

## Surveillance of emerging infectious diseases for biosecurity

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Emerging infectious diseases, such as COVID-19, continue to pose significant threats to human beings and their surroundings. In addition, biological warfare, bioterrorism, biological accidents, and harmful consequences arising from dual-use biotechnology also pose a challenge for global biosecurity. Improving the early surveillance capabilities is necessary for building a common biosecurity shield for the global community of health for all. Furthermore, surveillance could provide early warning and situational awareness of biosecurity risks. However, current surveillance systems face enormous challenges, including technical shortages, fragmented management, and limited international cooperation. Detecting emerging biological risks caused by unknown or novel pathogens is of particular concern. Surveillance systems must be enhanced to effectively mitigate biosecurity risks. Thus, a global strategy of meaningful cooperation based on efficient integration of surveillance at all levels, including interdisciplinary integration of techniques and interdepartmental integration for effective management, is urgently needed. In this paper, we review the biosecurity risks by analyzing potential factors at all levels globally. In addition to describing biosecurity risks and their impact on global security, we also focus on analyzing the challenges to traditional surveillance and propose suggestions on how to integrate current technologies and resources to conduct effective global surveillance.

**surveillance, biosecurity, early warning, emerging infectious disease**

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### Introduction

The COVID-19 pandemic is still impacting the world, and human beings are experiencing the most serious global public health crisis since World War II. Since medical technology and sanitary conditions have been greatly improved and popularized in modern society, emerging infectious diseases (EIDs) have caused great disasters for

human survival and social development. This makes people feel the significance of biosafety. In the 21st century, the subject of global infectious disease transmission and how to mitigate associated risks has become an intensely discussed topic. In 2001, the intentional release of anthrax in the United States (US) changed the world. Similarly, the emergence of Ebola in West Africa in 2014 and the Democratic Republic of the Congo in 2018 resulted in over 11,000 and 2,000 deaths, respectively (Eurosurveillance Editorial, 2019; <https://apps.who.int/gho/data/node ebola-sitre>). Furthermore, these biosecurity issues primarily affected the related countries,

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caused an increased burden on global public health services, and significantly threatened the security of directly and indirectly affected countries.

Biosecurity is closely related, both directly and indirectly, to human health and survival through changes to animals, plants, and other resources. Biosecurity refers to a country's state or capability to ensure its safety through countering the impact of biological events and related risk factors (Zheng, 2011). There are numerous examples of the impact of infectious diseases on human events or security, including bubonic plague that caused the collapse of the Mamluk dynasty of Iraq, smallpox virus from Europe that resulted in the dramatic decline of the native American population (Abdullah, 2014), the 1918 influenza pandemic (Spanish flu) that caused the loss of 20–100 million lives and changed the course of World War I (Oxford et al., 2002), and the COVID-19 pandemic that had a significant impact on the world (Casale, 2020). Figure 1 shows some important biosecurity events that have occurred over the past century.

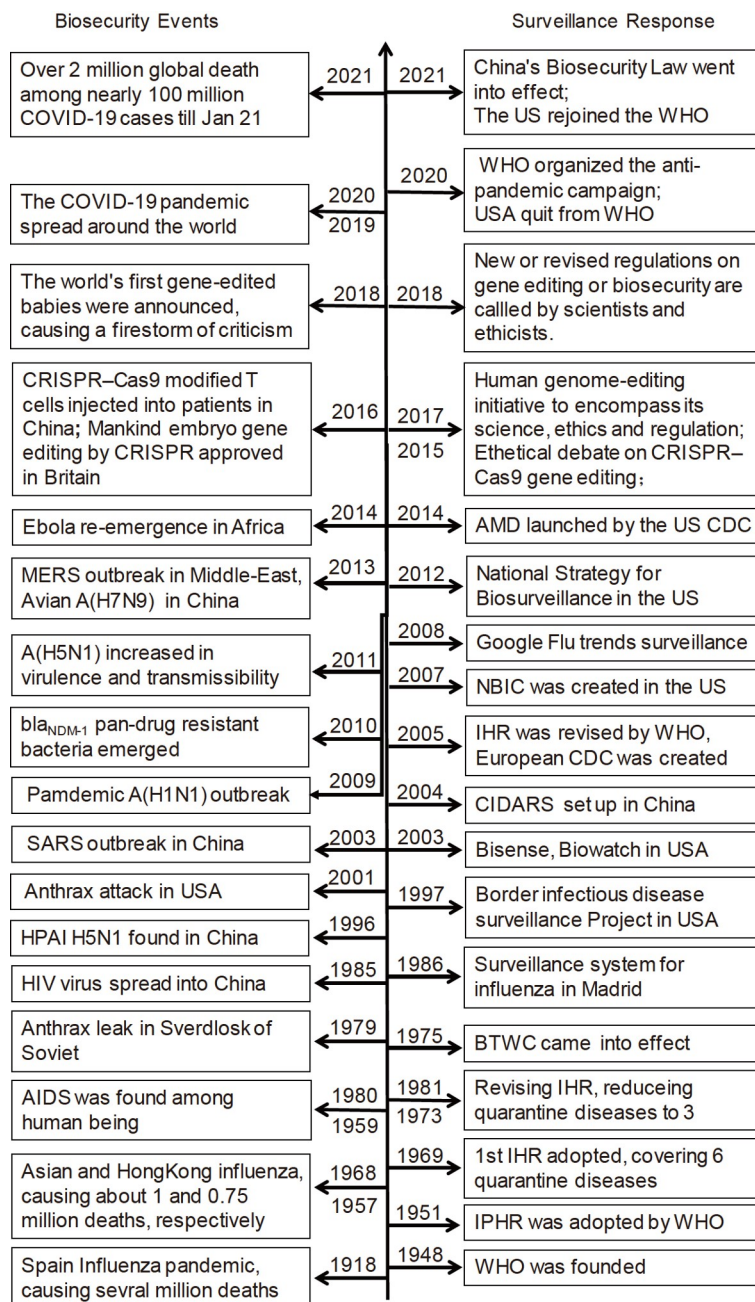
The 21st century has witnessed increased risks from infectious diseases through the emergence or reemergence of highly infectious pathogens, including severe acute respiratory syndrome coronavirus (SARS-CoV), avian influenza virus A(H5N1) and A(H7N9), Middle Eastern respiratory syndrome coronavirus (MERS-CoV), Ebola virus, and SARS-CoV-2. Infectious microbes previously restricted to a narrow geographic distribution or host range are experiencing altered transmission pathways due to the expansion of human activities and the rapid growth of global commerce and travel, thus adversely affecting humans (Wolfe et al., 2007). Furthermore, biosecurity risks arise from deliberate destruction using biological methods, such as bioterrorism attacks or the use of biological warfare agents (Meyerson and Reaser, 2002). In 2001, the anthrax attack in the US, which resulted in social panic, is a well-known example of such bioterrorism. Additionally, biological accidents also often occur. The leakage of pathogenic microorganisms from pathogen institutes or factories has frequently been reported. This caused severe damage to humans and the environment (Berger, 2016). In 2014, incidents related to the inactivation of *Bacillus anthracis* occurred in the high containment laboratories of the US Centers for Disease Control and Prevention (CDC). Although no infections resulted from these events, a wave of international concern was sparked (Palmer et al., 2015). It is estimated that there are over one thousand bacteria/virus banks, which are distributed to hundreds of affiliates globally. The risk of leakage of these pathogens cannot be ignored. Biological accidents can occur during use, custom clearance, and exchange of these pathogens (Bayot and Limaïem, 2019; Pham et al., 2017).

Moreover, biosecurity issues might also come from dual-use research, which is intended for benefit but misapplied to

cause harm (Parker and Kunjapur, 2020). The recent rapid development of sophisticated biotechniques has raised concern about the impact of dual-use research on biosecurity. One recent controversial example that illustrates this concern is the assessment of the potential risk associated with highly pathogenic avian influenza strains through “gain-of-function” research (Fouchier et al., 2013). This project's main research strategy is the artificial synthesis of virulence factors through accelerating reassortment with other pathogens, expanding the range of immunogenicity for more effective vaccines, evaluating host adaptations to novel pathogen strains, evaluating drug resistance, assessing transmissibility, and so on. The very essence of the research initiative creates biosecurity risks (Fouchier et al., 2013). Similarly, clustered regularly interspaced short palindromic repeats-Cas9 (CRISPR-Cas9), a recently fast developed gene-editing technique, can change the DNA sequence at specific targets. Some scientists worry about using the CRISPR-Cas9 in the clinical treatment of infertility as it should be used cautiously because of human genetic variation (Scott and Zhang, 2017). Shockingly, scientists have used CRISPR-Cas9 to treat patients and edit human embryonic genes, thus triggering a heated debate about the ethics of this technology (Cyranoski, 2018). The US Director of National Intelligence placed genome editing techniques on the lists of weapons of mass destruction that threaten national security (<http://www.laboratoryequipment.com/news/2016/02/director-national-intelligence-calls-crispr-weapon-mass-destruction>).

Furthermore, biosecurity risks also result from artificially synthesized life forms. Some biologists pursue the *de novo* construction of pathogens to understand the relationship between microbial form and function. These experiments would result in pathogens with high virulence, containing a wide-spectrum antimicrobial resistance, and/or with the possibility of high transmissibility. If these pathogens were accidentally or intentionally released, they would present a significant public health risk because they would create biosecurity risks that might pose a challenge of detecting, diagnosing, and treating (Ashford et al., 2003). Scientists have obtained completely new nucleotides different from and independent of the four basic nucleotides (GACT) using artificial synthesis methods, which is of particular concern. These two novel nucleotides could match each other and GACT to hybridize and form a double helix via complete Watson-Crick base pairing (Zhang et al., 2015). Furthermore, adding these two artificial bases to the classical four-base nucleotide library has created completely novel life forms (Kolby et al., 2015), which might cause potential biological risks.

Modern biological technologies are becoming available to a greater number of people. In theory, laboratories that are not under governmental control can participate in the artificial synthesis of pathogens. In 1975, scientists and



**Figure 1** Important biosecurity events and surveillance related response in the past century. Abbreviation: 1st IHR, the first “International Health Regulations”, covering six kinds of “quarantine diseases”; AIDS, aquired immune deficiency syndrome; AMD, advanced molecular detection; BTWC, the United Nations’ convention on the prohibition of biological weapons; CIDARS, The China Infectious Disease Automated-alert and Response System; HIV, human immunodeficiency virus; HPAI H5N1, highly pathogenic avian influenza H5N1 virus; IHR, International Health Regulations, be reduced to three quarantine diseases (yellow fever, plague and cholera); IPHR, International Public Health Regulations; NBIC, the National Surveillance Integration Center; SARS, severe acute respiratory syndrome; WHO, World Health Organization.

politicians established the Asilomar Process to determine the framework for managing biological risk, including emerging recombinant DNA technology (Mackenzie et al., 2014). However, the rapid development and widespread use of modern biological technologies continue to pose challenges to the Asilomar Process, significantly threatening global biosecurity.

The above biosecurity risks could be divided into three

types (Table 1). Type I refers to the transmission risk of infectious diseases from human beings, crops and livestock, quarantined pests, invasive alien species, and so on. Type II refers to deliberate sabotage using modern biological technology or biowarfare agents, such as bio-terrorism attacks. Type III refers to the potential negative effects of dual-use biotechnology. EIDs and other types of biosecurity risks might be great challenges to biosecurity, impacting the

**Table 1** Types of biosecurity risks and the corresponding surveillance

Type	Biosecurity risks	Surveillance
Type I	The transmission risk of infectious diseases from human being, crops and livestock, quarantined pests, invasive alien species and so on.	Disease surveillance, most of which is infectious disease surveillance, carried out based escalation of all levels of public health data, accompanied with very serious omission and delay problems in the disease reports.
Type II	Deliberately utilizing modern biological technology, such as bio-terrorism attack or deliberate destruction using biowarfare agents.	Focusing on bioterrorism-related syndromic surveillance, pathogen detection, and bioterrorism-related internet media search, to alert on potential bioterrorism attack, or reduce the mortality and morbidity.
Type III	Potential negative effects from dual-use biotechnology.	Strengthening active and systematic surveillance through broadening its range onto “the full spectrum risk” on the health of human being, animal, and plant.

economy, development, and overall stability of societies. These biosecurity issues are important part of global security because the world is a community with a shared future. All the countries are in one world with one health intimately connected with each other in biosecurity. Thus, we should monitor and prevent major biosecurity risks in a timely manner and build a strong biosecurity system accordingly (Table 1).

It is urgent to strengthen surveillance to build a common biosecurity shield for the global community of health for all (<http://www.oneworlddonehealth.org/>). The surveillance for EIDs, reemerging infectious diseases (REIDs), and other biosecurity risks has received increased attention. In 2012, the *National Strategy for Biosurveillance* bill came into law in the US, with the intent to strengthen biosurveillance in the US to provide early warning and situational awareness of public health risks for better decision-making.

We are living in a global community, with unprecedented increases in trade and travel, along with rapid biotechnological growth and modernization. The increased vulnerability to terrorist attacks has also come with these changes, and the ready access to biological materials has increased the likelihood of bioterrorism and biological warfare. Biosecurity, an important part of national security, has become a global security issue, impacting not only public health but also economic operations and social stability (Daszak et al., 2020).

Meanwhile, surveillance has developed continuously from traditional infectious disease surveillance and bioterrorism surveillance to biosurveillance of health risks at all levels, global human, animal, plant, microorganism, and environment, and all other potential factors that are naturally existing or deliberately made (Berger et al., 2019). However, current surveillance systems do not meet the challenges posed by emerging biosecurity risks. Therefore, strengthening surveillance through a global international cooperation strategy based on efficient integration of current surveillance and its correlated factors is urgently required.

### Surveillance of emerging infectious diseases

Surveillance is an important guarantee for timely detection

of emerging infectious diseases and other biosecurity risks, protecting human health, ensuring public health and biosafety, and maintaining economic and social stability. It is imperative to improve the capabilities of early surveillance and warning as a top priority to improve the public health system and strengthen the surveillance system for infectious disease epidemics and public health emergencies (<https://www.nppa.gov.cn/nppa/contents/718/74320.shtml>). Although this focuses on infectious diseases and public health, it is also applicable to extend it to the biosecurity field.

Methods of surveillance might be able to provide important support for global biosecurity. The former President of the US, Barack Obama, noted that surveillance is one of the first lines of defense against EID risks (Table 1) (Wendell, 2014). Biosurveillance aims to mitigate the impacts of biosecurity threats to health and the associated economic, political, and societal consequences (Figure 1) (Wendell, 2014).

### Surveillance strategies dependent on national conditions

In response to changing biosecurity risks, various countries and organizations have developed surveillance systems (as shown in Tables S1 and S2 in Supporting Information). In 1952, the World Health Organization (WHO) created Global Influenza Surveillance and Response System to track influenza viruses, make recommendations on laboratory diagnostics, vaccines, and risk evaluation and provide global alerts. Currently, the WHO supports 6 collaborating centers, 4 essential regulatory laboratories, and 143 institutions in 113 WHO member states.

In 2000, the Global Outbreak Alert and Response Network (GOARN) was formed as a technical collaboration of the existing institutions and networks to rapidly respond to international biosecurity outbreaks. GOARN also contributes to long-term epidemic preparedness and capacity building, comprised of over 250 institutions or technical partners and networks in the world (Johns et al., 2011; Mackenzie et al., 2014). In 2005, the WHO revised the International Health Regulations (IHR) for surveillance system tracking. The IHR 2005 no longer only focuses on specific high-priority infectious diseases, such as cholera and yellow fever, but has

expanded to include novel and changing public health risks. The IHR 2005 is more than a guideline, but not legislation. It relies on individual countries to self-report and is not strictly enforceable. In 2011, after the 2009 influenza A(H1N1) epidemic—a potential public health emergency of international concern—an independent review committee warned that “the world is ill-prepared to respond to a global, sustained, and threatening public health emergency” (Fineberg, 2014). This was also exemplified by the inefficient response to the 2014 Ebola epidemic in its early stages (Gostin and Friedman, 2014).

Many countries have increased their investment in bio-surveillance, strengthening their early detection capabilities and timely alert to biosecurity threats. Several US administrations have sought to strengthen biosurveillance as a priority since the anthrax attacks in 2001, and more than 32 billion US dollars have been spent on creating or strengthening surveillance systems (Kman and Bachmann, 2012). For example, BioSense, initiated by the CDC in 2003, collects electronic data from multiple governmental sources. Additionally, the US Department of Defense launched the Antimicrobial Resistance Monitoring and Research Program. This program uses molecular characterization to understand and control antimicrobial resistance (Lesho et al., 2014). The US has enhanced biosurveillance capabilities at the federal, state, local, tribal, and territorial levels of government and has even bolstered private organizational capabilities (Wendell, 2014). In November 2009, the White House issued the National Strategy for Countering Biological Threats to manage the risks from naturally occurring and deliberately introduced diseases. The US biosurveillance system has tried to encompass human-, animal-, and plant-related health for a “full-spectrum type threat” (Dobalian et al., 2017; Koenig, 2003). More than 4,000 surveillance sites in more than 30 major US cities have been established with an international biosurveillance network that impacts at least 92 countries (Larkins et al., 2020; Russell et al., 2011).

In 2005, the EU established the European Center of Disease Control and Prevention (ECDC) to help member states develop surveillance systems for timely alerts of infectious disease outbreaks. This surveillance covers 46 diseases, including severe acute respiratory syndrome, West Nile fever, and avian influenza. The surveillance system is integrated into the national crisis prevention system to support early evaluation and decision-making in response to potential biosecurity threats. In June 2021, the ECDC launched Epi-Pulse (the European surveillance portal for infectious diseases) to collect, analyze, and disseminate surveillance data about infectious diseases and associated health problems, such as global epidemic intelligence and whole-genome sequencing, for European public health authorities and global partners through integrating several surveillance systems, including the European Surveillance System (TESSy), Epi-

demic Intelligence Information System, and the Threat Tracking Tool into an online portal (<https://www.ecdc.europa.eu/en/publications-data/epipulse-european-surveillance-portal-infectious-diseases>).

In 2004, the National Notifiable Disease Reporting System (NNDRS) was established in China after the SARS epidemic for outbreak detection and rapid response to infectious diseases. The NNDRS covers almost all of the mainland of China (Yang et al., 2011; Zheng et al., 2018). Additionally, the Chinese National Influenza Surveillance Network (CNISN) plays an important role in the surveillance and control of influenza-like cases, notably in the fight against avian influenza A(H7N9) in 2013. Currently, the CNISN covers 408 network laboratories and 554 sentinel hospitals (<http://ivdc.chinacdc.cn/cnic/en/Aboutus/>). In response to the sudden outbreak of COVID-19, China obtained the whole-genome sequence of its pathogen (SARS-CoV-2) in less than a week and shared it with the world. China has not only timely controlled the COVID-19 epidemic but also effectively contained the imported epidemic situation and repeatedly controlled the domestic epidemic rebound by adopting timely detection, tracking, strict isolation, protection, and other prevention and control policies. Furthermore, the use of digital technologies, such as health codes and infrared thermometers, plays an important role in epidemic monitoring and analysis and virus traceability. China’s successful fight against the COVID-19 has made important contributions to the international fight against the epidemic and safeguarded global biosecurity. Richard Horton, editor-in-chief of *The Lancet*, said: “Chinese doctors and scientists have made the most outstanding contributions” (<https://news.cgtn.com/news/2020-05-01/Richard-Horton-China-s-reaction-is-decisive-and-quick-Q98QQ5Tkk0/index.html>). In April 2021, China’s Biosecurity Law went into effect to strengthen biosurveillance through risk monitoring and early warning on biosecurity.

The biosurveillance system is much less sophisticated in Africa. For example, many health information systems depend on household surveys. Few African countries have civil registration systems for tracking mortality and causes of death. The African region is considered the only WHO region where communicable, maternal, neonatal, and nutritional conditions still dominate. Moreover, biosurveillance systems do not fully cover this region (Foddai et al., 2014). Fortunately, Integrated Disease Surveillance and Response (IDSR) programs have been initiated in 43 countries in the African region (Mbondji et al., 2014). However, the 2014 Ebola outbreak and its rapid spread in West Africa indicate the deficiency of surveillance systems in this region ([http://www.who.int/gho/mortality\\_burden\\_disease/causes\\_death/region/en/](http://www.who.int/gho/mortality_burden_disease/causes_death/region/en/)). Following the 2014 Ebola epidemic, many African countries have strengthened surveillance by increasing public health investment and constructing

surveillance systems (Tambo et al., 2014). Dr. Margaret Chan, former Director-General of the WHO, pointed out that a well-functioning surveillance system should be able to capture early signals of an unusual biosecurity event to stop it quickly and early, keeping it from becoming an international threat. However, among the 194 WHO member states, only 64 (32%) have such surveillance capabilities. Fortunately, the establishment of the Africa CDC in 2017 has greatly improved surveillance, emergency response, and prevention of infectious diseases. Since the COVID-19 pandemic, the Africa CDC has worked with the WHO to perform surveillance on SARS-CoV-2 and its variants (<https://reliefweb.int/report/world/covid-19-genomic-surveillance-africa>).

### ***Surveillance system driven by technique development***

Surveillance requires systems whose type, range, and other characteristics determine effectiveness. Traditional surveillance is mainly toward infectious disease, which is based on case reports (Velasco et al., 2014). Medical and CDC departments need to report confirmed cases about notifiable infectious diseases to their superior department level by level or through an infectious disease reporting system, which is less efficient and might cause omission. Syndromic surveillance systems actively use data from emergency departments, intensive care units, hospital admission and discharge systems, and so on to monitor healthcare utilization patterns and track changes (often in real-time), looking for alarm patterns. Furthermore, disease syndrome-based automated surveillance is available for early detection of bioterrorism events and could increase the timeliness of responses but is limited by poor specificity and reliability (Hiller et al., 2013; Martin et al., 2019). Laboratory-based surveillance identifies the pathogen and analyzes its origin, virulence, and antimicrobial resistance based on detection capabilities at a molecular level, normally through network laboratories, such as the Laboratory Response Network that covers about 160 reference laboratories (Wagar, 2016). This network was established in 1999 by the CDC, the Federal Bureau of Investigation, and the Association of Public Health Laboratories to maintain an integrated network of laboratories and detect biothreats (Wagar, 2016). Environment-based surveillance mainly analyzes biological risks through sampling aerosols from key areas. Environmental detection systems comprise remote detection of aerosol clouds and environmental point detection systems. In 2003, the BioWatch program was launched in the US to promote the detection of aerosolized biological agents. The air sampling devices of BioWatch cover 31 major American cities, and samples are tested daily (<https://www.ncbi.nlm.nih.gov/pubmed/25032347>).

In comparison with the above surveillance, event-based Internet surveillance systems use the information on events

impacting health from the Internet and other sources, which have significantly broadened the surveillance information sources and improved its timeliness and sensitivity for early warning and emergence preparedness. Web-based surveillance uses unstructured data from diverse web-based sources, such as local and international media. Public health information from social media sources, including blogs, microblogs, social networks, and mobile networks, has a great potential value for data mining. It could serve as a real-time complementary approach to traditional surveillance methods for public health officials, healthcare workers, and the public and private sector (Sintchenko and Gallego, 2009). The Early Aberration Reporting System is an early example of a web-based surveillance system, which uses nontraditional public health data sources such as school/work absentee estimates, over-the-counter medication sales, 911 calls, ambulance run data, and veterinary data (Kman and Bachmann, 2012). It was demonstrated that over-the-counter electrolyte sales could detect respiratory or gastrointestinal diseases 2.4 weeks earlier than hospital visits. Google Flu Trends, another example of a web-based surveillance system developed by Google Inc. and the CDC to monitor daily health-searching behavior, detected influenza epidemics 7–14 d before the US CDC surveillance reports. However, with the predicting results much larger than the actual influenza-like illness provided by the US CDC, there was doubt that its predictions were accurate enough (Ginsberg et al., 2009; Lazer et al., 2014). The HealthMap Project, another web-based surveillance system, which has been operated for free since September 2006, integrates data from various electronic sources, including news media, professional records, and official warnings, and uses automated data mining and analysis to classify warnings by location and disease and label them on the interactive map. It detected news coverage about a strange fever in Guinea on March 14, 2014, nine days earlier than official information confirming the outbreak of Ebola (Milinovich et al., 2015). HealthMap, aided by artificial intelligence, has actually alarmed the COVID-19 as early as December 30, 2019 (<https://www.sciencemag.org/news/2020/05/artificial-intelligence-systems-aim-sniff-out-signs-covid-19-outbreaks>). Furthermore, there are also many other social media-based surveillance systems, such as ProMED-mail with over 60,000 subscribers in 185 countries, the Global Public Health Intelligence Network, and the Innovative Support to Emergencies Diseases and Disasters. An unprecedented opportunity for surveillance has been provided by expanding mobile phone networks for developing countries or regions. In 2020, the number of mobile phone users exceeded the global population, and the mobile phone signal covered nearly 97% of inhabitants worldwide (<http://www.itu.int/en/ITU-D/Statistics/Pages/default.aspx>). Furthermore, 93% of the world's population lives within reach of a mobile broadband (or

Internet) service. Compared to traditional means, the transmission of information about a pandemic outbreak in developing countries is more rapid with mobile phone communication, particularly by individual citizens (Generous et al., 2014). In the past decade, the rapid growth of Internet access in developing countries (e.g., increasing from 2.1% in 2005 to 24.4% in 2018 in Africa) has greatly benefited the Internet-based surveillance (<http://www.itu.int/en/ITU-D/Statistics/Pages/default.aspx>).

## Weakness of current surveillance strategies

### Limited detecting capability

Many approaches for data collection and analysis have been applied to surveillance systems. However, none completely meets the challenges posed by all biosecurity threats (Table 2). Current surveillance systems lack accuracy in data detection and analysis. For example, since 2003, there have been several BioWatch Actionable Results from the BioWatch surveillance system, but none have resulted from a biological attack. Furthermore, false alarms negatively impact community confidence in the public health system. Although developing countries have significantly improved their data analysis capabilities, most surveillance systems do not have sufficient real-time and automatic surveillance capabilities. Most countries do not have sufficient resources or capabilities to detect, analyze and respond to emergent biosecurity events that have the potential to spread worldwide. Internet and mobile health technologies have significantly accelerated data production for surveillance, but methods are needed to collect and analyze the data effectively. Moreover, in the developing world or resource-limited countries, poor Internet infrastructure poses challenges to surveillance efforts. Of particular concern is that current surveillance systems mainly target biological risks caused by known pathogens that would generally cause limited biose-

curity problems due to prearranged disposal plans. For example, the NNDRS failed in sending out warning signals at the early outbreak of the COVID-19. One of the reasons is that the system is only suitable for the early detecting and warning of statutory infectious diseases but cannot provide early warning of new and unknown infectious diseases.

The methods designed to detect new biological risks caused by unknown or novel pathogens remain a challenge for technologies used by surveillance systems. Moreover, current surveillance systems and technologies cannot distinguish cases of natural infectious diseases from deliberate ones.

### Fragmented surveillance data

Current surveillance data are significantly fragmented, decentralized, and operated under the direction of local governments. In the US, there are hundreds of surveillance systems operated by different governmental departments at the federal, state/territorial, and local levels. However, information sharing between departments is hindered due to the lack of mechanisms for secure information dissemination. Effective surveillance requires data integration and resource utilization from various governmental levels. In 2007, the National Biosurveillance Integration Center (NBIC) was created in the US to integrate biosurveillance information and support an interagency biosurveillance community (<https://www.gao.gov/products/gao-10-171>). However, an evaluation report by the US General Accounting Office revealed that NBIC still lacked coordination and interoperability across agency borders to meet the biosurveillance requirements in terms of timeliness, sensitivity, specificity, and routine analysis of data (Kman and Bachmann, 2012).

To date, the primary target of biosurveillance activities has been human infectious diseases, and zoonotic diseases have received only a fraction of attention (Peiris et al., 2012; Watsa and Wildlife Disease Surveillance Focus Group, 2020). It has been reported that 60% of EIDs are zoonotic

**Table 2** Challenge of current surveillance strategy

Type	Challenge	Suggestion
Technical shortage	(i) Lacking accuracy in data analysis. (ii) Lacking sufficient capability of real-time and automatic surveillance. (iii) Lack of specificity, reliance on chief complaint data. (iv) Insufficiency in detecting unknown pathogen.	(i) Using the technique of big data based on multiple stream information for accurate surveillance. (ii) Using automatic biosensing detection techniques, combining with modern networking and communication technology. (iii) Interdisciplinary integration in high techniques including internet, big data and molecular detection. (iv) Developing multiplexed detection methods and novel gene sequencing technique.
Fragments in management	Lacking enough coordinate and interoperability across agency borders to share data to meet the surveillance requirement.	Establishing well-integrated surveillance across different departments.
Scarce international cooperation	(i) Current surveillance sources are not well-allocated around the world. (ii) Some countries are unwilling to share pathogen materials.	Establishing global effective surveillance system under the frame of WHO, through integrating current surveillance systems among various countries.
Others	(i) Privacy of protected health information (ii) High cost to run surveillance system.	(i) Legislation to regulate surveillance activities. (ii) Maintaining sufficient investment on this field.

and over 70% are from wildlife, which suggests the great impact of wildlife-originated pathogens on human beings (Watsa and Wildlife Disease Surveillance Focus Group, 2020). Recently, several major epidemics have been caused by infectious agents transmitted to humans from animals, such as SARS, avian influenza A(H5N1) and A(H7N9), and Ebola. In China, zoonotic disease surveillance involves numerous governmental departments, including the Ministry of Agriculture, the National Health Commission, and the Import and Export Inspection and Quarantine Bureau. Fragmentation of information and lack of cooperation between these departments hinder the application of advanced biosurveillance techniques, such as automatic biosurveillance networks based on biosensors (Ecker et al., 2008).

The prevention and control of COVID-19 have exposed problems such as incomplete disease control system networks and biosurveillance systems, unclear functions, and lack of coordination between medical departments and the CDC. The infectious disease information should be reported to the NNDRS after the clinician completes the information card on infectious disease cases, followed by multilevel manual approval. Strict and cumbersome procedures are required to ensure the integrity and accuracy of the reported data, which seriously affect the efficiency of biosafety emergency response. The NNDRS lacks the horizontal information sharing function, and hospitals lack data comparison of patients with the same symptoms. The infectious disease report card is only uploaded vertically, and there is no horizontal information sharing. For other hospitals, the reminder and early warning can only rely on the NNDRS. If different hospitals cannot see the same cases in other hospitals and think that their cases are occasional, they cannot be alert.

### ***Isolated surveillance system***

Biosecurity threats transcend borders. Infectious diseases and biological outbreaks can spread globally via highly developed transportation systems very rapidly, in less time than the incubation period of most infectious diseases. However, the distribution of current global biosurveillance systems does not overlap well with that of EIDs and REIDs. Most biosurveillance systems are distributed in developed countries and few in developing countries (such as those in the African region) where EIDs are prevalent. In African countries, the significant scarcity of surveillance systems not only restricts the timely response to biosecurity events such as Ebola but also potentially causes global risk due to its rapid spreading characters throughout the world. Thus, enhancing biosurveillance capabilities in vulnerable areas, including Africa, is necessary. However, it is difficult for regions lacking the infrastructure to establish digital surveillance systems. This might impact the biosecurity of these regions and may negatively impact the global biosurveillance system

development (Milinovich et al., 2015). The US 2018 National Biodefense Strategy, unveiled by President Trump, highlighted the importance of that domestic and international biosurveillance and information sharing systems (<https://www.hsdl.org/c/2018-national-biodefense-strategy/>).

Lack of integration of global biosurveillance networks and response mechanisms has led to difficulties preventing the spread of infectious diseases such as cholera in Latin America and pneumonic plague in India (Castillo-Salgado, 2010; Hii et al., 2018). Many countries are reluctant to report infectious diseases due to the potential negative repercussions on tourism and trade. The necessity of global cooperation was demonstrated in response to the outbreak of SARS, the influenza A(H1N1)09 pandemic, and the 2013–2016 West Africa Ebola (Castillo-Salgado, 2010). In 2003, China initially hesitated to report SARS, influencing its timely control. The SARS epidemic was soon controlled after the Chinese government revised its strategy concerning epidemic information sharing and global cooperation. However, in response to avian influenza A(H7N9) in 2013, China's immediate response and sharing of data and isolates with the international community played a key role in controlling the outbreak's spread. However, many developing countries at high risk of infectious diseases lack the economic and political will and the public health infrastructure to conduct effective biosurveillance. For example, some countries have been unwilling to share pathogen samples due to concerns about the disproportionate access to vaccines by wealthier countries, potentially creating a cost barrier to developing countries (Gostin et al., 2014).

Insufficient global cooperation might hinder the effective control of COVID-19, including its origin tracing (Wang et al., 2021; Wu et al., 2021). After the global outbreak of COVID-19, to effectively control it and maintain global biosecurity, more international cooperation is needed. However, this is now facing huge challenges, especially with the insistence of the US on withdrawing from the WHO. *The Lancet* commented that when the world was facing a historic public health emergency, the withdrawal of the US from the WHO would threaten the health and safety of the world and the American people and impact global biosecurity (Gostin et al., 2020). Rejoining the WHO was one of the most important things after Biden took office as the President of the US, which also demonstrated the significance of the global cooperation on fighting against the COVID-19 pandemic and other biothreats.

### **Recommendations for establishing global surveillance system**

#### ***Interdisciplinary technical innovation to improve detecting capability***

The surveillance and early warning of infectious disease



outbreaks and other biosecurity events is a complex and systematic task, which requires a comprehensive assessment based on various aspects of information to obtain relatively accurate judgments. Both false positives and false negatives have significant negative effects. Various technical principles should be comprehensively used to improve the monitoring mechanism for unexplained diseases and abnormal health events, increase the sensitivity and accuracy of surveillance, and establish intelligent early warning based on a multipoint trigger mechanism.

Effective surveillance should use multiple data collected and integrated from several sources covering the domains of human health and threats to animals or plants. This approach requires integrating multiple technologies and data resources from various fields, including social media, the Internet, syndrome surveillance, laboratory detection, outpatient or emergency treatment, public health, food safety, environmental disasters, absenteeism, and over-the-counter (OTC) drug sales (Milinovich et al., 2015). The accuracy and timeliness of surveillance can be promoted by electronic systems, which could benefit the reach, visualization, and analysis of various data, including chief complaints, diagnosis, and OTC drug sales. Automated electronic systems, widely used in countries with sophisticated Internet connectivity and good healthcare systems, could significantly accelerate surveillance. However, poor information technology infrastructure hampers data collection, particularly in remote areas. Mobile platforms, such as short messaging systems, could address this limitation. Electronic surveillance might be greatly improved by integrating big data techniques, which could obtain knowledge of biosecurity issues by analyzing data in the digital domain, including Internet searches, social media, and online news media (Milinovich et al., 2015). The COVID-19 pandemic significantly accelerates the application of big data in EID surveillance. For example, the John Hopkins University Center for Systems Science and Engineering's COVID-19 dashboard developed COVID-19 map to provide real-time and visualized COVID-19 data for the access of the world, including public health authorities, researchers, and the general public, which also illustrates the great need for the standardization and sharing of public data (Dong et al., 2020).

The search engine-based method can be used to monitor the attention on biosecurity events, thereby detecting abnormal biosecurity signals, providing timely data sources for biosurveillance, and making up for the shortcomings of traditional surveillance systems. Even for remote areas, we can also learn about their concerns about biosecurity incidents by collecting people's retrieval (Madoff and Li, 2014).

To improve the technical capabilities of surveillance, we should comprehensively use big data and artificial intelligence. On June 11, 2020, the COVID-19 epidemic rebounded in Beijing. The relevant departments conducted a detailed epidemiological investigation on the scope of ac-

tivities of each confirmed case with the help of data resources and information technology and used information technology to quickly track it. Nucleic acid tests were also performed on key populations, key industries, and key regions personnel, which significantly avoided the possible negative effects of city lockdown. Actually, the emergence of COVID-19 might accelerate the application of big data and artificial intelligence to detect, predict, and control infectious diseases (Bansal et al., 2020).

However, simultaneously, it should be noted that big data is not omnipotent. There is still room for improvement in improving data accuracy and systematization and ensuring data security. Currently, big data only plays a role in analysis and decision-making assistance. Only by further strengthening information sharing, improving data accuracy, and computing capabilities while protecting personal privacy and data security can it be able to fight the epidemic and achieve scientific, precise, and efficient decision-making.

The rapid development of molecular diagnosis, especially continuously renewal sequencing techniques, has significantly improved microbiological and bioinformatics capabilities, revolutionizing the approach to biosurveillance. Current rapid sequencing techniques might help determine whether an EID occurs naturally or due to genetically modified microorganisms. In 2014, the CDC launched a program of advanced molecular detection, which can identify and retrospectively determine the origin of infectious pathogens, such as polio or MERS coronavirus, in fewer than two days (Fung et al., 2018). Novel biosensors could automatically identify viral, bacterial, and fungal pathogens from patient samples within a few hours. Novel surveillance systems could improve real-time surveillance capabilities by combining automatic detection techniques with modern networking and communication technologies, which would play an important role in the warning and prevention of EIDs and bioterrorism attacks (Meyerson and Reaser, 2002; Westfall et al., 2020).

Human beings are intimately connected with their surroundings, as well as animals and plants. Thus, adequate resources should be provided to support global wildlife disease surveillance, and more available strategies should be developed and implemented, such as decentralized model, including in situ biosampling, whole-genome sequencing, and metagenomic and metabarcoding analysis on wildlife pathogen, to strengthen wildlife disease surveillance (Hamelin and Roe, 2020; Watsa and Wildlife Disease Surveillance Focus Group, 2020).

#### ***Interdepartmental effective integration to provide multiple-source surveillance data***

Early and comprehensive surveillance is the key to the timely warning, and its premise is an unblocked source of

information. Therefore, establishing data-sharing mechanisms is necessary to strengthen the surveillance capability of infectious disease epidemics and other biosafety incidents, especially to develop intelligent early warning based on multipoint trigger mechanisms.

Moreover, a mechanism for multichannel surveillance and early warning should be established to improve the capability of real-time analysis and comprehensive judgment. It is necessary to strengthen the construction of pathogen detecting networks and establish a coordinated monitoring mechanism between public health and medical institutions so that they can play a surveillance role as frontier sentinels.

Furthermore, it is necessary to establish and improve surveillance's departmental responsibility division, coordination, and linkage and information sharing mechanism, clarify the responsibilities of each department, innovate the departmental coordination mechanism, and establish an information-sharing mechanism to meet the challenges of various biosecurity risks.

By learning from the experience and lessons in the prevention and control of the COVID-19 epidemic, China's Hubei Province is deploying to reform its CDC system: rationalizing the system and mechanism, clarifying functions and responsibilities, enhancing professional capabilities, strengthening the administrative functions of disease control agencies, and implementing supervision responsibilities, nominating the head of the disease control agency concurrently as the leader of the health department at the same level.

Establishing well-integrated biosurveillance systems at the national governmental level, integrating infectious disease surveillance with bioterrorist defense to detect potential biosecurity risks, especially those arising from the dual-use of biotechnology, is urgently needed. Strengthening cooperation among government, the private sector, non-governmental organizations, the medical establishment, public institutions, and veterinary departments for biosurveillance, data sharing, and biothreat responses is pivotal. For example, the first four confirmations of the 2009 influenza pandemic were made by cooperation between the Global Emerging Infections Surveillance program of the US Department of Defense and the CDC. An ideal biosurveillance system should include all biosecurity factor-related departments, including health, agriculture, environment, quality control, and food and drugs, and should establish mechanisms to coordinate between these departments and the expert system of risk evaluation for real-time surveillance of all potential biosecurity threats.

Developing simple and standard protocols for effective sharing of discrete and multisource data would help to achieve efficient integration of current surveillance resources (Gardner et al., 2021). It is meaningful to encourage the participation of various departments at all levels, especially

taking full advantage of the value of surveillance information resources at the community level. This would facilitate the national mobilization of potential initiatives. Moreover, addressing the gaps between the translation of scientific results and policymakers on biosecurity by strengthening their communications is important (Berger et al., 2019).

Additionally, it is necessary to advance the formulation and improvement of the laws and regulations on infectious disease prevention and control, the public health emergency response, and other biosecurity issues, and improve the law enforcement mechanisms on surveillance with clear powers and responsibilities, standardized procedures, and strong enforcement.

### ***International deep cooperation to establish global surveillance system***

Viruses know no borders, and epidemics do not distinguish between races. In the face of the COVID-19 epidemic, the most serious common crisis for all human beings in a century, no country can take care of itself. Thus, we should strengthen international cooperation, build a human health community, and unite a strong joint force to defeat the pandemic and ensure global biosecurity.

Once well-integrated domestic biosurveillance resources, technologies, and systems have been established, these should be integrated into a global strategic biosurveillance resource for effective cooperation in response to common biothreats. In 2005, the WHO revised the IHR to strengthen international cooperation in biosurveillance. However, there exist many difficulties in the practical operation of the IHR, including insufficient infrastructure for biosurveillance in developing countries, legal enforcement, and maintenance of individual human rights.

The WHO has played a core and key role in the early warning, overall prevention, and control of the COVID-19 epidemic. Meanwhile, the epidemic also exposed WHO's lack of decision-making influence and financial support. The COVID-19 epidemic should be considered an opportunity to build and maintain a global biosafety system, relying on the WHO to establish a global biosurveillance and early warning system and establish a working mechanism for regular research on major epidemics and biosafety risk evaluation. Thus, we can make scientific risk judgments through sharing information, formulating measures appropriately, and executing them efficiently.

Establishing effective biosurveillance needs broad participation and cooperation among numerous departments from various nations at all levels. More countries should be encouraged to participate in constructing global biosurveillance networks and share essential information with each other to enhance the global response to biosecurity events (Wendell, 2014). To develop and strengthen influenza surveillance of

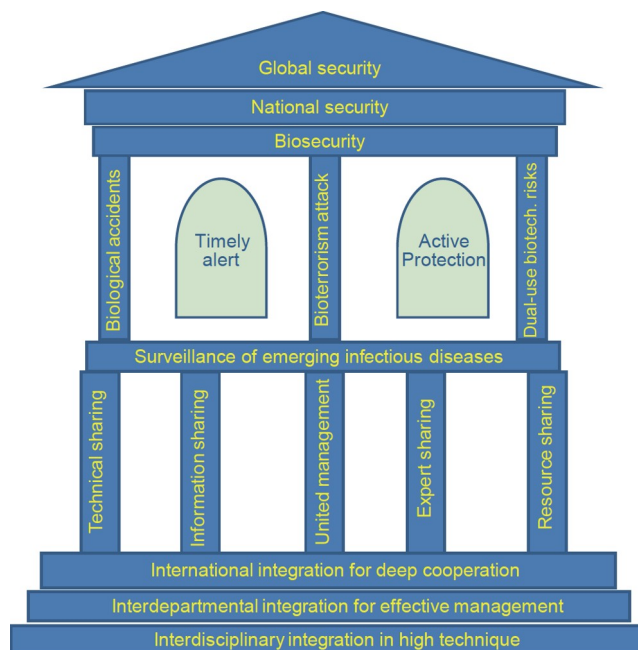
eight countries in the African region, the WHO funded the Strengthening Influenza Sentinel Surveillance in Africa project in 2011. This project demonstrated that a functional influenza surveillance system could be created by integrating the existing national IDSR systems (Kebede et al., 2013). International cooperation could significantly enhance bio-surveillance efficiency (Emanuel et al., 2011). For example, international cooperation based on open-source genomic sharing accelerates the analysis of Shiga toxin-producing *E. coli* O104:H4, allowing results from Germany within a week (Rohde et al., 2011). The CDC approaches its mission of improving global health security through building cooperative partnerships, which also benefit its overseas security. The US collaborates with overseas host countries to jointly conduct biosurveillance based on sharing their techniques and data. Furthermore, strengthening the Biological Weapons Convention by broadening its range and international cooperation is also vital for global biosecurity (Dando, 2016). Fortunately, a few international programs, such as the Global Health Security Agenda and Global Virama Project, have been launched recently to reduce the impact of various biosecurity risks in the world (Gao, 2019).

Figure 2 shows the surveillance strategy of emerging infectious diseases to ensure global biosecurity, including interdisciplinary integration in high technique, interdepartmental integration for effective management, and international integration for deep cooperation. Through technical sharing, information sharing, united management, expert sharing, and resource sharing, global surveillance of emerging infectious diseases could realize effective surveillance on bioterrorism attacks, biological accidents, dual-use biotechnology risks, and other biothreats for timely alert and active protection to ensure global biosecurity.

Global biosecurity is in a common community. Now, the international community's top priority is to do its best to prevent and control the epidemic, contain the spread of the epidemic as soon as possible, do everything possible to prevent the epidemic from spreading across borders, and support the WHO to play a leading role. We should also increase support for underdeveloped countries and regions, such as Africa, and help them build a strong biosecurity line of defense, strengthen international cooperation, and jointly build a global biosecurity shield.

## Conclusions and future perspective

New biosecurity problems threaten global security and challenge traditional surveillance strategies. One World, One Health. Solidarity and cooperation are the most powerful weapons to overcome the epidemic and other biosecurity issues and are also the foundation for building a human health community and maintaining global biosecurity.



**Figure 2** Illustration for the surveillance strategy of emerging infectious diseases to ensure global biosecurity.

Novel surveillance is expected to provide early warning and situational awareness of biosecurity risks covering the full spectrum of targets on humans, animals, and plants. Moreover, information on drug resistance, virulence, transmissibility, and variation of infectious pathogens, as well as information on clinical syndromes, is required. Further, surveillance should be able to automatically detect and provide real-time surveillance of potential biosecurity threats. This could be realized based on multiple sourced data and comprehensive analysis. An effective, global surveillance system should be constructed as soon as possible. Its range should include not only developed countries or regions but also underdeveloped areas with a high risk of EIDs.

Establishing an effective global surveillance system to combat increasing biosecurity risks will promote a better understanding of emerging biosecurity risks at the global level and address challenges created by current surveillance strategies. In the effort to establish a well-integrated surveillance system for collecting, analyzing, and transforming various types of data from different partners, many practical challenges related to technology, politics, legislation, and ethics exist. Extensive and meaningful cooperation is needed to integrate the surveillance systems of various countries. An internationally united and well-integrated surveillance department should be established under the framework of the WHO for effective management, including information, techniques, expert, and resource sharing through coordinating participating countries. We can ensure global biosecurity only through effective cooperation in both biosurveillance

and continuous response.

## Search strategy and selection criteria

We performed a literature search of the electronic databases PubMed and Web of Science (1980–2021) using the following search terms: “surveillance,” “biosurveillance,” “surveillance system,” “biosafety,” “biosecurity,” “infectious disease,” “bioterrorism,” “biological accident,” “dual-use research,” “public health,” and “pathogen.” We also performed a literature search with publications from the WHO, Centre for Disease Control and Prevention, and reports from related governments and their authority websites. The search included literature published in English and Chinese.

**Compliance and ethics** *The author(s) declare that they have no conflict of interest.*

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## SUPPORTING INFORMATION

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