies.²² Finally, there is no feasible experimental approach that will scale to generate the scientific information necessary for epidemic prediction and

prevention. Hence, modeling will continue to be the primary means for generating knowledge about contributing factors and potential outcomes of emerging diseases.

The fact that pandemic prediction and prevention is a multidisciplinary challenge means that diverse theories, concepts, and frameworks from across the natural, biomedical, and social sciences must be integrated. The inherent incompleteness of science, which precludes the development of any single “master model,” makes this challenge formidable. For example, while phylodynamic analysis offers valuable insights into the historical trajectory of an epidemic, it falls short of providing actionable intelligence. On the other hand, although detailed simulation models may be used for scenario analyses, their tendency to overparameterization renders them suboptimal for inference.

Here we explore the idea that the SOS paradigm can be used to understand and anticipate the impacts of emerging diseases. The SOS approach provides a framework for the integration of heterogeneous, interdependent systems incorporating diverse sources of information across multiple scales and, crucially, enables understanding how those systems interact when there are feedbacks among systems. Feedbacks are reciprocal causal processes through which interactions in 1 domain propagate to others and ultimately alter the dynamics of the originating system.

In a traditional SOS, each system has its own control processes and decentralized decisionmaking. Nevertheless, global behavior is not simply the summation or centralized coordination of systems. Instead, it evolves from feedback among the independent systems to produce emergent global behavior. The whole is not the sum of its components. We envision adapting this paradigm (which has been applied successfully to a variety of design tasks)²³⁻²⁵ to epidemic modeling (which traditionally involves separate representations for spillover, transmission, movement, pathology, evolution, etc.). We believe an effective system of predictive epidemic intelligence can be built using the SOS paradigm, with individual component models representing systems with operational and managerial independence (eg, ecology, epidemiology, engineering, public health, business and economic impact, risk communication) and distinct geographies (eg, countries, regions, cities, communities).

ANALYTIC CHALLENGES FOR ADVANCING EPIDEMIC INTELLIGENCE

We define epidemic intelligence as the systematic collection, analysis, and interpretation of data on outbreaks of infectious diseases for understanding, predicting, and mitigating their spread. Components include real-time surveillance of disease outbreaks, modeling to predict the spread of the disease, and decision-support systems to enhance public health responses.^{26,27} To address the global need for better epidemic intelligence, the World Health Organization

(WHO) Hub for Pandemic and Epidemic Intelligence is advancing a new vision for integrated information gathering that includes traditional surveillance, event-based surveillance, participatory or community surveillance, and on-the-ground investigations²⁷ to (1) ensure that global actors are aligned around top priorities and sharing of information, (2) identify and adopt effective solutions to surveillance challenges, and (3) ensure these solutions are scaled up widely around the world. In the era of big data and advanced analytics, this surveillance has increasingly come to involve sophisticated algorithms and computer models that can analyze vast and diverse datasets, ranging from medical records and laboratory tests to social media posts and personal geolocation data, all aimed at providing a real-time picture of how a disease is spreading and identifying what interventions may be most effective.

In its strategy plan for pandemic and epidemic intelligence, the WHO identifies as a key obstacle that “technology has not yet been fully harnessed to suit the full range of public health contexts, and the different systems have not yet been able to combine their strengths and information to give better insights.”²⁸ This obstacle arises from the disparate sources of information and methods used across disciplines. These diverse approaches often lack effective intercommunication and even shared concepts. This challenge has several layers, each contributing to the problem of ineffective or suboptimal informational support for decisionmakers tasked with managing outbreaks. Specific challenges include:

- **Variability in data types and sources.** Different disciplines generate and make use of different kinds of data. For example, epidemiologists focus on case reports, environmental samples, and genomic sequences; economists study market trends and employment; and social and behavioral scientists investigate human beliefs, behaviors, and social norms. These diverse data often exist in silos, which make it challenging to develop a comprehensive understanding of the multifaceted nature of disease outbreaks.
- **Disparate analytical approaches.** Methods used for data interpretation also vary widely among disciplines. The statistical models that epidemiologists find useful may be drastically different from the game theory models employed by economists or the qualitative methods of social scientists.
- **Terminological and ontological gaps.** Another obstacle is the lack of common terminology and theoretical ontologies. Each discipline has its specialized language and frameworks for understanding, making interdisciplinary communication difficult. Without a common language or set of concepts, there is a serious risk of misunderstanding and overlooked insights.
- **Lack of established platforms for collaboration.** In many cases, formal infrastructure to support interdis-

ciplinary collaboration remains underdeveloped. Even if experts from various fields wish to collaborate, the absence of a central platform can inhibit effective communication and data sharing.

- **Competing interests and objectives.** Different stakeholders have different priorities and objectives. For instance, public health officials are primarily concerned with reducing morbidity and mortality, while economic advisors might focus on minimizing economic disruption. These diverging objectives, which reflect genuinely different values, can impede consensus about the best course of action.

To overcome these challenges, it is necessary to develop mechanisms for interdisciplinary collaboration in the context of epidemic intelligence, including common data repositories, shared analytical tools, and theories or conceptual frameworks that facilitate multidisciplinary understanding.

HOW A SYSTEM-OF-SYSTEMS APPROACH CAN MEET THESE CHALLENGES

Because an SOS approach focuses on designing, engineering, maintaining, and evolving a collective of systems that are interactive yet largely autonomous, it could emphasize

the strategic management of system interactions to achieve broader objectives and overcome the traditional boundaries between disciplines without reinventing them. Within an SOS, distinct constituent systems—each with its own operational priorities and governance—interact via feedback mechanisms that are often nonlinear. This interactivity, a defining characteristic, distinguishes SOS from simple system aggregations or linear progressions.

Figure 1 illustrates how each system in a minimal SOS (comprising just 2 constituent systems) is agnostic about the structure of systems exogenous to it, but flows within the system are affected by a set of interactions that are a function of the states of the exogenous system. In this example, System 1 is a model of a vaccine supply chain, and System 2 is a compartmental disease transmission model. The raw materials in System 1 are vaccine precursors such as mRNA, and manufacturers include both the manufacturing activity (production systems) and the vaccine distribution (wholesalers and distribution networks). System 2 may be affected by states of System 1 (eg, vaccine inventory) via parameters reducing the flow from the susceptible state to the infectious state, and from susceptible to removed. In turn, System 1 may be affected by states of System 2 (eg, disease prevalence) via parameters affecting the rate of flow along the manufacturing chain (eg, increased demand, worker absenteeism).

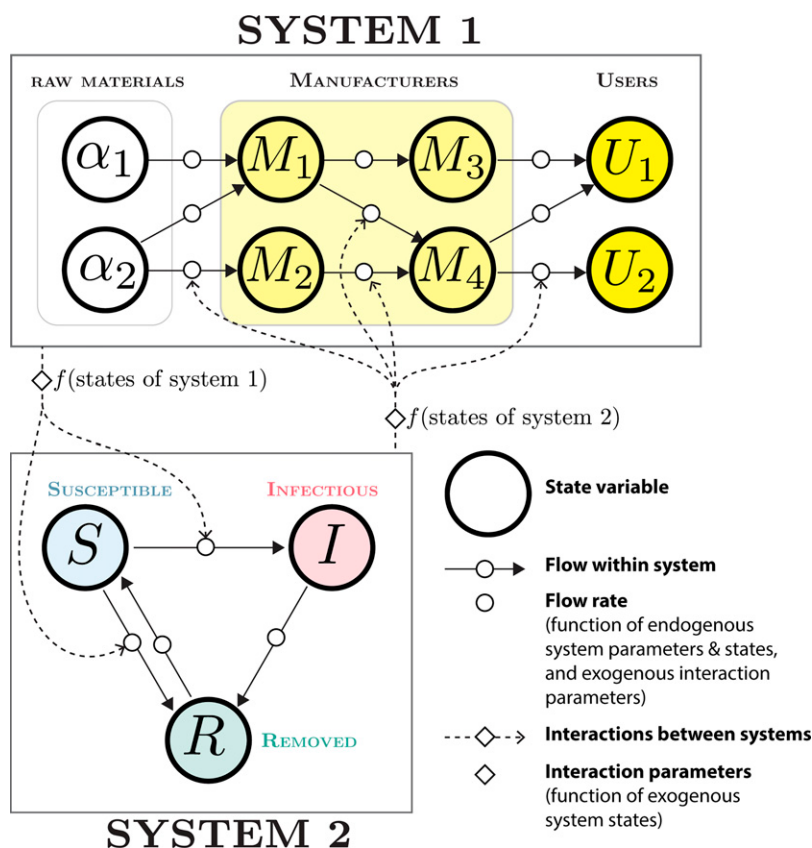


Figure 1. Conceptual diagram of a minimal system-of-systems with 2 constituent systems.

A foundational challenge in SOS research is how to define the system for a problem of interest. A common approach consists of (1) identifying the important feedbacks among constituent systems, which determines what systems should be included as constituents in an SOS, and (2) identifying candidate systems, with their actors, motivations, and processes. The method of identifying feedback is most insightful because other features of constituent systems—such as their interests and objectives—need not be aligned and are frequently competing. Moreover, the feedback among constituents of an SOS results in emergent behaviors in the global properties that would remain obscured if analyzing only 1 constituent at a time. Identifying candidate systems can be accomplished by understanding the potential stakeholders—such as public health decisionmakers, citizens, clients, or customers—and what technological, sociotechnical, and organizational processes affect these stakeholders.

One of the key benefits of SOS research is the ability to quantitatively operationalize heterogeneous approaches. These approaches may represent fundamentally different natural systems, come from different disciplines, or be encoded in different models and data types. Importantly, an SOS approach enables the discovery of dynamics and behaviors that are only possible when considering multiple constituent systems together. Thus, SOS research is enabled by both a way of thinking and by domain-specific models of natural and engineered systems. For instance, an SOS could be defined through the physical decomposition of a complex, spatially distributed system into constituents—such as social processes or epidemiological processes in different parts of the world—and considering their interactions. An SOS could also be defined by examining how epidemiological, sociotechnical, political, and economic processes are encoded in models and data.

APPLYING SOS THINKING TO EPIDEMIC INTELLIGENCE

SOS thinking provides both conceptual and operational value to epidemic intelligence. Implementing an SOS approach to epidemic intelligence would require a purposeful study of the interdependencies between state variables and parameters for distinct models. For example, infectious disease dynamics may be modeled using compartmental models that have state variables (such as the number of susceptible individuals in a geographic region) and parameters (such as transmission rates).^{29–31} Similarly, models of supply chains may have state variables (such as the number of products manufactured or services delivered) and parameters (such as production capacity and number of available workers).¹⁶ In most circumstances, the interactions among these models are negligible because the states of 1 system do not strongly affect the other systems. However, in

situations of public health emergency, the coupling between such systems, which may be bidirectional, becomes critical for understanding global processes. For example, transmission rates (parameters in epidemiological models) depend on products and services (vaccine or medical supply), while production capacity and available workers (states of the supply chain) depend on the number of infected individuals or fatalities (epidemic states). Thus, creating more accurate models in each domain also requires careful analysis of the dependencies of the states and processes in others.

Much knowledge exists (and is ever increasing) at the boundaries of the biomedical sciences, environmental sciences, and human behavior that are essential to understanding these couplings. We distinguish these boundary phenomena from disciplinary core phenomena. For example, epidemiological estimates of R_0 , serial interval, ascertainment rate, and asymptomatic fraction were quickly assimilated during the early days of the COVID-19 pandemic but were inadequate to guide official responses in the absence of related information about public policies, personal beliefs, individual health-related decision considerations, and community behavior. We are only just learning about how the presentation of information affects risk perception and the translation of these perceptions into behaviors, which then feed back into transmission at the population level.^{32,33} Similarly, behavioral patterns can affect the evolution of emerging viruses, both through demographic effects (eg, larger epidemics present more opportunities for mutation)³⁴ and selection (eg, when imperfect vaccines select for escape mutants).³⁵ We believe these 2 issues—behavioral change and the genetic evolution of variants—conspired to give rise to the multiple “waves” of SARS-CoV-2 transmission in 2020 and 2021.³⁶

The first step in understanding an SOS is to identify its parts, which involves breaking down the SOS into its constituent elements, each potentially a quasi-independent system. A key challenge is defining the system ontology (the set of concepts and categories in a subject area and their relations) so that shared quantities are commensurable across systems. Once the structure is defined, the next step is to analyze how each of these components can be understood with existing knowledge. For instance, in the context of a pandemic SOS, we might already understand the dynamics of a contagion process, movement patterns among various social groups like commuters, workers, and school children, and the research and development pipeline for vaccines. The SOS approach can link these together.

It is also essential to identify the knowledge domains that interact with the constituent systems to obtain a holistic understanding. These could range widely, including epidemiology, sociology, data science, logistics, and healthcare policy, each with a set of tools, methods, and information that could aid in understanding and managing the SOS. In any system, pinpointing what can be observed and measured is crucial. In an epidemiological context, for

example, hospitalizations might be a more reliable indicator of transmission than the number of cases, many of which might be unreported.³⁷ Equally important is defining how outcomes of interest are related to model states such as infection, vaccine distribution, or public trust.

Another significant aspect is determining the essential couplings between the constituent systems that significantly impact the SOS's target states. Criteria for establishing what makes a coupling "essential" could include factors like the absence of separable time scales—meaning that all processes in the system affect each other concurrently—and cause/effect relationships that produce significant changes in the magnitudes of target states. The scale of the effect and its feedback loops within the SOS also have to be considered. Examples of essential couplings in epidemiological systems might include the rate at which a virus mutates and how that impacts its transmissibility, the feedback between hospitalization rates and revision of public policies, and the coupling between vaccine distribution logistics and the rate of immunization in the population.

EXAMPLE: HIGHLY PATHOGENIC AVIAN INFLUENZA IN NORTH AMERICA

In this section, we imagine how SOS thinking might be applied to understanding the ongoing multispecies epizootic of highly pathogenic H5N1 avian influenza (HPAI H5N1) in the United States (Figure 2). This event affects many different sectors and stakeholders whose diverse interests, possibilities for action, and ways of interpreting the situation naturally lead to varying perspectives—some potentially incompatible.

Here we illustrate the SOS approach by thinking about 4 constituent systems: (1) dairy production; (2) the health and wellbeing of farmworkers; (3) human epidemiology, in the sense of possible human-to-human transmission in the general population; and (4) the spatial flows of cattle, animal products, farmers, and equipment. Of course, these are not the only aspects of the epidemic that are worth considering. For instance, one might be interested in transmission between dairy farms and poultry operations or the spread

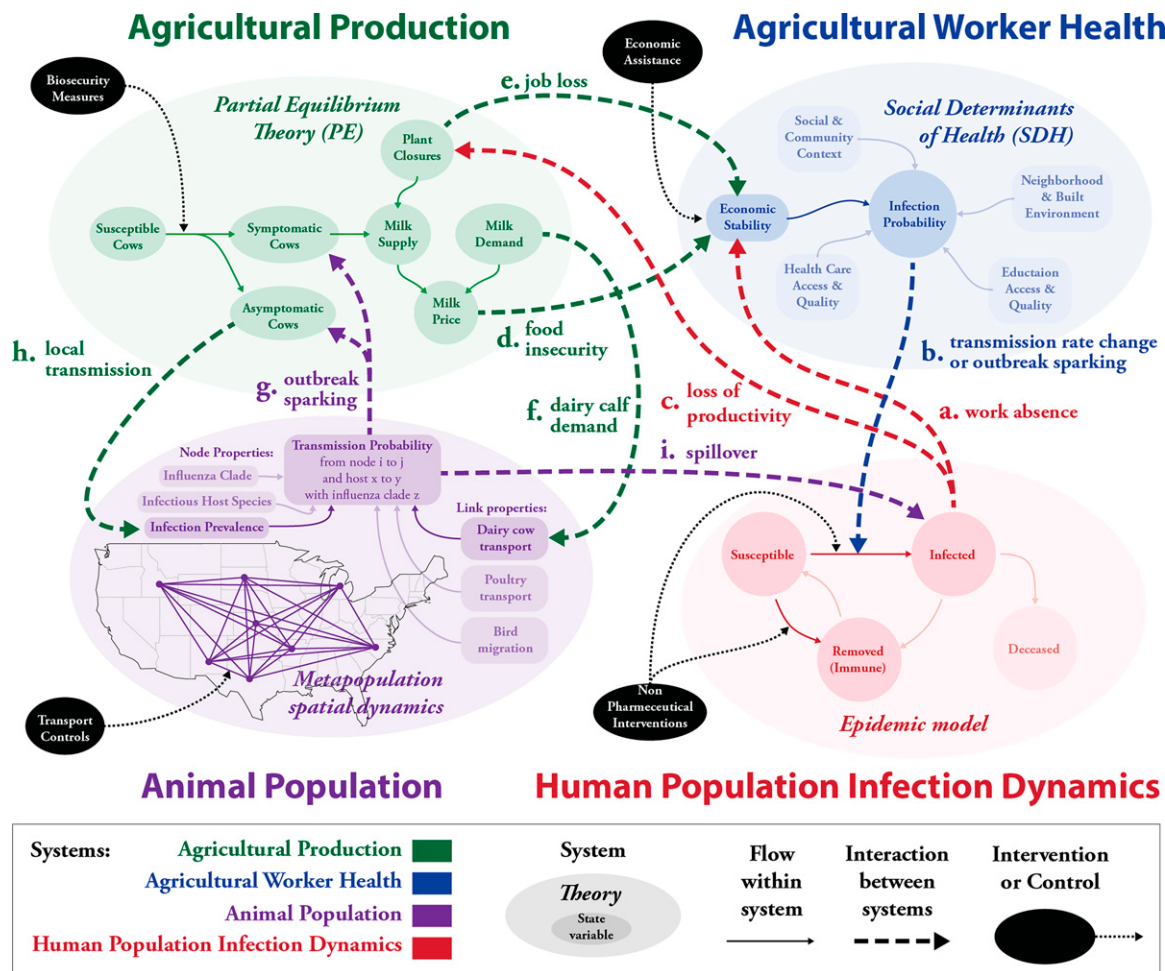


Figure 2. Conceptual diagram of a system-of-systems for avian influenza in the United States. See the main text for more details about (a) work absence, (b) transmission rates, (c) loss of productivity, (d) food insecurity, (e) job loss, (f) dairy calf demand, (g) outbreak sparking, (h) local transmission, and (i) spillover.

of HPAI H5N1 in wildlife. By design, the SOS is extensible so that these and other aspects of the event may be considered as they are discovered or become of interest.

In this case, the dairy production system might be modeled according to a partial equilibrium (PE)³⁸⁻⁴⁰ analysis, shown in green in Figure 2. The chosen framework for understanding worker health might be the Social Determinants of Health (SDH) model.⁴¹ Obviously, these are very different paradigms, each of which is appropriate to its own interests. However, a state of the dairy production system (plant closure) relates to a key feature of worker health (economic stability) through a shared concept (job loss). We can understand further aspects of the event by adding additional frameworks. For instance, a dynamical epidemic model⁴² could describe infection dynamics in the general human population (red) while spatial movements of the animal population across the United States can be modeled using a multihost metapopulation network (purple).⁴²⁻⁴⁴ Interventions and controls (black) can be applied to the states or parameters of constituent systems. These states or parameters are influenced by exogenous systems through linking processes (dashed colored arrows), which, in turn, create feedback loops among the systems.

Our diagram illustrates just a subset of these feedback loops, informed by interactions documented in past epidemics. For example, increased infection levels in the human population would be expected to lead to worker absences (a),⁴⁵ which lowers economic stability in populations without paid sick leave or job protections,⁴⁶ as in the agricultural worker system. Increased infection probability in that subpopulation, in turn, has some effect on transmission in the general population⁴⁷ via increased transmission rate or sparking of new clusters (b). Worker illness can lead to plant closures in the production system due to loss of productivity or as a biosecurity intervention (c),^{48,49} which, in turn, directly impacts the economic stability of agricultural workers through job loss (d).⁵⁰ In the production system, plant closures affect milk supply, which may drive price changes that contribute to food insecurity (e)⁵¹ among low-income workers, including agricultural workers. Pressures on milk supply and changes in demand can lead to increased demand for dairy calves (f),^{52,53} leading to increased interstate transport of cattle. In the animal metapopulation system, increased dairy cow transport increases the probability of HPAI transmission between dairy farms, leading to increased infection in cows via outbreak sparking (g)⁵⁴ and a decrease of milk production in the production system. Increased prevalence among asymptomatic dairy cows (h) increases the probability of point-to-point transmission among cattle⁵⁵ and spillover between cattle and humans in the animal metapopulation system. These spillover events (i) can spark new outbreaks in the general human population.⁵⁶ This example illustrates how feedback mechanisms within an SOS can lead to counterintuitive

outcomes, including unintended consequences of control measures made with limited understanding of the interacting systems. For instance, plant closures might reduce transmission in the agricultural system, but feedback with the spatial animal metapopulation, such as shifts in dairy calf shipments to adjust milk supply, could inadvertently increase disease spread among dairies. While the likelihood of this scenario is uncertain, an SOS framework is crucial for quantifying such feedback and assessing potential impacts.

WHAT IS THE VALUE ADDED BY TAKING AN SOS APPROACH TO EPIDEMIC INTELLIGENCE?

Adopting an SOS approach for epidemic intelligence offers several advantages over the traditional, siloed approach. First, an SOS framework allows for a nuanced understanding of the interactions and emergent properties that are often overlooked when considering systems individually, providing a richer, more complete view of the relevant processes and dynamics. Second, an SOS approach is scalable and may incorporate multiple layers of complexity across diverse scales. It more seamlessly integrates various interconnected systems like economics, healthcare delivery, and even social behavior, to provide a holistic view. This cross-system integration can be of special value in crafting policies or interventions that are both robust and flexible, and maximizes cobenefits across sectors.

Another significant aspect of the SOS approach is its flexibility and actionable value to a wide range of stakeholders. Government agencies and decisionmakers can glean insights for better policy formulation, while actors from privatized sectors like finance, trade, and tourism can obtain insights for risk mitigation. Companies that provide biomedical goods or services might benefit by aligning research, development, and production with short- and long-term demand. Thus, while each actor accesses the SOS from a different perspective, they do so with a shared foundational understanding about the core principles and interactions that structure the SOS. Moreover, there are many times that a multi-perspectival approach can yield valuable insights. For example, as viral sequence data became more available throughout the SARS-CoV-2 pandemic, their availability was biased towards populations more likely to be tested for SARS-CoV-2. Combining economic and behavioral models with data from molecular epidemiology might provide a less biased picture relevant to informing public policy.

While quantitative metrics offer transparency, comparability, and efficiency in guiding decisions, they are embedded in broader political and economic contexts that shape how information is used. The SOS approach is designed to support, not supplant, decisionmaking across levels—from clinical care to international diplomacy—by organizing diverse forms of information in ways that acknowledge

both technical and value-laden dimensions of pandemic response. The SOS approach is particularly suited for avoiding simplistic aggregate metrics or indicators favored by one interest group. By allowing for the complex interactions of various domains, the SOS approach provides both a comprehensive view and enables stakeholders to query the model or information system for the data pertaining to their area of interest. For example, understanding how discriminatory legislation or social stigma affect the overall system can only be captured by a comprehensive SOS approach that allows for the integration of heterogeneous sources of information. Generally, a holistic understanding is needed to account for contextual details that have significant consequences, especially those generated by feedback loops. When considered individually, these details may be overlooked.

While we cannot alter fundamental physical or biological processes, society does have the ability to modify other factors, such as educational systems, public policies, financial structures, and regulatory frameworks. These human systems that we have constructed can be reconfigured—if not fundamentally remade—to better meet the challenges we face. Adopting an SOS approach could potentially lead to more resilient, adaptable strategies for managing complex crises like pandemics.

ADVANCING SOS FOR EPIDEMIC INTELLIGENCE

Developing effective SOS for epidemic intelligence requires not just technical infrastructure but also human expertise to bridge disciplinary boundaries across interacting systems. Akin to the way application programming interfaces (APIs) function, serving as conduits between different software applications, it will be essential to create “interdisciplinary ontologies” that ensure standardized “apples-to-apples” comparisons across varied domains, enhancing the coherence and effectiveness of system-wide interventions. A critical aspect of this work is determining the relationships and interactions between constituent systems. This cross-system analysis is inherently an interdisciplinary endeavor, requiring contributions from specialists of diverse fields to collaboratively construct the conceptual frameworks, data systems, and models that will set the stage for advanced SOS modeling efforts.

Modeling an SOS cannot rely on a single, monolithic representation. Rather, an overall picture can be constructed through a pluralistic approach to modeling, employing multiple models to predict the same phenomena but based on different assumptions or perspectives. This pluralism adds robustness to the understanding of the system’s behavior, making it more resilient to uncertainties and more amenable to nuanced interpretation.

SOS thinking enables connectivity between heterogeneous domains that may be otherwise siloed. These connections raise the question of how a common ontology can be developed to accommodate such interconnections. This question could be answered in each domain by exploring the factors that are otherwise considered exogenous disturbances. For example, in a production system, the number of workers calling in sick could disrupt production. Understanding and modeling the factors that affect the number of ill workers is beyond the scope of manufacturing-specific models. However, the fact that the number of ill workers is a quantity of interest could be the starting point in identifying the gaps in the ontology needed to capture interfaces among the submodels in an SOS approach.

Lastly, the effectiveness of an SOS approach is amplified by data sharing across systems and stakeholders. Sharing data is frequently limited by privacy risks and fear of competition. Data sharing can be facilitated by aggregating or masking individual data points to address these concerns. Here, the SOS approach provides a unique opportunity to allow data sharing especially when concepts are quantified abstractly (eg, average economic loss, case fatality rate) that are not directly relatable to private information (eg, farm-level damages, private health information). In this sense, the sharing of relationships between inputs and outputs of submodels for the overall SOS can be done without the need to share the actual data that resulted in each input/output relationship. For example, sharing the relationship between worker illness and plant closures in a production system does not need to specify the actual numbers of ill workers or the actual number of closed plants. Specifically, such a relationship could be shared as a lookup table, regression model, or neural network whose weights encode the needed information. The model alone, isolated from the overall SOS model, does not provide information for analysis. Enabling such open communication channels and data-sharing frameworks would facilitate a more transparent, collaborative environment, enabling quicker, more informed decisionmaking. This in turn contributes to the overall resilience and adaptability of the SOS, ensuring it can better navigate the complexities and uncertainties inherent in multidisciplinary challenges.

It will be crucial to develop an operational plan to advance the SOS approach from concept to implementation. To be effective, this effort must obtain the buy-in and support of regulatory authorities that manage critical health and agricultural data—such as the Centers for Disease Control and Prevention, World Health Organization, national health services, and ministries of health, as well as private and grassroots organizations that administer scientific data platforms like GISAID. Rather than constructing a centralized bureaucracy, the SOS should function as a distributed, adaptive ecosystem with voluntary participation, modular interoperability, and the ability to scale across levels of governance. While the SOS framework is designed to enable

coordination at the global scale, its effectiveness ultimately depends on empowering national, subnational, and local actors, where the most timely and consequential interventions for epidemic prevention and response must occur. Likewise, leadership should not rest solely with either academic or governmental institutions; instead, a diverse coalition—including public health agencies, researchers, technical experts, and civil society—must be brought to the table. A broadly representative kickoff workshop could catalyze this effort, followed by working groups tasked with developing flexible, extensible ontologies and data standards, drawing largely on existing (domain-specific) concepts and specifications. These groups should be supported in a manner similar to National Academies committees or the Intergovernmental Panel on Climate Change but could also draw support from sections or working groups of disciplinary societies in fields such as virology, epidemiology, economics, and the social sciences. Experience from climate science and policy offers a useful precedent, demonstrating how collaborative, multilevel, and cross-sectoral governance structures can tackle complex global challenges while remaining actionable at local scales.

Epidemics and pandemics are complicated events that cause a multitude of health, social, and economic effects, defying simple approaches to situational awareness and intelligence gathering. Our understanding of them must be similarly comprehensive, which means that only a multifaceted interdisciplinary approach can hope to represent the variety of relevant natural and social processes. However, such a pluralistic picture inevitably will encounter conceptual ambiguity and divergence. Managing this ambiguity requires a flexible and adaptive approach to system representation, data analysis, and inference. The SOS paradigm provides such an approach.

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