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In recent years, emerging infectious diseases (EIDs), such as Middle East Respiratory Syndrome (MERS), Ebola and Zika virus diseases, have indicated that infectious diseases pose a current and major global health threat to humanity. The rapid global movement of people and goods increases the hidden dangers and the potential spread of infectious diseases across international borders. EIDs that occur in one part of the world may be found in other places within a short period of time. In 2015, for instance, MERS was imported into South Korea by an infected traveler, resulting in an increased number of MERS cases (186 cases total) and one exported case to China in only 2 months (Moran, 2015). Early detection and identification of abnormal increases in surveillance data are essential for the effective control of infectious disease outbreaks and subsequent spread of emerging or unexplained diseases.

The early warning of infectious diseases is to analyze surveillance data with specialized technologies for early detection and warning of notable aberrations. “Surveillance” and “early warning” are closely connected: the former provide the foundation for the latter, and the latter is an essential application of the former. In recent years, the rapid development of epidemiology, bioinformatics, computer science, measurement and statistics, systems engineering, environmental science, geography, medicine, veterinary science, artificial intelligence, and other surveillance-related interdisciplinary theories and technologies have boosted the rapid development of surveillance and early warning technologies with an increasingly important role in controlling infectious diseases.

1.1 BASIC TERMINOLOGIES: SURVEILLANCE, EARLY WARNING, AND PREDICTION

Disease surveillance often refers to the continuous, systematic collection, analysis, and interpretation of disease outbreaks and their related factors and to the use of such findings in guiding disease control practice. Infectious disease
surveillance is often the earliest and most commonly used field. The most basic applications of surveillance include describing the magnitude and patterns of infectious diseases, predicting epidemic trends, early detecting outbreaks, and discovering EIDs. Surveillance data can be directly applied to formulating, implementing and evaluating infectious disease control programs to help decision makers rationally plan and allocate resources and to inform public health education (Wagner et al., 2006).

Infectious disease early warning sends out signals related to an outbreak of infectious disease(s), before or at the early stage of the event(s) in order to warn people of the potential public health risks, and scope or extent of its occurrence. Different terms are used in the documentation to describe infectious diseases warning, and among the most commonly used are “early warning” and “outbreak detection,” and the term “detection of aberration” refers to infectious disease early warning based on quantitative data analysis. Early warning generally analyzes surveillance information, giving out timely warnings on any signs or abnormalities in line with laws, regulations, and relevant provisions of the emergency plan, allowing for the facilitation and ease of making appropriate and corresponding recommendations.

Early warning system for infectious disease is an essential component of public health emergency work and has four characteristics:

1. Surveillance information-based: Scientific early warning must be based on timely and accurate surveillance data. Information on the occurrence and influencing factors of infectious diseases can be collected via several effective and sensitive surveillance systems and channels and analyzed to reveal the occurrence and development of infectious diseases for timely detection of “abnormal increase” of the incidence, so as to warn relevant responsible departments, institutions, and population that may be affected by the diseases.

2. Timeliness: It is essential for infectious disease early warning to be timely in its detection and warning during the early stages of outbreaks. During the course of the outbreak, the negative impact caused by infectious diseases rapidly increase over time. As shown in Fig. 1.1, when people in the community are infected with the Ebola virus, cases will increase rapidly without timely detection or measures to control the epidemic (WHO, 2016). Early warning provides an opportunity to implement response measures early that may otherwise be missed. For a specific early warning system, timeliness is represented by the lag time between the onset of the outbreak and when the outbreak is actually detected by the early warning system. Therefore, enhancing timeliness means reducing the lag time, either by using different types of data, improving the collection of surveillance data, or by adopting optimized early warning algorithms.

3. Information for action: The aim of early warning is to provide evidence-based guidance resulting in an informed and targeted response for the purpose of controlling the outbreaks, or at the very least, ensuring they are reduced to a minimum. Therefore, early warning and response are closely linked, hence the so-called “information for action.” The Early
Warning and Response System, or EWARS is advocated by the World Health Organization (WHO) and concretely embodies this approach.

(4) Information inadequacy: In the early stages of infectious disease outbreaks, information is extremely limited and the allotted time to make response decisions is very short. Similarly, it is quite difficult to identify causes rapidly for the outbreaks as the lack of information on fluctuations in infectious disease incidence or small changes to pathogens and epidemiological factors, as well as evidence of dose-response relationships is initially sparse during the acute phase of any disease event. Despite the inadequacy of information and the uncertainty of the hazard in question, early warning should still be exercised in places where measures need to be taken.

Prediction is a notion closely related to early warning. It is characterized by speculation and the description of uncertain events in the future. Furthermore, it is an analysis and estimation of the future development trends of objective things as well as the various consequences of human activity. Prediction explores the trends and changes of objective reality for the purpose of circumventing, avoiding, or changing the expected results. Conceptually, prediction has basically the same meaning as the word “forecast,” but the latter stresses the expressed publication of various predictions.

Infectious disease predictions are most often used to estimate the level and trends of future epidemics based on existing information closely related to infectious diseases, such as routine surveillance data, pathogenic factors, host information and environmental data, etc. The trends and scale of future incidences are then depicted by using a certain forecasting model in the context of a simulation analysis. According to the predicted time frame, predictions can yield long- (5–10 years), medium- (3–4 years), and short-term (0.5–2 years) projections. The predicted information is frequently used to prepare long- and short-term plans for preventing and controlling infectious diseases.
Different from prediction, infectious disease early warning is not only detection of signals, but include decision making, information dissemination, and verification/response capacity. The most common approach of early warning is disseminating alerts when the number of reported cases or morbidity levels is above that of the historic average; indicating the potentiality of an outbreak which necessitates that certain response measures be taken (Fig. 1.2).

The concepts of early warning and prediction are interconnected and different because both serve to describe future events and inform decisions about future outbreaks control based on existing facts (such as surveillance data). To some extent, early warning can be seen as special types of prediction, or a special application of prediction technology. Nevertheless, these two concepts vary greatly in their use:

1. Early warning emphasizes detecting possible or ongoing events and issuing of warning messages, whereas prediction describes events that have yet to occur.
2. Early warning makes a judgment regarding a specific event, whereas prediction focuses on estimating and measuring short-, medium- and long-term trends, rather than a particular event.
3. The results from early warning are used to guide timely responses to possible or ongoing outbreaks. In contrast, prediction results are used to develop infectious disease control plans or programs.
4. For methods, early warning is based on easily available and limited information (such as infectious disease surveillance data). It uses simple and rapid analysis methods that lead to qualitative results. In contrast, more extensive information can be used to build more complex forecasting models, such as a time-series, infectious disease dynamic, discriminative, and regression analyses. Prediction results can be presented qualitatively but are usually expressed quantitatively.

### 1.2 A CONCEPTUAL FRAMEWORK FOR EARLY WARNING

An efficient and functional early warning system includes five basic elements (Fig. 1.3): (1) setting of early warning targets, (2) data collection, (3) data analysis, (4) early warning information dissemination, and (5) response action, which also reflect the operational steps for early warning. These targets determine the specific needs of the early warning system and the system’s function,
performance, structural characteristics, and data collection methods. The data that are necessary for early warning are the surveillance data that are collected according to the system requirements, which form a basis for operating the early warning model. Early warning signals are generated after carefully analyzing and calculating the collected data via appropriate methods, which are disseminated in line with early warning information delivery strategies, before suitable response actions are implemented. In a complete process of early warning operation, the system needs to be monitored and evaluated, ensuring that all its elements are adjusted in accordance with the feedback/data gathered, making certain that the early warning system is in good working condition.

1.3 SETTING OF EARLY WARNING TARGETS

As early warning and follow-up actions inevitably involve the use of resources, the consumption of manpower, materials and time, some response actions may have a great impact on society and the public, so the determination of early warning targets is crucial. In principle, some infectious diseases are taken as priority warning targets given limited social resources; diseases which may result in more serious outcomes and have the potential to spread rapidly, inciting grave and immense socioeconomic consequences, if not handled in a timely manner.

The Global Outbreak Alert and Response Network (GOARN) advocated by WHO gives top priority to highly pathogenic diseases with increased potential for international spread, having the ability to severely impact the global economy and international trade. One such example is poliomyelitis, caused by wild strains; human influenza caused by new subtypes; SARS, cholera, pneumonic

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**FIG. 1.3**

Conceptual framework for an early warning system.
plague and yellow fever, and EIDs (such as Ebola hemorrhagic fever, Lassa fever, Marburg fever, and West Nile virus infections).

The target diseases for early warning in the Pacific Public Health Surveillance Network, or PACNET, which was jointly established by WHO and the South Pacific Commission (SPC), focuses on dengue, measles, rubella, influenza, leptospirosis, typhoid fever, cholera, and HIV/STIs, whereas FluNet, which was co-founded by the WHO and the Institut National de la Santé et de la Recherche Médicale (INSERM), is an infectious disease early warning system of focused primarily on detecting influenza, a disease that has extreme pandemic potential.

Established in 2008, the China Infectious Diseases Automated-alert and Response System (CIDARS; Yang et al., 2011a,b) includes notifiable infectious diseases that are common, severe in impact, or already eliminated or close to elimination, such as plague, cholera, polio, measles, and hand, foot, and mouth disease, given the infectious disease situation in China and the need to prevent infectious diseases (see Chapter 7).

1.4 EARLY WARNING DATA COLLECTION

As a basis of early warning, high-quality sources of existing data are a must. However, even in a time where information is so readily accessible, it is still very difficult to obtain high-quality data. Despite the large variety of data, only a selected few can actually be used in decision making or for the purposes of technical/scientific guidance. As is often the case, the data required is either unavailable, expensive, or necessitates a lot of time to obtain. It is far from an easy task to timely collect data needed for early warning.

What kind of data can be selected for the early warning of outbreaks? In principle, the first consideration is availability, such as data collected from existing surveillance systems. The second consideration is timeliness, meaning, how much of an advance warning is needed in order to take appropriate action. The value of early warning is considerably reduced if one cannot access real-time data. Third, multisource or open-source data, as data from varied sources reflects the event from different perspectives. Comprehensive analysis of this type of data may significantly enhance the sensitivity of the early warning system.

Most of the current early warning systems in the world rely on infectious disease surveillance systems based on cases, events, and/or symptoms/syndromes, etc. The reports, especially those on pathogens and susceptible populations, from the laboratory are also important. Data from other sectors also have some non-negligible contributions for early warning of infectious diseases. For instance, abnormal weather and disaster information may indicate the outbreak of respiratory and intestinal infectious diseases. In addition, further attention should be paid to the news from TV, radio, the Internet, newspapers, and other media/information sources. Public rumors also need to be taken seriously.
1.5 EARLY WARNING DATA ANALYSIS

The data are collected, analyzed, and processed for the early identification of ongoing health threats that may occur. A complete early warning data analysis contains three basic steps: (1) building an early warning model, (2) setting the threshold, and (3) generating early warning signals. The model of early warning is closely connected with the setting of the threshold. For some types of threshold, such as using the fixed value of the number of cases as the threshold value, there is no need to build a complicated model. However, a model is needed when relative values or statistical values are used as thresholds. The choice of types and values of thresholds is subject to early warning strategies and resources.

The types of early warning thresholds commonly used are described as follows:

1. Absolute thresholds: the number of cases or incidence rate of diseases is used. For example, an alert is generated when there is a report of one suspected/probable/confirmed case of a plague or SARS, or a signal is detected once the weekly morbidity of measles exceeds two cases per 1,000,000 persons in a county.

2. Relative thresholds: According to historical data, when the observed indicators deviate from the historical time series, e.g., early warning signals will be produced when the ratio exceeds 0.85 by comparing the averages for the past 4-weeks to the averages for the same 4-week period from the past 3 years, or an increase of two standard deviations from the baseline.

Early warning signals are produced when the observed indicators (such as the incidence or morbidity) in the early warning model exceeds the threshold values. Thus, the early warning signals that are generated will first be verified for reliability and authenticity. The alert will then be evaluated and interpreted prior to dissemination (Fig. 1.4).

1.6 EARLY WARNING INFORMATION DELIVERY AND DISSEMINATION

The delivery of information constitutes an indispensable part of the early warning system. Only when an early warning signal is delivered to relevant institutions and personnel will it guide the required response actions.

Persons and units responsible for taking action against infectious diseases such as CDC staff, are the first target audience for early warning information. For serious infectious diseases, early warning information will also be delivered to higher level public health departments and specialists in neighboring areas that may be affected by the disease.

It is crucial to prepare and send alerts to the media and/or the public. Public health messaging and recommendations should be clear and easy to understand,
so as not to cause unnecessary social panic. In most cases, it is not necessary to release early warning information to the media or the public, except when (1) the information originates from media reports, or from public rumors, and is confirmed to be true; and (2) the target event is very serious and will involve social mobilization. There are several ways to release early warning information using some mechanisms include the news, reports, announcements, or modern technologies, e.g., fax, phone, mobile phone text messages, emails, and Internet bulletins.

### 1.7 EARLY WARNING RESPONSES

After receiving early warning signals, health departments or CDCs must take action and respond in order to prevent and control the outbreak(s) including field investigations, risk assessments, and public health control measures.

Disease prevention and control institutions dispatch specialists to conduct field investigations and conduct active data collection. In an early warning system, it is important conduct an epidemiological investigation to determine the presence of spatiotemporal clusters of cases that may provide evidence that confirms an outbreak and its evolution/progress. As part of the field investigation, and initial risk assessments should be conducted to analyze the features of the event that are consistent with existing data and information from other sources. This helps in assessing possible the threats, the population and the areas at risk, as well as its potential impact on society and the economy.
Although the most targeted measures are based on a full understanding of the features of infectious disease outbreak(s), this does not imply that prevention and control measures will only occur at the end of a field investigation. In contrast, control measures must occur in a timely manner. Once an event is identified as an infectious disease outbreak or epidemic, emergency measures should be rapidly deployed based on the available information and immediately implemented. As the field/outbreak investigation continues to evolve and the findings/evidence integrated, response measures should be adjusted and improved to reflect the updated findings as this will result in more effective epidemic control and prevention; imparting a better understanding of the nature, scale, trend, and causes of the outbreak, as well as the route of transmission.

1.8 EVALUATING EARLY WARNING SYSTEMS

Evaluation has a special role in the entire process of the infectious disease early warning system. For a newly established system, evaluation can determine whether the system has achieved its objectives, identify the problems with the core components of the system, and examine the system operations. For an existing early warning system, the evaluation results can support adjustments, improvements, and adaptations to the changing application environments and demands. In addition to its regular tasks, infectious disease early warning requires scientific research on problems that arise from developing early warning theory and technology, and evaluation is often used as a tool in such evidence-based research.

Early warning system evaluations often review the status of the entire system, but when necessary, it can focus on one or several components within the system, such as the early warning model, data quality, the hardware platform, and management processes. In general, the most important evaluations are implemented at two levels: the model or algorithm and the system. The former is concerned with the performance of the model and the evaluation results are used to optimize models, algorithms and parameters, and define influential factors. For additional information, please refer to Chapter 3. Evaluating the latter examines the overall operational characteristics of the system, which includes early warning functions, platforms, response capabilities and system benefits. The results are used to guide adjustments and improvements in early warning systems. For additional information, please refer to Chapter 6.

1.9 EARLY WARNING CLASSIFICATION

Currently, there is no consensus for systematically classifying early warnings. Some researchers divide these into early warning analysis and early warning monitoring. Early warning analysis refers to management activities that practice surveillance as well as identify, diagnose, and evaluate early warning targets for the purpose of delivering signals in a timely manner. Early warning monitoring
refers to the management activities that correct, prevent, and control adverse
trends of disaster indications based on the results from early warning analyses.

Researchers have also classified early warning into direct/indirect early warning,
qualitative/quantitative early warning, and long-term/short-term early warning
according to the methods employed. Direct early warning is the direct reporting
of acute infectious diseases or, e.g., easily transmitted diseases, unexplained dis-
eases, or severe food poisoning. Qualitative early warning is using comprehen-
sive predictions, control charts, likelihood estimations, Bayesian probabilities,
stepwise discriminant analysis and other statistical methods, and with the help
of the computer, to complete qualitative estimates of the trends and strength of
the disease, identifying whether the trends/strength is upward or downward, epide-
mic, or transmitted. Quantitative early warning refers to the use of univariate
or multivariable regression models to establish early warning equation or the use
of traditional or modern time series or spatiotemporal analyses to provide quan-
titative early warnings of diseases. Long-term warning uses expert advice for the
early warning of long-term disease trends.

Both classification methods that are discussed above have some scientific, sys-
tematic, and logical limitations. Classification that is based on the surveillance
type would be more reasonable. The world’s current infectious disease warning
systems are all based on surveillance information: several developed from origi-
nal infectious disease surveillance systems, whereas others were an inherent
part of the surveillance system, or the so-called “surveillance/early warning
and response system.” According to the differences in the surveillance system,
early warning can be divided into four types: case-based, incident-based,
and lab-based. However, this classification is rudimentary, as most early
warning systems use multiple methods; i.e., they may be case-, incident-, and
laboratory-based at the same time.

1.10 CASE-BASED EARLY WARNING

Most countries have established their own infectious disease reporting systems,
and cases that are reported via routine notifiable infectious disease surveillance
provide favorable conditions for implementing early warnings for infectious dis-
eases. CIDARS was constructed by the Chinese Center for Disease Control and
Prevention (China CDC) in 2008 and is based on a conventional infectious dis-
 ease surveillance and reporting system. Advantages of a case-based early warning
system are as follows:

(1) It is available to simultaneously detect several infectious diseases, as long
as the infectious diseases are included in the reporting system.

(2) Because most infectious disease reporting systems encompass the entire
nation, it is easy to establish national early warning systems.

(3) The high requirements for early warning and effectively applying the sur-
veillance data promote improvements in surveillance.
The high-quality requirements for case surveillance data are determined by the specificity of early warning. Regular case-based surveillance systems cannot be used for early warnings of outbreaks early warning unless they meet the following conditions:

1. Real-time reporting of surveillance cases once they are diagnosed. Weekly or monthly reports may not adhere to the time demands of the early warning system.
2. Real-time delivery of data, i.e., to send the reported cases for the early warning analysis in a timely manner. Therefore, it is difficult to use data from a surveillance system without access to the Internet.
3. High data reliability. A surveillance system that has a high proportion of omission and misinformation will directly affect the performance of the early warning system.
4. Accumulating historical surveillance data is not a requirement because it depends on the early warning model. However, for some common infectious diseases, the algorithm is usually based on comparing the current incidence with historical levels; thus, it is necessary to have historically accumulated data.

### 1.11 EVENT-BASED EARLY WARNING

Event-based surveillance and early warning is achieved by surveilling several targeted public health events. It focuses on signs of the occurrence of outbreak(s), rather than on specific diseases, so it is also referred to as an early warning of signals of events. In implementation, the types of events are first defined, specifically, the outbreaks that will be included in the scope of surveillance. Next, it clearly defines and describes each public health event. Early warning information will be generated after verifying and analyzing each event that occurs. Common surveillance events in early warning include the following:

1. Clustering: There is the possibility for disease (including infectious disease) outbreaks when several cases that have similar clinical manifestations or unexplained deaths occur suddenly and simultaneously in a particular population (for example, a village, school, or unit) in a short period of time.
2. Similar events: When poisoning, outbreaks of infectious diseases and other public health emergencies occur in a population, community or area, early warning signals are sent to units or areas potentially affected by similar events. For instance, when poisoning events are caused by water pollution, early warning is transmitted to downstream users and regions quickly; in case of rapidly spreading infectious diseases, such as influenza and meningitis, neighboring areas are warned immediately; in cases of food poisoning/toxicity, early warning is sent to areas where food that is found to be toxic and may be consumed.
3. Climate anomalies: Large changes in temperature, air humidity, the amount of sunlight, rainfall and other climate conditions can influence
infectious pathogens, vectors, the distribution and density of host animals, and human. They create conditions for infectious disease outbreaks and can be used as signs of potential outbreaks.

(4) Disaster events: Besides their devastating impact, natural disasters such as earthquakes, tsunamis, and floods, can easily lead to deterioration and a public health crisis, as well as outbreaks of acute infectious diseases. Therefore, disaster events are often used as a warning sign for infectious diseases.

(5) Pollution: Pathogenic microbial contaminations of food and drinking water due to natural or man-made disasters are common causes of infectious diseases outbreaks.

(6) Vectors and host animals: Changes in the number of biological vectors and host animals can directly affect the transmission of natural foci and vector-borne diseases. Significant increases in the biological density of host animal and vectors, or severe abnormal deaths of host animals indicate potential outbreaks of related infectious diseases.

1.12 LAB-BASED EARLY WARNING

Complete and efficient laboratory surveillance can identify sporadic cases that appear to be unrelated at first glance, and when these sporadic cases can be intrinsically related (identical genetic fingerprints) to a pathogen, there is a common source of infection, which is often an early sign of an infectious disease outbreak. When there is an epidemiological investigation in a timely manner, the source of the infection can be tracked and controlled, and the epidemic will be quickly contained. The foundation of an effective laboratory surveillance network that is based on standardized molecular biology typing and technology as well as the sharing information and resources across regions actively supports the early warning of outbreaks. Specifically, they have an irreplaceable role in the early warning of infectious diseases with extensive coverage, long duration, and complex suspicious factors.

Establishing laboratory surveillance networks allows for the sharing of surveillance and classification results in different areas. Comparing data in these areas facilitates the effective tracking of pathogenic microorganisms. It can also contribute to understanding the epidemiological features and early detection of public health emergencies.

Laboratory surveillance is a very important component of the global epidemic outbreak surveillance and early warning network and of early warning networks for infectious diseases that are established in some countries. Laboratory surveillance allows the monitoring of pathogens, vectors, reservoir hosts, and human immunity and provides strong evidence for the early detection of infectious disease outbreaks. Moreover, it facilitates verifying the outbreaks, tracking the sources of infection, and identifying the paths of transmission. The current early warning laboratory surveillance includes the following:
Pathogen monitoring: including antigenic changes in pathogens, virulence, or resistance that suggests an outbreak or an increased risk of infectious diseases. To improve global surveillance and early warning capabilities for avian influenza, WHO strengthens laboratory surveillance and attaches great importance to the prevalence of H5N1 strains that are based on the FluNet because the early symptoms observed in human beings who are infected with H5N1 are similar to those of general respiratory tract infections; thus, syndromic surveillance alone is not conducive to the early detection of H5N1.

Host animal surveillance: Attention is given to the host animal to identify whether there is any increase in carried pathogens or rare pathogenic microorganisms.

Susceptibility surveillance: According to the dynamics of infectious diseases, outbreaks of specific diseases are closely related to susceptibility in the human population. Therefore, periodic surveillance of antibody levels in high risk populations can reflect level of susceptibility. Generally, low immunization may suggest the increased of risk of outbreaks.

It is important to note that laboratory-based surveillance is frequently part of early warning systems. Given the costly, time-consuming, and technically demanding laboratory tests, it is often challenging to meet the requirement of timeliness by solely relying on laboratory surveillance for early warning.

**1.13 SYNDROMIC SURVEILLANCE-BASED EARLY WARNING**

Syndromic surveillance is designed to detect disease outbreaks via early signs. It provides an opportunity to take timely measures to control disease outbreaks before a confirmed case is reported to the public health agency. This surveillance has basic characteristics of the early warning system.

The advantage of syndromic surveillance is in its early detection of abnormalities, which meets the demand for timeliness. In addition to collecting medical records on the syndrome, it comprehensively uses other sources of information, such as drug sales, laboratory tests, medical examinations, ambulance response records, school or factory absences, and other symptoms and signs in emergency rescue. Early warning is based on comprehensive analysis and decisions; therefore, well-designed syndromic surveillance will perform well for early warning.

Syndromic surveillance is a new monitoring method, and its theory and technology are still in development. Given the high cost of data collection and the difficulty of data analysis and processing, it is difficult to conduct syndromic surveillance in areas where health information systems are underresourced or underdeveloped. Currently, syndromic surveillance is primarily used for the early warning of key infectious diseases in cities that have sound health information systems (Ye et al., 2011).
Influenza-like illness surveillance on a global scale is a typical syndromic surveillance system. The surveillance system monitors common and nonspecific influenza-like cases, and indicates the onset of the influenza epidemic season based on whether the incidence of symptomatic cases that exceeds the established baseline. It focuses on changes in epidemic patterns rather than confirmed individual influenza cases. Syndromic surveillance-based early warning monitors and reports infectious disease-related symptoms, producing alerts when abnormal changes spatiotemporally occur for certain symptoms.

The main target of syndromic surveillance early warning is to provide warning signals during the early stages of the epidemic. The syndromic surveillance system in the United States was enhanced after the 9/11 terrorist attacks and played an important role in the monitoring and early warning of anthrax “white powder” bioterrorism and SARS cases. Defining the target symptoms is key to syndromic surveillance, and a stronger correlation between the monitored symptoms and the indicated target disease leads to a better performance of early warning systems.

1.14 STATUS QUO AND SURVEILLANCE AND EARLY WARNING TRENDS FOR INFECTIOUS DISEASES

1.14.1 History of Infectious Disease Early Warning

Modern infectious disease early warning technology benefits from the disease surveillance and statistical methods that rapidly developed in the mid-20th century, which had extensive applications in several fields. After prediction theory was introduced to the medical field, it has been highly valued by medical workers, especially for its methods and applications for controlling infectious diseases. Since the 1980s, global outbreaks and pandemics of infectious diseases have been caused by poverty, war, population movement, global trade and tourism, antibiotic abuse, and bioterrorism. To minimize the losses caused by infectious diseases, it is essential to detect abnormal epidemics and respond with appropriate measures. Based on the rapid development of infectious disease prediction technology, adding anomalies analysis to surveillance system could be conducive for the early detection of changes in diseases.

The perspective of early warning indicated a significant change in public health surveillance systems, but it was only referred to as “early detection” because there was no real early warning theory at that time. In Apr. 1990, the US CDC constructed a “Current/Past Experience Graph” module in the national notifiable infectious disease surveillance system that used a historical limit chart as a statistical method. Using the infectious disease surveillance report as the data source, it analyzed 14 infectious diseases, including measles, rubella and hepatitis A, and presented detected anomalies in the Morbidity and Mortality Weekly Report (MMWR). Subsequently, France, Australia, Japan, Canada, and several other countries performed infectious diseases early warning research, and proposed several methods and techniques.
In the mid- and late-1990s, some countries began to incorporate laboratory, meteorological and environmental data and spatial information into the early warning database, which further improved the early warning system for infectious diseases and enhanced the ability to cope with infectious diseases emergencies. Several types of early warning systems have emerged to prevent EIDs and bioterrorism.

For example, GOARN was formally established by the WHO in 2000 as an effort to strengthen international cooperation. This network can link multiple existing networks, when necessary, to combine technical and operational resources from research institutions in its member states, medical and surveillance operations, regional technical networks, laboratory networks, UN organizations, the Red Cross, and international humanitarian nongovernmental organizations. Its mandate is to foster effective collaboration and cooperation in the gathering of data, experience and technologies for the quick identification, confirmation and response to major international outbreaks. It ensures that the international community remains vigilant against the threat of disease outbreaks and is prepared to respond.

The Global Public Health Intelligence Network (GPHIN) was founded in 1997 by the WHO and the Ministry of Health of Canada and uses the Internet to address disease outbreaks, infectious diseases, food and water pollution, bioterrorism, chemical leaks, natural hazards and product safety, pharmaceuticals, medical equipment, radioactive materials and other potential sources of global public health threats, and to perform necessary and reliable “early forecast and early warnings.”

BioSense is an information platform for the National Syndromic Surveillance Program (NSSP) of the US CDC (2017). It was designed to provide surveillance information that is obtained from unified and broadly applicable health surveillance methods for all levels of public health to detect diseases and related health problems early with a timely assessment and response. BioSense uses many forms of surveillance information, including complaints, symptoms and laboratory tests that are required for clinical diagnoses. Focusing on clinical symptoms and symptoms of diagnosed or undiagnosed cases, it reflects syndrome surveillance and constitutes, together with BioWatch and NBIS, the three core biological surveillance programs. BioSense is an international, multijurisdictional, information-sharing surveillance platform that applies to all levels of the public health sector. At the same time, given its use of standardized data elements and analytical methods, BioSense analysts can compare the public health status in different countries or regions in the same country. BioSense can visualize time, space, people and other information via maps, charts, tables and other forms, and the information that it presents can indicate data anomalies. When receiving a prompt, users can confirm the anomalies with related information and may provide an early warning of health problems. Since its development in 2003, BioSense has been greatly improved and developed to meet changing demands and user feedback, and its sources of information have expanded to the US Department
of Veterans Affairs, health-related information from the US DOD and treatment information for all citizens. It is jointly maintained and managed by the national CDC, state and district health departments, and other departments that apply this system.

With the support of the Federation of American Scientists (FAS), in Aug. 1994, infectious diseases experts from the International Society of Infectious Diseases (ISID) founded ProMED-mail, which is an Internet-based reporting system that is dedicated to rapid global dissemination of information on outbreaks of infectious diseases and acute exposure to toxins that affect human health, including those in animals and in plants grown for food and animal feed. Electronic communications allow ProMED to provide up-to-date and reliable news about threats to human, animal, and food plant health around the world, 7 days a week. By providing early warning of outbreaks for emerging and re-emerging diseases, public health precautions can be implemented at all levels in a timely manner to prevent epidemic transmission and save lives. ProMED is open to all sources and is free from political constraints. Sources of information include media reports, official reports, online summaries, local observers, and others. Reports are often contributed by ProMED subscribers. A team of expert human, plant, and animal disease moderators screens, reviews, and investigates reports before posting them to the network. Reports are distributed by email to direct subscribers and are immediately available on the ProMED web site. ProMED has reached over 70,000 subscribers in at least 185 countries.

In addition, the United States, Canada, and Mexico jointly established Early Warning Infectious Disease Surveillance in response to terrorist attacks. Since 2000, the WHO has helped Sudan, Iraq, Serbia, Morocco, Macedonia, and other countries establish early warning systems for infectious diseases and explored the possibilities, difficulties and problems that occur when constructing early warning systems for infectious diseases in developing countries.

Currently, the early warning system of infectious diseases is primarily based in developed countries. Many developing countries have not yet started to build these systems due to economic and technical constraints. Given the precautionary role of early warning systems for preventing and controlling communicable diseases, specifically for EIDs and bioterrorist attacks, the IHR (2005) strongly recommends that countries, specifically developing countries, establish early warning systems for infectious diseases as soon as possible.

### 1.15 EARLY WARNING TECHNOLOGY AND SYSTEMS FOR INFECTIOUS DISEASES IN CHINA

As stipulated in Article 19 of the Law on the Prevention and Treatment of Infectious Diseases of the People’s Republic of China (2004), the state should establish an early warning system for infectious diseases. The Emergency Response Law of the People’s Republic of China (2007) has provisions for the early
warning of natural disasters, accidents and public health emergencies and interprets “early warning” as “to take measures beforehand on finding certain signs that may lead to unexpected events.”

In the 1950s, China established its notifiable infectious disease reporting system, which primarily used mail and telephone for reporting infectious diseases in the country. The data from diagnosed cases were reported by hospitals to the local CDCs at the county level in a prescribed time limit, and the aggregated counts of cases were reported monthly to CDCs at provincial and national levels. In 1990, China established the PHIS (Public Health Information System), which uses computer technology and epidemic prevention stations across all provinces and municipalities to complete infectious disease statements for their respective jurisdictions and report to higher authorities. In 2004, China established a national “Notifiable Infectious Disease Reporting Information System” (NIDRIS). This system allows for the direct reporting of individual case data to a national database that is located in China’s CDC, which decreases the time interval from diagnosis to report from 5 days to only 4 hours and significantly improves the timeliness and information about infectious diseases.

The infectious disease surveillance reports have accumulated abundant epidemiological information over time and provide data that are necessary to systematically analyze situations and trends of infectious diseases in China. Based on the infectious disease surveillance data, Chinese researchers have conducted a series of studies on infectious disease prediction and early warning. For example, a “gray dynamic model” was proposed by Feng et al. (2003) and a “Z-D Phenomenon” by Zeng et al. (1997) for predicting infectious diseases.

Beginning in 2002, Yang et al. (2004) engaged in the study of automated-alert response theory and technology, and initially started control charting techniques for seven infectious diseases that were simple to operate, extensively applied, and highly efficient for early warning. They selected the thresholds for seven infectious diseases and used the results to establish a national automated-alert response system.

Given its vast territory, varied natural environment and diverse socio-economic levels, the incidence of infectious diseases greatly varies in China, and there is a need for both a simple and practical early warning method and an operational system. Notifiable infectious disease reporting is a systematic and complete data resource for infectious diseases. In 2004, China officially launched an information platform to establish the NIDRIS, “Information System for Public Health Emergency Management” and “Management System for Single Disease Report,” which indicates that China’s infectious disease surveillance reporting research has embarked on electronic and network tracks. The system provides broad coverage in China for reporting notifiable diseases and includes all health institutes across the country, while routine supervision and evaluation are conducted by health authorities to assess the quality of the reports. NIDRIS has a good quality control process for improving timeliness and the completeness
of data and avoiding duplicative reporting. At the county level or higher, 98% of all hospitals could directly report data to the NIDRIS via the Internet, which includes 87% of the township hospitals. These direct network reports of infectious diseases have changed the previous monthly report into a daily report.

NIDRIS provides a large number of complete and reliable time series analyses for developing early warning methods. Since 2002, China’s CDC has adopted the Moving Percentile Method to establish an automated-alert response concept model and its thresholds for different infectious diseases, while evaluating their sensitivity, specificity and timeliness. In 2006 and 2007, there was a pilot of CIDARS, and it operated nationwide on Apr. 21, 2008. CIDARS is the first complete and practical early warning system for infectious diseases in China (Yang et al., 2011a,b).

The existing disease surveillance system contains some valuable spatial information about cases, which supports the study of spatial clustering early warning. Further studies are conducted to build models for detecting spatiotemporal clusters. In addition, by using infectious disease reports and from hospital out-patient information, some areas in China have increased their use of syndromic surveillance and early warning methods.

The performance of China’s early warning system based on infectious disease surveillance needs to be fully evaluated and validated, as it has continuously improved. The construction, composition, operation, and evaluation of early warning systems in other countries provide inspiration and reference for establishing infectious disease surveillance and an early warning system in China. Additionally, applying syndromic surveillance and early warning technology from American and European researchers provides evidence for China’s research and application of syndromic surveillance. The early warning systems that were in use during the 2008 Beijing Olympic Games and the 2010 Shanghai World Expo also act as a valuable technical reference for public health response and preparations for mass gatherings all over the world.

1.16 TRENDS IN EARLY WARNING TECHNOLOGY

The research on infectious disease early warning will continue to make progress in technology that detects spatiotemporal clustering, syndromic surveillance and early warning technology, the combined use of various early warning technologies, the development and utilization of multiple sources of data for infectious disease related risk factors, lab-based surveillance and early warning, the utilization of new media, and evaluating early warning methods.

(1) Technology for detecting spatiotemporal clustering for early warning: With the recent development of geographic information system (GIS) and computer technology, this field has developed rapidly and it will be widely used in the near future.

(2) Syndromic surveillance technology for early warning: More efficient surveillance and early warning systems are needed to "move the strategic
pass forward” to prevent and control infectious diseases. Different from traditional surveillance systems, syndromic surveillance systems are designed to identify signs of an outbreak before a doctor discovers and reports the first case. Such a system may be defined as “syndrome” or “pre-diagnosis” surveillance. Compared to data on definitive diagnoses, syndromic surveillance data (such as complaints from emergency department patients and sales of over-the-counter (OTC) drugs) has lower specificity and can only be analyzed and processed with specific early warning methods. When using all of the available information to enrich and develop low-dimensional data methods for early warning, research is needed on high-dimensional data methods for improving the sensitivity, specificity and timeliness of early warning.

(3) The combined use of multiple early warning technologies: Integrated prediction primarily refers to applying two or more prediction models, combining qualitative and quantitative predictions, and using spatial-temporal technologies for early warning.

(4) Developing and utilizing new surveillance resources for early warning: It is important to explore new and available surveillance data for early warning, such as data from hospital emergency departments, OTC, biological media, animal epidemics, environmental meteorology, and to identify better ways to collect information and promote data use through multifactor analyses.

(5) Early warning based on lab surveillance: The popularity and refinement of modern laboratory networks with molecular biology and bioinformatics will greatly enhance early identification of the intrinsic relations (e.g., gene fingerprints) among seemingly unrelated sporadic cases for early warning. It will substantially enhance the early identification of the epidemiological significance of pathogens, and provide strong evidence for the early warning of infectious disease outbreaks.

(6) Evaluating early warning methods: Evaluating early warning methodology is also very important in current early warning research. This primarily refers to studying evaluation standards for early warning methods, systems, and test data. Sensitivity and specificity are two important indicators of evaluation. Other common indicators include the positive predictive value, receiver operating characteristic curve, activity monitoring operating characteristic, and the probability for successful detection.

Chinese infectious disease early warning researchers will continue to summarize theories and the practical experiences of public health surveillance in China. Thus, to increase China’s surveillance and early warning of infectious diseases and share this information with the world, researchers will conduct in-depth research, fully utilize the latest achievements in modern computer, network, communications, and data analysis technologies, explore and develop more abundant infectious disease automated-alert response methods and information systems.
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