Research Report

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Syndromic Surveillance 2.0

Emerging Global Surveillance Strategies for Infectious Disease Epidemics

For more information on this publication, visit **www.rand.org/t/RRA1812-1**.

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About This Report

This report documents research and analysis conducted as part of a project entitled *Syndromic Surveillance 2.0: Identifying Emerging Epidemics in the 21st Century*, sponsored by the U.S. Army Office of the Surgeon General. The purpose of the project was to identify how new technologies and approaches (economic indicators, social media scanning, and others) can be harnessed to gain early insights into emerging global epidemics to monitor health and safety threats to American soldiers across the globe and identify the epidemic's potential for widespread infection. The project also recommended promising strategies the Army could adopt to better monitor such biologic threats.

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We are grateful to the many individuals we interviewed for this report. Those who agreed to have their names listed are named in Appendix A.

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Summary

The research reported here was completed in June 2022, followed by security review by the sponsor and the U.S. Army Office of the Chief of Public Affairs, with final sign-off in August 2023.

The U.S. Army has a long history of preventing, detecting, and treating infectious diseases for American and allied forces and, by extension, protecting populations worldwide. Like other organizations and agencies involved in public health, the Army is increasingly interested in *syndromic surveillance strategies*—those that are designed "to identify illness clusters early, before diagnoses are confirmed and reported to public health agencies, and to mobilize a rapid response, thereby reducing morbidity and mortality" (Henning, 2004).

The Army asked the RAND Corporation's Arroyo Center to research how the next generation of epidemic surveillance strategies could identify emerging epidemics and pandemics in the near and far future. We focused this task to investigating how new strategies might be used to gain early insights into emerging epidemics across the globe.

Sources of Information

This report synthesizes information from multiple sources, including data from:

- **Peer-reviewed literature:** We conducted a systematic literature review to identify and describe strategies for surveillance of syndromes indicating potential outbreaks, to characterize their implementation and effectiveness, and to describe their potential for continued or expanded use. Our search strategy resulted in 80 unique articles describing syndromic surveillance strategies.
- **Global patent search:** We searched a global patent database for patents filed between 2010 and 2020. Twelve patents, including two duplicates, were deemed relevant.
- **Media scan:** RAND Arroyo conducted a search of news and working papers limited to the dates 2010 to 2020. The news search returned 75 articles that described a company, service, or method relevant to the research question.
- **Market environmental scan:** When literature, news, patents, or company information identified other services, institutions, or strategies, we examined the company using MarketLine or simple web searches.
- **Interviews with subject-matter experts:** We conducted interviews with 27 subject-matter experts to confirm findings from the literature review and scan of private enterprises and to capture new insights.

A Framework for Surveillance

We created a three-phase epidemic surveillance framework to categorize the strategies used to conduct syndromic surveillance of infectious diseases. The phases are:

- **Phase 1—Emergence: Strategies for surveilling for the potential emergence of an outbreak** track the prevalence and characteristics of pathogens in reservoir populations, known and unknown, with the potential for jumping to human populations.
- **Phase 2—Outbreak: Strategies for surveilling for the presence of an outbreak** identify localized events of novel or alarming infections in human populations to determine whether a particular pathogen has spread to or across humans within a region.
- **Phase 3—Spread: Strategies for tracking the extent of or potential for geographic disease spread** indicate how widely diseases that have progressed beyond outbreaks have spread within or among populations and the potential for continued spread.

Across these phases, several factors might directly relate to the benefits and limitations of specific syndromic surveillance strategies. We categorized these factors as:

- **Mathematic factors:** Epidemics are relatively rare, so probabilistically many strategies designed to detect them will suffer from high rates of false positives.
- **Biologic factors:** Systems can be designed to identify specific biologic pathogens, or they could be pathogen agnostic.
- **Geographic and environmental factors:** Illnesses might exhibit seasonal variation in their rate of spread, and geographic and environmental factors influence the types of surveillance systems that are developed and implemented.
- **Social and economic factors:** Social and economic factors might determine the extent of the human-animal interface in a society, affect public health system resources, affect the efficacy of surveillance systems, and influence behaviors and settings that affect disease spread.
- **Behavioral and cultural factors:** Behavioral and cultural factors influence how individuals in society interact, how they perceive health risks, and the extent to which they follow public health guidance and engage with the health care system.
- **Historic, political, and institutional factors:** History, particularly past experiences with outbreaks or epidemics, could influence future responses. Political will, transparency, data infrastructure, and logistics affect whether and how accurately pathogen spread is reported. Political and institutional factors influence the design and implementation of disease surveillance systems.
- **Demographic factors:** For many communicable diseases, large differences in the disease burden across population characteristics, such as age, gender, ethnicity, and race, influence surveillance efforts.

Strategies for Surveillance

Table S.1 lists the strategies for syndromic surveillance identified across the three epidemic phases.

Table S.1. Summary of Syndromic Surveillance Strategies

Strategy	Benefits	Limitations	Private-Sector Enterprises
Phase 1—Strategies for surveilling the potential emergence of an outbreak			
Veterinary public health surveillance: surveillance in animal populations to detect known and novel zoonotic diseases to prevent a spillover event	• Ability to identify potential outbreaks early • Ability to be implemented in regions with high levels of human-animal interface • Affordability	• Possibility of missing diseases with high and rapid mortality (e.g., highly pathogenic avian flu) • Inability of some pathogen-specific systems to detect novel diseases • Reliance on humans and associated delays • Less effective in remote areas with spotty mobile phone coverage	• IDseq • PREDICT (a collaboration between U.S. Agency for International Development and EcoHealth Alliance)
Remote sensing: use of satellite imagery to track environmental (e.g., rising sea levels, forest fires) or socioecological (e.g., urbanization) drivers of infection	• Broad geographic coverage • Little need to rely on other governments for information	• Technologically complex • Currently primarily academic • Gap between where surveillance systems are developed (richer countries) and where they are needed (low-income settings with weaker infrastructure)	• None identified
Phase 2—Strategies for surveilling for the presence of an outbreak			
Surveys: high frequency, geographically disaggregated indicators (e.g., self-reports of symptoms, symptom severity, and/or risk and protective behaviors) to capture the severity of the outbreak	• Ability to flexibly collect data on factors that are known to affect risk	• Potential data lag • Possible intensive and costly data processing • Possible unavailability of in-person collection of surveys during epidemics	• Magpi
Web searches: tracking internet search terms to detect new or emerging disease outbreaks or disease symptoms, or to track the course of an outbreak	• Timeliness of data • Nonreliance on government data • Inclusion of symptoms outside the health care setting • Ability to aid with forecasting	• Voluminous amounts of data • Regional variation in source data • Limited data availability (from third party owners) • Time dependency • Potential bias for cities in regions with low internet penetration or media coverage on the disease	• BlueDot • Google Trends

Strategy	Benefits	Limitations	Private-Sector Enterprises
Social media mentions: tracking mentions of diseases and/or symptoms on social media platforms	• Timeliness of data • Nonreliance on government data • Inclusion of symptoms outside the health care setting • Ability to aid with forecasting	• Voluminous amounts of data • Regional variation in source data • Poor data availability • Time dependency • Potential bias for cities in regions with low internet penetration • Sensitivity to targeted disinformation	• Bellingcat • Kinsa Health • Sickweather
Media monitoring and web scraping: algorithms that scan electronic news sources for indicators of confirmed or potential outbreaks	• Quicker identification of emerging issues than traditional systems and ability to support secondary prevention	• Limitation to local news media because of language and accessibility • Selection bias in reporting that could unduly influence predictive ability • Resource-intensive manual scanning and abstraction	• Travax by Shoreland, Inc. • ProMED • HealthMap • BlueDot • Google Trends • Bellingcat
Pharmaceutical sales: examining the trends in over-the-counter (OTC) drug sale data, which measures consumers' purchasing immediately upon recognizing symptoms	• Timeliness of data • Inclusion of symptoms outside the health care setting	• Limited data availability • Lack of specificity because most sales are for a broad variety of symptoms • Possible reflection of only certain populations	• Real-time Outbreak and Disease Surveillance (RODS)
School and work absences: tracking absences from school and from work	• Low-cost • School-based programs that focus on children (key population for spread) • Inclusion of symptoms outside the health care setting	• Unreliable data collection across systems • Best detection only for rapid and severe symptom onset resulting in absenteeism • Possible inability to capture work-from-home arrangements	• None identified
Data collection by health care staff: health care workers and/or administrative staff report prespecified surveillance data (e.g., temperatures or respiratory symptoms) in health care or other high-risk settings (e.g., postdisaster)	• Ease of use • Low cost	• Poor data quality • Resource burden • Difficulty to assess utility (i.e., sensitivity, positive predictive value) • Requirement of a known symptom set or syndrome to aggregate cases	• nference • IBM Explorys solutions
Consumer expenditure data: examining trends in	• Behavioral indicator of epidemic risk and	• Poor data access and availability	• None identified

Strategy	Benefits	Limitations	Private-Sector Enterprises
consumer expenditures to measure and map the extent of an outbreak	spread that does not rely on health infrastructure • Potential for the inclusion of symptoms outside the health care setting	• Lack of specificity about the type of pathogen • Different expectations for different populations or socioeconomic conditions	
Geospatial techniques: use of user-supplied or automated geographic information system data to identify geographic concentrations of disease risk and map epidemic emergence and spread	• Low cost • Online dashboards and mapping technologies that provide the public with information about epidemic spread and risk levels in their community	• Ethical concerns regarding privacy • Techniques that are not well established • Lack of formal systems in government or other institutions	• Kinsa Health (uses location and thermometer data to show large-scale fever data)
Wastewater sampling: collecting and testing municipal wastewater	• Cost- and time-efficient approach • Targeted monitoring based on geographic area or population • Ability to provide early warnings of outbreaks in new areas	• Inability to perform contact tracing or to identify affected persons • Reliance on municipal sewer systems • Lower effectiveness among highly mobile or transient populations	• Biobot Analytics (samples wastewater systems for viral RNA and maps findings over time)
Phase 3—Strategies for tracking the extent of or potential for geographic disease spread			
Population movement indicators: tracking day-to-day population mobility, mass migrations, and/or gatherings among displaced populations or those gathering for cultural events	• Promising evidence for tracking spread • New tools in development	• Data that is generally derived from proxy indicators of time spent places and moving between places	• Travax by Shoreland, Inc.

Notable Surveillance Systems

The syndromic surveillance strategies listed above are already in use in some surveillance systems or could be added to these systems in the future. We identified the following U.S. Department of Defense (DoD) surveillance systems currently in use:

- **Global Emerging Infections Surveillance (GEIS):** a global laboratory network tasked with providing technical support to geographic combatant commands (GCCs); conducting infectious disease surveillance; improving DoD laboratory readiness for outbreak; and enhancing collaboration among the GCCs, GEIS partners, and U.S. and international interagency partners
- **Defense Medical Surveillance System (DMSS):** person-level collection of medical events, personal characteristics, and military deployments of all service members

- **Electronic Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE):** a secure web-based system that primarily receives and categorizes electronic emergency department data for both civilian health systems and military treatment facilities
- **Disease Reporting System internet (DSRi):** integrated database from DoD's electronic health records (Armed Forces Health Longitudinal Technology Application and Military Health System [MHS] Genesis), laboratory results, DMSS, and ESSENCE.

In addition, the following systems were mentioned routinely in our literature review and/or our interviews:

- **PREDICT EcoHealth:** a collaborative that characterizes the virome at the human-wildlife interface by sampling wild animals across the globe and using metagenomic methods to identify viruses
- **Global Public Health Intelligence Network:** a big data aggregator, run by Public Health Agency of Canada, that scans online news reports in nine languages for potential signals of emerging public health threats, then uses machine learning algorithms and human analysts (who use their expertise in medicine, public health, and additional scientific fields to comb through the news reports, social media, and manually identified sources) to assess health threats
- **ProMED:** a service that invites and accepts reports of potential outbreaks from a variety of sources, including local media, professional networks, on-the-ground experts, and the general public; adds expert review; and curates reports to help disseminate potential threats
- **European Centre for Disease Prevention and Control tools for epidemiological threats and outbreaks:** tools used for surveillance and to respond to epidemiological threats and outbreaks.

Perspectives on the Application of Syndromic Surveillance Strategies

Interviewees reported on a variety of factors that might influence the strategies available for outbreak surveillance. There were many issues related to the data that are used, including the quality, biases, availability, and the ways that data are presented to consumers. Interviewees also noted the importance of evaluating systems to ensure that they yield accurate and useful information. They discussed the challenge of data silos—wherein systems for detecting one disease could be used for other diseases, but, according to one interviewee, "people only look for what they're funded to look for." Interviewees also discussed leaders' political will for surveilling for and reporting on outbreaks and how the culture of a region or community influences its surveillance capabilities. Western approaches are viewed as myopic in this regard, particularly if they rely on individuals to report illness or seek out care in traditional health care settings. Finally, experts consistently said that one of the key problems with syndromic surveillance is not the lack of systems but ensuring those who need the systems are able to access them and support upgrades and developments that improve the systems for future use.

Our interviews with representatives with DoD suggested uneven knowledge about or access to surveillance systems—different commands prioritize different strategies to retrieve information about disease threats—and some described syndromic surveillance activities as a "patchwork" approach. We were told that, to support the combatant command (CCMD), the Defense Health Agency's Armed Forces Health Surveillance Division is working to establish an improved biosurveillance hub that incorporates existing capabilities to eventually streamline the number of systems, but this is a new effort as of this writing.

Recommendations

Recommendation 1. The Army should track academic and private enterprise efforts to detect diseases during the outbreak phase of epidemic surveillance. Because there is so much activity in this domain—activity that we assume will grow in the context of the coronavirus disease 2019 pandemic—the Army should continue to monitor progress but not necessarily invest in additional methods above and beyond its current investments in GEIS, DSRi, DMSS, and ESSENCE.

Recommendation 2. The Army should establish more routine training to aid general medical officers in identifying and obtaining credible data and analyzing and interpreting the data. Our interviews with defense agency and CCMD representatives revealed that, although numerous systems exist to help CCMDs and services track possible disease outbreaks, there appears to be uneven awareness among some military medical personnel regarding what systems and information they can—or should—use for this purpose.

Recommendation 3. The Army should consider investing in surveillance efforts that detect the possible emergence of an epidemic for use during the emergence phase of epidemic surveillance. Detecting viruses in animal populations is crucial to understanding the risk to humans at the human-animal interface, where most spillover events occur. The Army Veterinary Corps might be exceptionally well positioned to create or complement existing global veterinary public health surveillance efforts in support of the operational force. The Army might also be able to contribute to science or systems that apply remote sensing strategies to identify where environmental changes could increase risk for the emergence of an outbreak. Currently, human health outbreak monitoring is anchored in the MHS and might pick up only threats warranting medical attention. Investment in the emergence phase might be more predictive and reduce risk.

Recommendation 4. The Army should consider investing in surveillance efforts that detect the confirmed or potential geographic spread of an outbreak for use during the spread phase of epidemic surveillance. If the Army has or can negotiate direct access to data on population movement, it might be able to contribute to modeling the potential for disease spread globally.

Recommendation 5. The Army should leverage opportunities to engage in regional and international dialogues, where appropriate, to enhance coordination and information-sharing. The Army should seek to inform or participate in engagements with foreign partners led by civilian counterparts in the U.S. Department of State, U.S. Agency for International Development, or U.S. Centers for Disease Control and Prevention, for example. In addition, military-to-military engagements led by CCMDs or defense agencies also provide opportunities for Army personnel to become better integrated into discussions regarding data sharing and integration.

Recommendation 6. The Army should sustain, maintain, and update current disease surveillance efforts and encourage the same investment throughout DoD. Current Army surveillance efforts are exemplified by GEIS, DMSS, DSRi, and ESSENCE. Sustaining, maintaining, and updating DoD systems and additional resources for syndromic surveillance can help mitigate risks to all the armed forces, not just the U.S. Army.

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Chapter 1. Introduction

The U.S. Army has a long history of preventing, detecting, and treating infectious diseases for American and allied forces and, by extension, protecting populations worldwide. It has been at the forefront of preventive medicine since its inception. For instance, Walter Reed's perceptive observations about the causal link between female mosquitoes and yellow fever informed mosquito abatement efforts and thus helped eradicate yellow fever during the Spanish-American War (McCarthy, 2001). The Army continues to be a global leader in vaccine research and preventive medicine (Ratto-Kim et al., 2018).

Among the reasons that the Army prioritizes preventing, detecting, and treating infectious diseases is that disease and nonbattle injury (DNBI) are persistent threats to the force. For example, DNBI accounted for 75 percent of all hospitalizations during the initial phases of Operation Iraqi Freedom (Belmont et al., 2010), which speaks to both the magnitude and severity of the threat. The U.S. Army Medical Department continues its mission to reduce DNBI, which also provides an opportunity to help the country and the world better control the current coronavirus disease 2019 (COVID-19) pandemic. Looking ahead, the Army can assist in global efforts to foresee and prepare for future threats with earlier detection, informed responses, and accurate tracking.

Outside the military context, public health systems rely on epidemiologic surveillance strategies based on detecting the presence of a disease that meets specific case criteria. For example, the World Health Organization's (WHO's) case definition for a confirmed case of COVID-19 requires a positive COVID-19 Nucleic Acid Amplification Test or a positive COVID-19 severe acute respiratory syndrome (SARS)-CoV-2 antigen rapid diagnostic test plus the presence of certain symptoms (WHO, 2020b). However, because definitive diagnostic testing for infectious diseases like COVID-19 requires time and access to the appropriate tests (and, in the case of a new pathogen, tests might not yet exist) syndromic surveillance strategies are designed "to identify illness clusters early, *before diagnoses are confirmed and reported* to public health agencies, and to mobilize a rapid response, thereby reducing morbidity and mortality" (Henning, 2004, emphasis added).

A useful syndromic surveillance strategy will identify the emergence of a disease *early* so that measures can be put in place to prevent its spread. We place the term *early* in italics because surveillance strategies can theoretically detect diseases before they enter human populations; before they become widespread in a region or population; or before they spread across communities, countries, and regions—with different approaches to mitigate the disease or its spread at each stage.

The Army asked the RAND Corporation's Arroyo Center to research how the next generation of epidemic surveillance strategies could identify emerging epidemics and pandemics

in the near and far future. RAND Arroyo focused this task to identify how new strategies might be used to gain early insights into emerging global epidemics. With this information, the U.S. Army Medical Department should be able to identify the most-promising strategies and ascertain which fit within their current suite of surveillance activities to meet the challenge of detecting disease outbreaks.[1]

Sources of Information

This report synthesizes information from multiple sources, including data from the peer-reviewed scientific literature, gray literature, information on private enterprise activity related to syndromic surveillance, and interviews with subject-matter experts. We briefly describe these methods below; more detail is provided in Appendix A.

Peer-Reviewed Literature

We sought to understand the state of the science of syndromic surveillance strategies by conducting a systematic literature review. Our objectives were to identify and describe existing strategies for the surveillance of syndromes (or *symptoms*, which, as described in Chapter 3, can be very broadly defined) indicating potential outbreaks, characterize their implementation and effectiveness, and describe their potential for continued or expanded use. Our goal was to identify as many syndromic surveillance strategies as possible, recognizing that it was beyond the scope of our effort to describe the entire evidence base for each strategy. We intentionally cast a wide, rather than deep, net. We defined syndromic surveillance as an approach or method for detecting and monitoring potential or confirmed infectious disease outbreaks. An included strategy could utilize single or multiple sources of data (e.g., triangulate information) to achieve its surveillance goals.

After applying our screening criteria (described in Appendix A), we were left with 80 unique articles describing surveillance strategies. Once we categorized these, we consulted additional peer-reviewed literature in each category, placing a priority on identifying systematic or other types of literature reviews.

Private Enterprise Efforts

We recognized that the peer-reviewed literature might miss surveillance efforts being conducted by private enterprises, particularly as the COVID-19 pandemic continues to have

[1] Throughout this report, we prefer the use of the term *strategies* but, in some instances, use *approaches* as a synonym, mostly for grammatic purposes. Syndromic surveillance "strategy" or "approach" is used when referring to the collection of unique data or use of data generated for other reasons for surveillance purposes. We use the term *activities* or *systems* to refer to the suite of strategies and approaches that institutions or organizations rely on for surveillance purposes, not necessarily limited exclusively to syndromic surveillance.

global impact. Thus, we crafted a search strategy of patents, news articles, and market information. Using this approach, we intended to identify companies or services using specific classes of data to inform disease surveillance strategies. However, companies and services might be difficult to find for several reasons. First, companies might be small or not publicly traded, or they might serve niche markets or customers that do not want the approaches or products they develop to be publicized. Second, news reports of company services appear in different forms and a wide variety of sources that might be collected, archived, or searchable. Third, companies or organizations developing algorithms for disease detection in data sources might not submit patents for processes. Algorithms and software are complex to patent, and some organizations might choose not to submit applications. When our search did reveal a commercial service, we searched related companies and products to provide a thorough view of the current market.

Global Patent Search

RAND has developed methods to detect emerging technologies using the technology classification systems of national and international patent offices (Eusebi and Silberglitt, 2014). We searched a global patent database for patents filed between 2010 and 2020. The search returned 98 patents; 30 of these were retained after a preliminary screen, and among these, we reviewed the patents they cited. Of these, 12 patents, including two duplicates, were deemed relevant. They include patent applications from the United States, Australia, China, and Canada. Most of these patents are products that use electronic health records (EHRs), one examines change in genetic sequences of pathogens as a source of information to map transmission, and one uses airline travel to project movement of infectious people in real time.

Media Scan

A search of news and working papers was conducted using ProQuest and limited to the dates 2010 to 2020. The initial search returned 7,885 articles, most frequently journal articles (n = 4,409), followed by dissertations and theses (n = 1,725), working papers (n = 1,522), features (n = 72) and news articles (n = 54).We excluded the journal articles, because they are expected to be captured in the literature review, and dissertations, because they are not expected to be reports on commercial services. The remaining 1,740 articles were reviewed to identify relevant services and companies. A review of the titles of the news search returned 293 articles. Of these, 75 (26 percent) were included for full extraction because they contained a company, service, or method relevant to the study. The news articles consisted predominantly of concepts for syndromic surveillance from academic white papers (research ideas were not peer reviewed). News articles also mentioned the efforts of specific companies developing analytic systems to facilitate analysis for organizations that hold pertinent data.

Market Environmental Scan

MarketLine is a service providing market research and company information on the automotive, consumer, energy, financial services, health care, and technology sectors. MarketLine supplies company profiles and news, including company-sourced data and press releases, which the service reviews for quality assurance.

We employed a snowball sampling technique for corporations: When literature, news, patents, or company information identified other services, institutions, or approaches, we researched the company on ProQuest, on MarketLine, and via a simple web search. Web searches and the gray literature were also consulted to identify U.S. Department of Defense (DoD) and global surveillance systems, described in Chapter 4.

Interviews with Subject-Matter Experts

We conducted interviews with subject-matter experts to confirm findings from the literature review and scan of private enterprises and to capture new insights. The interviews were divided into academic and scientific experts ($n = 9$), national government and international organization representatives ($n = 7$), and U.S. military representatives ($n = 11$). Interview participants were selected from the literature review and private-sector search or recommended by our research sponsor. A list of interviewees who consented to being identified is provided in Appendix A.

Organization of This Report

The remainder of the report is structured as follows: In Chapter 2, we describe a framework for categorizing the phases of epidemic surveillance, from the emergence (or potential for emergence) of a disease within humans to it becoming an outbreak and then spreading. We also discuss mathematic, economic, cultural, and other factors that affect surveillance efforts across these stages. In Chapter 3, we review existing strategies and their utility for conducting effective syndromic surveillance and discuss private enterprises using specific approaches. Chapter 4 includes DoD and other relevant global surveillance systems with a focus on the data sources they rely on. Chapter 5 provides a synthesis of subject-matter experts and DoD personnel perspectives on the utility of syndromic surveillance strategies. In Chapter 6, we end with conclusions and recommendations. We provide additional detailed information about all the research methods we used in Appendix A. Last, Appendix B includes surveillance systems not included previously in the report.

Chapter 2. A Framework for Surveillance

In this chapter, we briefly describe the Convergence Model and One Health, two frameworks that are useful for conceptualizing epidemic risk. Although an *outbreak*—which is the focus of most syndromic surveillance strategies—refers to a greater-than-expected increase in the number of cases of a disease within a limited geographic area (i.e., localized incidence), an *epidemic* refers a severer spread of a disease that affects larger numbers of people within a population or region. Because epidemics are usually associated with poorly controlled or uncontrolled outbreaks, understanding epidemic risk offers a valuable lens from which to evaluate systems aimed at detecting outbreaks. The weaker these systems are, the more transmissible a pathogen is, and the harder a pathogen is to detect, the more likely an epidemic will spread to multiple countries in two or more regions around the world, affecting larger populations and becoming a *pandemic*.

Using these two frameworks, we provide an overview of a three-phase epidemic progression framework developed for this project that is useful for thinking about different surveillance approaches and strategies. We then discuss mathematic, biologic, geographic, and other factors affect surveillance across these stages.

Frameworks for Conceptualizing Epidemic Risk

In the early 2000s, an interdisciplinary project to study potential microbial threats to human health was commissioned by multiple U.S. agencies.[2] The project team drafted the following framework for understanding the variety of factors capable of influencing epidemic risk (National Academy of Medicine, 2003, emphasis added):

> The emergence and spread of microbial threats are driven by a complex set of factors, the convergence of which can lead to consequences of disease much greater than any single factor might suggest. *Genetic and biological factors* allow microbes to adapt and change, and can make humans more or less susceptible to infections. Changes in the physical environment can have an impact on the ecology of vectors and animal reservoirs, the transmissibility of microbes, and the activities of humans that expose them to certain threats. *Human behavior, both individual and collective*, is perhaps the most complex factor in the emergence of disease. Emergence is especially complicated by *social, political, and economic factors*—including the development of megacities, the disruption

[2] These include the U.S. Centers for Disease Control and Prevention's (CDC's) Infectious Disease National Centers, DoD, the U.S. Agency for International Development (USAID), the U.S. Department of Agriculture's Food Safety and Inspection Service, the National Institutes of Health, and the U.S. Food and Drug Administration.

> of global ecosystems, the expansion of international travel and commerce, and poverty—which ensure that infectious diseases will continue to plague us.

The report introduced the Convergence Model as a framework for thinking about how biologic, genetic, and ecological factors all interact with the physical environment and with evolving economic, social, and political forces to drive disease emergence and spread. The report listed factors that influence disease emergence and spread in these domains, including microbial adaptation and change, human susceptibility to infection, climate and weather, changing ecosystems, economic development and land use, human demographics and behavior, technology and industry, international travel and commerce, breakdown of public health measures, war and famine, and lack of political will. These forces affect the risk of pathogen emergence in human populations; the spread of new epidemics; the capability of existing surveillance systems; and, ultimately, the ability of public health systems to respond to outbreaks. In Box 2.1, we briefly describe the role of armed conflict in fueling outbreaks and limiting disease surveillance activities.

Although, for scoping purposes, we focus primarily on the role of natural biologic threats as a source of disease emergence in this report, it is worth mentioning that deliberate or accidental biologic threats also exist (Office of the Assistant Secretary for Preparedness and Response, 2022). Examples of safety risks and accidental pathogen emergence suggest that there might be a benefit to monitoring these potential sources of disease outbreaks as well (MacIntyre et al., 2020; Noyce and Evans, 2018).[3] Furthermore, the threat of pathogen emergence from laboratory sources might increase over time given an increase in the quantity of laboratories working with high-risk pathogens (defined as biosafety level 3 and level 4) around the world (Peters, 2018). Many of these laboratories exist in nondemocratic countries that might lack public health transparency—a major challenge for disease surveillance.

Interdisciplinary-systems approaches have been developed to conceptualize the complex interactions between human, animal, and environmental health beyond the Convergence Model.[4] Among these, the One Health framework has arguably received the most attention, and the WHO, the Food and Agriculture Organization of the United Nations, and the World Organization for Animal Health agreed to lead efforts and cooperate on One Health in 2010 (Mi, Mi, and Jeggo, 2016). The One Health framework brings front and center the interdisciplinary nature of confronting epidemic risks from bacterial and viral mutations to novel zoonoses to the resurgence and spread of pathogens.

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[3] Examples include *Burkholderia pseudomallei* (Neporent, 2015), smallpox (Kaiser, 2014), and anthrax (Russ and Steenhuysen, 2014).

[4] Others include the EcoHealth and Planetary Health frameworks (Harrison et al., 2019; Hill-Cawthorne, 2019; National Academy of Medicine, 2003; Mi, Mi, and Jeggo, 2016).

Box 2.1. The Role of Armed Conflict in Fueling Outbreaks and Limiting Surveillance

Armed conflict facilitates disease emergence: Conflict can enable the biologic emergence of new pathogens into human populations by altering how and where humans live and interact with their environment. Many modern-day conflicts involve informal armies or nonstate armed groups that are often funded through illicit or extractive economic activities, such as mining or logging (Muggah and Sullivan, 2018). Because such activities as mining and logging (especially when remote and unregulated) alter the environment and bring humans and wildlife into closer contact, they have the potential to contribute to disease emergence. Venezuela provides an example case. Conflict has eroded public health resources, and illegal mining activities on its border with Brazil has left behind stagnant water in pits, creating new mosquito habitats and triggering malaria epidemics that have spread to neighboring countries (Boseley and Graham-Harrison, 2019, Grillet et al., 2020). Conflict also moves populations and hinders measures to mitigate disease spread. Globally, the United Nations High Commissioner for Refugees (UNHCR) estimates that some 84 million people are forcibly displaced because of conflict. These population movements often leave individuals without formal health care institutions, increasing vulnerability to disease emergence and spread (UNHCR, 2021).

Armed conflict hampers disease surveillance: Conflicts can also influence disease spread by weakening resources available for public health institutions or restricting the access of public health professionals. In the 1990s, post-Soviet conflicts were associated with epidemics of malaria, measles, pertussis, and tuberculosis in some central Asian and southern Caucasus countries (Hirschfeld et al., 2022), and civil wars in West Africa hampered health care response and monitoring (Moran, 2018). More recently, in their areas of control, cartels in Mexico and Central America enforced their own lockdowns at the onset of COVID-19 pandemic (Sullivan and Bunker, 2020).

Multiple dimensions of the progression of epidemics merit monitoring; we briefly discuss three main roles of surveillance strategies, each tracking a separate phase of a potential or ongoing epidemic.

Surveillance Systems and the Phases of Epidemic Monitoring

To understand surveillance systems, it is helpful to classify the phases of (confirmed and potential) epidemics. For this report, we have developed a three-phased nomenclature:

Phase 1—Emergence: Strategies for surveilling for the potential emergence of an outbreak track the prevalence and characteristics of pathogens in reservoir populations, known and unknown, with the potential for infecting and spreading to human populations.

Phase 2—Outbreak: Strategies for surveilling for the presence of an outbreak identify localized events of novel or alarming infection in human populations to determine whether a particular pathogen has spread to or among humans within a region.

Phase 3—Spread: Strategies for tracking the extent of or potential for geographic disease spread indicate how widely diseases that have progressed beyond outbreaks have spread within or across populations. These systems could also inform about the potential for continued spread.

Our three phases of surveillance map onto the WHO's six phases of a pandemic, as shown in Figure 2.1. Taking influenza viruses as an exemplar case, our phase 1 category, surveilling for the emergence of an outbreak, covers the WHO's first two phases:

1. Viruses circulate among animal populations, so-called *reservoir hosts*. However, at this point, no transmission from animals to humans has been reported.

2. Zoonotic transmission from host to human occurs, and the pathogen is considered a potential pandemic threat.

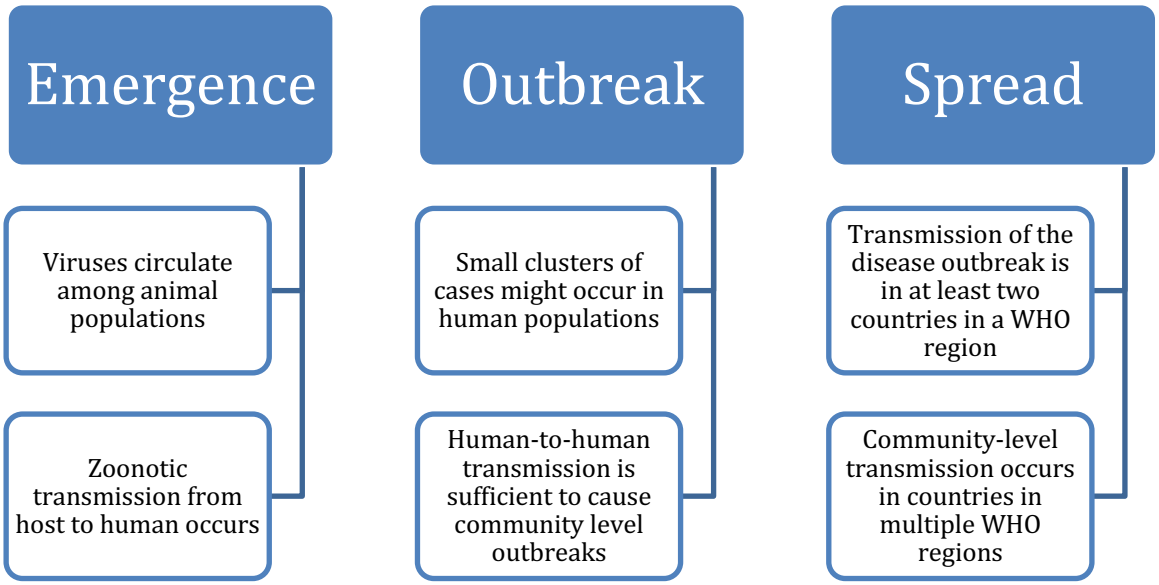
Our phase 2 outbreak surveillance category covers WHO phases 3 and 4:

3. Small clusters of cases might occur in human populations, likely because of animal-to-human transmission, but there are not sufficient cases to suggest human-to-human transmission.
4. The presence of human-to-human transmission that is sufficient to cause community-level outbreaks signifies entry into phase 4 and a substantially increased likelihood of a pandemic.

Our phase 3 spread surveillance category overlaps with WHO phases 5 and 6:

5. Recorded transmission of the disease outbreak is in at least two countries in one WHO region.
6. Community-level transmission occurs in countries in multiple WHO regions—the criteria used to define a pandemic.

Figure 2.1. Mapping of RAND Phases of Epidemic Surveillance to WHO Phases of a Pandemic



SOURCE: Adapted from WHO, 2009.

Although not a surveillance phase, it is important to recognize that before, during, and after an epidemic, there is a need to monitor the capabilities of government and public health entities to *respond* to such crises. An in-depth analysis of health system capacity to respond to outbreaks is beyond the scope of the current project; however, the need for this type of surveillance was evidenced in our literature review and our interviews. There is an existing international system in place to monitor and report on health system capacity based on the reporting requirements of the

WHO's 2005 International Health Regulations (IHR). The IHR require that countries collect data through relevant government ministries and agencies and use this information to complete a State Party Self-Assessment Annual Report (SPAR) on their own capabilities "to detect, assess, notify, report and respond to public health risk and acute events of domestic and international concern," such as health workforces and health financing (WHO, 2019). The WHO standardizes and aggregates this information and publishes the Global Health Security Index (GHSI), which provides stakeholders with an up-to-date assessment and benchmark of these capabilities across countries.

Here, we describe surveillance across these phases; in the next chapter, we review the specific types of strategies used in each phase.

Phase 1—Emergence: Surveilling the Potential Emergence of an Outbreak

The first set of strategies focuses on predicting and ideally mitigating the possibility that a pathogen emerges in human populations. A confluence of technological innovation and academic research has established new methods of disease surveillance relying on the identification and mapping of human, animal, and insect population habitats, movements, and interfaces to better understand epidemic risk and spread. Most of these systems track known risk factors for zoonotic and vector-borne illnesses. Fundamental information on emerging infectious diseases is provided in Box 2.2. Notably, epidemic surveillance strategies in this phase include efforts to monitor environmental conditions that create insect habitats and the forces that influence the level of interaction between human and insect populations, such as population spread.

Box 2.2. The Fundamentals of Emerging Infectious Diseases

In the case of zoonotic infections, many diseases easily transmit among animals without severe symptoms but can cause severe disease when they infect a human through close contact. These close contacts might result from higher-risk interactions between humans and animal populations, such as occur in the bushmeat industry or during urban encroachment on wildlife territories. Diseases such as Ebola are a ready example of such transmissions, often called *spillover events*. Such spillover events are further facilitated by interactions between animals and humans that are shaped by both naturally occurring (e.g., disaster) and manmade (e.g., deforestation) processes. For this reason, epidemic surveillance strategies in this phase include both disease surveillance among animal populations and monitoring social, economic, and environmental conditions that facilitate interactions between human and animal populations.

Vector-borne illnesses are often transmitted via insects, such as mosquitos, ticks, and fleas. These vectors can spread viral infections (e.g., dengue fever, Rift Valley fever, yellow fever, Zika, and encephalitis), bacterial infections (e.g., plague, typhus, and Lyme disease), and parasites (e.g., schistosomiasis and leishmaniasis) (WHO, 2020a). The extent of human interaction with disease reservoirs receives most of the surveillance focus. For example, the spread of insect habitats and the level of human-insect interaction depend on socioeconomic factors, such as population density, urbanization, migration, and building materials in homes, and ecological factors, such as weather and climate.

Phase 2—Outbreak: Surveilling the Presence of an Outbreak

Once a pathogen has spilled over into human populations, many strategies seek to rapidly identify and monitor the outbreak threat. For example, as part of its influenza surveillance program in the United States, the CDC routinely monitors influenza-related deaths, hospitalizations for laboratory-confirmed cases, outpatient visits for influenza-like illness (ILI), and virologic surveillance, which in addition to monitoring the occurrence of influenza also assists in tracking virus types, subtypes, and lineages (CDC, 2021). Many approaches to epidemiologic surveillance are based on health systems and thus might collect information only from those individuals with symptoms severe enough to warrant medical attention and who can access medical care. Strategies to augment traditional surveillance include outreach and testing among populations at increased risk for disease but who might not access care (e.g., the "seek, test, treat, and retain" initiative for human immunodeficiency virus [HIV]) (Chandler et al., 2015) and population-based surveys that monitor, for example, vaccination uptake (surveilled in the CDC National Immunization Surveys) (CDC, 2018).

DoD is unique in that routine, compulsory annual medical screening among the entire force and screening anchored to specific events help ensure that emerging outbreaks or other conditions can be identified routinely. These DoD surveillance efforts are important because many national systems exclude servicemembers during standard surveillance; for example, many soldiers receive care exclusively within the Military Health System (MHS), which, although part of large public health surveillance programs, does not always connect to local public health offices. In addition, some national household surveys exclude those who live in barracks.

Phase 3—Spread: Tracking the Extent of or Potential for Geographic Disease Spread

Once an outbreak has occurred and has been identified as circulating within a population, surveillance can detect how widely it has spread or has the potential to spread. The distinction between phases 2 and 3 is minor; the approaches in phase 3 are concerned with tracking the *movement* of pathogens or humans. For example, strategies that track how people move within their own communities, how they travel across regions, and when and how they migrate, including the conditions of these routes of travel, can affect disease acquisition and spread. Strategies surveilling the spread or potential spread of a pathogen generally require coordination across geographic entities and are maintained both by government (local, state, federal, and military) and nongovernment entities. Many academic and private-sector organizations from the Johns Hopkins Center for Health Security to Google have also entered the business of surveilling for the spread of known pathogens and providing this information publicly. The reach and sophistication of these strategies has expanded dramatically during the COVID-19 pandemic.

Factors That Affect Surveillance Strategies in All Phases

Here, we describe factors that affect surveillance strategies across the three phases of monitoring. Our goal is to describe the implications that these factors have for surveillance, as they might directly relate to the benefits and limitations of the syndromic surveillance strategies we identified and describe in the next chapter. However, the interplay among these factors is complex and could be classified in different ways.

Mathematic Factors

With 20th century public health efforts and modern sanitation, the rate of emerging epidemics has decreased over time (CDC, 1999). However, as the natural prevalence of emerging infectious disease epidemics falls, the probability of any monitoring strategy returning a true, positive signal decreases: There are simply fewer true positives to find. This means that false positive signals will likely comprise most surveillance strategy warning signs (see Box 2.3 for a description of the most-common statistical concepts used to evaluate surveillance systems). As a result, public health officials seeking to detect a truly emerging epidemic will need a way to identify and rule out false positives quickly. In clinical practice and traditional public health surveillance, rare diseases are found by *combination testing*: a sensitive test is applied first, followed by a specific test. The first test reduces false negatives, and the second test reduces false positives. Applying this method to syndromic surveillance, one might be able to identify incidence of a disease indicator above baseline rates. However, one would need to carefully evaluate context to discern whether those primary positives are indicators of an emerging epidemic and not a false alarm.

Box 2.3. Statistical Concepts

Here we give brief definitions of the statistical measures mentioned in this report that are used to quantify how useful a test or system is.

Sensitivity: Sensitivity is a measure of how well a test or system correctly identifies what it is designed to test for, commonly referred to as *true positives*. For example, the sensitivity of a diagnostic test for a disease is the percentage of the time that the test correctly identifies people with the disease. For syndromic surveillance systems that monitor and notify users of a potential outbreak, the sensitivity of a system would be the percentage of time that the system alarms of an infectious disease outbreak when there is an outbreak.

Specificity: Specificity is a measure of how well a test or system correctly identifies when the situation it is designed to test for is *not* occurring, commonly referred to as *true negatives*. For example, the specificity of a diagnostic test for a disease is a percentage of time that the test correctly identifies people who do not have the disease. For syndromic surveillance systems that monitor and notify users of a potential outbreak, the specificity of a system would be the percentage of time during which the system did not alarm when there was not an outbreak.

Positive predictive value (PPV): PPV is a measure of how well the positive results of the test or system results translate into a real-world effect. For example, the PPV of a diagnostic test for a disease is the percentage of the time that people who test positive for the disease develop the disease. For syndromic surveillance systems that monitor and notify the users of a potential outbreak, the PPV would be the percentage of the time that the system alarms of an infectious disease outbreak and that outbreak becomes a significant public health concern.

Biologic Factors

Surveillance strategies can be designed to test for known pathogens (i.e., disease surveillance) or can be pathogen agnostic (i.e., syndromic surveillance). Classic disease surveillance tests for a known pathogen, and no others, in a population (e.g., combing children's hair to identify lice). In general, pathogens that are well-known and easy to test for are easily detected and eradicated. However, even with known pathogen systems, there could be some uncertainty about treatability and the potential for transmission and spread. For example, antimicrobial resistant (AMR) bacteria are anticipated to be the next emerging infectious disease and possibly the next pandemic (Dall, 2021). Disease surveillance can be used to measure AMR and extensively drug-resistant (XDR) bacteria that resist multiple antimicrobials (e.g., XDR tuberculosis and XDR gonorrhea) (Basak, Singh, and Rajurkar, 2016). To detect the spread of these known organisms, disease surveillance is used.

Pathogen-agnostic strategies are valuable when the next emerging infectious disease is caused by a novel pathogen. As an example, health care professionals might investigate all school children with itchy scalps, looking for lice but also for other causes, such as allergies or poor hygiene. Such a surveillance strategy would be pathogen agnostic and, under some circumstances, more useful than classic disease surveillance.

In addition to the pathogen itself, some syndromic surveillance might detect the emergence of a rare disease that can be caused by bioterrorism (e.g., pulmonary anthrax). Most prime candidates for bioterror are rare diseases or unusual presentations, so even a small cluster of a possible bioterror agent infection should raise suspicion that the detected cluster is or has the potential to become an outbreak or epidemic.

Geographic and Environmental Factors

Geographic and environmental factors have implications for disease surveillance in multiple ways. One reason for this is that many illnesses exhibit seasonal variation in their rate of spread (e.g., cold and influenza seasons). This variation arises in two primary ways. First, environmental conditions, such as moisture and temperature, play a role in influencing pathogen survival in the environment and the overall pathogenicity in hosts (Polozov et al., 2008; Shaman and Kohn, 2009). Second, variation also arises from corresponding behavioral changes that occur in systematic ways related to time. For instance, populations could alter their time spent indoors, their time spent socializing, or their migration patterns because of such seasonal factors as variation in the weather or holidays (Moriyama, Hugentobler, and Iwasaki, 2020).

Nearly one-half of the world lives in cities (United Nations Department of Economic and Social Affairs, 2018). Both animal and insect populations can still thrive alongside humans in cities, suggesting potential for natural epidemic emergence (Dunn, 2021). Although illegal wildlife activities might commonly originate in rural areas, they typically reach into urban areas as well, exposing larger populations to risks (‘t Sas-Rolfes et al., 2019). Urban characteristics also have the potential to support disease spread or inhibit disease surveillance. For example, marginalized communities in urban areas often live closely together; these areas have little scope for distancing during outbreaks and low levels of institutional support and governance. Informal housing settlements might also lack critical sanitation infrastructure, and the absence of formal sewage systems limits the scope for novel wastewater surveillance strategies discussed in the next chapter.

Geographic and environmental factors also play a large role in influencing which surveillance strategies are developed and implemented in the first place. For example, environmental conditions, such as the density of flora and fauna in an area, pooling of rainfall or flooding, or ecotones that support interaction between human populations with risk reservoirs, all affect the risk of pathogen emergence. Similarly, at any given point, socioeconomic factors, such as the pattern of urban morphology; deforestation; and the location of populations near reservoirs, lakes, and other standing bodies of water have the capability of influencing pathogenic risk to human populations. Where these risk factors are high, institutions and researchers tend to set up surveillance systems that assess the general level of risk and the likelihood of new pathogen emergence. Examples include remote sensing applications that measure risk factors that can be used to forecast subsequent vector-borne and zoonotic disease outbreaks (Buczak et al., 2012; Olivero et al., 2017; Palaniyandi, 2012; Parselia et al., 2019; Rulli et al., 2017; Wimberly et al., 2021).

Social and Economic Factors

Economic Influences on Public Health System Capacity

An important economic factor is the role of public health system resources. Both across and within countries, lower-income settings are more likely to lack the necessary public health resources for surveillance. With tighter budget constraints, they might also place a lower level of prioritization on communicable disease surveillance relative to other funding needs (Phalkey et al., 2015). One recent study estimates that per capita spending on surveillance for vaccine-preventable communicable diseases in low- and middle-income countries amounts to roughly four cents per person per year (Hossain et al., 2018). Prepandemic estimates in Organization for Economic Co-operation and Development economies range as high as 0.9 percent of all health care expenditures, and studies estimate a willingness to pay of closer to 5 percent of all health spending (de Vries et al., 2021).

Differences in public health resources across geographies generates a phenomenon epidemiologists call *surveillance bias*, a recognized form of information bias in collected public health data (Haut and Pronovost, 2011). In colloquial terms, surveillance bias occurs when the more you search for a disease, the more cases of it you find. In practice, better public health surveillance systems are simply more effective at reducing the number of infections that occur but go uncounted, arriving at an estimate for the rate of infection that is closer to the true population value. Surveillance bias translates into lower accuracy for measured levels of infection, morbidity, and even mortality, simply because resources are insufficient for tracking or for diagnosis among some populations both across and within some countries. Where resource constraints are even severer, lack of public health resources also often means that important surveillance data is simply unavailable.

Surveillance bias complicates our understanding of disease risk because public health resources vary within society as well. This variation can cause public health authorities to inaccurately assess risk and spread along critical dimensions such as race, ethnicity, age, and gender. In the case of COVID-19, researchers have shown that lower-income countries are significantly less likely to track rates of infection that are disaggregated by sex even though pathogenicity and spread have been shown to statistically differ along these dimensions (Hawkes et al., 2021). Discrepancies in the level of available resources across geographies complicate disease surveillance greatly, particularly when trying to make inferences across levels of governance within federated units of administration (Rocco et al., 2021).

In better-funded public health systems, corresponding surveillance systems might access richer data and have the knowledge base to interpret these results more clearly. However, this phenomenon is not limited to those systems that rely on public health funding alone. For example, in populations with high levels of income and education, citizens might have more training and resources to support and participate in the construction and improvement of surveillance systems (Abourashed et al., 2021). Surveillance systems that are based on survey

data must also account for the possibility that response rates might vary along socioeconomic dimensions, although the direction of this bias is not always clear. For instance, within country, low-income respondents were less likely to respond to health questionnaires in Finland, whereas cross-country survey nonresponse bias is often much higher for respondents in high-income settings (Lallukka et al., 2020).

Another concern is that many surveillance technologies' general efficacy might be affected by socioeconomic conditions. This is because socioeconomic conditions could affect the propensity for individuals to seek formal health care or the degree to which populations actively report cases in a particular system (Buckee, Noor, and Sattenspiel, 2021). For example, surveillance strategies that rely on social media risk being overrepresentative of outcomes among higher-income and higher-education groups and underrepresentative of those with fewer resources (Nsoesie et al., 2016). These strategies are also potentially overrepresentative of technologically savvy and younger individuals who are more likely to adopt these technologies relative to other segments of the population.

Socioeconomic Considerations for Measuring Disease Spread

A variety of socioeconomic factors affect surveillance for infectious disease threats. Economic factors are important for surveillance of epidemic risk levels because they might help to determine the extent of the human-animal interface in a society. Typically, economic conditions influence the opportunity cost of engaging in the wildlife trade, hunting, or other activities that entail zoonotic risk, because the presence of these and other industries could create possible infection channels. An example can be found in the analysis of Ebola. Bats can harbor the virus without showing illness, acting as reservoir hosts. When they transmit the virus to other animals that are susceptible, such as gorillas and chimpanzees, the virus can circulate within these populations, causing large die-offs. Typically, such die-offs occur in remote parts of the wilderness and would not be detected by humans living in the region. However, such events pose a threat to human populations when hunting is present. Hunters not only handle the raw meat of potentially infected carcasses but also are often in contact with bodily fluids without ready access to appropriate sanitation measures.

Socioeconomic factors provide valuable contextual information for how other variables might influence disease spread and surveillance. Although the full array of socioeconomic influences on disease spread is beyond the scope of this analysis, population mobility can provide an exemplar case that is generally illustrative of how such forces influence spread. At the macroeconomic level, international trade and globalization are often linked to population flows and disease spread (Farzanegan, Feizi, and Gholipour, 2021; Wu et al., 2017). For this reason, surveillance systems at the onset of the COVID-19 pandemic often analyzed flight data and border crossings.

At the microeconomic level, socioeconomic status has been strongly linked to varied levels of individual risk, behavior, and spread. Using mobility data, researchers have shown that

individuals with better internet access who live in higher-income areas are more likely to comply with social distancing requirements during the COVID-19 pandemic (perhaps because they are better able to do so) (Chiou and Tucker, 2020). Similarly, using data from New York City, Coven and Gupta, 2020, showed that higher-income individuals were more likely to flee the city. Individuals who resided in low-income neighborhoods were less likely to comply with shelter-in-place activities, possibly because a larger portion of these individuals was deemed front-line or essential workers, and possibly because lower-income households make more-frequent shopping trips for essential goods and services. Finally, higher-income individuals often have more-flexible work arrangements or work in industries in which these benefits are more common. This could be because of the nature of the work in some industries; because of greater white-collar employer acceptance of remote work; or because higher-income households have more resources to facilitate working from home, such as high-speed internet and access to video conferencing equipment (Papageorge et al., 2021; Papanikolaou and Schmidt, 2020). Many groups within society, such as younger workers, those with lower education levels, and immigrants, appear to be concentrated in industries with lower levels of remote work (Yasenov, 2020). Similarly, in some societies around the world, gender roles and occupational choices differ strongly between men and women, leading to males traveling farther and interacting with larger number of individuals than women (Buckee, Noor, and Sattenspiel, 2021).

These examples suggest that surveillance systems should be understood in the socioeconomic milieu from which they are derived, or policymakers risk misinterpreting the situation or failing to capture the full extent of the epidemic's burden for population subgroups, which might be disproportionally larger or smaller when groups exhibit differing socioeconomic conditions.

Behavioral and Cultural Factors

Behavioral and cultural factors influence the way in which individuals in society interact, the way that they perceive health risks, and the extent to which they comply with public health guidance and engage with the formal health system. Many of these factors both overlap and interact with the social and economic influences discussed in the preceding section. All these factors can influence both the spread of pathogens within a society and the reliability of systems designed to identify and track these pathogens.

One example of a cultural factor that can influence disease surveillance is the extent to which gender inequality influences the provision of medical resources in a country. There are large, documented differences between men's and women's health and sanitation knowledge and ability to access to health care services around the world (Heise et al., 2019). This has important repercussions for both disease spread and surveillance within populations. For instance, in countries with high rates of gender inequality, women are both less likely to seek health care services when ill and less likely to be tested for COVID-19 (Akter and Kim, 2020). High levels of gender inequality might then inhibit disease surveillance and facilitate disease spread.

Social practices and lack of health information can interact to enhance disease spread. One WHO estimate suggests that over half of Ebola cases in Guinea can be traced to traditional burial practices. Funeral practices throughout West Africa have been associated with the spread of Ebola, the plague, and other pathogens (Park, 2020). The existence of traditional or spiritual healing practices in societies can have an influence on disease spread—particularly when religious or spiritual authority figures purport to have cures or preventive measures—as these can influence individuals to eschew formal health care or to make choices that are more likely to expose them to pathogens (Manguvo and Mafuvadze, 2015).

Individual and societal perception, politics, and personal belief systems have the potential to affect behavior in ways that affect disease surveillance. For example, cultural factors influence how likely populations are to support the implementation of surveillance technologies that involve a loss of privacy. Researchers examining Asia's COVID-19 pandemic response argue that populations in the region were significantly more accepting of digital track-and-trace smartphone applications than individuals in Europe and the United States. This facilitated their adoption, implementation, and ultimate efficacy in amenable populations and hindered it elsewhere (Cha, 2020; Zimmermann et al., 2021).

An important consideration for health behavior and public health decisionmaking is cognitive bias. As COVID-19 spread through the United States, Europe, and the United Kingdom, researchers uncovered evidence suggesting that individuals held different beliefs about the probability that others would be infected by the virus in comparison with the probability that they themselves could become infected. These patterns could help explain the slow adoption of policy goals, such as social distancing, and discrepancies between official warnings and individual assessments of threat levels (Bottemanne et al., 2020).

Cultural attitudes and beliefs affect buy-in both for surveillance and for disease spread. For instance, belief in science and trust in authorities have been linked to compliance with COVID-19 mitigation measures, such as shelter in place orders. Using cell phone mobility data, Brzezinski et al., 2021, found that counties in the United States with higher levels of skepticism toward science and toward the notion of scientific consensus were less likely to obey local and regional government policies. Such attitudes and beliefs could affect essential components of surveillance systems, such as compliance with mandatory testing after periods of travel.

For surveillance of disease spread, determinants of the frequency, duration, and nature of gatherings are also relevant. Disease spread could be influenced by any number of cultural activities, such as sporting events, political assembly, and religious gatherings. In the case of COVID-19, researchers studying the U.S. National Basketball Association found that each additional mass-gathering event at the onset of the pandemic was associated with an 11 percent increase in deaths in the subsequent period (Ahammer, Halla, and Lackner, 2020). Scholars outside the United States have linked religiosity to the spread of the pandemic both directly through attendance at religious gatherings and indirectly through its influence on cultural values

and practices (Vermeer and Kregting, 2020). Some surveillance systems have been developed specifically to monitor outbreaks during planned mass gatherings.

Finally, as highlighted by the case of COVID-19, one of the major behavioral challenges can be the rise of misinformation. Misinformation affects behavioral risk, public health awareness, uptake of testing, willingness to accept treatment or vaccines, and interaction with the formal health care system—all of which have repercussions for disease surveillance. Furthermore, some demographic groups, such as the elderly and those with lower education, have been shown to be more susceptible to misinformation, complicating surveillance and reporting (Bapaye and Bapaye, 2021).

Historic, Political, and Institutional Factors

Historic, political, and institutional factors can influence disease surveillance. In terms of historic experience, the occurrence of a prior pandemic can help build vital institutions and knowledge to support future responses. For example, South Korea might have been better prepared to respond to the COVID-19 pandemic because it had learned lessons from the 2015 Middle East respiratory syndrome outbreak (Moon, 2020). Institutional experience can affect pandemic readiness not just at the federal level. Leavitt, 2021, argues that during the 1918 influenza pandemic, the city of Milwaukee outperformed most other major cities in the United States, quickly responding with public-private partnerships and benefiting from local buy-in for public health initiatives. Although other cities had attempted similar policies, they were less effective, potentially because of the local legacy of disease epidemics. Milwaukee suffered a disastrous smallpox epidemic in 1894 through which public health officials had learned valuable lessons about the importance of public education, trust building, and transparency.

A vital concern is the necessary political will to conduct and accurately report pathogen spread when it does occur. Research during the COVID-19 pandemic has demonstrated that countries, regions, and individual politicians have often failed to report, or deliberately misreported, the results of disease surveillance for political reasons. Misreporting is a problem in many settings, although evidence suggests that it is higher where checks and balances are fewer, such as in nondemocracies and in countries without free and fair elections (Adiguzel, Cansunar, and Corekcioglu, 2020; Annaka, 2021). Some misreporting of disease incidence reflects not malfeasance but institutional and organizational challenges. For example, researchers examining surveillance during the COVID-19 pandemic have found that there are statistically significant associations between the quality of subnational data and indicators of fiscal decentralization and the robustness of civil-societal institutions (Rocco et al., 2021). This research suggests that coordination challenges across the levels of government might complicate disease surveillance. Similarly, surveillance systems could face additional challenges in crises and natural disasters during which it might be harder to collect data or even estimate the size of the population at risk (Hall and Ross, 2021). In this regard, preparedness and institutional resilience become important factors in surveillance system readiness.

Political and institutional factors also play a large role in the effective design and implementation of disease surveillance programs writ large. For example, in a systematic review of the factors influencing farmer engagement with livestock surveillance systems, researchers found that farmers are more likely to report disease outbreaks when there is a financial incentive to report, when the potential economic repercussions of reporting are smaller for the farmer, when the regulatory hurdles are smaller, when the farmers believe that the health authorities' response will be efficacious, when there are higher levels of trust in public health institutions, and when the clinical signs to report are more clearly communicated (Gates, Earl, and Enticott, 2021). These results suggest multiple channels through which transparent and efficient public health and political systems can support surveillance systems.

Another factor involves ethical questions raised by surveillance techniques that rely on health records access and by digital surveillance tools (Mello and Wang, 2020). Countries have elected to strike very different levels of personal privacy protections, which have resulted in large repercussions in nature of available surveillance data. As discussed earlier, these factors might be influenced by cultural values, but they also depend on political norms and the level of checks and balances on government reach in society.

Finally, it is possible that multiple political and institutional factors jointly determine effective public health responses and surveillance during epidemics. In a comparison of five East Asian countries' responses to COVID-19, researchers concluded that such factors as competent leadership, efficient public health infrastructure, and populations supportive of public health goals are important, but that these factors are ultimately most effective when working in concert (An and Tang, 2020).

Demographic Factors

There is a wide variety of demographic factors that are important to track when conducting disease surveillance. For example, in an analysis of COVID-19 cases in Sub-Saharan Africa, researchers found that the share of the population over 65, urbanization, and population density were all significant predictors of disease spread (Nguimkeu and Tadadjeu, 2021). Some of these factors might even be dynamic, complicating surveillance efforts. As a disease becomes endemic, the amount of preexisting immunity to many pathogens rises in the population. This generates a tendency to observe lower infection rates of many communicable diseases among older individuals (Laskowski et al., 2011). For novel pathogens introduced into society, the reverse might be true because immune responses to an initial disease exposure tend to decrease with age. These patterns are especially important for symptomatic surveillance based on morbidity or mortality.

The case of COVID-19 is again illustrative as both age and sex have been robustly linked to the severity of outcomes. Because of this, when analyzing mortality surveillance data, it is essential to account for demographic factors in the analysis, or one risks drawing inferences

regarding the efficacy of policy responses that are confounded by characteristics of the age and sex distribution in a society (Gallo et al., 2021).

It is well documented that there are large differences in the disease burden for many communicable diseases, including COVID-19, across racial and ethnic groups. These stem from both biologic factors and socioeconomic factors correlated with race and ethnicity (Kniffin et al., 2021; Kopel et al., 2020). Although a complete discussion of the full list of systemic cultural, social, and economic drivers of these differences is beyond the scope of this report, many of these factors influence not only the spread of disease but also the ability to surveil for diseases. For example, disparities in access to the health care system affect both health outcomes after infection and testing capacity in systematic ways. These issues extend across racial and ethnic groups and across the geographies in which they inhabit. Urban populations are also associated with higher levels of socioeconomic inequality and, as a result, inequal access to health care resources during epidemics (Patterson-Lomba et al., 2016). Underreporting—both of race and ethnicity in health records and of disease incidence among many groups in the United States, including individuals identifying as African American and Latinx—is also a major issue (Tai et al., 2021).

Conclusion

In this chapter, we introduced two frameworks (the Convergence Model and One Health) for conceptualizing epidemic risk and for understanding the progression of an epidemic when an outbreak does occur. We then highlighted how surveillance needs will vary over three phases of epidemic progression, wherein surveillance systems are designed to identify and track epidemic emergence, outbreaks, and disease spread. The conceptual frameworks make clear that the effectiveness of epidemic surveillance strategies in each of these moments will be affected by a wide variety of factors, including characteristics of pathogens themselves; human biology and demographics; geographic and environmental influences; and social, cultural, behavioral, economic, historic, and political settings. Grouping these factors, we highlighted several vulnerabilities and limitations to existing and planned surveillance strategies and to the application of emerging approaches to surveillance. Not all surveillance strategies are equally affected by each of these factors, but understanding these nuances requires a deeper exploration of the strategies themselves. In Chapter 3, we take an in-depth approach to describing surveillance systems, grouping efforts to predict and measure epidemics based on the underlying surveillance strategies used.

Chapter 3. Strategies for Surveillance

In this chapter, we describe strategies currently in use for conducting syndromic surveillance. Each strategy is placed in the surveillance phase in which it is used most often, although there might be instances when it is used in other phases. For example, remote sensing is placed under Phase 1—Emergence, but there are applications in which remote sensing is being used in other phases. For each phase, we present a summary table that includes the specific strategy, examples based on our literature review, and private-sector enterprises we identified. After this table, we present a more-detailed description of each strategy, curated evidence of the strategy stemming from our literature review, benefits of the approach, limitations of the strategy, and private-sector enterprises utilizing the strategy, if they exist.

One limitation of our approach is that the description of the evidence is not comprehensive. As described in Chapter 1, our goal was to identify as many syndromic surveillance strategies as possible, and it was beyond our scope to describe the entire literature for each strategy. Thus, the evidence we present is based on the most-relevant evidence derived from our literature review, supplemented by other articles we identified post hoc, particularly literature or systematic reviews focused on a given surveillance approach.

Phase 1—Surveilling the Potential Emergence of an Outbreak

Our investigation revealed two strategies for surveilling for the potential emergence of an outbreak: veterinary public health (VPH) surveillance and remote sensing (see Table 3.1).

Table 3.1. Strategies for Surveilling the Potential Emergence of an Outbreak

Strategy	Examples	Private Enterprises
VPH surveillance	• Wildlife mortality surveillance • Farmer and veterinarian call-in centers • PREDICT Project	• IDseq: Open-source system to map and track microbe sequence information
Remote sensing	• Using satellite imagery to observe factors that affect the emergence of mosquito-borne diseases, such as malaria, and land-use change to map human exposure to wildlife disease reservoirs	• None identified

Veterinary Public Health Surveillance

VPH professionals conduct disease surveillance to detect specific pathogens and preempt possible animal-to-human transmission. Most citizens in the developed world are beneficiaries of

routine VPH programs that ensure a safe meat and dairy supply. VPH programs also screen imported live animals to ensure livestock diseases are not transported with them around the world: Direct losses attributed to one case of imported livestock-only disease for one year exceed $141 billion (Berthe, 2020). VPH surveillance strategies focus on preventing zoonotic diseases from passing between animal populations and humans through food and live animal transport and at the so-called human-animal interface wherein which humans, such as farmers, hunters, abattoir workers, and those who live in remote areas, have routine close contact with animals.

Of the zoonotic surveillance programs, there are currently two strategies: programs to detect known zoonotic pathogens and programs to detect as-yet unknown zoonotic pathogens. We discuss the two programs based on our literature review to illustrate the versatility of VPH programs. Another VPH effort, the PREDICT program, is a collaborative effort between USAID and EcoHealth Alliance (a National Institutes of Health–funded scientific nonprofit organization). The PREDICT project works to characterize the virome at the human-wildlife interface by sampling wild animals across the globe and using metagenomic methods to identify viruses. PREDICT is described more fully in Chapter 4.

Kuisma et al., 2019, conducted a study to detect Ebola virus in wildlife in rural Republic of the Congo. Over a 12-year study period, the team ran 520 outreach visits to remote villages across a 50,000-acre region, asking to be notified by phone if a carcass was seen in the area. Fifty-eight carcasses were reported and sampled, and all tested negative for Ebola (which is somewhat unsurprising because the Republic of the Congo has not had a confirmed Ebola virus outbreak since 2005). The program sought to detect Ebola virus in wild apes, which are known pathogen hosts.

In contrast, Thumbi et al., 2019, took a pathogen-agnostic approach. In villages in Kenya where farmers live in the same shelter as their animals, zoonotic transmission is likely. The team set up a system for these rural farmers to call a veterinary professional when their animals became sick. During the five-year study period, more than 10,000 validated disease reports were collected and categorized by syndrome pattern and species affected. Once alerted, the veterinary staff could diagnose and treat the disease, then counsel farmers about zoonotic risk, if applicable. This program was more effective at early detection of disease outbreaks than a veterinary professional regularly rotating among several villages. The program is unique; through screening all reported diseases, it seeks to detect zoonotic disease transmission prior to knowing which pathogens are present.

Benefits

The benefits of a program to encourage reporting of carcasses through prolonged educational outreach efforts in rural communities could facilitate long-term behavior changes, reducing hunters' contact with diseased carcasses and thus the risk of zoonoses. These programs can also be low cost, especially relative to their benefit: The estimated marginal cost of initiating the carcass-testing program was approximately $30,000, with one-tenth of that for each additional

year of surveillance (Kuisma et al., 2019). If the program was rerun with the PREDICT model in mind, the collected samples could be screened for other viruses to characterize the virome at the human-wildlife interface. Such efforts would be a substantial benefit for both citizens living at the human-wildlife interface and for scientific endeavors more broadly.

Providing access to veterinarians in remote regions of Kenya, which has suffered two large outbreaks of Rift Valley fever in the past two decades, was effective at detecting severe diseases in animal populations in rural areas. In fact, in 2006, the number of human Rift Valley fever fatalities was 75 percent lower than in 1997; this was attributed in large part to mobile phone technology enabling rapid deployment of VPH professionals. Not only are these programs effective, they are also substantially more affordable than characterizing the virome worldwide (as in the PREDICT model) and are likely to detect spillover events rapidly enough to enable robust public health response and intervention.

Limitations

VPH strategies are not without drawbacks. For pathogen-agnostic strategies, syndromes with severe disease might be more likely to be reported than diseases with rapid mortality. As a result, diseases characterized by high and rapid mortality, such as highly pathogenic avian influenza, might not be reported as readily as Rift Valley fever, which has distinct and severe clinical signs. Pairing the surveillance system with an incentive to report livestock deaths could improve this aspect of the syndromic surveillance strategy. As observed in the study monitoring carcasses, the effort resulted in a very low carcass-reporting rate. In addition, there might be challenges associated with delays in reporting, sampling, obtaining and testing results, and relying on patchy mobile networks in remote areas. The program was also testing for known pathogens; although it is very helpful to detect one disease in one vulnerable region, this type of program cannot detect novel pathogens at the human-wildlife interface unless the sample residuals are tested for a wider array of viruses. It is unclear whether the type of samples collected would support broader metagenomic testing or at what cost. As a result, such surveillance programs will not detect spillover events of novel viruses or any other pathogen not tested for.

Private Enterprises Using Biologic or Veterinary Data for Disease Surveillance

Although there are limited commercial products for the identification of emerging diseases, IDseq provides “an open-source cloud-based metagenomics pipeline and service for global pathogen detection and monitoring” (Kalantar et al., 2020). To date, there is no evidence that IDseq has been used for VPH surveillance, but it has the potential to detect novel diseases, especially if combined with a program like the carcass-sampling program. The service allows uploading of metagenomic next-generation sequences into a system that overlays them with known viral and microbial sequences. The process allows for identification of microbes and virus sequences in the sample with use of specific markers or sequences for a known organism.

Because of this advance, the IDseq system can be used to identify and track specific pathogens, and potentially specific variants, using collection time and location as markers.

IDseq was a critical tool in identifying a SARS-related virus in Cambodia in January 2020, which was later determined to be SARS-CoV-2, and is used in other countries throughout Asia and Africa (Zeeberg, 2021). Users can upload information about a pathogen into IDseq to achieve a clinical diagnosis, which can be especially useful for advancing knowledge about possible emerging outbreaks in resource-poor settings. In our interviews, Jessica Manning, director of the International Center of Excellence in Research Cambodia, stated that advanced scientific and technical training are not necessarily required to use IDseq. Users are trained on the system, but, in Manning's laboratory in Cambodia, those responsible for uploading samples typically have a two-year degree with some basic understanding of math and biology, although others who perform quality assurance and quality control duties might be working toward a bachelor's degree. IDseq users also have access to online resources to help troubleshoot problems and connect with other users across the world.

Remote Sensing

Advances in the capabilities, coverage, and availability of satellite imagery, coupled with the development of associated geospatial resources such as Google Earth Engine and crowdsourced data projects like OpenStreetMap, have meant that far more detailed and useful information is available to researchers and practitioners, both for modeling epidemic risk and for tracking disease spread in settings where traditional health system surveillance might be poor, such as in the aftermath of disasters (Bernardo et al., 2020). In broad terms, remote sensing applications of disease surveillance fall into two categories. The first comprises environmental biosurveillance strategies—those established to track the influence of environmental factors and climate change on known drivers of infection, such as the habitat impacts of rising sea levels, flooding events, or forest fires on animals and insects that constitute disease reservoir risks to humans. The second comprises strategies used to track socioecological drivers of infection—human factors, such as urbanization, migration, poverty, and human-wildland interfaces, that can also be tracked through satellite observation (Peckham and Sinha, 2017).

Zoonoses and vector-borne diseases are two very promising targets on which satellite imagery has been used to assess risk and track outbreaks. As an example, a recent *Lancet* commission that centered on global malaria eradication identified remote sensing as a vital source of information for monitoring both human populations and the surrounding disease environment (Feachem et al., 2019). In the case of malaria outbreaks, remotely sensed data has been used for more than 20 years in research and monitoring applications. Over this span, the technologies, capabilities, and raw data available to researchers have rapidly evolved, and, today, the utility of remotely sensed data sources has been robustly demonstrated for monitoring the effects of urbanization, deforestation, and water management on malaria incidence. Wimberly et al., 2021, provides a summary of these studies, discusses malaria risk assessment systems, and

compiles all freely available remotely sensed data products available for monitoring malaria outbreaks.

Our literature review also identified research examining a broader set of remote sensing applications, including studies examining urban morphologies, landscape features in urban environments, and rainfall and water cover patterns that are useful for tracking mosquito-borne illnesses such as chikungunya (Lorenz et al., 2020), dengue fever (Pham et al., 2018), West Nile virus (Ozdenerol, Taff, and Akkus, 2013), and Zika (Weinstein, Leslie, and von Fricken, 2020). Parselia et al., 2019, provides a comprehensive review of 43 studies employing earth observation methods and data to study mosquito-borne diseases.

While mosquito-borne illnesses provide several well-developed case studies, numerous other health risks, such as leptospires and Lyme disease, have been studied using remote sensing technology (Biscornet et al., 2021; Cheng et al., 2017). In this literature, one promising area of growing satellite data monitoring is in land-use change studies to map human exposure to wildlife disease reservoirs. Researchers have demonstrated that forest loss and fragmentation are significantly associated Ebola outbreaks in West and Central Africa (Olivero et al., 2017; Rulli et al., 2017). Rulli et al. notes that centers of initial outbreak are more likely to occur in regions where the average degree of forest fragmentation within a 25 km distance from the infection center was significantly higher than in other parts of the country.

Benefits

One of the most-promising features of remotely sensed measures of disease risk is the extent of geographic coverage. Earth observation techniques and databases have the potential to provide global warning systems. In addition, many governments struggle to maintain accurate health records and others lack transparency in sharing data with the international community. In most cases, remote sensing methods can be used without any reliance on foreign governments to share data.

Limitations

Despite these proof-of-concept studies, numerous institutional challenges remain to developing, implementing, and monitoring satellite-based rapid detection systems to track Ebola and other disease outbreaks (Peckham and Sinha, 2017). Disease forecasting using geospatial data involves a high level of complexity, requiring expertise to read, manipulate, and analyze data from such sources as satellites as well as an understanding of the ecological factors important for disease emergence in human populations (Sudmanns et al., 2020). In practice, technological, financial, and political barriers to analysis, implementation, and maintenance have also meant that, outside academic research, there are few on-the-shelf, user-friendly systems in place for epidemic surveillance relying on remote sensing (Pepey et al., 2020; Tibbetts, 2017). Finally, a major challenge is that there is a disconnect between innovation, which often occurs in academic settings in rich countries, and field implementation of these developments, which often

is required in lower-income settings with weaker health infrastructure. Misaligned incentives between developers and practitioners and institutional barriers often prevent new forms of disease surveillance from evolving into formal systems (Buckee, Noor, and Sattenspiel, 2021).

Private Enterprises Using Remotely Collected Data for Disease Surveillance

We did not identify any private enterprises using remotely collected data for disease surveillance.

Phase 2—Surveilling for the Presence of an Outbreak

Several new strategies are being used to surveil for the presence of an outbreak in a community (see Table 3.2).

Table 3.2. Strategies for Surveilling for the Presence of an Outbreak

Strategy	Examples	Private Enterprises
Surveys	• Surveys for tracking infections or symptoms in households or at mass-gathering events	• Magpi—surveying through mobile phones
Web searches	• Google and Baidu search terms for pathogen names and/or symptoms	• BlueDot—search (and other) data to detect outbreaks • Google Trends—search data to monitor trends
Social media mentions	• Weibo, WeChat, and Twitter mentions of pathogen names and/or symptoms	• Bellingcat—investigative journalism that uses open-source intelligence to advance forensic research transparency and accountability • Sickweather—social media mentions, in addition to other data, that predict disease incidence • Kinsa Health—temperature measurement with smart thermometers to predict spread
Media monitoring and web scraping	• Manual scanning of local news media for health risk events, specific disease of concern	• ProMED—collection and curation of relevant media information • HealthMap—application for querying, filtering, integrating, and visualizing unstructured media reports • Travax by Shoreland, Inc.—medical experts that evaluate reports for determining health risks using several data sources • BlueDot—web scraping (and other) data to detect outbreaks • Google Trends—search data to monitor trends

Strategy	Examples	Private Enterprises
		• Bellingcat—investigative journalism that uses open-source intelligence to advance forensic research, transparency, and accountability
Pharmaceutical sales	• Over-the-counter (OTC) and prescription drug sales for specific symptoms such as ILI and gastrointestinal health	• Real-time Outbreaks and Disease Surveillance (RODS)—OTC sales (and other data) that are suggestive of disease outbreaks • Sickweather—social media mentions, in addition to other data, to predict disease incidence
School and work absence (absenteeism) data	• Tracking of absenteeism in school districts and workplaces	• None identified
Data collection by health care staff	• Clinical health system and emergency responder data of symptoms and/or diseases • Clinicians report on forms (on paper or electronically) for symptoms and/or diseases • Community health workers log rumors of events	• nference—text analysis of symptoms • IBM Explorys solutions—comparison of medical cases to identify patterns (disease clusters) • IDseq—open-source system that maps and tracks microbe and virus sequence information
Consumer expenditure data	• Patterns of consumer spending, such as hoarding, that indicate behavioral responses to epidemic threats and spread	• None identified
Geospatial techniques	• Satellite data map population movements and economic activity via night lights • Crowdsourced initiatives that volunteer geographic information • Smartphone apps and contact tracing, geostatistical modeling, and hot and cold spot analysis	• Kinsa Health—location and thermometer data that shows large-scale fever data
Wastewater sampling	• Use of sampling with the municipal wastewater system to determine viral load from specific regions or neighborhoods	• Biobot Analytics—sampling of wastewater systems for viral RNA and maps findings over time

Surveys

The COVID-19 pandemic has seen an increased use of survey instruments for self-reporting of symptoms as a screening approach as well as to understand broader prevalence in geographic areas. For example, to track the contemporaneous effects of COVID-19, the U.S. Bureau of Labor Statistics launched two new high-frequency digitally collected surveys, the weekly household pulse survey and the weekly small-business pulse survey (Buffington et al., 2020; Nguyen et al., 2021). Using digital surveillance techniques, these surveys provide high-

frequency, geographically disaggregated indicators intended to capture the severity of the outbreak. In the context of epidemic surveillance, they contain information that can be useful for assessing population risk factors and population behaviors or attitudes relevant for spread and mitigation. For instance, the household pulse survey has fielded questions on vaccine access and uptake, delays in the receipt of other forms of medical care, use of telehealth, telework, food insecurity, and household mobility. However, recent evaluations have criticized the household pulse survey and its sampling technique for limited generalizability (Bradley et al., 2021).

Community and public health strategies have also been deployed at mass-gathering events (Hoy et al., 2016; Lami et al., 2019) and typically entail survey-based data capture of symptoms, often enhanced by a web-based application (e.g., Hoy et al., 2016). Studies suggest that these event-specific strategies have been effective at detecting potential outbreaks, often without large costs to implement (Lami et al., 2019).

Benefits

The use of survey instruments for data collection as part of syndromic surveillance has limited application but some benefits. Epidemic surveys designed to provide rapid information on the impacts of an ongoing disease outbreak have the advantage of allowing policymakers to flexibly collect data on behavioral factors that influence population risk. Examples include population health knowledge and sanitation practices, access to and uptake of formal health system resources, and attitudes regarding vaccination and other treatment. Many of these risk factors can be collected prior to an outbreak and can help policymakers and scholars contextualize the risk of further disease spread within populations. Another promise of survey approaches is that they can be added on to existing national survey efforts for a more cost-effective data collection approach. In addition, surveys can be a low-tech approach to data collection in resource-sparse but high-risk contexts. For example, a brief questionnaire used across 40 mobile clinics along the road to Karbala, Iraq, during a mass gathering was effective at detecting and tracking multiple communicable disease syndromes by surveilling gastrointestinal symptoms, fever, cough, and rash (Lami et al., 2019). Surveys can be paper based, online, or conducted by telephone, allowing for flexibility in implementation. As described in the previous section on VPH surveillance, mobile phone survey reporting of livestock disease tied to Ebola was similarly effective, but faster and less resource intensive, at outbreak detection than in-person digital survey data collection (Thumbi et al., 2019).

Limitations

Unlike most measures of epidemic surveillance, surveys are typically collected with some degree of lag. Design, enumeration, data cleaning, anonymization, and processing can add to this time. Traditional surveys require significant time to field, clean, and interpret. They also often involve in-person enumeration. In addition, as mentioned, there can be issues with

generalizability. These factors render surveys' utility quite low when attempting to monitor epidemics.

Private Enterprises Using Surveys for Disease Surveillance

Magpi is a platform that enables survey data collection using text messaging and includes data analytics and visualization features. The platform was developed with experts from the CDC and WHO with the aim to deploy forms and collect health and population data in real time. Magpi is frequently reported as a platform in health- and disease-related surveys in Africa (Enriquez, Udhayashankar, and Niescierenko, 2020; McQuilkin et al., 2017; Merrill et al., 2020).

Web Searches

Syndromic surveillance has been conducted using internet search terms as indicators of new and emerging disease outbreaks or to track the course of an outbreak. In certain cases, the search term was the name of the pathogen itself and thus could be used only for tracking the spread of a known pathogen into a new region or increased incidence within a region. For example, Mavragani, 2020, examined Google searches for "coronavirus" in early 2020 across European countries, and Milinovich, Magalhães, and Hu, 2015, examined Google searches for "Ebola" worldwide. The first study found strong correlation between the search term and COVID-19 cases and deaths in these countries, although the strength of relationship monotonically decreased after a point. The global examination revealed that countries with high-volume searches for Ebola were highly affected countries; search frequency in a country correlated with the nation's Ebola epidemic curve. In a related study, Dai and Wang, 2020, examined search volume in Baidu, a popular search engine in China, for "pneumonia" and "SARS" from November 2019 to March 2020 and found that search volume peaked 20 days earlier than the official warnings about COVID-19. Dong et al., 2017, interviewed patients with confirmed flu and asked, "If you've searched for influenza in the early stages of illness, what search queries or terms have you used among alternative keywords below?" "Fever" was the most frequent, and searches for fever on Baidu had the strongest correlation with influenza laboratory data in Tianjin, China.

Use of internet searches for influenza-like symptoms was also assessed relative to COVID-19 incidence in articles identified in the literature review. Rajan et al., 2020, and Higgins et al., 2020, found respiratory and gastrointestinal symptom-related search terms correlated with COVID-19-related case counts and fatalities and laboratory-confirmed surveillance, and search terms often correlated with cases by days to weeks. However, in one study of search terms considered separately from each other on Baidu, only a few terms ("SARS," "*feidian*" [i.e., severe acute respiratory syndrome in Chinese], "pneumonia," and "coronavirus") deviated from the norm and only one day before the official outbreak announcement (Wang et al., 2020).

One study uncovered in our literature review used data from Google Flu Trends (GFT) and found positive correlations with GFT data and emergency department (ED) presentations for flu

in Queensland, Australia, from 2006 to 2009 (Boyle et al., 2011). GFT was historically one of the more widely used and studied tools using internet search terms for disease surveillance but was discontinued in 2015 (Kandula and Shaman, 2019). Beginning in 2013, a series of articles that were critical of GFT was published, finding that the model, at times, significantly inflated the presence of influenza in communities (Butler, 2013; Lazer et al., 2014; Lazer and Kennedy, 2015); more on the critiques of GFT is provided in Box 3.1.

Box 3.1. Google Flu Trends

GFT was developed to predict the incidence of flu in a specific location based on key terms in Google Searches. The algorithm for search terms and frequencies was tuned to CDC official estimates of ILI case rates. Initial results, in 2008, were able to predict rate of flu two weeks before CDC reporting of official case rates (Kandula and Shaman, 2019; Lazer and Kennedy, 2015).

However, in 2013 to 2014, GFT was inaccurate in its predictions, and the program was terminated by Google. Analyses of the GFT algorithm found many issues. The high volume and wide variety of Google's nonstandardized (i.e., search) data meant that it was difficult to identify which search terms were associated with ILI (Butler, 2013). Google used automation techniques to create the algorithm based on which search terms were most associated with ILI, but it did not check the automated process retrospectively to discern what search terms the resulting algorithm was using to predict ILI cases (Lazer et al., 2014). There could have been popular search terms unrelated to ILI that followed the same trend as ILI cases.

One of the main reasons for the inaccuracy of the GFT algorithm a few years after it was created is that the algorithm was fit to the initial ILI data too well—Google "overfit" the algorithm. When the algorithm was applied to new ILI data, the algorithm was no longer a good fit, resulting in inaccurate predictions (Lazer and Kennedy, 2015). This was problematic because of the time dependency of the data. Internet search data changes over time as it is influenced by changing search recommendations, advertisements, and media coverage of the flu (i.e., whether influenza is discussed frequently in the news; and whether the Google searches done by those who have the flu, those who think they have the flu, or those who are interested in learning more about flu), among other factors (Butler, 2013; Lazer et al., 2014).

Benefits

Search data can precede official case, virologic, mortality data, or official notices about an existing outbreak. For example, search data indicated an increased volume of respiratory illness in China weeks before official warnings of COVID-19 and prior to increases in case counts and fatalities (Dai and Wang, 2020; Higgins et al., 2020; Rajan et al., 2020). In addition, public health agencies within or outside a country or region can often access data originating in another country or region (Mavragani, 2020; Milinovich, Magalhães, and Hu, 2015). Search data also enable tracking symptoms associated with diseases that are unrecognized in health care settings because they might represent less severe cases. And finally, search data can assist in forecasting the course of an outbreak, either independently or in combination with another data source. Approaches that combine internet data with existing data might outperform traditional methods used for forecasting, based primarily on different approaches applied to historic trends (Aiken et al., 2020; Liu et al., 2020).

Limitations

The sheer volume of search data available requires a well-developed, vigilant analytic strategy. Without a well-specified index of terms, the model is prone to lack specificity, resulting in overestimates of disease burden projections. This is particularly problematic when there is an unknown pathogen, and one is trying to monitor for any of number of symptoms. To identify influenza-related search terms, Dong et al., 2017, conducted phone-based interviews with confirmed cases and surveyed them about their internet search histories. Wang et al., 2020, found that only some words deviated from normal frequency distributions in web searches ahead of the official COVID-19 warning in China. In addition, different sources of internet data are common in different parts of the world (e.g., Google in Africa, Europe, and Korea and Baidu in China). Most internet data are owned by the third party that hosts that platform, (e.g., Google and Baidu), and the amount of data available and the format of available data vary and can change. As was seen in the GFT example, the models for using internet data are time dependent and will need to be updated over time. This can be because disease symptoms, the words to describe diseases or symptoms, and the course of the outbreak and its relationship with one or more words change over time. For example, the strength of the relationship between Google searches for "coronavirus" and case and death counts in Europe decreased after a point (Mavragani, 2020). In addition (and related to the point made about regional variability above), new internet platforms could gain in popularity, which requires adaptation as surveillance systems incorporate new platforms into their systems. Finally, the source data used to populate internet platforms might be biased. Aiken et al., 2020, put forth that, in developing regions where internet penetration is low, internet-based surveillance might be regionally biased toward cities and capital regions. There might be other factors that distinguish internet users to noninternet users in a region or, similarly, users of a specific internet platform relative to nonusers of that platform.

Private Enterprises Using Web Search Data for Disease Surveillance

BlueDot is a Canadian company founded in 2013 (as BioDiaspora) that aims to "track, contextualize, and anticipate infectious disease risks" by applying data analytics to web-scraped information from news and search data (BlueDot Inc., 2019). Source information for the BlueDot algorithm is reported to include online news outlets, health expert mailing lists, and health-related queries in internet search engines (Khan et al., 2012). BlueDot was reported to beat the WHO to the identification of COVID-19 in Wuhan by seven days. Later news sources indicate that other public, freely available systems (i.e., HealthMap and ProMED, discussed later under "Media Monitoring and Web-Scraping") had released earlier warnings (Macaulay, 2020).

Google Trends is a publicly available system, managed by Google, to compare the frequency of use of specific search terms put into Google temporally and spatially. This is a centralized web search based on the use of Google as a search engine and, therefore, reflects the understanding and constraints described earlier regarding web searches. There is evidence that Google Trends provides some predictive power for the progression of diseases that are common

but that receive only minor media coverage and for rare diseases with high media attention (Cervellin, Comelli, and Lippi, 2017). Overall media attention to a disease or condition will lead to an increase of Google searches for related search terms. Therefore, the pattern of media coverage must be considered in the use of Google Trends for surveillance. Google has made available a data set of search terms related to COVID-19 for over 400 terms searched in the United States and identified at the county level—the COVID-19 Search Trends data set (Gabrilovich, 2020). Google intends this data set to be used by public health researchers to improve understanding of the further progression of the epidemic.

Social Media Mentions

Syndromic surveillance is also being conducted by tracking mentions of diseases or symptoms on social media platforms. As with internet searches, in some instances studies tracked mentions of known pathogens by name, whereas in others the focus was on symptoms. In the former of these categories, Zhang et al., 2015, documented that mentions of "A(H7N9)" (avian flu) on Weibo (a social media platform popular in China) occurred on average one hour and two minutes ahead of official documentation and, in some cases, 20 hours prior to official documentation on the Chinese National Health and Family Planning Commission website and 24 hours sooner than on the Event Information Site of the WHO. This was largely driven by postings from Chinese media that were then amplified or reposted. Data from Weibo were also used to examine Chinese public's awareness and concern about spread of Ebola in 2014, particularly after a woman in China exhibited symptoms consistent with Ebola infection (Feng et al., 2018). Mentions of COVID-19–related terms on WeChat (a popular social media application in China) were tested against each other, many of which had abnormal posting volume in the days leading up to the announcement of the outbreak (Wang et al., 2020).

Outside China, our literature review identified two studies using Twitter data to surveil cholera outbreaks in Haiti, with the mentions of "cholera" on Twitter preceding case data reports by as much as two weeks. Furthermore, researchers were able to use Twitter mentions of "cholera" to produce a preliminary of estimate the virus's reproductive number (Chunara, Andrews, and Brownstein, 2012). Sarker et al., 2020, identified Twitter posts from individuals who self-reported positive COVID-19 tests but showed no symptoms or disclosed only anosmia and/or ageusia, which were not being covered in COVID-19 symptom studies that were based on clinical case presentations, suggesting that such data might be useful in assisting with case definitions among those who do not present.

Benefits and Limitations

Many of the benefits and limitations described for web search terms apply to social media data as well. These benefits include the timeliness of data (e.g., social media mentions of cholera in Haiti preceded official case data reports by as much as two weeks) (Chunara, Andrews, and Brownstein, 2012), nonreliance on government data (e.g., researchers in Singapore could use

mentions of A[H7N9] on social media to monitor an evolving epidemic in China before official data was released) (Zhang et al., 2015), inclusion of symptoms outside the health care setting, and help with forecasting. Similarly, limitations of using social media data for syndromic surveillance include the voluminous amounts of data, regional variation in source data (e.g., Weibo, Twitter, and WeChat), whether those who own such data make it available, time dependency, and the potential for biased source data based on who has access to the internet and who uses social media. In our interviews, Edward Holmes of the University of Sydney also described social media monitoring as particularly useful, citing Twitter as one platform in which data on disease trends can easily be monitored; however, challenges persist with how to determine the quality of social media data because it comes from such a wide variety of sources.

Private Enterprises Using Social Media Data for Disease Surveillance

Bellingcat is an investigative journalism organization using open-source intelligence to advance forensic research, transparency, and accountability. Bellingcat works through a small staff funded through workshops, grants, and contributions from citizen journalists in many countries. The organization posts a data privacy policy concerning data collection, use, and retention. Researchers glean findings from available electronic data sources and, in the process, provide transparent analysis of data from social media platforms.

Sickweather is an application that maps the incidence of social media posts related to disease and health. The application has three kinds of inputs: analysis of posts on social media that reference diseases or symptoms, crowdsourcing instances and rates of illnesses from members and partners, and clinical information from the CDC. Disease predictions are considered according to local population and verified using medication point of sale and CDC reports. Sickweather states on its website that it can "predict the rate of illnesses up to 15 weeks in advance with 91% accuracy" (Sickweather, undated). No peer reviewed studies were identified to support this claim.

Kinsa Health uses social media in a unique way: The company produces smart thermometers that can report location and temperature if they are internet connected. According to a news report, the company has used this information to predict the spread of the flu over two seasons, (McNeil, 2020). Kinsa Health displays a map and a county-level report of change in reported fevers on its website. Kinsa works with schools and business to track the rate of fever and in work sites and classrooms to identify clusters for targeted testing and early access to medical services in their FLUency program (Kinsa Health, undated).

Media Monitoring and Web Scraping

Digital disease surveillance is a low-cost and time-efficient approach to outbreak detection relative to traditional surveillance. Real-time and rapid dissemination of information on emerging diseases around the world is a reason these tools are being increasingly used as part of surveillance systems (Bhatia et al., 2021). A key method in this arsenal is media monitoring,

often using web-scraping methods to quickly extract information from online news sources. Our review suggests that, although media monitoring might not be efficient as a standalone surveillance tool, if used in combination with other informal (e.g., social media information) or formal (e.g., case reports) data sources, it might help to augment surveillance capabilities and efficacy. Our literature review identified articles describing media monitoring methods as an approach to syndromic surveillance. Ao et al., 2016, found that manual scanning of local news media (e.g., articles, television news reports, and recorded video clips) for health risk events detected 70 percent of 30 outbreaks during the study period. Liu et al., 2020, tracked Chinese media websites for COVID-19-related words and ,when used in combination with Baidu search data (described earlier under Web Searches), found that the approach helped to outperform traditional data collection, as described earlier.

Benefits

Media outlets are often the first providers to call attention to potential threats by highlighting unusual health events. Use of media-monitoring approaches can help to identify outbreaks faster than other approaches. Aggregator systems like ProMED (described later) go one step further by combining data from multiple media networks with expert analysis to offer a more-curated and comprehensive view of a potential outbreak. In addition, these systems offer a standardized and efficient approach to filtering and integrating unstructured media reports on health risk events.

Limitations

Although automated media-scanning approaches can reduce the resource intensity of this surveillance approach, key limitations of both manual and automated methods are the time, training, and costs associated with media monitoring. Individuals might need to be trained on how and what to scan and how to process and evaluate scanned information as relevant to surveillance. Data might need to be additionally verified by health officials and other experts to determine what warrants an outbreak response. Importantly, the utility of this approach is constrained by the information that local media decides to report, which introduces significant selection bias that could be mitigated if used in conjunction with other surveillance approaches.

Private Enterprises Using Media Monitoring and Web Scraping for Disease Surveillance

ProMED was launched in 1994 as an email service to identify and disseminate potentially relevant health events among public health leaders, government officials, and health providers, among others (Carrion and Madoff, 2017). It has since been continually expanded to collect and curate information from formal and informal sources, including media reports, official reports, social media, local observers, and a network of clinicians throughout the world. Reports generated through bottom-up surveillance are reviewed, vetted, and commented on by a team of subject-matter experts before being posted to the ProMED network. ProMED reports data on outbreaks globally, 24 hours a day, seven days a week, averaging eight outbreak reports per day.

Dissemination of ProMED findings now occurs not only via its website but also through social media channels, expanding its reach and utility. Its reliance on informal disease surveillance facilitates faster dissemination than traditional surveillance systems. We also discuss ProMED in Chapter 4.

HealthMap is an automated system for querying, filtering, integrating, and visualizing unstructured reports on disease outbreaks (Freifeld et al., 2008). It utilizes online news aggregators, eyewitness reports, and other formal and informal sources of information and allows for visualization of alerts on a map. One study found that media collected via HealthMap combined with Twitter data were correlated with official case counts of cholera in Haiti, which helped to estimate patterns of cholera outbreak (Chunara, Andrews, and Brownstein, 2012). As mentioned earlier, HealthMap and ProMED use these tools and were among the first sources to release notifications about COVID-19 (Macaulay, 2020).

Travax is a travel medicine risk analysis product produced by Shoreland, Inc. Shoreland, Inc., uses expert, physician, and epidemiologist analysis of reports and data to generate current risk characterization of specific regions for commercial clients. Reports are risk characterizations of known regional diseases, not forecasts or projections.

Other enterprises described earlier that use media monitoring include BlueDot, Google Trends, and Bellingcat.

Pharmaceutical Sales

Drug sales are a measure with a clear theoretical link to syndromic surveillance: When individuals experience symptoms of illness, their first response might be to seek drugs to alleviate these symptoms. Therefore, OTC drug sale data hold promise as a leading indicator, because consumers could make purchases immediately on recognizing symptoms and, in some cases, even before engaging with health care professionals for formal diagnosis and treatment. A systematic review found that 17 of 19 studies using drug sales demonstrated a positive association between clinical outcomes and sales data (Pivette et al., 2014). Promisingly, drug sales provided a leading indicator—predicting subsequent patterns in clinical data in four of these cases.

One category of these studies provides suggestive evidence that purchases of drugs used to treat ILI symptoms match patterns displayed in other syndromic measures and diagnostic health records. For instance, in China, OTC drug sales tracked from 2013 to 2014 displayed a moderately strong positive correlation with counts of hospital diagnoses, with Baidu web searches for related symptoms, and with school-based ILI monitoring systems (Dong et al., 2017). A larger study in the United States using prescription drug sales data from a pharmacy chain with over 8,000 locations in all 50 states over the period of 2007 to 2011 demonstrated that sales of respiratory tract infection and cold medicines correlated strongly with contemporaneous search results from GFT and with CDC ILI data (Patwardhan and Bilkovski, 2012). Not all research focused on ILI symptoms, however. For example, correlative analysis suggests that

sales of both prescription and OTC antidiarrheals closely tracked the rate of general practitioner consultations for gastroenteritis in France (Pivette et al., 2014).

Benefits

A particular benefit of tracking drug sales data is that they might capture illnesses that generate symptoms that are below the threshold for forcing individuals to seek formal health care but for which we might hope to contain the spread regardless (e.g., the common cold).

Limitations

Academic and public health interest in using drug sales data has waned since the early 2010s, perhaps because of limitations to tracking drug sales. This includes limited availability of data, particularly for prescription drug sales. Another shortcoming is that drug sales typically provide proxy information about a likely disease outbreak because purchases treat symptoms that could be common to wide classes of infections (e.g., ILI and gastrointestinal distress). This means that a flu outbreak could generate similar impacts as a COVID-19 outbreak in a system tracking drug sales.

Private Enterprises Using Drug Sale Data for Disease Surveillance

RODS is a software interface designed to facilitate the real-time examination of aggregated, deidentified data collected through both clinical and information systems for trends or anomalies that might be suggestive of disease outbreaks ("The RODS Open Source Project," undated). The system monitors ED visits and tracks the sales of OTC medications. It is maintained by the Department of Biomedical Informatics at the University of Pittsburgh.

Sickweather, described earlier, uses medication point of sale as one of its inputs for the prediction of diseases.

Absenteeism Data

An additional area in which economic data has played a large role in syndromic surveillance systems is the monitoring of absenteeism. Databases that track absences from school and from work have been shown to correlate with alternative measures of disease outbreaks. For instance, using school sign-out sheets from a large middle school in Atlanta, Georgia, researchers showed that absences were correlated with locally reported cases of ILI and were available daily rather than with the two-week lag for the officially produced ILI data (Weiss, 2019).

Similarly, an automated school-based alert system was able to accurately detect all ILI outbreaks in Miami-Dade County in the year after the H1N1 outbreak in April 2009 and in Singapore from June to October 2009 during H1N1 (Mann et al., 2011; Soh et al., 2012). School-based systems are further capable of tracking a wider variety of pathogens than just the flu, including such diseases as mumps and varicella, and could be used to immediately alert local populations about within-school and community-level outbreaks (Fan et al., 2014; Ward et al.,

2019). A systematic review tracking the efficacy of school-based surveillance systems concluded that such systems could provide one to two weeks of lead time, with high reliability, for the diagnosis of influenza outbreaks (Donaldson et al., 2021). However, we did find one study with mixed results related to school absenteeism data (Ding et al., 2015). The authors surveilled for several diseases of concern, including acute respiratory infectious diseases and gastrointestinal infectious diseases, using symptom data from health facilities, absenteeism data from primary schools (dates, numbers, ages, gender, classes, addresses, reasons for absence, and diseases or symptoms), and sales of selected medicines from pharmacies. They found that the number of daily reported events per unit was the highest at pharmacies and lowest at the primary schools, but that the highest costs associated with reporting was at the primary schools, calling into question the cost-effectiveness of this approach in some contexts.

Workers also provide a critical source of absenteeism data. Research in France has demonstrated that worker absence data was able to detect nine out of ten epidemics and to do so approximately two and one-half weeks before the French Sentinelles System—a high-quality, well-established sentinel syndromic surveillance system among primary care doctors—was able to do so (Duchemin et al., 2021). The potential for absenteeism data to provide weeks of advance notice has been replicated for ILI absenteeism among Belgian railway workers and London transport employees during H1N1, and it has been suggested that longer lead times of up to a month might exist when such systems track absenteeism among health care workers (Bollaerts et al., 2010; Drumright et al., 2015; Paterson, Caddis, and Durrheim, 2011). However, we again identified a single study suggesting that worker absenteeism data is not the most-precise or most-effective approach to surveillance, and that it might be best utilized in conjunction with other data sources (Zhang, May and Stoto, 2011). Zhang, May, and Stoto, 2011, triangulated health center visit data, ED visit data, student ILI cases reported to nonmedical staff, and employee absenteeism data to surveil and track patterns of student ILI at two universities and found that student visit data provided the most-accurate depiction of disease transmission.

Work to analyze the reliability of absenteeism systems has also been conducted in the United States. The National Institute for Occupational Safety and Health, a division of the CDC, analyzed Current Population Survey data collected by the U.S. Bureau of Labor Statistics. Its study found that for 2017 to 2018, the prevalence of health-related workplace absenteeism was consistent with the official characterizations of ILI in the same period (Groenewold et al., 2019). The institute regularly monitors workplace absenteeism in the United States.

Benefits

Absenteeism data provides a unique form of syndromic surveillance that can be used in real time to help slow the spread of an epidemic in an affected population. Sentinel systems based on teacher or school system monitoring can provide low-cost methods of detection in resource-poor settings, as has been demonstrated by school districts across the United States during the COVID-19 pandemic. Similarly, school-based monitoring systems provide various

complementary use cases to laboratory-based surveillance systems. For some illnesses, such as influenza, school morbidity or absenteeism data provide direct evidence on a segment of the population that plays a key role in the spread of these outbreaks. School alert systems can be used to rapidly close schools, distance students, and shut down transmission channels.

The same is true when focusing on workers, particularly with systems that track absenteeism of those in the health care industry. These systems provide not only an indicator of the degree of infectiousness of a particular illness but also of the strength and capacity of the health system to cope with these shocks. Systems that specifically monitor health care employees have demonstrated that those on the front lines can provide an early warning for influenza epidemics (Gianino et al., 2017; Ip et al., 2015; Sadarangani et al., 2010). Early reports of first responder absenteeism were common at the onset of the COVID-19 pandemic.

Absenteeism data is possibly more useful for estimating epidemic case numbers when people are sick and miss work but do not seek medical care. This situation could happen when hospitals and doctors' offices are or are perceived to be overfull, when there is fear of contracting or passing on the illness in the medical setting, when people are sick enough to miss work but not sick enough to seek medical care, and when symptoms can be managed by OTC medication, among other reasons.

Limitations

Absenteeism relies on reporting by schools, businesses, or other institutions that might not regularly collect such data or report it to public health officials. The data might also fail to reliably provide early warnings about epidemic emergence unless the symptom onset is rapid or severe. Furthermore, during epidemics, individuals could move to remote work or schooling, inherently making student and worker absenteeism and illness monitoring more challenging to conduct.

Private Enterprises Using Absenteeism Data for Disease Surveillance

Private companies doing disease or syndromic surveillance using employee absenteeism as a data source were not identified.

Data Collection by Health Care Providers

Because symptomatic individuals often present to a health care site and because symptom information is commonly collected by health care workers, many surveillance systems rely on data collected at the point of care by health care or community health workers (Bordonaro et al., 2016; Clara et al., 2018; Jephcott, Wood, and Cunningham, 2017; Sarma et al., 2018). The type of data and data collection process vary. In some cases, clinical data is directly recorded into an individual's medical record that is then surveilled and aggregated. For example, as part of a disease surveillance study in Massachusetts, temperature measurements collected in local EDs were surveilled for fever (temperatures greater than equal to 100.4 degrees Fahrenheit) and

compared with regional disease surveillance program data on influenza. Authors note that fever data collected this way appeared to provide a stronger signal than other markers of influenza, such as flu-like symptoms, but a weaker yet more-timely signal than others, such as counts of laboratory-confirmed influenza cases (Bordonaro et al., 2016).

Utilization data is also typically captured by health care workers and then used for surveillance. For example, the New York City Department of Health and Mental Hygiene syndromic surveillance system receives data on patient visits from all 53 hospital EDs in the city and uses that data to surveil for a variety of conditions, including heat-related illness, postdisaster syndromes (e.g., asthma after building collapse and medical needs after severe weather), meningitis, and Ebola (Lall et al., 2017). Similarly, the North Carolina Disease Event Tracking and Epidemiologic Collection Tool (NC DETECT) system processes and classifies ED visit records and screens ED triage notes to detect a variety of syndromes using CDC-established definitions (Haas et al., 2014; Zhao et al., 2011). These data are combined with information from poison control centers, prehospital records, urgent care centers, and veterinary labs. Another article identified in our literature review described the use of ambulance data to surveil for various syndromes (e.g., fever, vomiting or nausea, dizziness, palpitation, unconsciousness, and breathing disorder). These data are typically recorded on transfer to an ED, making it feasible to systematically collect and monitor (Sugishita et al., 2020). The National Emergency Medical Service Information System (NEMSIS) provides the architecture for collecting, transferring, and storing emergency medical service data for analysis across the United States (NEMSIS, undated).

In some cases, health care workers capture relevant syndromic information using paper or electronic forms created for proactively surveilling specific events—natural or human made—that pose high health risks (Iwata et al., 2013; Zhang, May, and Stoto, 2011). Although these could take significant time and labor, the strategy allows for tailored data collection and could be useful in very specific contexts (e.g., a mass gathering prior to an anticipated but novel outbreak in which the symptoms are known). For example, a surveillance system in Japan that was initiated posttsunami used data recorded on surveillance reporting forms by clinicians working in interdisciplinary teams (Iwata et al., 2013).

Data collected by health care providers are often captured at a postdisaster point of care. Our literature review identified three articles describing examples of this. Sheel et al., 2019, describe a smartphone-enabled approach deployed at 34 health care facilities after the 2016 cyclone in Fiji. Smartphones with preinstalled early warning, alert, and response system applications were used to monitor target cases and facilitated immediate reporting if case numbers rose above specific weekly thresholds, indicative of a suspected disease outbreak. Surveillance officers provided positive feedback about the system, indicating that it was flexible and easy to modify; was low cost and low burden to use; minimized human error; and was successful at generating appropriate alerts and identifying confirmed outbreaks, specifically influenza, typhoid, and conjunctivitis. In contrast, two other more-resource-intensive approaches were identified, one

that focused on posttsunamic data reporting, and one that used an interdisciplinary medical team collecting information from clinics and health care sites using a simple data reporting form, following and earthquake (Babaie et al., 2015; Iwata et al., 2013). Like Iwata et al., 2013, Babaie et al., 2015, described the simplicity and utility of the reporting form but also noted poor data quality, low (or unable to calculate) sensitivity and PPV, and a high resource burden.

One particularly novel approach to surveillance in this category involved the use of logbooks maintained by local health centers to capture "rumors" of events (e.g., flooding), health conditions (e.g., watery diarrhea in a population), or potential disease outbreaks from citizens, health care workers, and patients (Toyama, Ota, and Beyene, 2015). Rumors were investigated by health volunteers, and relevant follow-up actions were taken. The use of this approach was evaluated in a single district in Ethiopia, although the logbook program had been nationally implemented with low uptake. The perceived feasibility and acceptability of this approach was very high, and, at least for one disease—measles, the accuracy of the rumor logbook system was comparable with the existing indicator-based surveillance system.

Benefits

Point-of-care data on their own might not provide a strong enough signal to serve as a standalone surveillance mechanism; however, they often form the foundation of more-systematic multisource surveillance systems. These data are also cost-effective to collect in part because they often rely on information already being routinely collected at health care sites, for example, via screening and intake forms administered at clinic visits to capture body temperature and symptoms. In some cases, newly developed and tailored data collection forms might be used when screening for a specific disease at the point of care. Moreover, point-of-care data are often a first and early signal of potential outbreaks. Although point-of-care data serve as a useful building block for disease surveillance, more-robust medical and informatics infrastructure might be needed to analyze the multiple streams of data necessary for effective syndromic surveillance.

Limitations

Challenges to these approaches included the ability of health care workers to identify aberrant signals and the amount of data necessary to collect before a deviation from typical disease prevalence could reliably be demonstrated. In addition, robust data on sensitivity and PPV (see Box 2.1) are still needed. However, these approaches were generally viewed as feasible and flexible and facilitative of early detection of potential outbreaks.

Private Enterprises Using Health Care Provider Data for Disease Surveillance

nference is a start-up developing technology that analyzes text from biomedical publications and EHR. The company has partnered with the Mayo Clinic to identify symptoms that are early indicators of COVID-19 and found that anosmia and dysgeusia were the earliest and most indicative of an infection (Wagner et al., 2020).

IBM Explorys provides a platform for the analysis of health data for life sciences companies. Academics with access to large numbers of EHRs can do case comparisons to identify patterns. Wang, Xu, and Volkow, 2021, found that dementia increased the risk of COVID-19 using a case control analysis of patient EHRs of 61.9 million adult and senior patients.

IDseq, described earlier, is "an open-source cloud-based metagenomics pipeline and service for global pathogen detection and monitoring" (Kalantar et al., 2020). It has been primarily used to sequence or identify pathogens and their variants collected from patients visiting health centers with signs of infection, often a fever.

Consumer Expenditure Data

In tracking the economic consequences of the COVID-19 pandemic, researchers have demonstrated that broader measures of consumer expenditure are also useful for mapping the extent of the outbreak. For instance, as the pandemic worsened, spending shifted visibly from in-person to online retailers (Chen, Qian, and Wen, 2021). The composition and timing of purchases also changed as households reacted to the pandemic. In the United States, households increased overall spending by nearly 40 percent in early March—clear evidence of precautionary hoarding when the pandemic took hold. Households then decreased spending on most categories of goods and services, especially travel and hospitality, but spending on groceries and food delivery purchases rapidly increased. These patterns indicate efforts by households to isolate and socially distance (Baker et al., 2020; Kim, Santacreu-Vasut, and Shin, 2020). Finally, by combining anonymized data from private companies, researchers have constructed a variety of publicly available indicators—both income and expenditure—to track the pandemic in households in the United States (Chetty et al., 2020). Although these methods are not directly focused on counting cases in each area, they can be employed to produce proxy measures of mobility and behavior and, thus, might be useful for modeling the spread of COVID-19 or other epidemics.

Benefits

Measures of economic expenditure can be produced even in settings where traditional health systems might lack transparency or the capacity to adequately monitor outbreaks. For instance, proxy measures of spread based on spending patterns require no health data and do not require information from individuals who might be sick. Instead, these indicators could be constructed from administrative data, financial intermediary data, transactions, or firm-level records, or even through an establishment survey. Survey-based measures are flexible enough that they can be tailored to inform policymakers about important trends in population health practices, behaviors, beliefs, and attitudes over the course of an epidemic.

Limitations

There are several limitations to using expenditure data, including data access burdens, as accurate tracking requires either relying on government statistics (which might be collected with substantial lag times) or cooperation of businesses. Consumer expenditure data is probably best suited for tracking existing outbreaks in a society, such as the existing COVID-19 pandemic. This is because consumer spending habits are likely to evolve with consumer and worker behavior in response to an ongoing epidemic. Finally, apart from drug sales data, expenditure data is less likely to provide meaningful information about the type of pathogen that is circulating.

Private Enterprises Using Consumer Expenditure Data for Disease Surveillance

Private companies doing disease or syndromic surveillance using consumer expenses as a data source were not identified.

Geospatial Techniques

Whereas the strategies described earlier are based primarily on data sources being leveraged for syndromic surveillance, this surveillance strategy uses geospatial technologies beyond remote sensing. With the spread of COVID-19, a variety of new mapping technologies, largely reliant on geographic information system methods, have come online. Kamel Boulos and Geraghty, 2020, describes online resources, such as HealthMap, WorldPop, EpiRisk, the WHO's ArcGIS dashboard, the Johns Hopkins University Center for Systems Science and Engineering dashboard, and China's "close contact detector" geospatial application and their application to the ongoing epidemic. In a review of emerging technologies with a focus on new COVID-19 applications, Saran et al., 2020, details advances across various geospatial techniques, including:

- citizen science, crowdsourced initiatives, and volunteering geographic information methods
- smartphone applications and contact tracing
- geostatistical modeling
- hot and cold spot analysis.

Benefits

Citizen science, crowdsourced, and volunteer information have the potential to produce data and insights at very low cost. The emergence of online dashboards and mapping technologies serve to provide the public with information about epidemic spread and risk levels in their own community.

Limitations

One of the major concerns with some geospatial technologies, such as contract tracing and mobility tracking, is the potential for these tools to invade privacy. As with remote sensing and

other emerging technological capabilities for tracking epidemic emergence and spread, many geospatial techniques are not well established and lack formal systems in government and other institutions.

Private Enterprises Using Geospatial Techniques for Disease Surveillance

Kinsa Health, described earlier, uses geospatial techniques to map data from its smart thermometers.

Wastewater Sampling

Because many infectious agents are excreted via bodily fluids, an increasing number of surveillance systems track and test wastewater to detect a variety of infectious diseases, waterborne and otherwise. In response to the COVID-19 pandemic, CDC and other agencies initiated the National Wastewater Surveillance System to help public health officials better understand the extent of SARS-CoV-2 infections in communities (CDC, 2022). The goal of this and most wastewater surveillance systems is to complement other surveillance data sources to provide and reinforce timely data on outbreaks. A recent study of a wastewater-based COVID-19 surveillance tool in Portugal found that trends of SARS-CoV-2 in wastewater followed trends of daily new cases in Portugal, underscoring the utility of this approach when used in conjunction with clinical surveillance data (Monteiro et al., 2022). Similar wastewater monitoring systems in the United States have been demonstrated at multiple levels of aggregation as tools for testing the efficacy of public health interventions to stop the spread of COVID-19 (Sharara et al., 2021).

Use of wastewater systems for surveillance is not new; many outbreaks are associated with use of drinking, recreational, and other water types. Since 1971, the CDC, U.S. Environmental Protection Agency, and Council of State and Territorial Epidemiologists have collaborated on the Waterborne Disease and Outbreak Surveillance System, which tracks data related to waterborne disease outbreaks associated with drinking water. Using data collected through this system, important surveillance information is captured. For example, more than one-half of the drinking water–associated outbreaks (both viral and bacterial) reported in the United States during the 2007 to 2008 surveillance period were found to be associated with untreated or inadequately treated groundwater, and many of the outbreaks were related to the growth of *Legionella* spp. in the drinking water system (Brunkard et al., 2011).

Prior work has also found evidence that, in urban areas, greater variability in water supply sources and in sanitation infrastructure were associated with higher incidences of avian influenza, further underscoring the potential of wastewater tracking—and, more generally, detection of water contamination—for syndromic surveillance (Saksena et al., 2015; Spencer, 2013).

Benefits

Because a single sample comprises a large pool of individuals, wastewater surveillance is a cost- and time-efficient approach to surveillance when used in conjunction with individual testing. Therefore, it can provide early warning and facilitate containment of cases in new areas and can be useful for tracking disease movement. It also provides targeted monitoring of case rates by population or subgroup and by geographic area.

Limitations

Although wastewater surveillance offers a bird's-eye view of disease movement and growth, it does not provide individual-level surveillance information and should be complemented by individual testing and clinical data. With novel diseases, it might take time to determine the concentration of the agent shed into wastewater across the duration of the illness, thus rendering its use limited at the beginning of a potential outbreak. This approach also relies on municipal sewage systems, which limits its use in underresourced communities. Finally, targeting of whole communities through wastewater surveillance could lead to stigma and discrimination against the targeted group.

Private Enterprises Using Wastewater Monitoring for Disease Surveillance

Biobot Analytics strategically samples municipal wastewater systems for viral RNA to track the amount and spread of COVID-19 according to the neighborhoods or municipal areas served by specific collection systems. It produces a map of the change in viral load by region over time.

Phase 3—Surveilling the Geographic Spread or Potential Spread of an Epidemic

Table 3.3 shows strategies being used to surveil for spread.

Table 3.3. Strategies for Surveilling the Geographic Spread or Potential Spread of an Epidemic

Strategy	Examples	Private Enterprises
Population movement indicators	• Mobility tracked with Google mobility index, Apple mobility data, cards for retail purposes, mobile phone towers, and flight data	• Travax by Shoreland, Inc.—medical experts that evaluate reports for determining health risks using several data sources

Population Movement Indicators

Multiple sources of data specific to population mobility were identified in the literature review. Some of these studies assess general population mobility day to day, whereas others

examine disease among vulnerable populations that are displaced by disasters or that are gathering for important cultural events, such as religious festivals.

During the COVID-19 pandemic, multiple scholars began to leverage new sources of mobility data to observe the impact of social distancing on the spread of the disease. For instance, Noland, 2021, and Unwin et al., 2020, examined U.S. resident mobility between retail and grocery stores, parks, transit, work, and home residences using the Google mobility index, gathered from anonymized and aggregated cell phone tracking data. In both cases, time spent in sites outside the home is associated with higher levels of COVID-19 spread. Nouvellet et al., 2021, found similar results in an analysis of Google and Apple mobility data spanning 52 countries.

As COVID-19 has spread and these tools have rapidly evolved, scholars have begun to use behavioral data to provide "nowcasts" and forecasts of epidemic spread. For instance, researchers employed daily public transport and small retail payment data from a ubiquitous card system, known as Octopus, used by 99 percent of the population in Hong Kong, to track mobility and population mixing. They were able to generate both contemporaneous estimates and forecasts of COVID-19 incidence by introducing this data into epidemiological models (Leung, Wu, and Leung, 2021).

Syndromic systems have also been designed to assess communicable diseases specifically among displaced populations. One such study demonstrated that a mobility index based on anonymized mobile phone operator data that recorded user movements from one cell tower to another could be used to measure the spread of cholera in Haiti during the 2010 outbreak. Mobility data for 2.9 million users were compared with a CDC-supported national surveillance system. The authors were able to demonstrate that the mobility data provide a significant predictor of disease spread across the country (Bengtsson et al., 2015).

Systems have also been designed to assess planned migration events. For example, researchers examined a set of mobile clinics set up to record communicable diseases during a major migration period in which 8 to 14 million people would travel to the region for religious ceremonies in Wassit Governorate, Iraq (Lami et al., 2019). The clinics used surveys to track nearly 90,000 individuals and record incidences of acute watery diarrhea, bloody diarrhea, fever and cough, vomiting with or without diarrhea, fever and bleeding tendency, and fever and rash. Nearly 5 percent of respondents reported symptoms associated with some form of communicable disease, and, as proof of concept, the study demonstrated that mobile clinics could be an effective means of tracking disease spread in migratory populations, even in developing economy settings.

Combining travel information with health records from countries with well-functioning health-reporting systems is a promising avenue for identifying and tracking disease outbreaks. For instance, research has shown that travelers to New Zealand could be used as sentinels for dengue fever outbreaks originating in Asia and throughout the Pacific including in the Cook Islands, Samoa, American Samoa, Fiji, Tonga, and French Polynesia (Lau, Weinstein, and

Slaney, 2013). This notion has been formalized by the GeoSentinel network, established by the International Society of Travel Medicine, the CDC, and the TropNetEurop sentinel surveillance system (Leder, 2009).

Mobility data have proved very effective at illustrating compliance with shelter-in-place orders and the extent of social mixing in populations and at assessing behavioral responses to disease risk in general. As with many other new measures of pandemic risk, there is a growing body of accessible mobility-related data. This includes RAND's flight-tracking tool, Google mobility reports, the Unacast Social Distancing Scoreboard, SafeGraph, and Baidu Maps (Brodeur et al., 2021).

Benefits

There are several benefits to mobility data. First, as discussed, sources of available mobility data have expanded widely. Second, although many surveillance systems provide information on the presence of an outbreak, mobility data is extremely useful in classifying the potential for disease spread across populations and areas. Third, surveillance using mobility data need not rely on medical records or tests, meaning that estimates of disease spread can be produced for parts of the world where these measures are limited.

Limitations

One of the major limitations of population mobility and migration data is that these sources of information track disease risk—providing only a proxy for actual disease spread. In addition, these data sources are generally not informative on the exact context of interactions, which might be useful for understanding disease spread.

Private Enterprises Using Population Movement for Disease Surveillance

Travax, the travel medicine product by Shoreland, Inc., includes a risk projection for specific known diseases in a geographic region that considers connectivity between affected countries.

Conclusion

Multiple, diverse, and overlapping strategies are being used in novel ways to surveil the spread or potential spread of infectious diseases before clinical presentation. The bulk of these occur in the outbreak phase of epidemic surveillance and include internet search terms, OTC drug sales, and data collected by health care providers. However, as described in this chapter, there are new—and, at times, low-tech—strategies for surveillance during the emergence phase of an epidemic and population movement indicators to help forecast disease spread. In Chapter 4, we review existing DoD and global surveillance systems and describe the methods employed to monitor for disease outbreaks to better understand how new data sources, new surveillance strategies, and new approaches could be leveraged assess disease risk.

Chapter 4. Current DoD Surveillance Systems and Notable Global Surveillance Systems

The approaches to syndromic surveillance described in Chapter 3 are already in use in some surveillance systems or could be added to these systems in the future. In this chapter, we describe DoD surveillance systems and tools that it uses for diseases surveillance, including a joint DoD-civilian system—the Electronic Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE). After that, we describe notable global surveillance systems that were mentioned frequently in the literature we reviewed, media articles we collected, and interviews we conducted. To the extent that they were referenced during our interviews, we provide interviewees' perspectives on these systems. Appendix B provides a table of other systems that were referenced in the literature review.

Current DoD Surveillance Systems

The systems described in this section are available to U.S. military organizations. However, as we discuss in Chapter 5, our interviews with active-duty and civilian DoD personnel revealed uneven awareness and use of these capabilities among geographic combatant commands (GCCs).

Global Emerging Infections Surveillance

A part of the Armed Forces Health Surveillance Division (AFHSD), Global Emerging Infections Surveillance (GEIS) conducts forward-looking surveillance in partnership with a global laboratory network to inform force health protection decisionmaking of GCCs. According to the 2021 AFHSD GEIS strategy document, GEIS is tasked with the following (Armed Forces Health Surveillance Branch, 2018):

- providing GCCs with technical support regarding emerging infectious threats
- conducting infectious disease surveillance to inform force health protection in the GCCs
- improving DoD laboratory readiness for outbreak response
- enhancing collaboration between the GCCs, GEIS partners, and U.S. and international interagency partners.

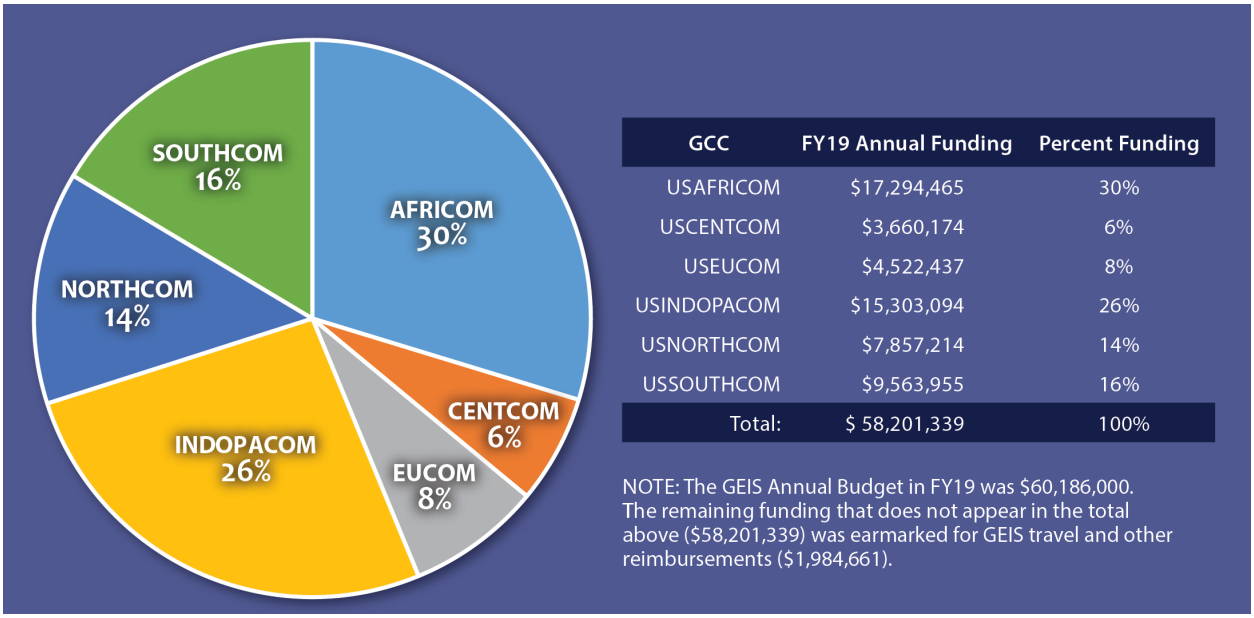
GEIS activities span four branches of focus:

- AMR surveillance
- enteric infection surveillance
- febrile and vector-borne infections surveillance
- respiratory infections.

Most notably, the febrile and vector-borne infections program works in surveillance projects to optimize disease risk modeling and prediction tools, to conduct in-depth genetic sequencing of zoonotic pathogens, and to discover novel pathogens in militarily relevant populations.

In fiscal year 2019, GEIS funded laboratories $60 million to support GCCs. Most funding went to organizations in U.S. Africa Command (30 percent) and U.S. Indo-Pacific Command (26 percent) (see Figure 4.1). According to GEIS branch chief, Guillermo Pimentel, GEIS funding is critical to the U.S. military's ability to retain overseas disease surveillance activities, conducted through enduring host-nation relationships, some reaching back to the mid-20th century.

Figure 4.1. Fiscal Year 2019 GEIS Funding by GCC



GCC	FY19 Annual Funding	Percent Funding
USAFRICOM	$17,294,465	30%
USCENTCOM	$3,660,174	6%
USEUCOM	$4,522,437	8%
USINDOPACOM	$15,303,094	26%
USNORTHCOM	$7,857,214	14%
USSOUTHCOM	$9,563,955	16%
Total:	$ 58,201,339	100%

NOTE: The GEIS Annual Budget in FY19 was $60,186,000. The remaining funding that does not appear in the total above ($58,201,339) was earmarked for GEIS travel and other reimbursements ($1,984,661).

SOURCE: AFHSD, 2020.
NOTE: AFRICOM = Africa Command, CENTCOM = Central Command, EUCOM = European Command, FY = fiscal year, INDOPACOM = Indo-Pacific Command, NORTHCOM = Northern Command, SOUTHCOM = Southern Command.

Defense Medical Surveillance System

Defense Medical Surveillance System (DMSS) is a comprehensive, retrospective collection of medical events (e.g., hospitalizations and outpatient visits), personal characteristics (e.g., rank, military occupation, and demographic factors), and military deployments of all service members over their entire military careers. These data are longitudinal and capture all health care purchased through the MHS (AFHSD, 2020). Such longitudinal data are important for AFHSD's queries and statistical analyses, including those published monthly in the Medical Surveillance Monthly Report, a publication of militarily relevant studies of infectious disease and

occupational health injuries. DMSS data are anonymized, then synchronized monthly with the Defense Medical Epidemiology Database (DMED), which is covered in a later section.

Disease Reporting System Internet

The Disease Reporting System internet (DRSi) collects certain medical events for DoD, primarily those with public health significance or the potential to degrade mission achievement (U.S. Navy and Marine Corps Public Health Center, 2020). It is integrated across all services and contains individual-level contextual data to enable users to better understand and track medical events, including certain infectious disease outbreaks (AFHSD, 2020).

Importantly, DRSi does not fractionate reportable medical events from other health data; instead, the system works to integrate data sources from DoD's EHRs (Armed Forces Health Longitudinal Technology Application and MHS Genesis), laboratory results, DMSS, and ESSENCE. Using this integration of information, system users, including public health nurses and preventive medicine physicians, can closely track syndromic surveillance programs (U.S. Army Public Health Center, undated). Combining data was useful during the COVID-19 pandemic, as it facilitated a list of service members who had contracted the disease. Other reporting systems, such as through chain-of-command, often became duplicated (e.g., unit personnel might report the same positive case to both medical and operational reporting channels, causing a duplication in case numbers at the Joint Staff level).

DoD Surveillance Tools

In addition to its data systems described in the previous section, DoD also invests in tools to make the data more readily available and actionable. This section describes three such tools.

Defense Medical Epidemiology Database

DMED provides access to a subset of the DMSS. Its user-friendly application performs queries regarding disease and injury rates in active component populations to inform decisionmaking and analysis (AFHSD, 2020).

During interviews, combatant command (CCMD) surgeon staff relayed that DMED has been extremely useful in tracking COVID-19 and other diseases of concern. Its custom query function and ease of use made it an indispensable resource in the face of crisis, but users retain it as a daily tool to inform themselves and decisionmakers on force health events.

Geographic Utilization of Artificial Intelligence in Real-Time for Disease Identification and Alert Notification

Geographic Utilization of Artificial Intelligence in Real-Time for Disease Identification and Alert Notification (GUARDIAN) is a DoD-funded proprietary beta research project that automates the process of detecting disease outbreaks using information collected by health care providers through the electronic medical records. Similar to nference, described in Chapter 3,

GUARDIAN uses natural language processing to extract medical terms; then uses geospatial and temporal clustering to look for abnormal numbers of cases; and lastly, if a cluster of concern is identified, sends an alert to health personnel. One study found that, when compared with other similar systems that detect ILIs, GUARDIAN was the most robust (Silva et al., 2013). The system was under development as of 2013 for eventual commercial availability to the civilian public health sector; its progress to market is unclear.

Health Surveillance Explorer

Health Surveillance Explorer (HSE) is a dynamic DoD Common Access Card–enabled application that allows GCCs to map global health threats in near real time (Armed Forces Health Surveillance Branch, undated). The portal tracks events of interest to CCMDs and events of concern to AFHSD. The information is timely, relevant, actionable, and comprehensive to support the CCMDs. In addition, health and disease events in proximity to U.S. embassy locations can be monitored specifically. All content on the site can be searched for historical context. Access to HSE is available only to U.S. military Common Access Card holders with a need to view.

Interviewees stated that, although the HSE interface was useful, epidemiology-trained staff preferred spreadsheets rather than graphical information; such tabular data is easier to analyze with advanced statistics methods. However, given that many military commanders are geographic in their orientation to an area of responsibility (AOR), the simultaneous delivery of graphical and tabular health events data might be useful to mixed audiences. Future HSE development might benefit from more-ready access to both tabular and graphical data from the application.

Joint DoD-Civilian Systems

Electronic Surveillance System for the Early Notification of Community-Based Epidemics

ESSENCE is a secure web-based system that primarily receives and categorizes electronic ED data for syndromic surveillance (Burkom et al., 2021). ESSENCE also enables the inclusion and integration of electronic data from other clinical and nonclinical sources, such as medication sales, poison control call center data, and school absentee data, to enhance surveillance. In addition to data collection and categorization, ESSENCE also offers temporal and spatial alerting for concerns requiring further investigation as well as data analysis and visualization. The inclusion of multiple data sources makes it easier for users to access a single source that includes a variety of data, according to an official familiar with the system. When ESSENCE detects a potential event of interest, the application provides an alert to users who are responsible for public health responses for that area or facility.

According to a government official interviewed for this report, ESSENCE is unique, with no other system comparable to it. It also has the advantage of being cost-effective in a variety of public health settings and user friendly for nontechnical specialists. The official estimates that nearly 70 percent of ED data in the United States is reported in ESSENCE. The AFHSD and military treatment facilities worldwide use ESSENCE to monitor 9.4 million military beneficiaries' health (Armed Forces Health Surveillance Branch, undated). AFHSD also partners with state governments to share anonymized ESSENCE data between military and civilian entities. According to Juan Ubiera, chief of AFHSD's Integrated Biosurveillance Branch, such partnerships also break down silos between installations and local communities by enabling faster communication of disease outbreaks than reporting through military operational channels.

AFHSD's Integrated Biosurveillance Branch works to mitigate infectious disease threats to the U.S. military through such programs as ESSENCE and serves as a central biosurveillance coordination unit for DoD medical and public health efforts. Although the division embraces the all-hazards aspect of biosurveillance, most efforts are directed to monitoring infectious diseases in humans (Armed Forces Health Surveillance Branch, undated).

Global Surveillance Systems

PREDICT: EcoHealth

PREDICT, led by the University of California, Davis, One Health Institution, is part of USAID's Emerging Pandemic Threats program and is a collaborative effort aimed at better understanding the threat of emerging pathogens. PREDICT is an effort to more-fully characterize the virome at the human-wildlife interface. This effort entails community partnership building around the world, laboratory training of on-the-ground teams in disease detection, outbreak response, biosafety, and ethical research practices. Leveraging these networks, the PREDICT consortium has sampled over 70,000 wild animals in 28 countries and, using metagenomic methods, identified 855 viruses, of which 721 were newly discovered.

The consortium convened an expert panel survey to rank-order 42 risk factors related to each virus's spillover risk to cause outbreaks. From this consensus, a risk assessment tool, SpillOver, was produced to inform policymakers, public health decisionmakers, and communities about the relative risk for each virus akin to pulling a credit score for the virus (Grange et al., 2021). However, there are limitations to this data source. Given the large numbers of viruses included and wide array of risk factors, many of the entries are incomplete. The required data fields for assessing risk vary broadly from environmental risk factors to host species—more specifically, to virus binding sites and other virological risk factors; many of these data are completely unknown, especially for novel viruses. Viruses with known worrisome characteristics thus rank as riskier than viruses whose worrisome characteristics have not yet been discovered.

Without complete data, such relative-risk ranking is somewhat misleading. The authors note that SARS-CoV-2 ranked second behind Ebola virus largely because of the paucity of scientific information about the novel virus, despite the recent pandemic presenting persuasive evidence to support reversing the ranking. With more-complete information, a more-accurate risk picture can be drawn. However, missing information becomes obfuscated behind a credit score–type categorization, which can be misleading to the unwary user.

This incongruity of the pandemic with the ranking order might stem from the relative valuation of animal-human transmission as more important than human-to-human transmission. The former prioritizes spillover events, whereas the latter prioritizes large human outbreaks. The distinction between risk of spillover and consequences of spillover creates a risk communication hurdle for decisionmakers who use the tool. Nevertheless, the authors make valiant entreaties to encourage others to contribute the missing data to the tool to serve as a crowdsourced repository of all knowledge about any virus across multiple disciplines. If the missing data is filled in by reputable scientists employing rigorous methods, the tool has promise to identify risky members of the virome before they cause the next pandemic spillover event; however, if the missing data is of stereotypical crowdsourced quality, the tool could be more misleading than informative. Such an exhaustive global effort to discover and understand future pathogens is laudable and shows how much work remains to protect public health globally from pandemics.

Global Public Health Intelligence Network and Global Outbreak Alert and Response Network

Global Public Health Intelligence Network (GPHIN) is a syndromic surveillance system run by the Public Health Agency of Canada, initially cofounded by the WHO, which was heavily used by the WHO as a source of integrated global surveillance in the late 1990s and early 2000s. Designed to serve as an early warning system, the GPHIN was focused on gathering information, assessing risk, and verifying threats in attempt to provide institutional capabilities for epidemic surveillance globally. The system ran from 1997 to 2019 when it was effectively shut down, only to be reinstated during the COVID-19 pandemic in August 2020.

Today, GPHIN remains operated and funded by the Public Health Agency of Canada. It is comprised of a big data aggregator that scans online news reports in nine languages for potential signals of emerging public health threats.[5] To assess health threats, it combines machine learning algorithms with human analysts who use their expertise in medicine, public health, and additional scientific fields to comb through the news reports, social media, and additional manually identified sources. GPHIN is intended to alert member nations to disease outbreaks as

[5] The languages are Arabic, English, Farsi, French, Portuguese, Russian, simplified Chinese, Spanish, and traditional Chinese.

early as possible and to get information on public health outbreaks that occur in countries that might otherwise hide or silence such outbreaks (Wenham, 2015).

Leveraging the information available in GPHIN, the WHO sought to create a set of coordinated responses to disease outbreaks through the Global Outbreak Alert and Response Network—a system coordinated by the WHO that included over 250 institutional partners and networks around the globe. The Global Outbreak Alert and Response Network was developed in 1997 and fully formalized in 2000 with a goal of taking reports assembled by such systems as GPHIN and ProMED (described later) and coordinating responses to them (Dixon, Dar, and Heymann, 2014; Wenham, 2015). At the time, the bulk of international risk assessment and reporting responsibility and effort originated with the WHO. This burden was reallocated to nation states with the adoption in 2005 of a set of legally binding IHRs that required 196 countries to strengthen disease surveillance capabilities and to report on the status of core health capabilities to the WHO annually (Wenham, 2015). Progress regarding epidemic surveillance and health care capacities by country are now tracked regularly through the WHO SPAR.

ProMED

As described in Chapter 3, ProMED takes a more-informal approach to surveillance by inviting and accepting reports of potential outbreaks from a wide variety of sources, including local media, professional networks, on-the-ground experts, and even the general public. It then adds expert review, curates reports, and disseminates potential threats (Carrion and Madoff, 2017). ProMED was established in the late 1990s when global communication was limited, especially at a time before the World Wide Web, and it was an important communication channel for international surveillance (Morse, Rosenberg, and Woodall, 1996). Many countries and governments recognized the importance of international surveillance but did not have an international mandate or funding for such surveillance, which left a gap—one that ProMED, according to one interviewee, was designed to fill. Surveillance information now is rapidly distributed via social media and smartphone applications and to subscribers to the ProMED service. A wide reach and easily accessible platform ensure a constant stream of data that can be disseminated globally 24/7, with an average of eight outbreak reports a day.

Interviewees noted that these aspects of ProMED—expert review, wide reach, and accessibility of information—are strengths. Moreover, ProMED is not commercially tied or tied to any governments, meaning that it is not influenced by those biases. ProMED has been helpful in the earliest detection of outbreaks. One interviewee told us that ProMED led to the early detection of SARS in China: The WHO's China office was alerted about SARS only after it was referenced in ProMED chat rooms but before official government reports about the SARS cases were released. Although it is easy to use, such a system is resource intensive and relies on manual expert curation of data to filter out noise and identify real threats in a timely manner.

The WHO's International Health Regulations—Global Health Security Index

The WHO's IHR system creates a GHSI, an attempt to provide benchmarks of country-level health security capabilities. The GHSI relies on self-reported data for 195 countries from the IHR SPAR tool and supplements this information with assessments of health system capability and resilience as well as information on country-specific norms and risk environments. Measures in the GHSI span six broad categories (prevention, detection and reporting, rapid response, health system, compliance with international norms, and risk environment), 34 indicators, and 85 detailed subindicators. One of the stated goals of the GHSI is to detail the existence of capabilities in countries to stop outbreaks at the source. The database and tools for the GHSI are updated annually and disseminated freely online.

Although the GHSI was only launched in 2019, some efforts have been made to assess its usefulness and reliability. In an assessment of value added by the GHSI, Razavi, Erondu, and Okereke, 2020, noted that although the data collection effort is impressive and useful for country-level gap analysis, users should be wary of applying country rankings across a wide range of weighted score indicators when any two particular indicators might not warrant equal attention. When researchers compared country-level outcome rankings for 37 Organization for Economic Co-operation and Development nations during the COVID-19 pandemic (as measured by cases, deaths, recovery rates, and testing) with individual rankings for indicators in the GHSI, they found that the index overstated the preparedness of some countries and understated that of others (Abbey et al., 2020). In correlative statistical analyses, GHSI scores were not found to be strongly predictive of testing, although deaths were positively correlated to GHSI preparedness measures—with the caveat that measurement error (particularly for something like COVID-19 deaths in less-developed economies) could confound the precise estimation of this relationship (Aitken et al., 2020).

European Centre for Disease Prevention and Control Tools for Epidemiological Threats and Outbreaks

The European Centre for Disease Prevention and Control (ECDC) has several tools and systems that are available for use and/or currently in use for the surveillance and response to epidemiological threats and outbreaks (ECDC, undated).

Arguably the most-popular tool is the ECDC's rapid risk assessment (RRA). In the earliest stages of an infectious disease outbreak or other public health threat, the RRA characterizes the level of risk and the population at risk and compiles any information that is already known about the threat. The ECDC published an RRA report very early in January 2020 about the cluster of pneumonia cases in Wuhan, China, and what was known about the disease at that time (even before the disease was identified as COVID-19) (ECDC, 2020). In at least one of our interviews, the ECDC RRA was described as extremely useful for quickly characterizing risk. The ECDC

has published materials, such as manuals and e-learning courses, on its RRA method, intended for public health experts working at the national or subnational level.

Another set of tools that the ECDC has are epidemic intelligence tools. One example is a public-access tool that automatically monitors Twitter for trends of interest. Another tool is a database, called the Threat Tracking Tool, in which the ECDC keeps track of events that are already known to affect public health or that have a possible public health impact (ECDC, 2021). One subject-matter expert discussing the reliability of syndromic surveillance systems indicated that the ECDC epidemic intelligence tools were particularly valuable because of the rich underlying data they leverage. The ECDC combines routine health surveillance records and additional sources of information, including genomic and unstructured data that has been web scraped.

Other Notable Systems

In April 2022, the CDC launched a new Center for Forecasting and Outbreak Analytics, which seeks to inform and improve public health decisionmaking in the United States. In addition to this and the other systems in this section, there are many other systems that are also notable for the Army's awareness; these are described in Appendix B. Many of the systems in Appendix B are set up to surveil at the regional or statewide (rather than global) level but are included in this report because they use a variety of strategies. Similar to the systems already discussed, we identified other notable systems from the literature, and we learned additional information about some of them from the interviews.

Conclusion

DoD has several systems designed to monitor the current health of servicemembers and potential outbreaks. However, most of these systems are anchored in the MHS, which, as described in Chapter 3, might pick up only threats that warrant medical attention. In comparison, structured global systems like GPHIN and unstructured systems like ProMED combine multiple sources of data, including many of the data sources described in Chapter 3. The utility of these systems, according to our interviewees, is described in Chapter 5.

Chapter 5. Perspectives on the Application of Syndromic Surveillance Strategies

In addition to specific tools, strategies, or approaches for conducting syndromic surveillance and related activities, the academic, government, and military experts we interviewed for this project raised multiple issues to consider from their firsthand experiences performing disease surveillance activities throughout the world.[6] These issues pertain to data, surveillance silos, political will, the role of culture, and user buy-in for syndromic surveillance tools. The chapter begins with a discussion of each of these issues. Then, we describe the key findings from our interviews with DoD personnel who perform, oversee, or are otherwise aware of service syndromic surveillance activities in the department.

Data: Quality, Bias, Availability, and Communication

Four principal issues regarding data emerged from our interviews: data quality, bias, data availability, and risk communication.

Data Quality

Data are still collected manually in many parts of the world. The lack of digitization affects quality and reliability and could impede the ability to compare data across populations within and outside a region or country. This, in turn, affects the quality of output. There are opportunities to digitize data collection by using smartphone apps, which is possible even in remote environments (e.g., with tools such as Magpi, described in Chapter 3, which is used by numerous private- and public-sector organizations to collect and analyze survey data).

Gaps in data might also affect the quality of information about emerging disease threats. Sara Del Valle from Los Alamos National Laboratory has observed that there is more data about disease spread between humans and not as much about spread from animal to human or environmental effects, although zoonotic spread and environmental effects are recognized gaps that initiatives, such as One Health and PREDICT: EcoHealth, are trying to fill. Behavioral information that could help fill this gap—for example, migration patterns in relation to disease outbreaks—is important but difficult to collect. Incorporating sociologists, anthropologists, or others conversant in human behavior into research and analysis on emerging disease threats

[6] A list of our interviewees who consented to being named in the report is provided in Appendix A. The themes described in this chapter were derived from the discussions we conducted. Additional interviews, or interviews with different experts, could have illuminated different themes.

could enable a more-holistic understanding of outbreaks than physical science alone. Because tracking behavioral patterns would require exploitation of many data sources, machine learning approaches will be critical to deciphering signal from noise. However, a former WHO official we interviewed cautioned that human engagement is still required to interpret and possibly correct technology-driven systems for processing data.

Interviewees we spoke to said that evaluating the data that informs disease surveillance tools is important but not always done. According to Jennifer Nuzzo, formerly of the Johns Hopkins Center for Health Security, evaluation can also foster a "culture of continuous improvement" with respect to data and system requirements that feed syndromic surveillance tools. Sometimes evaluation is difficult because of concerns over the validity of data. This is especially true for social media data, in which there is such a high volume of information whose quality can be difficult to judge. Experts agreed that evaluation mechanisms should be incorporated into the research design to ensure evaluation is done. This was the case for the flight-tracking tool developed by RAND to map the early spread of COVID-19. By comparing data from the tool with the Johns Hopkins University COVID-19 tracker, the developers were able to spot-check their results to ensure their findings tracked with the COVID-19 case data compiled by Johns Hopkins University, which was considered the gold standard at the time. The COVID-19 flight-tracking tool required the use of two databases because one database had delays of around three months in its data and needed to be compared with more-current information.

Bias

Bias, both intentional and unintentional, can challenge the quality of data for syndromic surveillance efforts. Many of the examples from our interviews described unintentional biases or errors; for example, a person responsible for entering data into a hospital records system is too busy to do so properly and enters inaccurate disease or death codes. However, intentional bias is possible when reportable illnesses are deliberately coded inaccurately, which, according to several academic experts we interviewed, has occurred in hospital settings when personnel find their reporting obligations too onerous. Bias also occurs in more-remote parts of the world where researchers or data collectors cannot speak local dialects, which might mean parts of the population are not accounted for in the data.

Availability

In the United States, issues regarding the availability of data relate to restrictions of sharing private health data, which is done differently in public versus private health systems and not uniformly fed to the CDC or other federal agencies. U.S. officials we interviewed expressed concern over the lack of information-sharing among departments responsible for tracking and controlling the spread of disease, such as Health and Human Services and the Department of Homeland Security. A further concern expressed by an academic researcher with government experience is that the lack of uniformity in data collection and sharing means public health

systems might miss early opportunities to detect disease spread, which could result in delayed diagnoses, response, and undue loss of life.

In the United States, health care data is increasingly being collected outside traditional health systems. One example of this trend that was provided by a physician we interviewed is private pharmacies, such as CVS, that administer vaccinations and deliver other primary care through their in-house clinics. A possible implication of this trend is that health data is collected in systems that do not typically have much engagement with the health care system, which could mean that systems, such as ESSENCE, that rely on data from health care systems do not include all available information.

Furthermore, access to costly databases could create roadblocks to organizations or governments that lack robust or reliable funding for syndromic surveillance. The RAND research team for the COVID-19 flight-tracker tool already had access to a key database that was needed to perform the analysis, so they were able to establish the tracker and the tool but could not maintain it because the license ran out and there was no additional funding available. The need to pay for data, including data sets, can also create barriers to scientific advancement in resource-poor countries.

Risk Communication

Accurate and timely communication of data to the public is also critical. In an emerging epidemic, this is a task that might fall largely to the government, which risks undermining its credibility without effective communication. Governments might proceed cautiously in the case of a possible disease outbreak so as not to alarm citizens. An overabundance of reporting might lead individuals to believe they have symptoms when they do not; should these individuals seek medical treatment, they could take up resources required to treat actual patients. However, U.S. government scientists we spoke to have also experienced tightened control over disease reporting in countries with authoritarian governments, a situation that we describe later in this section.

Incorporating visualizations into scientific communications was one approach suggested by Del Valle to improve translations of findings for public health action, particularly with respect to conveying uncertainty. The PREDICT project implemented this approach through projects such as *Living Safely with Bats*, a cartoon book produced through One Health to promote behavioral changes in West Africa after a strain of the Ebola virus was found in bats (USAID, undated-b). The book has been translated into numerous African and Asian languages and dialects and delivered to communities via local partners, as depicted in Figure 5.1.

Figure 5.1. Living Safely with Bats Demonstrations in Africa

SOURCE: USAID, undated-a.

Avoiding Surveillance Silos

Nuzzo noted that surveillance is part of a constellation of systems, activities, and actors that need to be regularly engaged. Focusing on early detection alone is not enough. Furthermore, it is important to remain open to finding something other than the disease or pathogen originally in question, particularly when working in a region where there is a higher likelihood of human-animal interaction, which might increase spillover potential. For example, a nongovernmental organization (NGO) representative we interviewed described challenges of extrapolating lessons learned from H1N1, Ebola, and Zika experiences in various parts of the world. Each disease required similar expertise and methods for surveillance and response, but this information was not always regularly shared between countries.

The challenge of securing reliable, consistent funding sources can also create surveillance silos. According to Stephen Morse of Columbia University's Mailman School of Public Health, "people only look for what they're funded to look for." Some systems are designed to look for only one disease, even if their structure could enable surveillance over multiple diseases that might be prominent in a region. Funding can drive what researchers work on, and valid observations from work in one system or project might not be transferred to others. Researchers from Los Alamos National Laboratory described similar problems. Another expert we spoke with, Gulrez Azhar, described related challenges conducting field work in India, where research

for polio appeared to be well funded, but other diseases that could have benefited from the same architecture received far fewer resources.

Political Will

At national and multinational levels, leadership decisions affect how openly a country participates in information-sharing with other entities to enable syndromic surveillance. As Holmes of the University of Sydney's Faculty of Medicine and Health told us, "Technology is not the problem. It's the politics and then the training." In Holmes's view, the tools already exist, but to perform surveillance globally, governments must make the decision to share data with one another. Then, training will be required in resource-poor settings that lack existing capability. Even though tools exist to detect emerging disease outbreaks, without political will to contribute accurate, timely information on a regular basis, the tools will not be as useful.

Political will can also determine how a country reacts to early information about a possible emerging epidemic within its own borders. Multiple interviewees described how important it is for information to flow between all relevant ministries or departments in a government, including those responsible for health, security, finance, foreign relations, and agriculture. However, information shared between relevant parts of government requires someone to act, which might not happen if leaders doubt information or have other motivations for keeping the information quiet. For example, a government might not want to be the first to report on a possible outbreak. Doing so could reflect poorly on their leadership, affect their ability to receive aid or assistance, or create panic among citizens. However, according to one of our interviewees, "disincentivizing accurate reporting leads to systematic underreporting."

A concern expressed by some of our interviewees is the possible lack of proactive work being done to prepare for the next pandemic, which relates to government decisions not to sustain funding for disease surveillance. According to one expert with military and civilian U.S. government experience, "In public health . . . if you do your job right, they cut your funding . . . there's a lack of understanding that it takes funding to look ahead. You need the staff [and] the resources to do more than put out fires but look ahead to see what the next fires might be." Another expert offered a similar analogy: "Think of it like a fire department—you don't shut it down if you haven't had a fire in a year. It's very hard to stand [disease surveillance capabilities] up in the midst of an emergency."

Although different from national political will, interviewees also described the will of researchers to share and provide credit where it is due. Those in academic institutions described tendencies for researchers from resource-poor organizations not to share their early findings with colleagues from larger organizations for fear that they will not receive credit or acknowledgment for their work in final publications.

The Role of Culture

As described in Chapter 2, culture is an element that is critical to recognize yet difficult to capture. For example, cultural differences affect whether individuals report illness and how symptomatic or infected individuals seek out care (if they do at all). During our interviews, experts suggested that Western approaches could be too myopic to capture these differences. Several scientists described a "culture of fear" that exists among scientists in countries whose leadership lack scientific backgrounds. Those we interviewed believed that this culture led scientists in China to withhold publishing their findings about a SARS-like virus in late 2019 because of the historic backlash that China experienced over its handling of the SARS outbreak in the early 2000s. One individual who spoke off record described this as a difference in Western and Chinese approaches to scientific discovery: "[In the West,] your general notion is, you have an interesting finding, you publish it as quickly as possible. [In China], there's more concern, care, and control. Although that's good for maintaining a compliant population, it's awful for a pandemic response."

Azhar described a somewhat related construct in India's government, in which public health is a newer discipline, and leadership might not have public health or scientific backgrounds. There is also a broad variety of practitioners in India who specialize in faith healing and do not report data to government systems. Therefore, health information collected by these practices does not contribute to governmentwide data for disease tracking. According to a U.S. government scientist who preferred to speak off record, when U.S. researchers are working in a foreign country, sometimes the best they can do is present data to ministry of health officials; if these officials do not accept the information, U.S. officials might not feel empowered to push back too strongly because they are "guests in the country."

Certain habits or ways of life inherent in some cultures also affect how diseases spread. According to Holmes, viruses will continue to evolve in resource-poor settings, which can have a great deal of biodiversity and greater human-animal interaction, and in industries that rely on wet markets and logging. For this reason, it is less important to invest in surveillance tools than it is to invest in skills training for those in resource-poor, biodiversity-rich settings where diseases have typically spread. In Holmes's opinion, this type of training takes a more-holistic approach, incorporating the social and economic dimensions of epidemics, which go beyond the disease itself.

There are also differences between urban and rural environments, including inequities in disease testing and reporting in large cities and small villages in places like India. Disparities also exist in the United States, according to a U.S. official who spoke off record. Better-funded hospitals in places like New York City have access to better facilities and more trained personnel, which enable them to perform more novel analyses than poorer cities and states.

User Buy-In

Experts consistently said that one of the key problems with syndromic surveillance is not a lack of tools but making sure those who need the tools are able to access them and obtain upgrades and developments that improve the tools for future use. According to Nuzzo, it is critical to start with the user, ensuring that the tools that are given to them help them make decisions more easily. In a military context, a user might need to report up the chain of command on an emerging disease event; understanding the data required to deliver timely, accurate reports can help developers design more-useful tools. Tabletop exercises could provide opportunities for military medical officers and commanders to test these processes and identify the right information sources, information-sharing processes, and tools available to aid decisionmaking.

If new tools, approaches, and strategies must be designed or modified from existing designs, these changes should be made with the needs of the user in mind, which includes incorporating user feedback into updates. In the context of military medicine, the purpose of the tool and its importance must be clearly communicated. Research and development processes should engage end users in the development of new tools and the modification of existing tools to ensure that any concerns about the utility, feasibility, or practicality of the tool are addressed. Then, users must receive adequate training, including follow-up, as necessary, to make sure that once the tool is introduced, it is operating as intended. Taking these steps can help achieve or maintain user buy-in that ensures that the tool is not relegated to the bottom of a to-do list—a common problem that interviewees described when tools are introduced without proper training or explanation.

In addition, issues arise because of the differing perspectives of developers and end users. A U.S. government scientist and retired military officer explained that these challenges have persisted for decades. In their view, people will not use tools until they appreciate the utility of the tools, which usually does not happen until they are incorporated into daily work. Furthermore, the interviewee described disconnects between information technology professionals and end users—a problem that the U.S. government officials we interviewed found still exists today. Efforts are underway to mitigate this challenge, which we discuss in the following section.

Perspectives on Syndromic Surveillance in the U.S. Military

In our second phase of interviews, we focused on understanding which syndromic surveillance tools, strategies, and approaches military stakeholders knew about and how effective these tools are at meeting user needs—whether the user is a command surgeon, an operational commander, or a soldier operating in a unit downrange or serves in a different role. These interviews also illuminated challenges that U.S. forces experience with identifying emerging disease threats and tracking outbreaks, which are discussed later in this section.

Awareness of Systems and Tools Currently in Use

Chapter 4 describes the systems that the military uses to track disease outbreaks worldwide, all of which were referenced at least once during our interviews with military personnel. However, there appears to be uneven knowledge about or access to these systems, with different commands prioritizing different methods to retrieve information about disease threats. According to the GCC representatives we interviewed, the primary method for performing syndromic surveillance activities is a patchwork approach that involves searching multiple individual civilian databases, including those provided by the WHO, Pan American Health Organization, the CDC, the U.S. Department of State, Johns Hopkins University, and Travax by Shoreland, Inc. (described in Chapter 3). Command surgeons we interviewed expressed confidence in data from such sources as Johns Hopkins University, which provided a COVID-19 tracking tool used by organizations throughout the world to monitor the spread of COVID-19. Some command representatives we spoke to were not aware of a single tool that could search multiple databases at once, and others from DoD agencies described a fluency using a broad variety of tools throughout DoD. Those who were familiar with the systems described in Chapter 4 highlighted GEIS and DMSS as especially useful.

According to numerous DoD personnel we interviewed, the Defense Health Agency (DHA) is working to address these disparities in knowledge and awareness of DoD surveillance tools through its AFHSD. AFHSD is working to establish an improved biosurveillance hub to support the CCMDs that incorporates existing capabilities to eventually streamline the number of systems, but this is a new effort as of this writing. The hub will also seek to incorporate capabilities that are in development. Officials cautioned that the hub will require significant back-end work to maintain, including data exchange agreements with software providers that could delay its rollout. However, GCC representatives said that access to a centralized resource was among the items that would improve their ability to conduct disease surveillance activities, so this initiative could improve current posture.

Challenges with Syndromic Surveillance Strategies in DoD

Like the academic researchers and NGO representatives we interviewed, military personnel we interviewed do not believe that there is a lack of available tools or systems; rather, the problem is a lack of training for end users and policymakers and scarce resources for maintaining and updating tools. Many active-duty military and civilian personnel we spoke to were reluctant to see a new tool or system because of the burdens that learning a new system could add to their workloads for uncertain payoff in improving their ability to do their jobs. Furthermore, although coordination between relevant DoD entities, such as the Office of the Secretary of Defense, the Joint Staff, CCMDs, DHA, and the services, is considered strong by many personnel we interviewed, challenges remain regarding how to collate data from the different systems

employed by these entities into timely, actionable information for operational commanders or other decisionmakers.

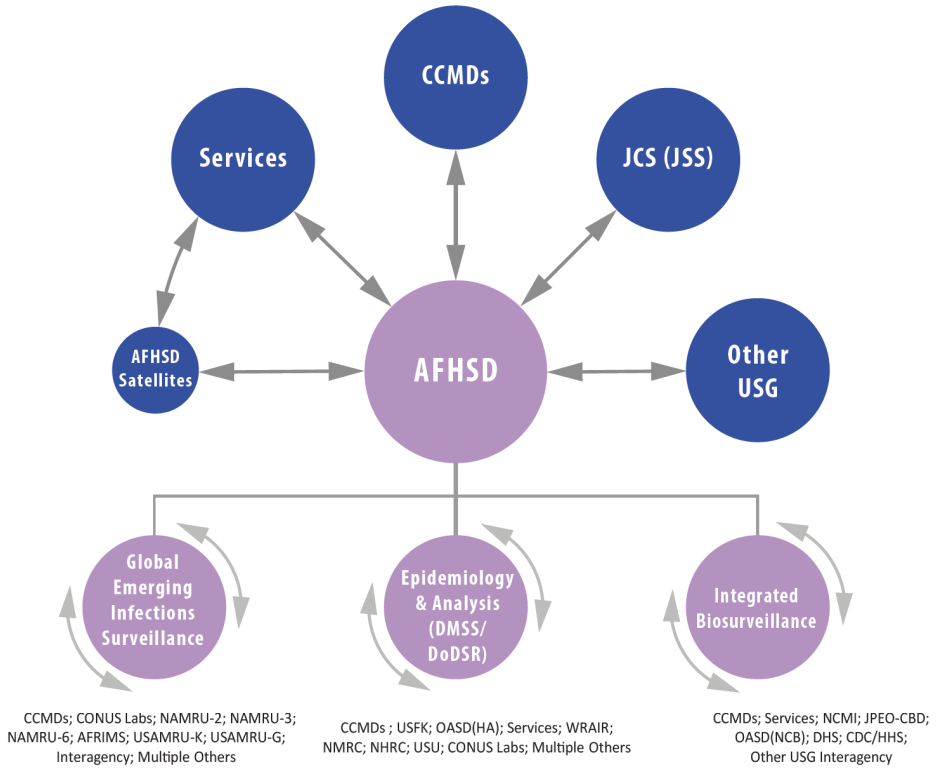
An additional challenge is the need for greater transparency in how a tool is developed, which was mentioned by a previously cited U.S. government official as critical for establishing user trust: "[There] has to be caution that you're not developing yet another system with a black box. [A user needs] to see how the sausage is made to have trust in the system's conclusion." The same official believed that establishing trust enables the user to take greater ownership of the tool to avoid creating a "solution in search of a problem." Nuzzo provided similar insights regarding the need to identify the questions for analysis before deciding which tool to use because different tools might be more appropriate at different stages of analysis. Furthermore, different tools might be required for identifying different diseases.

Similar information-sharing challenges that impede progress in government and academic communities, including time lags in sharing data between services, are also present in the U.S. military. In addition, GCC personnel must often rely on reporting from host nation governments; in countries where there are no U.S. entities to evaluate or validate these data, it can be difficult to understand unexpected changes that arise in reporting. For example, a service component command representative noticed a large spike in COVID-19 cases reported in a South American country in 2020 that dropped back down after a few days, but no U.S. entities had information to explain the sudden increase in cases or confirm that it was not caused by a reporting irregularity.

However, there are examples of more collaborative relationships. One is the Joint West Africa Research Group, which was established after the Ebola outbreak in 2015 (Armed Forces Research Institute of Medical Sciences [AFRIMS], undated). Through this initiative, U.S. military researchers have worked closely with their African counterparts, which, according to Nelson Michael, director of the Center for Infectious Diseases Research at Walter Reed Army Institute of Research, has fostered trust and close cooperation with such key partners as Nigeria (U.S. Military HIV Research Program, 2016).

GEIS laboratories throughout the world have defined processes for sharing information about possible disease outbreaks with AFHSD, who can then perform additional analysis and relay the information to appropriate GCC entities. GEIS also produces monthly reports for the GCC's medical teams; these reports are sometimes shared more broadly in DoD or with civilian agencies, such as CDC, if needed. AFHSD leaders spoke of the potential benefits of DoD Directive 6420.02, *DoD Biosurveillance* in codifying the roles and responsibilities in the department for comprehensive health surveillance (DoD, 2020). Figure 5.2 depicts the DoD entities that regularly engage in health surveillance activity with AFHSD.

Figure 5.2. AFHSD Cooperation with DoD and the U.S. Government



SOURCE: AFHSD, 2020, p. 6. (See p. 27 for acronyms.)

In addition, in regular coordination meetings, DHA divisions, the CCMDs, the services, and others have sought to incorporate international partners to improve military-to-military information-sharing. However, attempts to provide even close U.S. allies with such tools as the HSE (described in Chapter 4) failed because recipient nations did not enter data into the system. International cooperation to improve timely information-sharing with allies and partners was also cited as an area for improvement by a Defense Threat Reduction Agency modeling expert with whom we spoke.

Data quality is also challenge for the U.S. military. According to Ubiera of AFHSD, reliable data often come from the services because there are quality-control checks at such places as the Army Public Health Center that ensure that reporting from Army installations is complete. However, the accuracy of information depends on the quality of individual data entry, which is difficult to track at the service public health centers because they might not collect installation-level data firsthand.

Resources are another challenge to sustaining biosurveillance efforts in DoD—specifically, sustaining and maintaining adequate funding, personnel, technology, and research and development to advance DoD's capability to monitor emerging disease threats. Officials we interviewed expressed worry that DoD will miss important data without personnel to conduct

surveillance activities in AORs of concern. Furthermore, concerns persist that medical officers might not receive enough training in basic epidemiology to collect and interpret public health data correctly. Officials we interviewed expressed unease that some GCC personnel who are responsible for tracking emerging disease threats lack the public health training necessary to fuse information from multiple data sources to derive actionable information for commanders.

A GCC representative we interviewed offered a solution to mitigate this gap: increasing the number of public health officers stationed at GCCs. The interviewee explained that this cadre of public health officers could also directly cooperate with one another to ensure that time-sensitive information is shared among GCCs more rapidly than existing coordination mechanisms at higher levels might enable. However, Michael suggested that greater investments should be placed in developing and training civilians to perform disease surveillance functions for the military because they do not rotate out of their positions every few years as military officers do. Alternatively, training organic military medical officers in additional public health skills has the added advantage of developing a deployable force with these capabilities.

A promising area for developing new tools is predictive analytics that can warn of a possible outbreak before it becomes widespread. Although such technology could improve force health security throughout the world, AFHSD's Ubiera does not believe that the technology has evolved enough yet to enable this type of prediction, in part because data points might be too diffuse to capture in one system. In addition, predictive analytics are useful in projecting only current data points and patterns into the future; novel viruses represent so-called *black swan* events whose novelty (or consequences) cannot be extrapolated from present data.

Conclusion

The experts we interviewed for this project raised concerns with approaches to identifying emerging disease threats across six key areas: gathering and validating data, undertaking effective evaluation, avoiding surveillance silos, ensuring transparency and political will, understanding the role of culture, and facilitating user buy-in. For the military, challenges persist with the availability and utility of systems currently in use for syndromic surveillance activities. However, ongoing efforts to streamline systems currently in use could help improve some of these challenges. In Chapter 6, we discuss these and other recommendations for the U.S. Army to consider going forward.

Chapter 6. Conclusion and Recommendations

There are strategies being used to identify potential outbreaks before clinical data are available. Some of these, such as remote sensing, make use of emerging technologies and methods (satellite imagery and artificial intelligence). More-traditional strategies, such as VPH surveillance efforts and the use of data collected from health care providers, can still yield timely and critical information from animal and human populations.

The Army has an interest in identifying and preventing epidemics early because of the organization's global presence and the national security threats created by an outbreak. Using RAND Arroyo's review of the state of the science, we identify recommendations across two domains: efforts that the Army should monitor and efforts that might be worthy of Army investments.

Efforts Worth Observing

Recommendation 1. The Army should track academic and private enterprise efforts that detect diseases during the outbreak phase of epidemic surveillance. The primary focus of this report was to describe the types of strategies that are being used to conduct syndromic surveillance. Most research activity and most available strategies, including efforts by health care organizations, internet users, and businesses and schools, are used in the outbreak phase of epidemic surveillance. For different reasons and in different contexts, all these strategies could be useful. For example, internet search data could be done by entities outside a nation where an outbreak is occurring but is not transparent in sharing data, and OTC drug sales can identify changes in behavior indicative of an outbreak prior to cases being identified in health care systems.

Because there is so much activity in this domain—activity that we assume will grow in the context of COVID-19 pandemic—the Army should continue to monitor progress (e.g., via academic literature or market scans—methods used for this report and detailed in Appendix A) but not necessarily invest in additional systems for the outbreak phase above and beyond its current investments in GEIS, DSRi, DMSS, and ESSENCE. The data used to create these newer outbreak detection systems could be inaccessible or costly and will likely duplicate work done by universities or private industries. As we discuss in Recommendation 2, the sheer amount of data available implies that adding new data sources and systems should be done with caution.

Research and development specialists spoke of the promise of greater cooperation with private industry for improving syndromic surveillance in the military. Interviewees highlighted BlueDot and EpiWatch as particularly promising tools, although additional testing is required to ensure that these tools can provide early warning of disease threats. A modeling expert at the

Defense Threat Reduction Agency cautioned that there could be challenges in interpreting civilian data for use in military analyses, which would require ample evaluation before a non-DoD system can be integrated with DoD systems.

As outbreak detection systems continue to be developed and marketed, we recommend the Army regard each with the following questions in mind:

- *How specific is the system?* The earlier in advance of an outbreak, the more likely there are to be false positives. A system that produces multiple false positive indications might ultimately be ignored or abandoned.
- *Is the system pathogen specific or pathogen agnostic?* A pathogen-agnostic system might be more beneficial for detecting novel pathogens but might also rely on vague symptoms that lack specificity.
- *Is the system prepared to adapt?* Existing systems might be based on data that will change. For example, internet search platforms and social media sites could be more or less popular in different regions and might change over time. Similarly, as was seen with GFT, algorithms based on voluminous data (e.g., Google searches, social media posts, and clinical notes) will need to be routinely updated to adapt to user behavior.

Jorge V. Zambrana, a research and development expert with North American Aerospace Defense Command and U.S. Northern Command, offered additional operational parameters that his command follows when considering investments in new systems or tools:

- does not add to commander, staff, or operator workload
- does not require continuous monitoring
- does not require a separate interface (e.g., does not add another screen or monitor to a workstation)
- complements existing systems until these systems are phased out (e.g., no snap replacements)
- does not require an organization to hire new staff
- can connect to or interact with existing systems
- seeks to integrate with partners in academia, industry, or other countries as appropriate.

Many of these parameters, including the need to avoid adding to the user's workload, the need to avoid adding an additional login or screen, and the need for compatibility with existing systems, were mentioned by other GCC and defense agency representatives.

As described in Chapter 5, the DHA, through its AFHSD, is spearheading an effort to gather information about the disease surveillance capabilities that are in use in the military and those that are in development to eventually streamline the number of systems, but this is a new effort that officials emphasized will require time to demonstrate results.

Efforts Worth Army Investment

Recommendation 2. The Army should establish more routine training to aid general medical officers in identifying credible data sources and interpreting the data. Our interviews with defense agency and CCMD representatives revealed a lack of public health and

epidemiological training opportunities for unit-level medical officers. As a result, although there might be numerous systems and tools to help CCMDs and services track possible disease outbreaks, there appears to be uneven awareness among some medical personnel regarding what systems, tools, and information they can—or should—use for this purpose. In addition, many years later, if assigned to such positions as command surgeon that require such knowledge, these individuals might be ill-prepared with the systems, tools, training, and professional network to fully comprehend the disease environment of their AOR. In addition to unit-level medical officers, universal training to better prepare all soldiers to identify and combat disease threats might be beneficial given the increasing threat of infectious disease outbreaks associated with conflicts across the globe to which the Army might deploy its troops.

Training for medical officers should address how to identify credible data sources, interpret the data, and communicate findings to key personnel. In the Army, additional training could be incorporated into routine professional military education opportunities that medical officers receive or through Post-Professional Short Course Programs at regular intervals. These opportunities need not be costly or time consuming; rather, they can likely be adapted into slides or short lectures from existing off-the-shelf products and informed by the DHA through their previously discussed efforts. Examination of existing public health training programs in the joint force might reveal ready sources to upscale training, such as the Uniformed Services University's Fundamentals of Global Health Engagement course, and many of the courses provided by Navy's Bureau of Medicine and Surgery. However, as the Army and DoD adopt new surveillance systems and tools, training will need to be updated to reflect these new investments.

Recommendation 3. The Army should consider investing in surveillance efforts that detect the possible emergence of an epidemic for use during the emergence phase of epidemic surveillance. In contrast to the many strategies for surveillance at the outbreak phase, there are relatively few at the emergence stage in which the Army could be uniquely poised to contribute. Setting aside deliberate and accidental biologic threats that will require unique surveillance and mitigation strategies, future human outbreaks will likely originate from animal populations through zoonoses. Currently, human health outbreak monitoring is anchored in the MHS and might pick up only threats warranting medical attention, so investment in the emergence phase could be more predictive and reduce risk. Detecting viruses in animal populations is crucial to understanding the risk to humans at the human-animal interface, where most spillover events occur. The evidence shows promise for relatively lower-tech systems, for example, encouraging those close to the human-animal interface to contact teams of scientist when they discover wildlife carcasses or when farmers' livestock is suddenly sick. However, there are more substantial efforts as well: as part of the EcoHealth Alliance, the PREDICT initiative sampled animals from global hot spots around the world to identify known and unknown pathogens. Such information could enable the production of vaccines and other preventive measures to safeguard the vulnerable people at the human-animal interface. The

Army could consider investing in existing systems, such as PREDICT, or could invest in complementary efforts. The Army Veterinary Corps, and specifically VPH Officers, might be exceptionally well positioned to leverage both small- and large-scale systems to create or complement existing global VPH surveillance efforts in support of the operational force.

The Army also has access to an arsenal of remote sensors (e.g., satellites and drones) that could assist in identifying regional drivers of infection, such as rising sea levels, flooding events, forest fires, urbanization, migration, poverty, and human-wildland interfaces. These strategies have proven useful for forecasting malaria hot spots for twenty years, but newer applications, although promising, have been limited to academic settings. The Army might be able to contribute to research efforts that apply remote sensing strategies to identify where environmental changes might increase risk for the emergence of an outbreak so that systems, including VPH efforts, could be strategically targeted.

Recommendation 4. The Army should consider investing in surveillance efforts that detect the confirmed or potential geographic spread of an outbreak for use during the spread phase of epidemic surveillance. Like the emergence phase, there are relatively few strategies in place to monitor the spread or potential spread of an outbreak—a surveillance phase in which again the Army could be uniquely able to contribute. The COVID-19 pandemic has seen the emergence and utility of data on population mobility to track the potential spread of a disease. For pandemic purposes specifically, combining travel information with health records holds potential promise for identifying and tracking disease outbreaks. RAND's flight-tracking tool is one example a product with potential real-world application, but we were informed by its developer that the cost of the underlying data made continuous updating and monitoring impossible. If the Army has direct access to this data or can negotiate such access, it might be able to contribute to modeling the potential for disease spread globally.

Recommendation 5. The Army should leverage opportunities to engage in regional and international dialogues, where appropriate, to enhance coordination and information-sharing. Political will was identified as a major barrier to conducting effective disease surveillance on a global scale. The U.S. government maintains active bilateral and multilateral relationships with countries and international organizations on matters related to public health, including syndromic surveillance. At embassies throughout the world, DoD representatives provide scientific expertise in support of diplomatic efforts to preserve and maintain health security. Where possible, the Army should seek to inform or participate in engagements with foreign partners led by civilian counterparts in the U.S. Department of State, USAID, or the CDC, for example. In addition, military-to-military engagements led by CCMDs or defense agencies provide opportunities for Army personnel to become better integrated into discussions regarding data sharing and integration.

Good relationships with host nation entities are critical to conducting syndromic surveillance efforts because, without trust, information-sharing between governments becomes more difficult. Civilian organizations in the U.S. government, including the U.S. Department of State, USAID,

and CDC, maintain robust connections with foreign partners worldwide that the Army can leverage alongside its own working relationships. A notable example is AFRIMS, which has leveraged its decades-long presence in Thailand to establish strong working relationships with military and civilian entities, including civilian ministries, NGOs, and academic organizations, throughout Southeast Asia (U.S. Embassy & Consulate in Thailand, undated). Another example is the Joint West Africa Research Group described in Chapter 5.

Army efforts to sustain such relationships will be critical to maintaining and enhancing efforts to identify emerging disease threats to troops. In Southeast Asia and Africa, relationships forged through such organizations as AFRIMS enable access to remote, sometimes dangerous, environments where zoonotic diseases might spread but that civilian organizations cannot safely access. Strengthening and maintaining these relationships, including expanding ties with regional partners based on relationships forged through such organizations as AFRIMS, will be critical to maintaining trust and open communications with foreign partners to share information about possible emerging disease threats.

Recommendation 6. The Army should sustain, maintain, and update current disease surveillance efforts and encourage the same investment throughout DoD. Existing Army surveillance efforts are GEIS, DMSS, DSRi, ESSENCE. U.S. government researcher and command surgeon interviewees alike emphasized the importance of maintaining these efforts because of how difficult it is to marshal the personnel, facilities, equipment, technology, and other resources needed to effectively track and stop outbreaks once they have begun. A failure to sustain, maintain, and update DoD resources for syndromic surveillance creates risks to all the armed forces, not just the U.S. Army.

Conclusion

This report provides RAND Arroyo Center's synthesis of data from multiple sources (scientific literature, private enterprise, and interviews) to understand systems in place and strategies used to identify epidemics before clinical confirmation. The strategies are many, so we created a three-stage epidemic surveillance framework to categorize systems that detect outbreaks before they occur, when they are occurring, and when and where they are likely to spread. There are opportunities for the Army to contribute to surveillance efforts, but equally critical is helping Army general medical officers interpret and respond to data when they are made available. Similarly, given its global presence, the Army can help promote ways to communicate epidemic threats across nations and integrate multiple streams of data across systems.

Appendix A. Research Methods

Peer-Reviewed Literature Review

We sought to understand the state of the science of syndromic surveillance systems by conducting a systematic literature review. Our objectives were to identify and describe existing systems for surveillance of syndromes indicating potential outbreaks, characterize their implementation and effectiveness, and describe their potential for continued or expanded use. For the purposes of this review, we sought to cast a wide, rather than deep, net. We defined *syndromic surveillance* as an approach or method for detecting, tracking, and monitoring potential or real infectious disease outbreaks. An included system could utilize single or multiple sources of data (e.g., triangulate information) to achieve its surveillance goals.

Search Strategy

A senior evidence-based practice center researcher designed all searches. Two researchers trained in literature review and extraction methods executed all searches with oversight from the senior researcher. A senior research librarian obtained all full-text documents. We searched PubMed (the most-comprehensive index of biomedical literature), Embase (index of pharmacological research to capture systems using drug prescriptions for surveillance), and Web of Science. We used search terms to reflect "disease," "condition," "outbreak," "surveillance," "tools," and "technology" with modifications for each database as needed (see Table A.1). Duplicate results from the various searches were removed. All searches were limited to English-language publications from 2010 forward to ensure relevance and recency of surveillance systems.

Table A.1. Literature Review Search Strategy and Yield

Database	Search Term	Yield
PubMed #1	("bioterrorism"[tiab] OR "disease outbreaks" [tiab] OR "pandemics" [tiab] OR "communicable diseases" [tiab] OR "zoonoses" [tiab] OR "drug resistance, microbial" [tiab] OR "emerging infectious diseases" [tiab] OR "biosecurity" [tiab]) AND population surveillance [MeSH] or syndromic surveillance [tiab])	*n* = 991
PubMed #2	"bioterrorism"[tiab] OR "disease outbreaks" [tiab] OR "pandemics" [tiab] OR "communicable diseases" [tiab] OR "zoonoses" [tiab] OR "drug resistance, microbial" [tiab] OR "emerging infectious diseases" [tiab] OR "biosecurity" [tiab] AND ("artificial intelligence" [MeSH] OR "remote sensing technology" [MeSH] OR "machine learning" [MeSH] OR "social media" [MeSH] OR "social networking" [MeSH] OR "web scraping" [tiab] or "geospatial" [tiab] or "biospatial" [tiab])	*n* = 200
PubMed #3	syndromic surveillance [tiab]	*n* = 619
Embase	'syndromic surveillance' AND	*n* = 25

Database	Search Term	Yield
	(2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py OR 2015:py OR 2016:py OR 2017:py OR 2018:py OR 2019:py OR 2020:py) AND ('article'/it OR 'review'/it) AND [embase]/lim NOT ([embase]/lim AND [medline]/lim)	
Web of Science	Basic search; "syndromic surveillance", [TOPIC], custom year range of 2010-2020	*n* = 1,031

NOTE: MeSH = Medical Subject Headings (used to index PubMed articles); tiab refers to search terms in the title and abstract fields only.

Article Selection

To select studies for inclusion in the review, we applied eligibility criteria determined a priori following a PICOTSS (population, intervention, comparator, outcome, timing, setting, and study design) framework.

- *Population*: Eligible populations included human adults or children, as well as animal studies *if* implications for human transmission are described as one objective of the surveillance system. Articles on surveillance systems that focused only on animal-to-animal transmission without explicitly stating human implication were excluded.
- *Intervention*: Articles had to describe a specific tool, technology, system or systematic approach or method for surveillance of potential and/or emerging outbreaks. The surveillance intervention could be pathogen agnostic. If surveillance focused on a known pathogen, it was included only if the system aimed to track outbreaks in novel populations or new geographic regions. For example, systems for tracking and recording annual influenza cases were not included unless they specifically aimed to track potential outbreaks in novel populations or regions.
- *Comparator*: If described, any *comparator*—that is, a prior version of the surveillance system or another approach to surveilling the same condition—was included.
- *Outcomes*: Included articles had to report on at least one of three main outcomes. These included implementation outcomes, such as reach, adoption, acceptability, utility and value, feasibility, and endorsement or credibility of the system; effectiveness outcomes, such as sensitivity and specificity of the approach and outbreak detection rates; and cost outcomes, including raw costs of implementation and use and efficiency outcome. We also abstracted and assessed unintended consequences of the system if described in the article, but articles were not included on this outcome only.
- *Timing*: We looked for short-term, medium-term, and long-term surveillance systems.
- *Settings*: Articles had to describe surveillance systems used at the global, regional (multiple countries in a geographic region), country, state, or smaller-than-state levels. This last category included districts, cities, and health systems, that is, systems of multiple hospitals and clinics. Articles describing surveillance efforts implemented in only a single site, such as a single hospital, were not included, based on limited generalizability.
- *Study design*: We included any descriptive or interventionist design if all other criteria were met. We excluded commentary, letters to the editor, and opinion pieces.

Screening Procedures

The screening flow is depicted in Figure A.1 below. Two trained researchers and one senior evidence-based practice center researcher screened citations that were identified in the literature searches. Citation titles and abstracts were screened first, then full-text articles, before moving on to data abstraction. At title and abstract screening, each reviewer screened a subset of citations independently, then met to discuss dispositions. Reviewers initially screened 100 titles and abstracts independently and, after three rounds, achieved interrater agreement of 97 percent; subsequent title/abstract screening was conducted separately by the three reviewers. Regular meetings ensured consistency of screening procedures; disagreements or uncertainties were resolved by consensus across the three reviewers, with larger project team input and consensus obtained if needed. Full-text screening was conducted following the same procedures.

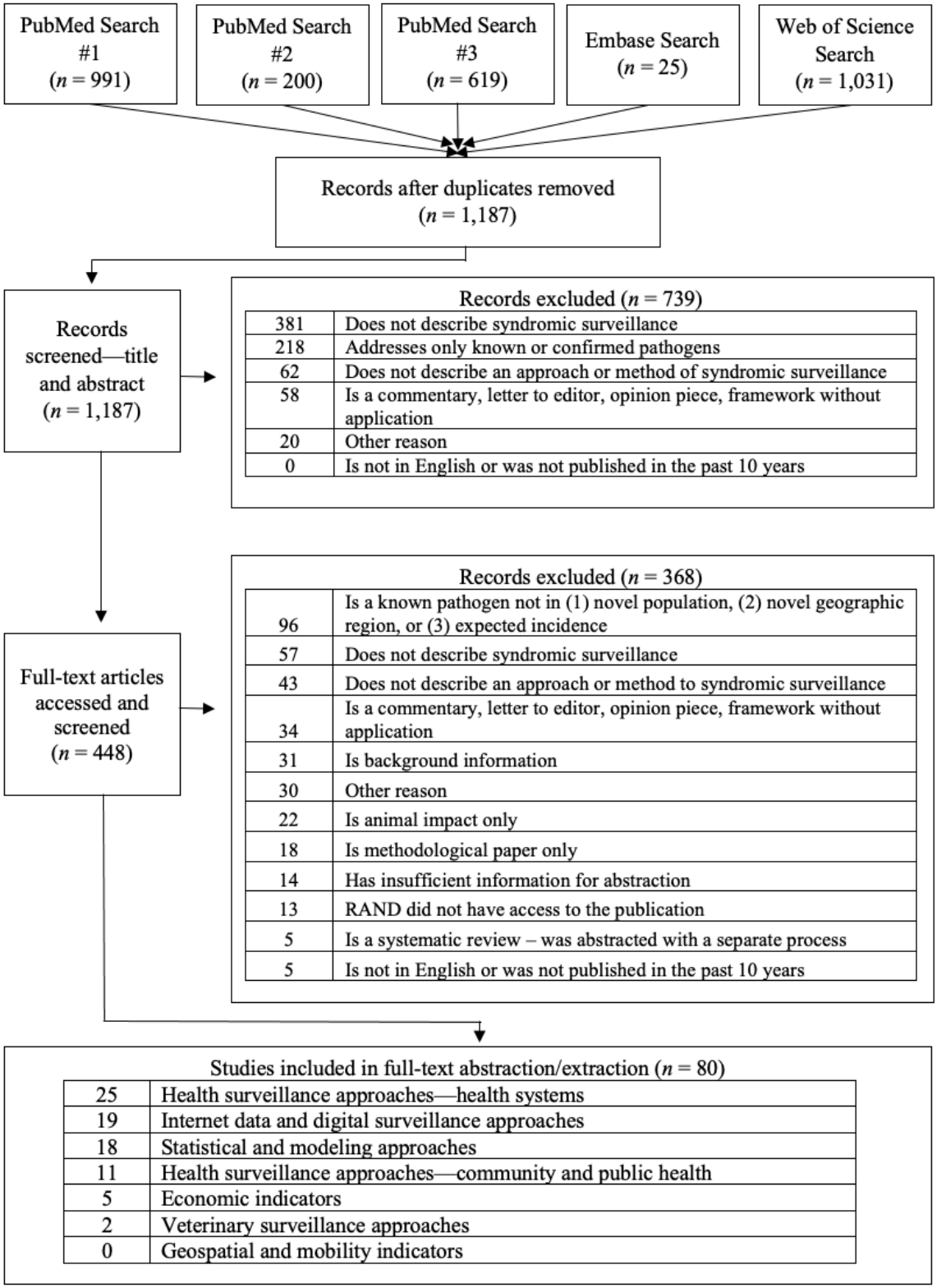
Data Abstraction and Synthesis

A structured abstraction form was developed by the reviewing team to extract relevant information from each included full-text citation. The form was informed by the aims of the review to include syndromic surveillance approaches and the key outcomes described above. The form abstracted article metadata and surveillance system information, including target pathogens, signs and symptoms captured, data capture methods, setting of use, and key outcomes of the system as described in the article—that is, efficiency, effectiveness, and implementation outcomes. Given the descriptive aim of the review to broadly identify and understand surveillance approaches, risk of bias assessment or other critical appraisal was not conducted.

A narrative synthesis of all included articles, by category, was conducted. First, based on a review of all included articles, the reviewing team identified an *initial* set of syndromic surveillance categories:

- internet- or social media–based approaches to surveillance
- geospatial mapping or location-based approaches
- artificial intelligence and machine learning approaches
- genotyping and genomic sequencing approaches
- use of economic indicators for surveillance
- computer simulation or modeling approaches
- animal surveillance approaches
- broader health systems and public health approaches.

Figure A.1. Preferred Reporting Items for Systematic Reviews and Metaanalyses Flow Diagram



The reviewing team then assigned each included article to one of the above categories and reviewed initial assignments with the full project team. Project team members with specialized expertise in each of the above categories then independently reviewed article assignments and proposed adjustments to the assignments. This process continued iteratively through the data abstraction process until the full team reached consensus on the final categories (and subcategories, where appropriate). These categories were created to facilitate extraction and used to inform the final categories presented in Chapter 3. These include the following:

- health surveillance approaches (*n* = 36)
  - health systems approaches (*n* = 25)
  - community or public health approaches (*n* = 11)
- internet data and digital surveillance approaches (*n* = 19)
- economic indicators (*n* = 5)
- veterinary surveillance approaches (*n* = 2)
- statistical and modeling approaches (*n* = 18)

For each of these categories, two members of the project team closely read each article and developed a narrative synthesis of the findings.

Private Enterprise Efforts

To identify a set of relevant services and companies, a systematic set of search queries was conducted of international patents, news stories, and market information. Importantly, the search terms and approach parallel the terms used for the peer-reviewed literature search.

Patent Search

RAND researchers have developed and reported on methods for detection of technology emergence using the technology classification systems of national and international patent offices (Eusebi and Silberglitt, 2014). They use a common set of search terms to identify related patent applications, develop a system of technology classification and subclassification for the subject area of interest, and fit the temporal publication of applications to an s-shaped or logistic curve describing the technology emergence. Patents were included from the Information for Industry CLAIMS database, which includes full-text patents from 45 countries. The database was queried on February 25, 2021. Patent applications include the time frame from 2010 to 2020. The search term used was ("bioterrorism" OR "disease outbreaks" OR "pandemics" OR "communicable diseases") AND (ttl: "syndromic surveillance" OR ttl: surveillance OR ttl: population OR ttl: predict OR ttl: screen OR ab: 'syndromic surveillance' OR ab: surveillance OR ab: population OR ab: algorithm OR ab: predict OR ab: screen) AND +cpcl3:g16h, where CPC is the Cooperative Patent Classification of G16H. The G16H group includes patents related to "information and communication technology specifically adapted for the handling or

processing on medical or health care data" and bioinformatics. The search returned 98 patents categories as follows: health, machine learning and artificial intelligence, remote sensing, social media, and genomic. The initial screen resulted in 30 patents. When each patent's content was reviewed, the patents that it cites and the patents that cite the original were considered as a part of the response.

For each reviewed patent, the Espacenet URL was reviewed. From the description, claims, cited documents, and citing documents, the following information was abstracted: issuing country or organization; human or animal population; diseases or symptoms targeted; system symptoms; data sources; method or technique; approach; indicator group; utilization; validation commercialization (value and/or size); differential and/or limited access to populations or groups; frequency of data update; geographic region; and forecasting, nowcasting, and/or backcasting. If additional sources related to the patent or associated entity were identified, then those references were recorded as well.

News Scan

A search of news and working papers was conducted using ProQuest and limited to the dates 2010 to 2020. The search string used is shown in Table A.2.

Table A.2. ProQuest Search String Used to Identify New Articles with References to Companies or Services for Syndromic Surveillance

Search	Search Term		Search Term		Search Term	Yield
News scan	(noft(algorithm) OR noft(AI) OR noft(machine learning))	AND	(noft(surveillance) OR noft(predict*))	AND	(noft(disease) OR noft(bioterrorism))	*n* = 7,782

This search string identified articles that have the terms *algorithm*, *AI*, or *machine learning* in any field (e.g., title, abstract, keywords, and source) except the full-text field. The articles identified were limited to those that contain the term *surveillance* or *predict* (*predicts*, *prediction*, etc.). This set of articles was limited to those that also contained either the word *disease* or *bioterrorism*. The initial search returned 7,782 articles. The most-frequent type of article was journal articles (4,409), followed by dissertations and theses (1,725), working papers (1,522), features (72), and news (54). From this set, we excluded journal articles because they are expected to be captured in the literature review and dissertations and theses because they are not expected to report on commercial services. The remaining 1,648 articles were reviewed to identify relevant services and companies.

Market Scan

MarketLine is a service providing market research and company information on the automotive, consumer, energy, financial services, health care, and technology sectors.

MarketLine supplies company profiles and news including company-sourced data and press releases, which the service reviews for quality assurance.

When literature, news, patents, or company information identified other services, institutions, or approaches, we researched the new services and entities in the databases listed here and using a simple web search. This snowballing of references identified several relevant companies and approaches and has been shown to improve efficacy in the context of clinical trials evidence.

Data Collection

For each entity or service that was identified, several pieces of information were collected, often from additional sources or the home website for the companies. The following information was searched for and noted when found: URL; issuing company or organization; human or animal population; diseases or systems targets; mechanisms; data sources; approach; indicator group; utilization; validation; commercialization; differential access to populations or groups; frequency of data update; geographic region; forecasting, nowcasting, or backcasting; potential contact; source; general description; and references.

Identified Private-Sector Activities

A review of the titles of the news search returned 293 articles to be reviewed. Of these, 75 were included for full extraction because they contained a company, service, or method relevant to the study. This acceptance rate was 26 percent. The news articles consisted predominantly of concepts for syndromic surveillance from academic white papers (research ideas that were not peer reviewed). News articles also mentioned the efforts of specific companies, such as Palantir, that develop analytic systems for data holders.

Thirty of the returned patents were reviewed. Of those, 18 were not summarized because they appeared to be unrelated to our effort because they either did not describe syndromic surveillance or did not describe an approach or method to syndromic surveillance (no tool or system). In the second case, many of the patents related to EHRs without the means to look across records for patterns or locations of activity for specific symptoms or conditions. The remaining 11 including two duplicates, are summarized in Table A.3. They include patent applications from the United States, Australia, China, and Canada. The descriptions of services are of three types. Most of these patents are systems to consider the pattern of syndromes or diagnoses across EHRs to look for emerging conditions. Another type is a system to look at the change in genetic sequences of pathogens as a source of information to map transmission. The third type is a model to use airline travel to project the movement of infectious people in real time.

Table A.3. Relevant Patents

Patent Number	Summary
US-10714213-B2	Automated processing of medical information comprised of software as a service, cloud storage, and information retrieval. Information analysis includes demographics and patient visit tracking and a public health surveillance interface.
EP-3566230-A1	A computer-implemented method for annotating a query nucleic acid sequence and applying a corresponding matching algorithm to compare the query nucleic acid sequence with an exemplar nucleic acid sequence.
WO-2018127785-A1	Same as EP-3566230-A1 above.
CN-110926655-A	A method for monitoring and processing infectious disease data (individual's illness time in the individual health file) to construct a group monitoring set using personal risk indicators. When the proportion of the population infected with a specific infectious disease in any monitoring group exceeds a set warning value, an early warning of the specific infectious disease is triggered.
US-10540787-B2	A platform for infection surveillance that can assist infection preventionists with infection detection rules and dynamic alerts by aggregating and processing infection surveillance data with contextual health care data regarding a facility, organization, and so on. The platform can enable proactive prevention of infection risks by detecting risk patterns in the data and generating alerts.
US-201261708292-P	A computer system to predict the likelihood, temporal or developmental state, possible locations, rate of spread or *infectiousness*, and so on, of a potential epidemic. There is a wide and diverse variety of inputs and associated parameters. The system statistically analyzes and reanalyzes the totality of all recently updated information (and in the context of all past information) as can efficiently be modeled by the dynamic Bayesian belief network or other adaptive or machine learning method to provide updated predictions and to suggest a recommended reactive protocol for an epidemic.
CN-102073783-A	A method of anticipating an epidemic in a population using a compilation of clinical symptoms of patients recorded via client computers to note any sudden increase of clinical symptom or specific combination of clinical symptoms. Thus, a trend might be observed before diagnosis and statistics can confirm infection outbreak.
CN-101681490-A	A system for predicting transmission of an infectious agent via air travel, including a modeling engine operative to map air passenger travel data with the infectious agent and a reporting engine operative to produce a probability of infection for an individual destination city.
US-28675608-A	Coordinated human-animal health monitoring that can provide an early warning system with fewer false alarms for naturally occurring disease outbreaks. This monitoring requires the integration and analysis of multifield, multiscale, and multisource data sets. This application provides a visual analytics framework for analyzing both human emergency room data and veterinary hospital data for Indiana Network for Patient Care Hospital and Banfield Pet Hospital.
US-20030187615-A1	A system provides early detection, classification, and reporting of health-related events in a population by capturing emergency room patient information from an EMR. The patient information is sorted and analyzed by the central computer facility to detect any health-related events in the population and to generate corresponding alerts. The alerts are electronically reported to designated authorities, such as health officials, and other government authorities, such as the CDC.
EP-1488355-A1	Same as US-20030187615-A1 above.

SOURCE: Patent information derived from a search of international patent documents in the World Intellectual Property Organization database.

Newspaper stories or other sources were occasionally identified outside the formal research method. When these additional companies or services were identified, the sources were archived, and the companies were researched. This snowball process yielded several results that were researched and archived in the same way as the patent and news process. Because of the means of the search process, the metrics for rate of acceptance and the source search details are not relevant to this group of results.

Interviews

The research team also conducted interviews with subject-matter experts worldwide to confirm findings from the literature review and capture new insights and developments. The interviews were divided into academic and scientific community experts, national government and international organization representatives, and U.S. military representatives. Interview participants were selected from the literature review and private-sector search or recommended by our research sponsor. Everyone that we interviewed was asked for their consent to be named in our report; Table A.4 lists the interview participants who agreed. We also provided the option to speak for or not for their affiliation. The interviews took place via video- or teleconference between May and September 2021.

Table A.4. Interviewees

Name	Affiliation
Gulrez Azhar	
Sara Del Valle	Los Alamos National Laboratory
Paul Cox	
Edward Holmes	University of Sydney and National Health and Medical Research Council
Aaron Kite-Powell	
Eric Lombardini	AFRIMS
Jessica Manning	National Institutes of Health and National Institute of Allergy and Infectious Disease International Center of Excellence in Research Cambodia
Jonna Mazet	University of California, Davis, School of Veterinary Medicine and One Health Institute
Ben McMahon	Los Alamos National Laboratory
Nelson Michael	Walter Reed Army Institute of Research
Stephen Morse	Columbia University's Mailman School of Public Health
Christopher Mouton	RAND
Jennifer Nuzzo	Formerly with Johns Hopkins Center for Health Security
Julie Pavlin	
Guillermo Pimentel	DHA AFHSD
Ben Rader	Boston Children's Hospital
Christine Sears	U.S. Southern Command
Joel Selanikio	Magpi
Michael Stoto	Georgetown University
Juan Ubiera	DHA AFHSD
Mike von Fahnestock	Battelle
Jorge V. Zambrana	North American Aerospace Defense Command and U.S. Northern Command

NOTE: Some participants who we spoke to declined to be identified in the report; others declined to include their professional affiliation.

Appendix B. Other Surveillance Systems

Table B.1 presents the surveillance systems described in the literature we reviewed. In addition, the following were referenced during our interviews:

- VirScan was mentioned as a promising system.
- WHO Resource Mapping Tool can identify gaps in a country's preparedness for epidemic response.
- BioFire was mentioned as a tool already in use in some parts of DoD; it is also commercially available.
- Cepheid has been used for the U.S. Southern Command AOR.

Table B.1. Other Notable Surveillance Systems

System	Developer	Coverage	Inputs	Findings
Military Active Real-time Syndromic Surveillance	DoD Armed Forces Medical Command, Biosurveillance Portal (BSP), and Johns Hopkins University Applied Physics Laboratory	Implemented in South Korea, can be implemented elsewhere	International Classification of Disease 2010 codes for a select list of syndromes from military medical records	Data suggest that sensitivity is good, but smaller data sets might need more-refined algorithms to maintain accurate and timely detection (Rhee et al., 2016).
Suite for Automated Global Electronic bioSurveillance (SAGES)	Johns Hopkins University Applied Physics Laboratory, DoD Armed Forces Medical Command, and BSP	Developed for mass-gathering events, is used in and adapted for locations as needed	Web communication data, such as email, web forms, Short Message Service data from cell phones (texting), digital logbooks, and interactive voice response systems	SAGES is built on top of the ESSENCE system. It uses a data analysis tool, OpenESSENCE, to provide a web-based interface for reporting, data visualization, and data analysis that can be used by epidemiologists and other health professionals (Lewis et al., 2011). SAGES has been pilot tested in a few places. Evaluation of SAGES demonstrates a few lessons. There is a need for good planning and preparation at least 12 months before the event to establish and test the surveillance tools. Also, it is imperative to run a test run of the surveillance system before the event. There needs to be specific planning for areas with low internet connectivity, which will require manual data entry. In addition, the connection with the laboratory must be efficient for identifying patterns. Last, the system requires daily operation, and there is a need to ensure adequate staffing when surveilling for several weeks (Lewis et al., 2011; White et al., 2017; White et al., 2018).
Pacific Syndromic Surveillance System	Individual Pacific Island Countries and Territories (PICTs), Secretariat of the Pacific Community, WHO regional office, academic	22 PICTs	Health data on patients who meet the definition of one of the four syndromes surveilled (acute fever and rash, diarrhea, ILI, and prolonged fever), collected by sentinel surveillance site	Many researchers have noted that the Pacific Syndromic Surveillance System is simple, acceptable, useful for public health decisionmakers, and effective at detecting many outbreaks in a timely manner. Regional reporting of alerts and outbreaks has increased under this system. It has greatly enhanced PICTs' ability to undertake early

System	Developer	Coverage	Inputs	Findings
	institutions, and CDC (Kool et al., 2012)		workers, and data on a suspicious outbreak, event of public health concern, or rumor	warning surveillance and has contributed to efforts to meet national surveillance-related capacity development obligations (Alsentzer et al., 2020; Kool et al., 2012; Paterson et al., 2012). Challenges with the system include issues with timeliness and completeness of reporting, data quality, and system stability.
NC DETECT	North Carolina Division of Public Health and Carolina Center for Health Informatics in the University of Chapel Hill Department of Emergency Medicine	State of North Carolina	ED records, Carolinas Poison Center, North Carolina's prehospital medical information system, pilot data from the North Carolina State University College of Veterinary Medicine Laboratories, and data from select urgent care centers	Continuing research is being conducted on NC DETECT to improve and evaluate the system in multiple ways to make sure it is meeting the needs of the users, particularly the public health epidemiologists who use NC DETECT regularly (Haas et al., 2014; Travers et al., 2013; Zhao et al., 2011).
Respiratory DataMart System	Public Health England	14 laboratories across 9 regions in England that do diagnostic services for their affiliated major regional and local hospitals	Respiratory virus test results (positive and negative) every week	When compared with other established surveillance systems, Respiratory DataMart System was shown to be helpful for early detection of the flu season. This system is used to identify potential H1N1 outbreaks quickly. In addition, it was used during international events and was successful at near real-time, daily surveillance. It continuously collects data year-round and is geographically representative. Given the potential sample size with combined data sources, this approach was deemed to be a robust supplementary surveillance mechanism with minimal additional costs because of the use of routinely collected lab data (Zhao et al., 2014).
Integrated Disease Surveillance and Response (IDSR)	CDC and WHO	Developed specifically for countries in the WHO African Region	Health worker detection and patient diagnoses of one or a small number of cases	IDSR is a framework created by the CDC and WHO for infectious disease surveillance within a country and is particularly useful for implementing the IHR. Included in the program are technical guidelines and training modules for different aspects of disease surveillance. One study evaluated the use of IDSR for emerging infectious diseases rather than common infectious diseases, which is what IDSR was set up to surveil

System	Developer	Coverage	Inputs	Findings
				for, and found that IDSR is much more successful at surveilling for common infectious diseases. In the case of an unknown or emerging infectious disease, there is a need for a surveillance system to collaborate with existing IDSR functionality. Facility-based surveillance, in which a health worker detects individual or small numbers of cases, has been used, but was found to be ineffective at detecting emerging infectious diseases because of variation in clinical care practices, resource limitations, and lack of diagnostic assays (Jephcott, Wood, and Cunningham, 2017).
Early Warning, Alert, and Response System (EWARS)	WHO	Used in locations as needed, developed for low- and middle-income countries to conduct disease surveillance after natural disasters	Frontline health worker data collection on mobile phones	EWARS is set up to be deployed within 24 hours of an event. It is a smartphone-based system, and its toolkit includes the technology, computing power, and other resources needed for the surveillance. Evaluation of EWARS shows that it is highly automated, and it is effective as a disease surveillance system during or after emergencies. It has received positive feedback from those who used it (Sheel et al., 2019).

Abbreviations

AFHSD	Armed Forces Health Surveillance Division
AFRIMS	Armed Forces Research Institute of Medical Sciences
AMR	antimicrobial resistant
AOR	area of responsibility
BSP	Biosurveillance Portal
CCMD	combatant command
CDC	U.S. Centers for Disease Control and Prevention
COVID-19	coronavirus disease 2019
DHA	Defense Health Agency
DMED	Defense Medical Epidemiology Database
DMSS	Defense Medical Surveillance System
DoD	U.S. Department of Defense
DSRi	Disease Reporting System internet
ECDC	European Centre for Disease Prevention and Control
ED	emergency department
EHR	electronic health record
ESSENCE	Electronic Surveillance System for the Early Notification of Community-based Epidemics
EWARS	Early Warning, Alert, and Response System
GCC	geographic combatant command
GEIS	Global Emerging Infections Surveillance
GFT	Google Flu Trends
GHSI	Global Health Security Index
GPHIN	Global Public Health Intelligence Network
GUARDIAN	Geographic Utilization of Artificial Intelligence in Real-Time for Disease Identification and Alert Notification
HIV	human immunodeficiency virus
HSE	Health Surveillance Explorer
IDSR	Integrated Disease Surveillance and Response
IHR	International Health Regulations
ILI	influenza-like illness
MHS	Military Health System
NC DETECT	North Carolina Disease Event Tracking and Epidemiologic Collection Tool
NGO	nongovernmental organization

OTC	over the counter
PICT	Pacific Island Country and Territory
PPV	positive predictive value
RODS	Real-time Outbreaks and Disease Surveillance
SAGES	Suite for Automated Global Electronic bioSurveillance
SARS	severe acute respiratory syndrome
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2 (same as COVID-19)
SPAR	State Party Self-Assessment Annual Report
USAID	U.S. Agency for International Development
VPH	veterinary public health
WHO	World Health Organization

References

Abbey, E. J., B. A. A. Khalifa, M. O. Oduwole, S. K. Ayeh, R. D. Nudotor, E. L. Salia, O. Lasisi, S. Bennett, H. E. Yusuf, A. L. Agwu, and P. C. Karakousis, "The Global Health Security Index Is Not Predictive of Coronavirus Pandemic Responses Among Organization for Economic Cooperation and Development Countries," *PLoS One*, Vol. 15, No. 10, 2020, p. e0239398.

Abourashed, A., L. Doornekamp, S. Escartin, C. J. M. Koenraadt, M. Schrama, M. Wagener, F. Bartumeus, and E. C. M. van Gorp, "The Potential Role of School Citizen Science Programs in Infectious Disease Surveillance: A Critical Review," *International Journal of Environmental Research and Public Health*, Vol. 18, No. 13, June 30, 2021.

Adiguzel, F. S., A. Cansunar, and G. Corekcioglu, "Truth or Dare? Detecting Systematic Manipulation of COVID-19 Statistics," *Journal of Political Institutions and Political Economy*, Vol. 1, No. 4, 2020, pp. 543–557.

AFHSD—*See* Armed Forces Health Surveillance Division.

AFRIMS—*See* Armed Forces Research Institute of Medical Sciences.

Ahammer, A., M. Halla, and M. Lackner, *Mass Gatherings Contributed to Early COVID-19 Spread: Evidence from US Sports*, Linz, Austria: The Christian Doppler (CD) Laboratory Aging, Health, and the Labor Market, Johannes Kepler University, working paper 2013, 2020.

Aiken, E. L., S. F. McGough, M. S. Majumder, G. Wachtel, A. T. Nguyen, C. Viboud, and M. Santillana, "Real-Time Estimation of Disease Activity in Emerging Outbreaks Using Internet Search Information," *PLoS Computational Biology*, Vol. 16, No. 8, 2020, p. e10081172020.

Aitken, T., K. L. Chin, D. Liew, and R. Ofori-Asenso, "Rethinking Pandemic Preparation: Global Health Security Index (GHSI) Is Predictive of COVID-19 Burden, but in the Opposite Direction," *Journal of Infection*, Vol. 81, No. 2, August 2020, pp. 318–356.

Akter, S., and D. Kim, "The Nexus Between Gender Inequality and Gender Difference in COVID-19 Infections and Mortality," preprint, June 2020.

Alsentzer, E., S.-B. Ballard, J. Neyra, D. M. Vera, V. B. Osorio, J. Quispe, D. L. Blazes, and L. Loayza, "Assessing 3 Outbreak Detection Algorithms in an Electronic Syndromic Surveillance System in a Resource-Limited Setting," *Emerging Infectious Diseases*, Vol. 26, No. 9, 2020, pp. 2196–2200.

An, B. Y., and S.-Y. Tang, "Lessons from COVID-19 Responses in East Asia: Institutional Infrastructure and Enduring Policy Instruments," *Annual Review of Public Administration*, Vol. 50, Nos. 6–7, 2020, pp. 790–800.

Annaka, S., "Political Regime, Data Transparency, and COVID-19 Death Cases," *SSM Population Health*, Vol. 15, September 2021, p. 100832.

Ao, T. T., M. Rahman, F. Haque, A. Chakraborty, M. J. Hossain, S. Haider, A. S. M. Alamgir, J. Sobel, S. P. Luby, and E. S. Gurley, "Low-Cost National Media-Based Surveillance System for Public Health Events, Bangladesh," *Emerging Infectious Diseases*, Vol. 22, No. 4, 2016, pp. 720–722.

Armed Forces Health Surveillance Branch, "Health Surveillance Explorer," webpage, undated. As of October 8, 2021: https://health.mil/Military-Health-Topics/Health-Readiness/AFHSD/Integrated-Biosurveillance/Health-Surveillance-Explorer

———, *Strategy FY 2019-2021: Global Emerging Infections Surveillance*, Defense Health Agency, May 3, 2018. As of October 8, 2021: https://www.health.mil/Reference-Center/Reports/2018/06/15/2019-to-2021-GEIS-Strategy

Armed Forces Health Surveillance Division, *Armed Forces Health Surveillance Division 2019 Report*, Washington, D.C.: U.S. Department of Defense, 2020.

Armed Forces Research Institute of Medical Sciences, "AFRIMS," undated. As of October 10, 2021: https://afrims.health.mil/

Babaie, J., A. Ardalan, H. Vatandoost, M. M. Goya, and A. Akbari Sari, "Performance Assessment of a Communicable Disease Surveillance System in Response to the Twin Earthquakes of East Azerbaijan," *Disaster Medicine and Public Health Preparedness*, Vol. 9, No. 4, 2015, pp. 367–373.

Baker, S. R., R. A. Farrokhnia, S. Meyer, M. Pagel, and C. Yannelis, "How Does Household Spending Respond to an Epidemic? Consumption During the 2020 COVID-19 Pandemic," *Review of Asset Pricing Studies*, Vol. 10, No. 4, 2020, pp. 834–862.

Bapaye, J. A., and H. A. Bapaye, "Demographic Factors Influencing the Impact of Coronavirus-Related Misinformation on WhatsApp: Cross-Sectional Questionnaire Study," *JMIR Public Health Surveillance,* Vol. 7, No. 1, 2021, p. e19858.

Basak, S., P. Singh, and M. Rajurkar, "Multidrug Resistant and Extensively Drug Resistant Bacteria: A Study," *Journal of Pathogens*, Vol. 2016, No. 4, 2016, Art. 4065603.

Belmont, P. J., Jr., G. P. Goodman, B. Waterman, K. DeZee, R. Burks, and B. D. Owens, "Disease and Nonbattle Injuries Sustained by a U.S. Army Brigade Combat Team During Operation Iraqi Freedom," *Military Medicine*, Vol. 175, No. 7, July 2010, pp. 469–476.

Bengtsson, L., J. Gaudart, X. Lu, S. Moore, E. Wetter, K. Sallah, S. Rebaudet, and R. Piarroux, "Using Mobile Phone Data to Predict the Spatial Spread of Cholera," *Scientific Reports*, 2015.

Bernardo, T. M., E. Perez Gutierrez, G. F. Hachborn, R. O. Forrest, and K. E. Sobkowich, "Innovating at the Human-Technology Interface in Disasters and Disease Outbreaks," *Revue scientifique et technique*, Vol. 39, No. 2, 2020, pp. 491–501.

Berthe, F., "The Global Economic Impact of ASF," *PANORAMA Bulletin*, No. 2020-1, 2020, pp. 22–23.

Bhatia, S., B. Lassmann, E. Cohn, A. N. Desai, M. Carrion, M. U. G. Kraemer, M. Herringer, J. Brownstein, L. Madoff, A. Cori, and P. Nouvellet, "Using Digital Surveillance Tools for Near Real-Time Mapping of the Risk of Infectious Disease Spread," *NPJ Digital Medicine*, Vol. 4, No. 1, April 16, 2021, Art. 73.

Biscornet, L. C. Révillion, S. Jégo, E. Lagadec, Y. Gomard, G. Le Minter, G. Rocamora, V. Guernier-Cambert, J. Mélade, K. Dellagi, P. Tortosa, and V. Herbreteau, "Predicting the Presence of Leptospires in Rodents from Environmental Indicators Opens Up Opportunities for Environmental Monitoring of Human Leptospirosis," *Journal of Remote Sensing*, Vol. 13, No. 2, 2021, Art. 325.

BlueDot Inc., "Digital Health Company BlueDot Secures $7M USD Series A Financing," PR Newswire, August 7, 2019. As of June 23, 2022: https://www.prnewswire.com/news-releases/digital-health-company-bluedot-secures-7m-usd-series-a-financing-300894210.html

Bollaerts, K., J. Antoine, E. Robesyn, L. Van Proeyen, J. Vomberg, E. Feys, E. De Decker, and B. Catry, "Timeliness of Syndromic Influenza Surveillance Through Work and School Absenteeism," *Archives of Public Health*, Vol. 68, No. 3, 2010, pp. 115–120.

Bordonaro, S. F., D. C. McGillicuddy, F. Pompei, D. Burmistrov, C. Harding, and L. D. Sanchez, "Human Temperatures for Syndromic Surveillance in the Emergency Department: Data from the Autumn Wave of the 2009 Swine Flu (H1N1) Pandemic and a Seasonal Influenza Outbreak," *BMC Emergency Medicine*, Vol. 16, No. 1, March 2016.

Boseley, S., and E. Graham-Harrison, "Venezuela Crisis Threatens Disease Epidemic Across Continent—Experts," *The Guardian*, February 21, 2019.

Bottemanne, H., O. Morlaàs, P. Fossati, and L. Schmidt, "Does the Coronavirus Epidemic Take Advantage of Human Optimism Bias?" *Frontiers in Psychology*, Vol. 11, August 2020, Art. 2001.

Boyle, J. R., R. S. Sparks, G. B. Keijzers, J. L. Crilly, J. F. Lind, and L. M. Ryan, "Prediction and Surveillance of Influenza Epidemics," *Medical Journal of Australia*, Vol. 194, No. 4, 2011, pp. S28–S33.

Bradley, V. C., S. Kuriwaki, M. Isakov, D. Sejdinovic, X. L. Meng, and S. Flaxman, "Unrepresentative Big Surveys Significantly Overestimated US Vaccine Uptake," *Nature*, Vol. 600, No. 7890, December 2021, pp. 695–700.

Brodeur, A., D. Gray, A. Islam, and S. Bhuiyan, "A Literature Review of the Economics of COVID-19," *Journal of Economic Surveys*, Vol. 35, No. 4, 2021, pp. 1007–1044.

Brunkard, J. M., E. Ailes, V. A. Roberts, V. Hill, E. D. Hilborn, G. F. Craun, A. Rajasingham, A. Kahler, L. Garrison, L. Hicks, J. Carpenter, T. J. Wade, M. J. Beach, J. S. Yoder, MSW, and CDC, "Surveillance for Waterborne Disease Outbreaks Associated with Drinking Water—United States, 2007–2008," *MMWR Surveillance Summaries*, Vol. 60, No. 12, 2011, pp. 38–68.

Brzezinski, A., V. Kecht, D. Van Dijcke, and A.L. Wright, "Science Skepticism Reduced Compliance with COVID-19 Shelter-in-Place Policies in the United States," *Nature Human Behaviour*, Vol. 5, No. 11, 2021, pp. 1519–1527.

Buckee, C., A. Noor, and L. Sattenspiel, "Thinking Clearly About Social Aspects of Infectious Disease Transmission," *Nature*, Vol. 595, No. 7866, 2021, pp. 205–213.

Buczak, A. L., P. T. Koshute, S. M. Babin, B. H. Feighner, and S. H. Lewis, "A Data-Driven Epidemiological Prediction Method for Dengue Outbreaks Using Local and Remote Sensing Data," *BMC Medical Informatics and Decision Making*, Vol. 12, November 2012, Art. 124.

Buffington, C., C. Dennis, E. Dinlersoz, L. Foster, and S. Klimek, *Measuring the Effect of COVID-19 on U.S. Small Businesses: The Small Business Pulse Survey*, Washington, D.C.: U.S. Census Bureau, working paper CES-20-16, May 2020.

Burkom, H., W. Loschen, R. Wojcik, R. Holtry, M. Punjabi, M. Siwek, and S. Lewis, "Electronic Surveillance System for the Early Notification of Community-Based Epidemics (ESSENCE): Overview, Components, and Public Health Applications," *JMIR Public Health Surveillance*, Vol. 7, No. 6, June 2021, Art. e26303.

Butler, D., "When Google Got Flu Wrong," *Nature*, Vol. 494, No. 7436, February 2013, pp. 155–156.

Carrion, M., and L. C. Madoff, "ProMED-Mail: 22 Years of Digital Surveillance of Emerging Infectious Diseases," *International Health*, Vol. 9, No. 3, 2017, pp. 177–183.

CDC—*See* U.S. Centers for Disease Control and Prevention.

Cervellin, G., I. Comelli, and G. Lippi, "Is Google Trends a Reliable Tool for Digital Epidemiology? Insights from Different Clinical Settings," *Journal of Epidemiology and Global Health*, Vol. 7, No. 3, September 2017, pp. 185–189.

Cha, V., "Asia's COVID-19 Lessons for the West: Public Goods, Privacy, and Social Tagging," *Washington Quarterly*, Vol. 43, No. 2, 2020, pp. 1–18.

Chandler, R. K., S. Y. Kahana, B. Fletcher, D. Jones, M. S. Finger, W. M. Aklin, K. Hamill, and C. Webb, "Data Collection and Harmonization in HIV Research: The Seek, Test, Treat, and Retain Initiative at the National Institute on Drug Abuse," *American Journal of Public Health*, Vol. 105, No. 12, December 2015, pp. 2416–2422.

Chen, H., W. Qian, and Q. Wen, "The Impact of the COVID-19 Pandemic on Consumption: Learning from High-Frequency Transaction Data," *AEA Papers and Proceedings*, Vol. 111, May 2021, pp. 307–311.

Cheng, A., D. Chen, K. Woodstock, N. H. Ogden, X. Wu, and J. Wu, "Analyzing the Potential Risk of Climate Change on Lyme Disease in Eastern Ontario, Canada Using Time Series Remotely Sensed Temperature Data and Tick Population Modelling," *Journal of Remote Sensing*, Vol. 9, No. 6, 2017, Art. 609.

Chetty, R., J. N. Friedman, N. Hendren, M. Stepner, and The Opportunity Insights Team, *How Did COVID-19 and Stabilization Policies Affect Spending and Employment? A New Real-Time Economic Tracker Based on Private Sector Data*, Cambridge, Mass.: National Bureau of Economic Research, working paper 27431, 2020.

Chiou, L., and C. Tucker, "Social Distancing, Internet Access and Inequality," Cambridge, Mass.: National Bureau of Economic Research, working paper 26982, 2020.

Chunara, R., J. R. Andrews, and J. S. Brownstein, "Social and News Media Enable Estimation of Epidemiological Patterns Early in the 2010 Haitian Cholera Outbreak," *American Journal of Tropical Medicine and Hygiene*, Vol. 86, No. 1, 2012 pp. 39–45.

Clara, A., T. T. Do, A. T. P. Dao, P. D. Tran, T. Q. Dang, Q. D. Tran, N. D. Ngu, T. H. Ngo, H. C. Phan, T. T. P. Nguyen, A. T. Lai, D. T. Nguyen, M. K. Nguyen, H. T. M. Nguyen, S. Becknell, C. Bernadotte, H. T. Nguyen, Q. C. Nguyen, A. W. Mounts, and S. A. Balajee, "Event-Based Surveillance at Community and Healthcare Facilities, Vietnam, 2016–2017," *Emerging Infectious Diseases*, Vol. 24, No. 9, 2018, pp. 1649–1658.

Coven, J., and A. Gupta, *Disparities in Mobility Responses to COVID-19*, New York: New York University, working paper, 2020.

Dai, Y., and J. Wang, "Identifying the Outbreak Signal of COVID-19 Before the Response of the Traditional Disease Monitoring System," *PLoS Neglected Tropical Diseases*, Vol. 14, No. 10, 2020, Art. e0008758.

Dall, C., "Antibiotic Development, Stewardship Advocates See Window of Opportunity," *CIDRAP News*, April 21, 2021.

de Vries, L., M. Koopmans, A. Morton, and P. van Baal, "The Economics of Improving Global Infectious Disease Surveillance," *BMJ Global Health*, Vol. 6, No. 9, September 2021, Art. e006597.

Ding, Y., R. Sauerborn, B. Xu, N. Shaofa, W. Yan, V. K. Diwan, and H. Dong, "A Cost-Effectiveness Analysis of Three Components of a Syndromic Surveillance System for the Early Warning of Epidemics in Rural China," *BMC Public Health*, Vol. 15, No. 1, 2015, Art. 1127.

Dixon, M. A., O. A. Dar, and D. L. Heymann, "Emerging Infectious Diseases: Opportunities at the Human-Animal-Environment Interface," *Veterinary Record*, Vol. 174, No. 22, 2014, pp. 546–551.

DoD—*See* U.S. Department of Defense.

Donaldson, A. L., J. L. Hardstaff, J. P. Harris, R. Vivancos, and S. J. O'Brien, "School-Based Surveillance of Acute Infectious Disease in Children: A Systematic Review," *BMC Infectious Diseases*, Vol. 21, No. 1, 2021, Art. 744.

Dong, X., M. L. Boulton, B. Carlson, J. P. Montgomery, and E. V. Wells, "Syndromic Surveillance for Influenza in Tianjin, China: 2013–14," *Journal of Public Health*, Vol. 39, No. 2, 2017, pp. 274–281.

Drumright, L. N., S. D. W. Frost, A. J. Elliot, M. Catchpole, R. G. Pebody, M. Atkins, J. Harrison, P. Parker, and A. H. Holmes, "Assessing the Use of Hospital Staff Influenza-Like Absence (ILA) for Enhancing Hospital Preparedness and National Surveillance," *BMC Infectious Diseases*, Vol. 15, March 2015, Art. 110.

Duchemin, T., J. Bastard, P. A. Ante-Testard, R. Assab, O. S. Daouda, A. Duval, J. P. Garsi, R. Lounissi, N. Nekkab, H. Neynaud, D. R. M. Smith, W. Dab, K. Jean, L. Temime, and M. N. Hocine, "Monitoring Sick Leave Data for Early Detection of Influenza Outbreaks," *BMC Infectious Diseases*, Vol. 21, No. 1, 2021, Art. 52.

Dunn, R., *A Natural History of the Future*, New York: Basic Books, 2021.

ECDC—*See* European Centre for Disease Prevention and Control.

Enriquez, K., K. Udhayashankar, and M. Niescierenko, "Understanding the Predictors That Contribute to Liberian Health Care Workers Feeling Protected from Ebola While at Work," *Disaster Medicine and Public Health Preparedness*, Vol. 15, No. 5, 2020, pp. 589–594.

European Centre for Disease Prevention and Control, "Current Threats and Outbreaks," webpage, undated. As of October 9, 2021: https://www.ecdc.europa.eu/en/threats-and-outbreaks

———, *Pneumonia Cases Possibly Associated with a Novel Coronavirus in Wuhan, China*, Solna, Sweden: ECDC, January 9, 2020.

———, "ECDC Activities on Epidemic Intelligence and Outbreak Response," webpage, 2021. As of October 9, 2021: https://www.ecdc.europa.eu/en/threats-and-outbreaks/epidemic-intelligence

Eusebi, Christopher A., and Richard Silberglitt, *Identification and Analysis of Technology Emergence Using Patent Classification*, Santa Monica, Calif.: RAND Corporation, RR-629-OSD, 2014. As of June 27, 2022: https://www.rand.org/pubs/research_reports/RR629.html

Fan, Y., M. Yang, H. Jiang, Y. Wang, W. Yang, Z. Zhang, W. Yan, V. K. Diwan, B. Xu, H. Dong, L. Palm, L. Liu, and S. Nie, "Estimating the Effectiveness of Early Control Measures Through School Absenteeism Surveillance in Observed Outbreaks at Rural Schools in Hubei, China," *PLoS One*, Vol. 9, No. 9, 2014, Art. e106856.

Farzanegan, M. R., M. Feizi, and H. F. Gholipour, "Globalization and the Outbreak of COVID-19: An Empirical Analysis," *Journal of Risk and Financial Management*, Vol. 14, No. 3, 2021, Art. 105.

Feachem, R. G. A., I. Chen, O. Akbari, A. Bertozzi-Villa, S. Bhatt, F. Binka, M. F. Boni, C. Buckee, J. Dieleman, A. Dondorp, A. Eapen, N. Sekhri Feachem, S. Filler, P. Gething, R. Gosling, A. Haakenstad, K. Harvard, A. Hatefi, D. Jamison, K. E. Jones, C. Karema, R. N. Kamwi, A. Lal, E. Larson, M. Lees, N. F. Lobo, A. E. Micah, B. Moonen, G. Newby, X. Ning, M. Pate, M. Quiñones, M. Roh, B. Rolfe, D. Shanks, B. Singh, K. Staley, J. Tulloch, J. Wegbreit, H. J. Woo, and W. Mpanju-Shumbusho, "Malaria Eradication Within a Generation: Ambitious, Achievable, and Necessary," *Lancet*, Vol. 394, No. 10203, September 2019, pp. 1056–1112.

Feng, S., L. Hossain, J. W. Crawford, and T. Bossomaier, "Quantifying Network Dynamics and Information Flow Across Chinese Social Media During the African Ebola Outbreak," *Disaster Medicine and Public Health Preparedness*, Vol. 12, No. 1, 2018, pp. 26–37.

Freifeld, C. C., K. D. Mandl, B. Y. Reis, and J. S. Brownstein, "HealthMap: Global Infectious Disease Monitoring Through Automated Classification and Visualization of Internet Media Reports," *Journal of the American Medical Informatics Association*, Vol. 15, 2008, pp. 150–157.

Gabrilovich, E., "Using Symptoms Search Trends to Inform COVID-19 Research," *The Keyword*, blog, Google, September 2, 2020.

Gallo, V., P. Chiodini, D. Bruzzese, E. Kondilis, D. Howdon, J. Mierau, and R. Bhopal, "Comparing the COVID-19 Pandemic in Space and over Time in Europe, Using Numbers of Deaths, Crude Rates and Adjusted Mortality Trend Ratios," *Scientific Reports*, Vol. 11, No. 1, 2021, Art. 16443.

Gates, M. C., L. Earl, and G. Enticott, "Factors Influencing the Performance of Voluntary Farmer Disease Reporting in Passive Surveillance Systems: A Scoping Review," *Preventive Veterinary Medicine*, Vol. 196, November 2021, Art. 105487.

Gianino, M. M., G. Politano, A. Scarmozzino, L. Charrier, M. Testa, S. Giacomelli, A. Benso, and C. M. Zotti, "Estimation of Sickness Absenteeism Among Italian Healthcare Workers During Seasonal Influenza Epidemics," *PLoS One*, Vol. 12, No. 8, 2017, Art. e0182510.

Grange, Z. L., T. Goldstein, C. K. Johnson, S. Anthony, K. Gilardi, P. Daszak, K. J. Olival, T. O'Rourke, S. Murray, S. H. Olson, E. Togami, G. Vidal, Expert Panel, Predict Consortium, J. A. K. Mazet, and University of Edinburgh Epigroup members who wish to remain anonymous, "Ranking the Risk of Animal-to-Human Spillover for Newly Discovered Viruses," *Proceedings of the National Academy of Sciences*, Vol. 118, No. 15, April 2021, Art. e2002324118.

Grillet, M. E., J. E. Moreno, J. V. Hernández-Villena, M. F. Vincenti-González, O. Noya, A. Tami, A. Paniz-Mondolfi, M. Llewellyn, R. Lowe, A. A. Escalante, and J. E. Conn, "Malaria in Southern Venezuela: The Hottest Hotspot in Latin America," *PLoS Neglected Tropical Diseases*, Vol. 15, No. 1, January 2021, Art. e0008211.

Groenewold, M. R., S. L. Burrer, F. Ahmed, A. Uzicanin, and S. E. Luckhaupt, "Health-Related Workplace Absenteeism Among Full-Time Workers—United States, 2017-18 Influenza Season," *Morbidity and Mortality Weekly Report*, Vol. 68, No. 26, July 2019, pp. 577–582.

Haas, S. W., D. Travers, A. Waller, D. Mahalingam, J. Crouch, T. A. Schwartz, and J. Mostafa, "Emergency Medical Text Classifier: New System Improves Processing and Classification of Triage Notes," *Online Journal of Public Health Informatics*, Vol. 6, No. 2, 2014, Art. e178.

Hall, T. F., and D.A. Ross, "Establishing Communicable Disease Surveillance Systems," *BMJ Military Health*, Vol. 168, No. 2, 2021 pp. 160–165.

Harrison, S., L. Kivuti-Bitok, A. Macmillan, and P. Priest, "EcoHealth and One Health: A Theory-Focused Review in Response to Calls for Convergence," *Environment International*, Vol. 132, November 2019, Art. 105058.

Haut, E. R., and P. J. Pronovost, "Surveillance Bias in Outcomes Reporting," *JAMA*, Vol. 305, No. 23, 2011, pp. 2462–2463.

Hawkes, S., S. Tanaka, A. Pantazis, A. Gautam, S. Kiwuwa-Muyingo, K. Buse, and A. Purdie, "Recorded but Not Revealed: Exploring the Relationship Between Sex and Gender, Country Income Level, and COVID-19," *Lancet Global Health*, Vol. 9, No. 6, 2021, pp. e751–e752.

Heise, L., M. E. Greene, N. Opper, M. Stavropoulou, C. Harper, M. Nascimento, D. Zewdie, and Gender Equality, Norms, and Committee Health Steering, "Gender Inequality and Restrictive Gender Norms: Framing the Challenges to Health," *Lancet*, Vol. 393, No. 10189, 2019, pp. 2440–2454.

Henning, K. J., "What Is Syndromic Surveillance?" *MMWR Supplements*, Vol. 53, September 2004, pp. 5–11.

Higgins, T. S., A. W. Wu, D. Sharma, E. A. Illing, K. Rubel, J. Y. Ting, and Snot Force Alliance, "Correlations of Online Search Engine Trends with Coronavirus Disease (COVID-19) Incidence: Infodemiology Study," *JMIR Public Health and Surveillance*, Vol. 6, No. 2, 2020, Art. e19702.

Hill-Cawthorne, G. A., "One Health/EcoHealth/Planetary Health and Their Evolution," M. Walton, ed., *One Planet, One Health*, Sydney, Australia: Sydney University Press, 2019, pp. 1–20.

Hirschfeld, Katherine, Kirsten De Beurs, Brad P. Brayfield, and Ani Melkonyan, "Ethnic Conflict as a Risk Amplifier for Resurgent *P. Vivax* Malaria in Temperate Zones: A Case Study from the Caucasus Region," *Global Environmental Change*, Vol. 74, May 2022, Art. 102495.

Hossain, A., C. Politi, N. Mandalia, and A. L. Cohen, "Expenditures on Vaccine-Preventable Disease Surveillance: Analysis and Evaluation of Comprehensive Multi-Year Plans (cMYPs) for Immunization," *Vaccine*, Vol. 36, No. 45, 2018, pp. 6850–6857.

Hoy, D., S. T. Saketa, R. R. Maraka, A. Sio, I. Wanyeki, P. Frison, D. Ogaoga, D. Iniakawala, C. Joshua, S. Duituturaga, C. Lepers, A. Roth, P. White, and Y. Souares, "Enhanced Syndromic Surveillance for Mass Gatherings in the Pacific: A Case Study of the 11th Festival of Pacific Arts in Solomon Islands, 2012," *Western Pacific Surveillance and Response Journal*, Vol. 7, No. 3, 2016, pp. 15–20.

Ip, D. K. M., E. H. Y. Lau, Y. H. Tam, H. C. So, B. J. Cowling, and H. K. H. Kwok, "Increases in Absenteeism Among Health Care Workers in Hong Kong During Influenza Epidemics, 2004–2009," *BMC Infectious Diseases*, Vol. 15, December 2015, Art. 586.

Iwata, O., T. Oki, A. Ishiki, M. Shimanuki, T. Fuchimukai, T. Chosa, S. Chida, Y. Nakamura, H. Shima, M. Kanno, T. Matsuishi, M. Ishiki, and D. Urabe, "Infection Surveillance After a Natural Disaster: Lessons Learnt from the Great East Japan Earthquake of 2011," *Bulletin of the World Health Organization*, Vol. 91, No. 10, 2013, pp. 784–789.

Jephcott, F. L., J. L. N. Wood, and A. A. Cunningham, "Facility-Based Surveillance for Emerging Infectious Diseases; Diagnostic Practices in Rural West African Hospital Settings: Observations from Ghana," *Philosophical Transactions of the Royal Society B Biological Sciences*, Vol. 372, No. 1725, 2017, Art. 20160544.

Kaiser, J., "Six Vials of Smallpox Discovered in U.S. Lab," *ScienceInsider*, July 8, 2014.

Kalantar, K. L., T. Carvalho, C. F. A. de Bourcy, B. Dimitrov, G. Dingle, R. Egger, J. Han, O. B. Holmes, Y.-F. Juan, R. King, A. Kislyuk, M. F. Lin, M. Mariano, T. Morse, L. V. Reynoso, D. R. Cruz, J. Sheu, J. Tang, J. Wang, M. A. Zhang, E. Zhong, V. Ahyong, S. Lay, S. Chea, J. A. Bohl, J. E. Manning, C. M. Tato, and J. L. DeRisi, "IDseq—An Open Source Cloud-Based Pipeline and Analysis Service for Metagenomic Pathogen Detection and Monitoring," *GigaScience*, Vol. 9, No. 10, 2020, Art. giaa111.

Kamel Boulos, M. N., and E. M. Geraghty, "Geographical Tracking and Mapping of Coronavirus Disease COVID-19/Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Epidemic and Associated Events Around the World: How 21st Century GIS Technologies Are Supporting the Global Fight Against Outbreaks and Epidemics," *International Journal of Health Geographics*, Vol. 19, No. 1, March 2020, Art. 8.

Kandula, S., and J. Shaman, "Reappraising the Utility of Google Flu Trends," *PLoS Computational Biology*, Vol. 15, No. 8, 2019, Art. e1007258.

Khan, K., S. J. N. McNabb, Z. A. Memish, R. Eckhardt, W. Hu, D. Kossowsky, J. Sears, J. Arino, A. Johansson, M. Barbeschi, B. McCloskey, B. Henry, M. Cetron, and J. S. Brownstein, "Infectious Disease Surveillance and Modelling Across Geographic Frontiers and Scientific Specialties," *Lancet Infectious Diseases*, Vol. 12, No. 3, 2012, pp. 222–230.

Kim, C., E. Santacreu-Vasut, and E. Keunuk Shin, "Trade-Off Between Health and Wealth? Insights from COVID-19 in South Korea," *Covid Economics*, Vol. 58, November 2020, pp. 57–84.

Kinsa Health, "Kinsa's School Health Program FLUency," undated. As of October 25, 2021: https://content.kinsahealth.com/hubfs/fluency-2021/Kinsa-FLUency-Overview_ARP.pdf

Kniffin, K. M., J. Narayanan, F. Anseel, J. Antonakis, S. P. Ashford, A. B. Bakker, P. Bamberger, H. Bapuji, D. P. Bhave, V. K. Choi, S. J. Creary, E. Demerouti, F. J. Flynn, M. J. Gelfand, L. L. Greer, G. Johns, S. Kesebir, P. G. Klein, S. Y. Lee, H. Ozcelik, J. L. Petriglieri, N. P. Rothbard, C. W. Rudolph, J. D. Shaw, N. Sirola, C. R. Wanberg, A. Whillans, M. P. Wilmot, and M. van Vugt, "COVID-19 and the Workplace: Implications, Issues, and Insights for Future Research and Action," *American Psychologist*, Vol. 76, No. 1, 2021, pp. 63–77.

Kool, J. L., B. Paterson, B. I. Pavlin, D. Durrheim, J. Musto, and A. Kolbe, "Pacific-Wide Simplified Syndromic Surveillance for Early Warning of Outbreaks," *Global Public Health*, Vol. 7, No. 7, 2012, pp. 670–681.

Kopel, J., A. Perisetti, A. Roghani, M. Aziz, M. Gajendran, and H. Goyal, "Racial and Gender-Based Differences in COVID-19," *Frontiers in Public Health*, Vol. 8, July 2020, Art. 418.

Kuisma, E., S. H. Olson, K. N. Cameron, P. E. Reed, W. B. Karesh, A. I. Ondzie, M.-J. Akongo, S. D. Kaba, R. J. Fischer, S. N. Seifert, C. Muñoz-Fontela, B. Becker-Ziaja, B. Escudero-Pérez, C. Goma-Nkoua, V. J. Munster, and J.-V. Mombouli, "Long-Term Wildlife Mortality Surveillance in Northern Congo: A Model for the Detection of Ebola Virus Disease Epizootics," *Philosophical Transactions of the Royal Society B Biological Sciences*, Vol. 374, No. 1782, September 2019, Art. 20180339.

Lall, R., J. Abdelnabi, S. Ngai, H. B. Parton, K. Saunders, J. Sell, A. Wahnich, D. Weiss, and R. W. Mathes, "Advancing the Use of Emergency Department Syndromic Surveillance Data, New York City, 2012–2016," *Public Health Reports*, Vol. 132, Supp. 1, July/August 2017, pp. 23S–30S.

Lallukka, T., O. Pietiläinen, S. Jäppinen, M. Laaksonen, J. Lahti, and O. Rahkonen, "Factors Associated with Health Survey Response Among Young Employees: A Register-Based Study Using Online, Mailed and Telephone Interview Data Collection Methods," *BMC Public Health*, Vol. 20, No. 1, 2020, Art. 184.

Lami, F., W. Asi, A. Khistawi, and I. Jawad, "Syndromic Surveillance of Communicable Diseases in Mobile Clinics During the Arbaeenia Mass Gathering in Wassit Governorate, Iraq, in 2014: Cross-Sectional Study," *JMIR Public Health and Surveillance*, Vol. 5, No. 4, 2019, Art. e10920.

Laskowski, M., L. C. Mostaço-Guidolin, A. L. Greer, J. Wu, and S. M. Moghadas, "The Impact of Demographic Variables on Disease Spread: Influenza in Remote Communities," *Scientific Reports*, Vol. 1, October 2011, Art. 105.

Lau, C. L., P. Weinstein, and D. Slaney, "Dengue Surveillance by Proxy: Travellers as Sentinels for Outbreaks in the Pacific Islands," *Epidemiology and Infection*, Vol. 141, No. 11, 2013, pp. 2328–2334.

Lazer, D., and R. Kennedy, "What We Can Learn from the Epic Failure of Google Flu Trends," *Wired Opinion*, October 1, 2015.

Lazer, D., R. Kennedy, G. King, and A. Vespignani, "Big Data. The Parable of Google Flu: Traps in Big Data Analysis," *Science*, Vol. 343, No. 6176, 2014, pp. 1203–1205.

Leavitt, J. W., "Pandemics and History: Context, Context, Context," *American Journal of Public Health*, Vol. 111, No. 6, 2021, pp. 996–998.

Leder, K., "Travelers as a Sentinel Population: Use of Sentinel Networks to Inform Pretravel and Posttravel Evaluation," *Current Infectious Disease Reports*, Vol. 11, No. 1, 2009, pp. 51–58.

Leung, K., J. T. Wu, and G. M. Leung, "Real-Time Tracking and Prediction of COVID-19 Infection Using Digital Proxies of Population Mobility and Mixing," *Nature Communications*, Vol. 12, No. 1, 2021, Art. 1501.

Lewis, S. L., B. H. Feighner, W. A. Loschen, R. A. Wojcik, J. F. Skora, J. S. Coberly, and D. L. Blazes, "SAGES: A Suite of Freely-Available Software Tools for Electronic Disease Surveillance in Resource-Limited Settings," *PLoS One*, Vol. 6, No. 5, 2011, Art. e19750.

Liu, D., L. Clemente, C. Poirier, X. Ding, M. Chinazzi, J. Davis, A. Vespignani, and M. Santillana, "Real-Time Forecasting of the COVID-19 Outbreak in Chinese Provinces: Machine Learning Approach Using Novel Digital Data and Estimates from Mechanistic Models," *Journal of Medical Internet Research*, Vol. 22, No. 8, 2020, Art. e20285.

Lorenz, C., F. Chiaravalloti-Neto, M. de Oliveira Lage, J. A. Quintanilha, M. C. Parra, M. R. Dibo, E. A. Favaro, M. M. Guirado, and M. L. Nogueira, "Remote Sensing for Risk Mapping of *Aedes Aegypti* Infestations: Is This a Practical Task?" *Acta Tropica*, Vol. 205, May 2020, Art. 105398.

Macaulay, T., "AI Sent First Coronavirus Alert, but Underestimated the Danger," *Next Web*, February 21, 2020. As of March 15, 2022: https://thenextweb.com/news/ai-sent-first-coronavirus-alert-but-underestimated-the-danger

MacIntyre, C. R. , X. Chen, M. Kunasekaran, A. Kannan, V. Nayak, K. Bayaraa, E. Sitnikova, P. Y. Nguyen, and T. German, "Tailored Intelligence to Detect Unusual Epidemic Activity Following the Explosion at Vector, Russia," *Global Biosecurity*, Vol. 1, No. 4, 2020.

Manguvo, A., and B. Mafuvadze, "The Impact of Traditional and Religious Practices on the Spread of Ebola in West Africa: Time for a Strategic Shift," *Pan African Medical Journal*, Vol. 22, Supp. 1, 2015, p. 9.

Mann, P., E. O'Connell, G. Zhang, A. Llau, E. Rico, and F. C. Leguen, "Alert System to Detect Possible School-Based Outbreaks of Influenza-Like Illness," *Emerging Infectious Diseases*, Vol. 17, No. 2, 2011, pp. 262–264.

Mavragani, A., "Tracking COVID-19 in Europe: Infodemiology Approach," *JMIR Public Health and Surveillance*, Vol. 6, No. 2, 2020, Art. e18941.

McCarthy, M., Jr., "A Century of the US Army Yellow Fever Research," *Lancet*, Vol. 357, No. 9270, 2001, Art. 1772.

McNeil, D. G., "Can Smart Thermometers Track the Spread of the Coronavirus," *New York Times*, March 18, 2020.

McQuilkin, P. A., K. Udhayashankar, M. Niescierenko, and L. Maranda, "Health-Care Access During the Ebola Virus Epidemic in Liberia," *American Journal of Tropical Medicine and Hygiene*, Vol. 97, No. 3, 2017, pp. 931–936.

Mello, M. M., and C. J. Wang, "Ethics and Governance for Digital Disease Surveillance," *Science*, Vol. 368, No. 6494, 2020, pp. 951–954.

Merrill, K. G., J. C. Campbell, M. R. Decker, J. McGready, V. M. Burke, J. K. Mwansa, S. Miti, C. Frimpong, C. E. Kennedy, and J. A. Denison, "Prevalence of Physical and Sexual Violence and Psychological Abuse Among Adolescents and Young Adults Living with HIV in Zambia," *PLoS One*, Vol. 15, No. 6, 2020, Art. e0235203.

Mi, E., E. Mi, and M. Jeggo, "Where to Now for One Health and Ecohealth?" *EcoHealth,* Vol. 13, No. 1, 2016, pp. 12–17.

Milinovich, G. J., R. J. Magalhães, and W. Hu, "Role of Big Data in the Early Detection of Ebola and Other Emerging Infectious Diseases," *Lancet Global Health*, Vol. 3, No. 1, 2015, pp. e20–e21.

Monteiro, S., D. Rente, M. V. Cunha, M. Carmo Gomes, T. A. Marques, A. B. Lourenço, E. Cardoso, P. Álvaro, M. Silva, N. Coelho, J. Valaça, F. Meireles, N. Brôco, M. Carvalho, and R. Santos, "A Wastewater-Based Epidemiology Tool for COVID-19 Surveillance in Portugal," *Science of the Total Environment*, Vol. 804, 2022, Art. 150264.

Moon, M. J., "Fighting COVID-19 with Agility, Transparency, and Participation: Wicked Policy Problems and New Governance Challenges," *Public Administration Review*, Vol. 80, No. 4, 2020, pp. 651–656.

Moran, B., "Fighting Ebola in Conflict in the DR Congo," *Lancet*, Vol. 392, No. 10155, 2018, pp. 1295–1296.

Moriyama, M., W. J. Hugentobler, and A. Iwasaki, "Seasonality of Respiratory Viral Infections," *Annual Review of Virology*, Vol. 7, No. 1, 2020, pp. 83–101.

Morse, S. S., B. H. Rosenberg, and J. Woodall, "ProMED Global Monitoring of Emerging Diseases: Design for a Demonstration Program," *Health Policy*, Vol. 38, No. 3, 1996, pp. 135–153.

Muggah, R., and J.P. Sullivan, "The Coming Crime Wars," 2018. As of March 15, 2022: https://foreignpolicy.com/2018/09/21/the-coming-crime-wars/

National Academy of Medicine, *Microbial Threats to Health: Emergence, Detection, and Response*, M. S. Smolinski, M.A. Hamburg, and J. Lederberg, eds., Washington, D.C.: National Academies Press, 2003.

National Emergency Medical Service Information System, "How NEMSIS Works," webpage, undated. As of October 10, 2021: https://nemsis.org/what-is-nemsis/how-nemsis-works/

NEMSIS—*See* National Emergency Medical Service Information System.

Neporent, L., "Dangerous Bacteria Mysteriously Escapes from Louisiana Monkey Lab," ABC News, March 2, 2015. As of March 15, 2022: https://abcnews.go.com/Health/dangerous-bacteria-mysteriously-escapes-louisiana-monkey-lab/story?id=29327907

Nguimkeu, P., and S. Tadadjeu, "Why Is the Number of COVID-19 Cases Lower Than Expected in Sub-Saharan Africa? A Cross-Sectional Analysis of the Role of Demographic and Geographic Factors," *World Development*, Vol. 138, 2021, Art. 105251.

Nguyen, K. H., K. Nguyen, L. Corlin, J. D. Allen, and M. Chung, "Changes in COVID-19 Vaccination Receipt and Intention to Vaccinate by Socioeconomic Characteristics and Geographic Area, United States, January 6–March 29, 2021," *Annals of Medicine*, Vol. 53, No. 1, 2021, pp. 1419–1428.

Noland, R. B., "Mobility and the Effective Reproduction Rate of COVID-19," *Journal of Transport & Health*, Vol. 20, March 2021, Art. 101016.

Nouvellet, P., S. Bhatia, A. Cori, K. E. C. Ainslie, M. Baguelin, S. Bhatt, A. Boonyasiri, N. F. Brazeau, L. Cattarino, L. V. Cooper, H. Coupland, Z. M. Cucunuba, G. Cuomo-Dannenburg, A. Dighe, B. A. Djaafara, I. Dorigatti, O. D. Eales, S. L. van Elsland, F. F. Nascimento, R. G. FitzJohn, K. A. M. Gaythorpe, L. Geidelberg, W. D. Green, A. Hamlet, K. Hauck, W. Hinsley, N. Imai, B. Jeffrey, E. Knock, D. J. Laydon, J. A. Lees, T. Mangal, T. A. Mellan, G. Nedjati-Gilani, K. V. Parag, M. Pons-Salort, M. Ragonnet-Cronin, S. Riley, H. J. T. Unwin, R. Verity, M. A. C. Vollmer, E. Volz, P. G. T. Walker, C. E. Walters, H. Wang, O. J. Watson, C. Whittaker, L. K. Whittles, X. Xi, N. M. Ferguson, and C. A. Donnelly, "Reduction in Mobility and COVID-19 Transmission," *Nature Communications*, Vol. 12, No. 1, 2021, Art. 1090.

Noyce, R. S., and D. H. Evans, "Synthetic Horsepox Viruses and the Continuing Debate About Dual Use Research," *PLoS Pathogens*, Vol. 14, No. 10, 2018, Art. e1007025.

Nsoesie, E. O., L. Flor, J. Hawkins, A. Maharana, T. Skotnes, F. Marinho, and J. S. Brownstein, "Social Media as a Sentinel for Disease Surveillance: What Does Sociodemographic Status Have to Do with It?" *PLoS Currents*, Vol. 8, December 2016.

Office of the Assistant Secretary for Preparedness and Response, "National Biodefense Strategy," Washington, D.C.: U.S. Department of Health and Human Services, January 25, 2022. As of March 15, 2022: https://www.phe.gov/Preparedness/biodefense-strategy/Pages/default.aspx

Olivero, J., J. E. Fa, R. Real, A. L. Márquez, M. A. Farfán, J. M. Vargas, D. Gaveau, M. A. Salim, D. Park, J. Suter, S. King, S. A. Leendertz, D. Sheil, and R. Nasi, "Recent Loss of Closed Forests Is Associated with Ebola Virus Disease Outbreaks," *Scientific Reports*, Vol. 7, No. 1, 2017, Art. 14291.

Ozdenerol, E., G. N. Taff, and C. Akkus, "Exploring the Spatio-Temporal Dynamics of Reservoir Hosts, Vectors, and Human Hosts of West Nile Virus: A Review of the Recent Literature," *International Journal of Environmental Research and Public Health*, Vol. 10, No. 11, 2013, pp. 5399–5432.

Palaniyandi, M., "The Role of Remote Sensing and GIS for Spatial Prediction of Vector-Borne Diseases Transmission: A Systematic Review," *Journal of Vector Borne Diseases*, Vol. 49, No. 4, 2012, pp. 197–204.

Papageorge, N. W., M. V. Zahn, M. Belot, E. van den Broek-Altenburg, S. Choi, J. C. Jamison, and E. Tripodi, "Socio-Demographic Factors Associated with Self-Protecting Behavior During the Covid-19 Pandemic," *Journal of Population Economics*, Vol. 34, No. 1, 2021, pp. 691–738.

Papanikolaou, D., and L. D. W. Schmidt, *Working Remotely and the Supply-Side Impact of Covid-19*, Cambridge, Mass.: National Bureau of Economic Research, working paper 27330), June 2020.

Park, C., "Traditional Funeral and Burial Rituals and Ebola Outbreaks in West Africa: A Narrative Review of Causes and Strategy Interventions," *Journal of Health and Social Sciences*, Vol. 5, No. 1, 2020, pp. 73–90.

Parselia, E., C. Kontoes, A. Tsouni, C. Hadjichristodoulou, I. Kioutsioukis, G. Magiorkinis, and N. I. Stilianakis, "Satellite Earth Observation Data in Epidemiological Modeling of Malaria, Dengue and West Nile Virus: A Scoping Review," *Remote Sensing*, Vol. 11, No. 16, 2019, Art. 1862.

Paterson, B., R. Caddis, and D. Durrheim, "Use of Workplace Absenteeism Surveillance Data for Outbreak Detection," *Emerging Infectious Diseases Summaries*, Vol. 17, No. 10, 2011, pp. 1963–1964.

Paterson, B. J., J. L. Kool, D. N. Durrheim, and B. Pavlin, "Sustaining Surveillance: Evaluating Syndromic Surveillance in the Pacific," *Global Public Health*, Vol. 7, No. 7, 2012, pp. 682–694.

Patterson-Lomba, O., M. Safan, S. Towers, and J. Taylor, "Modeling the Role of Healthcare Access Inequalities in Epidemic Outcomes," *Mathematical Biosciences and Engineering*, Vol. 13, No. 5, 2016, pp. 1011–1041.

Patwardhan, A., and R. Bilkovski, "Comparison: Flu Prescription Sales Data from a Retail Pharmacy in the US with Google Flu Trends and US ILINet (CDC) Data as Flu Activity Indicator," *PLoS One*, Vol. 7, No. 8, 2012, Art. e43611.

Peckham, R., and R. Sinha, "Satellites and the New War on Infection: Tracking Ebola in West Africa," *Geoforum*, Vol. 80, March 2017, pp. 24–38.

Pepey, A., M. Souris, A. Vantaux, S. Morand, D. Lek, I. Mueller, B. Witkowski, and V. Herbreteau, "Studying Land Cover Changes in a Malaria-Endemic Cambodian District: Considerations and Constraints," *Journal of Remote Sensing*, Vol. 12, No. 18, 2020, Art. 2972.

Peters, A., "The Global Proliferation of High-Containment Biological Laboratories: Understanding the Phenomenon and Its Implications," *Revue scientifique et technique*, Vol. 37, No. 3, 2018, pp. 857–883.

Phalkey, R. K., S. Yamamoto, P. Awate, and M. Marx, "Challenges with the Implementation of an Integrated Disease Surveillance and Response (IDSR) System: Systematic Review of the Lessons Learned," *Health Policy and Planning*, Vol. 30, No. 1, 2015, pp. 131–143.

Pham, N. T. T., C. T. Nguyen, D. T. Vu, and K. Nakamura, "Mapping of Dengue Vulnerability in the Mekong Delta Region of Viet Nam Using a Water-Associated Disease Index and Remote Sensing Approach," *APN Science Bulletin*, Vol. 8, No. 1, 2018.

Pivette, M., J. E. Mueller, P. Crépey, and A. Bar-Hen, "Surveillance of Gastrointestinal Disease in France Using Drug Sales Data," *Epidemics*, Vol. 8, September 2014, pp. 1–8.

Polozov, I. V., L. Bezrukov, K. Gawrisch, and J. Zimmerberg, "Progressive Ordering with Decreasing Temperature of the Phospholipids of Influenza Virus," *Nature Chemical Biology*, Vol. 4, No. 4, 2008, pp. 248–255.

Rajan, A., R. Sharaf, R. S. Brown, R. Z. Sharaiha, B. Lebwohl, and S. Mahadev, "Association of Search Query Interest in Gastrointestinal Symptoms with COVID-19 Diagnosis in the United States: Infodemiology Study," *JMIR Public Health and Surveillance*, Vol. 6, No. 3, 2020, Art. e19354.

Ratto-Kim, S., I. K. Yoon, R. M. Paris, J.-L. Excler, J. H. Kim, and R. J. O'Connell, "The US Military Commitment to Vaccine Development: A Century of Successes and Challenges," *Frontiers in Immunology*, Vol. 9, June 2018, Art. 1397.

Razavi, A., N. Erondu, and E. Okereke, "The Global Health Security Index: What Value Does It Add?" *BMJ Global Health*, Vol. 5, No. 4, 2020, Art. e002477.

Rhee, C., H. Burkom, C.-G. Yoon, M. Stewart, Y. Elbert, A. Katz, and S. Tak, "Syndromic Surveillance System for Korea-US Joint Biosurveillance Portal: Design and Lessons Learned," *Health Security*, Vol. 14, No. 3, 2016, pp. 152–160.

Rocco, P., J. A. J. Rich, K. Klasa, K. A. Dubin, and D. Béland, "Who Counts Where? COVID-19 Surveillance in Federal Countries," *Journal of Health Politics, Policy and Law*, Vol. 46, No. 6, 2021 pp. 959–987.

"The RODS Open Source Project," webpage, undated. As of March 15, 2021: http://openrods.sourceforge.net/index.php?page=introduction

Rulli, M. C., M. Santini, D. T. Hayman, and P. D'Odorico, "The Nexus Between Forest Fragmentation in Africa and Ebola Virus Disease Outbreaks," *Scientific Reports*, Vol. 7, February 2017, Art. 41613.

Russ, H., and J. Steenhuysen, "CDC Reassigns Director of Lab Behind Anthrax Blunder," Reuters, June 24, 2014.

Sadarangani, S., M. I. C. Chen, A. L. P. Chow, A. Earnest, M. K. Win, and B. S. P. Ang, "Use of Healthcare Worker Sickness Absenteeism Surveillance as a Potential Early Warning System for Influenza Epidemics in Acute Care Hospitals," *Annals of the Academy of Medicine of Singapore*, Vol. 39, No. 4, 2010, pp. 341–342.

Saksena, S., J. Fox, M. Epprecht, C. C. Tran, D. H. Nong, J. H. Spencer, L. Nguyen, M. L. Finucane, V. D. Tran, and B. A. Wilcox, "Evidence for the Convergence Model: The Emergence of Highly Pathogenic Avian Influenza (H5N1) in Viet Nam," *PLoS One*, Vol. 10, No. 10, 2015, Art. e014519.

Saran, Sameer, Priyanka Singh, Vishal Kumar, and Prakash Chauhan, "Review of Geospatial Technology for Infectious Disease Surveillance: Use Case on COVID-19," *Journal of the Indian Society of Remote Sensing*, Vol. 48, No. 8, 2020, pp. 1121–1138.

Sarker, A., S. Lakamana, W. Hogg-Bremer, A. Xie, M. A. Al-Garadi, and Y. C. Yang, "Self-Reported COVID-19 Symptoms on Twitter: An Analysis and a Research Resource," *Journal of the American Medical Informatics Association*, Vol. 27, No. 1, 2020, pp. 1310–1315.

Sarma, N., A. Ullrich, H. Wilking, S. Ghozzi, A. K. Lindner, C. Weber, A. Holzer, A. Jansen, K. Stark, and S. Vygen-Bonnet, "Surveillance on Speed: Being Aware of Infectious Diseases in Migrants Mass Accommodations—an Easy and Flexible Toolkit for Field Application of Syndromic Surveillance, Germany, 2016 to 2017," *Eurosurveillance*, Vol. 23, No. 40, 2018, Art. 1700430.

Shaman, J., and M. Kohn, "Absolute Humidity Modulates Influenza Survival, Transmission, and Seasonality," *Proceedings of the National Academy of Sciences*, Vol. 106, No. 9, 2009, pp. 3243–3248.

Sharara, N., N. Endo, C. Duvallet, N. Ghaeli, M. Matus, J. Heussner, S. W. Olesen, E. J. Alm, P. R. Chai, and T. B. Erickson, "Wastewater Network Infrastructure in Public Health: Applications and Learnings from the COVID-19 Pandemic," *PLOS Global Public Health*, Vol. 1, No. 12, 2021, Art. e000061.

Sheel, M., J. Collins, M. Kama, D. Nand, D. Faktaufon, J. Samuela, V. Biaukula, C. Haskew, J. Flint, K. Roper, A. Merianos, M. D. Kirk, and E. Nilles, "Evaluation of the Early Warning, Alert and Response System After Cyclone Winston, Fiji, 2016," *Bulletin of the World Health Organization*, Vol. 97, No. 3, 2019, pp. 178–189C.

Sickweather, "How Sickweather Works," undated. As of October 25, 2021: https://www.sickweather.com/how/

Silva, J. C., S. C. Shah, D. P. Rumoro, J. D. Bayram, M. M. Hallock, G. S. Gibbs, and M. J. Waddell, "Comparing the Accuracy of Syndrome Surveillance Systems in Detecting Influenza-Like Illness: GUARDIAN vs. RODS vs. Electronic Medical Record Reports," *Artificial Intelligence in Medicine*, Vol. 59, No. 3, 2013, pp. 169–174.

Soh, S. E., A. R. Cook, M. I. Chen, V. J. Lee, J. L. Cutter, V. T. K. Chow, N. W. S. Tee, R. T. P. Lin, W.-Y. Lim, I. G. Barr, C. Lin, M. C. Phoon, L. W. Ang, S. K. Sethi, C. Y. Chong, L. G. Goh, D. L. M. Goh, P. A. Tambyah, K. C. Thoon, Y. S. Leo, and S. M. Saw, "Teacher Led School-Based Surveillance Can Allow Accurate Tracking of Emerging Infectious Diseases—Evidence from Serial Cross-Sectional Surveys of Febrile Respiratory Illness During the H1N1 2009 Influenza Pandemic in Singapore," *BMC Infectious Diseases*, Vol. 12, December 2012, Art. 336.

Spencer, J. H., "The Urban Health Transition Hypothesis: Empirical Evidence of an Avian Influenza Kuznets Curve in Vietnam?" *Journal of Urban Health*, Vol. 90, No. 2, 2013, pp. 343–357.

Sudmanns, M., D. Tiede, S. Lang, H. Bergstedt, G. Trost, H. Augustin, A. Baraldi, and T. Blaschke, "Big Earth Data: Disruptive Changes in Earth Observation Data Management and Analysis?" *International Journal of Digital Earth*, Vol. 13, No. 7, 2020, pp. 832–850.

Sugishita, Y., T. Sugawara, Y. Ohkusa, T. Ishikawa, M. Yoshida, and H. Endo, "Syndromic Surveillance Using Ambulance Transfer Data in Tokyo, Japan," *Journal of Infection and Chemotherapy*, Vol. 26, No. 1, 2020, pp. 8–12.

Sullivan, John P., and Robert J. Bunker, eds., *COVID-19, Gangs, and Conflict*, McLean, Va.: Small Wars Foundation, 2020.

't Sas-Rolfes, M., D. W. S. Challender, A. Hinsley, D. Veríssimo, and E. J. Milner-Gulland, "Illegal Wildlife Trade: Scale, Processes, and Governance," *Annual Review of Environment and Resources*, Vol. 44, 2019, pp. 201–228.

Tai, D. B. G., A. Shah, C. A. Doubeni, I. G. Sia, and M. L. Wieland, "The Disproportionate Impact of COVID-19 on Racial and Ethnic Minorities in the United States," *Clinical Infectious Diseases*, Vol. 72, No. 4, 2021, pp. 703–706.

Thumbi, S. M., M. K. Njenga, E. Otiang, L. Otieno, P. Munyua, S. Eichler, M.-A. Widdowson, T. F. McElwain, and G. H. Palmer, "Mobile Phone-Based Surveillance for Animal Disease in Rural Communities: Implications for Detection of Zoonoses Spillover," *Philosophical Transactions of the Royal Society B Biological Sciences*, Vol. 374, No. 1782, 2019, Art. 20190020.

Tibbetts, J. H., "Remote Sensors Bring Wildlife Tracking to New Level: Trove of Data Yields Fresh Insights—and Challenges," *Journal of BioSciences*, Vol. 67, No. 5, 2017, pp. 411–417.

Toyama, Y., M. Ota, and B. B. Beyene, "Event-Based Surveillance in North-Western Ethiopia: Experience and Lessons Learnt in the Field," *Western Pacific Surveillance and Response Journal*, Vol. 6, No. 3, 2015, pp. 22–27.

Travers, D., S. W. Haas, A. E. Waller, T. A. Schwartz, J. Mostafa, N. C. Best, and J. Crouch, "Implementation of Emergency Medical Text Classifier for Syndromic Surveillance," *Proceedings of the AMIA Annual Symposium*, Vol. 2013, November 2013, pp. 1365–1374.

UNHCR—*See* United Nations High Commissioner for Refugees.

United Nations Department of Economic and Social Affairs, "68% of the World Population Projected to Live in Urban Areas by 2050, Says UN," New York, 2018. As of March 15, 2022:
https://www.un.org/development/desa/en/news/population/2018-revision-of-world-urbanization-prospects.html

United Nations High Commissioner for Refugees, "Mid-Year Trends," Geneva, 2021. As of June 30, 2022:
https://www.unhcr.org/en-us/mid-year-trends.html

Unwin, H. J. T., S. Mishra, V. C. Bradley, A. Gandy, T. A. Mellan, H. Coupland, J. Ish-Horowicz, M. A. C. Vollmer, C. Whittaker, S. L. Filippi, X. Xi, M. Monod, O. Ratmann, M. Hutchinson, F. Valka, H. Zhu, I. Hawryluk, P. Milton, K. E. C. Ainslie, M. Baguelin, A. Boonyasiri, N. F. Brazeau, L. Cattarino, Z. Cucunuba, G. Cuomo-Dannenburg, I. Dorigatti, O. D. Eales, J. W. Eaton, S. L. van Elsland, R. G. FitzJohn, K. A. M. Gaythorpe, W. Green, W. Hinsley, B. Jeffrey, E. Knock, D. J. Laydon, J. Lees, G. Nedjati-Gilani, P. Nouvellet, L. Okell, K. V. Parag, I. Siveroni, H. A. Thompson, P. Walker, C. E. Walters, O. J. Watson, L. K. Whittles, A. C. Ghani, N. M. Ferguson, S. Riley, C. A. Donnelly, S. Bhatt, and S. Flaxman, "State-Level Tracking of COVID-19 in the United States," *Nature Communications*, Vol. 11, No. 1, 2020, Art. 6189.

U.S. Agency for International Development, "Connecting Human and Forest Health in West Africa," webpage, undated-a. As of August 2, 2022: https://www.usaid.gov/biodiversity/stories/connecting-human-forest-health-west-africa

U.S. Agency for International Development, "Living Safely with Bats," Washington, D.C., undated-b. As of October 10, 2021: https://p2.predict.global/living-safely-with-bats-book

USAID—*See* U.S. Agency for International Development.

U.S. Army Public Health Center, *Surveillance of COVID-19 in the Department of Defense*, U.S. Army Public Health Center, Technical Information Paper No. 98-122-0720, undated.

U.S. Centers for Disease Control and Prevention, "Achievements in Public Health, 1900–1999: Control of Infectious Diseases," *Morbidity and Mortality Weekly Report*, Vol. 48, No. 29, 1999, pp. 621–629.

———, "National Immunization Surveys," Atlanta, Ga., January 23, 2018. As of October 5, 2021: https://www.cdc.gov/vaccines/imz-managers/nis/index.html

———, "U.S. Influenza Surveillance System: Purpose and Methods," Atlanta, Ga., October 15, 2021. As of June 30, 2022: https://www.cdc.gov/flu/weekly/overview.htm

———, "National Wastewater Surveillance System (NWSS)," Atlanta, Ga., March 21, 2022. As of June 30, 2022: https://www.cdc.gov/healthywater/surveillance/wastewater-surveillance/wastewater-surveillance.html

U.S. Department of Defense Directive 6420.02, *DoD Biosurveillance*, Washington, D.C.: Office of the Under Secretary of Defense for Personnel and Readiness, September 17, 2020.

U.S. Embassy & Consulate in Thailand, "US Army Medical Directorate of the Armed Forces Research Institute of Medical Sciences (USAMD-AFRIMS)," Bangkok, undated. As of October 10, 2021: https://th.usembassy.gov/embassy-consulate/bangkok/us-agencies/usamd-afrims/

U.S. Military HIV Research Program, "MHRP—Nigeria," Bethesda, Md., 2016. As of October 10, 2021: https://www.wrp-n.org/joint-west-africa-research-group-profile/

U.S. Navy and Marine Corps Public Health Center, "Reportable Medical Events," webpage, 2020. As of June 30, 2022: https://www.med.navy.mil/Navy-Marine-Corps-Public-Health-Center/Population-Health/Epi-Data-Center/Reportable-Medical-Events/

Vermeer, P., and J. Kregting, "Religion and the Transmission of COVID-19 in the Netherlands," *Religions*, Vol. 11, No. 8, 2020, Art. 393.

Wagner, T., F. N. U. Shweta, K. Murugadoss, S. Awasthi, A. J. Venkatakrishnan, S. Bade, A. Puranik, M. Kang, B. W. Pickering, J. C. O'Horo, P. R. Bauer, R. R. Razonable, P. Vergidis, Z. Temesgen, S. Rizza, M. Mahmood, W. R. Wilson, D. Challener, P. Arand, M. Liebers, Z. Doctor, E. Silvert, H. Solomon, A. Anand, R. Barve, G. Gores, A. W. Williams, W. G. Morice II, J. Halamka, A. Badley, and V. Soundararajan, "Augmented Curation of Unstructured Clinical Notes from a Massive EHR System Reveals Symptoms of Impending COVID-19 Diagnosis," *eLife*, July 7, 2020.

Wang, Q., R. Xu, and N. D. Volkow, "Increased Risk of COVID-19 Infection and Mortality in People with Mental Disorders: Analysis from Electronic Health Records in the United States," *World Psychiatry*, Vol. 20, No. 1, 2021, pp. 124–130.

Wang, W., Y. Wang, X. Zhang, X. Jia, Y. Li, and S. Dang, "Using WeChat, a Chinese Social Media App, for Early Detection of the COVID-19 Outbreak in December 2019: Retrospective Study," *JMIR mHealth and uHealth*, Vol. 8, No. 10, 2020, Art. e19589.

Ward, M. A., A. Stanley, L. E. Deeth, R. Deardon, Z. Feng, and L. A. Trotz-Williams, "Methods for Detecting Seasonal Influenza Epidemics Using a School Absenteeism Surveillance System," *BMC Public Health*, Vol. 19, No. 1, 2019, Art. 1232.

Weinstein, J. S., T. F. Leslie, and M. E. von Fricken, "Spatial Associations Between Land Use and Infectious Disease: Zika Virus in Colombia," *International Journal of Environmental Research and Public Health*, Vol. 17, No. 4, 2020, Art. 1127.

Weiss, Z., "Detecting the Onset of Infectious Disease Outbreaks Using School Sign-Out Logs," *Epidemiology*, Vol. 30, No. 3, 2019, pp. e18–e19.

Wenham, Clare, "GPHIN, GOARN, GONE? The Role of the World Health Organization in Global Disease Surveillance and Response," in S. E. Davis and J. R. Youde, eds, *The Politics of Surveillance and Response to Disease Outbreaks*, London: Routledge, 2015.

White, P., S. Saketa, A. Durand, S. Vaai-Nielsen, T. A. Leong-Lui, T. Naseri, A. Matalima, F. Amosa, A. Mercier, C. Lepers, V. Lal, R. Wojcik, S. Lewis, A. Roth, Y. Souares, O. E. Merilles Jr., and D. Hoy, "Enhanced Surveillance for the Third United Nations Conference on Small Island Developing States, Apia, Samoa, September 2014," *Western Pacific Surveillance and Response Journal*, Vol. 8, No. 1, 2017, pp. 15–21.

White, P., S. Saketa, E. Johnson, S. V. Gopalani, E. Edward, C. Loney, A. Mercier, T. Toatu, R. Wojcik, S. Lewis, and D. Hoy, "Mass Gathering Enhanced Syndromic Surveillance for the 8th Micronesian Games in 2014, Pohnpei State, Federated States of Micronesia," *Western Pacific Surveillance and Response Journal*, Vol. 9, No. 1, 2018, pp. 1–7.

WHO—*See* World Health Organization.

Wimberly, M. C., K. M. de Beurs, T. V. Loboda, and W. K. Pan, "Satellite Observations and Malaria: New Opportunities for Research and Applications," *Trends in Parasitology*, Vol. 37, No. 6, 2021, pp. 525–537.

World Health Organization, *Pandemic Influenza Preparedness and Response: A WHO Guidance Document*, Geneva, 2009.

———, "e-SPAR: State Party Annual Report," Geneva, 2019. As of October 5, 2021: https://extranet.who.int/e-spar#capacity-score

———, "Vector-Borne Diseases," Geneva, 2020a. As of October 5, 2021: https://www.who.int/news-room/fact-sheets/detail/vector-borne-diseases

———, "WHO COVID-19 Case Definition," Geneva, 2020b. As of October 7, 2021: https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-Surveillance_Case_Definition-2022.1

Wu, T., C. Perrings, A. Kinzig, J. P. Collins, B. A. Minteer, and P. Daszak, "Economic Growth, Urbanization, Globalization, and the Risks of Emerging Infectious Diseases in China: A Review," *Ambio*, Vol. 46, No. 1, 2017, pp. 18–29.

Yasenov, V., *Who Can Work from Home?* Cambridge, Mass.: Institute of Labor Economics, No. 13197, 2020.

Zeeberg, A., "Piecing Together the Next Pandemic," *New York Times*, February 16, 2021.

Zhang, E. X., Y. Yang, R. Di Shang, J. J. P. Simons, B. K. Quek, X. F. Yin, W. See, O. S. H. Oh, K. S. T. Nandar, V. R. Y. Ling, P. P. Chan, Z. Wang, R. S. M. Goh, L. James, and J. S. H. Tey, "Leveraging Social Networking Sites for Disease Surveillance and Public Sensing: The Case of the 2013 Avian Influenza A(H7N9) Outbreak in China," *Western Pacific Surveillance and Response Journal*, Vol. 6, No. 2, 2015, pp. 66–72.

Zhang, Y., L. May, and M. A. Stoto, "Evaluating Syndromic Surveillance Systems at Institutions of Higher Education (IHEs): A Retrospective Analysis of the 2009 H1N1 Influenza Pandemic at Two Universities," *BMC Public Health*, Vol. 11, July 2011, Art. 594.

Zhao, H., H. Green, A. Lackenby, M. Donati, J. Ellis, C. Thompson, A. Bermingham, J. Field, P. Sebastianpillai, M. Zambon, J. Watson, and R. Pebody, "A New Laboratory-Based Surveillance System (Respiratory DataMart System) for Influenza and Other Respiratory Viruses in England: Results and Experience from 2009 to 2012," *Eurosurveillance*, Vol. 19, No. 3, 2014, Art. 20680.

Zhao, Y., D. Zeng, A. H. Herring, A. Ising, A. Waller, D. Richardson, and M. R. Kosorok, "Detecting Disease Outbreaks Using Local Spatiotemporal Methods," *Biometrics*, Vol. 67, No. 4, 2011, pp. 1508–1517.

Zimmermann, B. M., A. Fiske, B. Prainsack, N. Hangel, S. McLennan, and A. Buyx, "Early Perceptions of COVID-19 Contact Tracing Apps in German-Speaking Countries: Comparative Mixed Methods Study," *Journal of Medical Internet Research*, Vol. 23, No. 2, 2021, Art. e25525.