CHAPTER 7

China Infectious Diseases Automated-Alert and Response System (CIDARS)

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Notifiable disease reporting system constitutes an important source of data for gathering disease prevalence information and monitoring infectious disease outbreaks (Wang et al., 2008). Following the outbreak of severe acute respiratory syndrome in 2003, China has made milestone innovations on the reporting system of the notifiable infectious disease reporting system. It successfully launched a web-based Nationwide Notifiable Infectious Diseases Reporting Information System (NIDRIS) in 2004. NIDRIS enables health facilities to directly report real-time notifiable infectious disease cases to the national infectious disease surveillance central database via the Internet. This system involves health facilities at all administrative levels of China, and it covers 30 notifiable infectious diseases. In addition, NIDRIS has achieved the data collection of individual case, timely reporting, electronic data management and centralized storage of information, which lays the foundation for real-time analysis, processing of surveillance data, as well as early detection of infectious disease outbreaks by CDCs at various levels. The increasingly extensive application of the Internet, telecommunication, and computer technologies has also created the conditions for automatic analysis and utilization of infectious disease surveillance data. On such a basis, China CDC assembled a research team composed of experts specializing in infectious diseases, epidemiology, statistics, geography, and computer science to develop the nationwide China Infectious Diseases Automated-Alert and Response System (CIDARS). This chapter will describe the development history, design framework, targeted diseases and methodology, dissemination

and response of warning signals, alert effectiveness, major features, challenges, and the future directions of CIDARS.

7.1 HISTORY OF DEVELOPMENT

Since 2002, with the support from the National Social Welfare Research Program, China CDC, West China School of Public Health, Sichuan University, and several local CDCs have jointly established a research team which carried out proactive studies and practices in terms of early warning methodology and application. In six provinces of China, the monthly numbers of reported cases of seven infectious diseases (hemorrhagic fever with renal syndrome, hepatitis A, bacillary dysentery, Meningococcal Meningitis, malaria, measles, and pulmonary tuberculosis) were collated to develop early warning models with the definition of epidemic determined by epidemiologists. The metrics of sensitivity, specificity, and positive predictive values of different methods were compared with ROC curves, and the moving percentile method (MPM) and its parameters was optimized for detecting infectious disease outbreaks. In 2006, the research team developed and finalized the infectious diseases automated-alert information system, and formulated a standardized protocol of signal response (China CDC, 2008a).

In order to further verify and evaluate the effectiveness of early warning methods and protocol, a pilot of the automated alert system for major infectious diseases in 33 counties/districts in 10 provinces of China was launched from Aug. 2006 to Apr. 2008. Meanwhile, to explore the roles of an sophisticated spatial model in detecting infectious disease outbreaks, with the support of the State Council Emergency Management Office, Chinese Ministry of Health and the World Health Organization (WHO) in 2007, the research team, in cooperation with the Institute of Geographic Sciences and Natural Resources Research of Chinese Academy of Sciences, explored and established the spatial-temporal clustering detection and alert model (hereinafter referred to as the "spatial-temporal model") on the basis of temporal model by leveraging the spatial information of current residential addresses of the reported cases and the Spatial Scan Statistics method (Kulldorff, 1997). On Apr. 21, 2008, CDCs at county, city and provincial levels launched temporal model-based CIDARS, and the piloting of spatial-temporal model-based CIDARS was launched in 221 counties/districts in 20 provinces (China CDC, 2008b).

In 2009, when the influenza A (H1N1) pandemic was emerging, the novel infectious disease was incorporated into the early warning system, thus accomplished the automated detection and warning of influenza A (H1N1). In the same year, the research team optimized the technical road map and related parameters for spatial-temporal model, introducing the function of eliminating duplicated warning signals. At the beginning of 2010, in consideration of the hand, foot, and mouth disease (HFMD) epidemic and the need for ensuring health at Shanghai World Expo, the research team developed HFMD early warning method in CIDARS. In Dec. 2010, the research team again made substantial improvement to the temporal model of the alert system: implementing single case early warning for measles while aligning with the national measles elimination initiative, and modifying
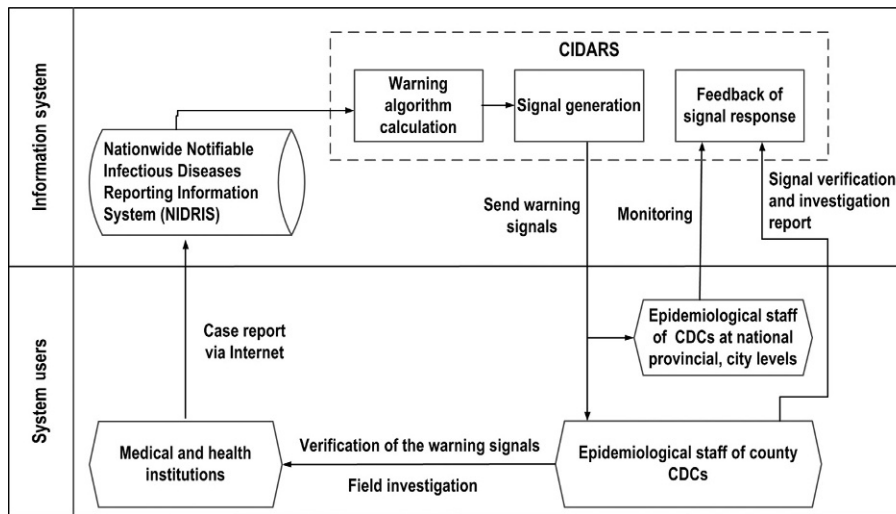
FIG. 7.1

The framework of China Infectious Diseases Automated-Alert and Response System (CIDARS).

the warning thresholds for certain diseases; meanwhile, different areas were allowed to flexibly determine warning thresholds appropriate for local situations, which further enhanced the ability of CIDARS in detecting outbreaks.

7.2 CIDARS DESIGN FRAMEWORK

Based on the Chinese Information Platform for Disease Control and Prevention, CIDARS has been designed as a uniform early warning tool that covers the whole country and multiple diseases to effectively assist CDCs for detecting infectious disease outbreaks as early as possible. The system constantly performs automatic analysis and calculation of nationwide notifiable infectious disease surveillance data by leveraging different early warning algorithms for different diseases, and timely sends signals on detected abnormal case increase or clustering to local county/district CDCs via short message service (SMS). Once the epidemiological surveillance staff at county/district CDC receive the SMS alert, they immediately have to verify or investigate the warning signal, and report the result in the system. Epidemiological surveillance staff at CDCs of prefectural, provincial and national levels can log in the system and view the results of warning signal investigation at any time (see Fig. 7.1).

7.3 TARGETED DISEASES AND METHODOLOGY FOR CIDARS

7.3.1 Targeted Diseases for Early Warning

Those infectious diseases with high burden, or highly concerned by the public and government of China, or require prompt response are incorporated into CIDARS. In addition, different areas can also incorporate additional diseases into CIDARS, in according to the local situations. In the initial phase of CIDARS,

Table 7.1	Early Warning Methods and Targeted Diseases for China Infectious Diseases Automated-Alert and Response System (CIDARS)
Methods	**Targeted diseases**
Fixed-threshold detection method	12 infectious diseases Plague, cholera, severe acute respiratory syndrome, polio, human infection with highly pathogenic avian influenza virus, pulmonary anthrax, diphtheria, filariasis, unexplained pneumonia, influenza A (H1N1), measles, hand, foot, and mouth disease (severe and death)
Temporal model (1) Moving percentile method (MPM)	18 infectious diseases Hepatitis A, hepatitis E, epidemic hemorrhagic fever, Japanese encephalitis, dengue, bacillary and amoebic dysentery, typhoid and paratyphoid, meningococcal meningitis, scarlet fever, leptospirosis, malaria, influenza, mumps, rubella, acute hemorrhagic conjunctivitis, epidemic and endemic typhus, and other infectious diarrhea
(2) Cumulative Sum Control Chart (CUSUM) method	Hand, foot, and mouth disease
Spatial-temporal model (MPM and spatial detection method)	17 infectious diseases Hepatitis A, hepatitis E, epidemic hemorrhagic fever, Japanese encephalitis, dengue, bacillary and amoebic dysentery, typhoid and paratyphoid, meningococcal meningitis, scarlet fever, leptospirosis, malaria, influenza, mumps, rubella, acute hemorrhagic conjunctivitis, epidemic and endemic typhus, and other infectious diarrhea

29 notifiable infectious diseases were included. In the subsequent operation, several diseases were removed or added according to the changes in the epidemic situations of infectious diseases in China and the needs of infectious disease prevention and control in certain areas. As of 2011, CIDARS covered a total of 30 notifiable infectious diseases (Table 7.1).

7.3.2 Early Warning Methods

By 2015, CIDARS has leveraged three early warning methods, namely, fixed-threshold detection method (FDM), temporal model, and spatial-temporal model. Among them, FDM and temporal model have been seen extensively applied throughout China, while spatial-temporal model is piloted in only 221 counties/districts.

FIXED-THRESHOLD DETECTION METHOD

FDM is primarily applicable to category A infectious diseases (as defined in the Chinese Law on Prevention and Control of Infectious Diseases), category B diseases that are managed as category A infectious diseases, rare diseases, or

diseases drawing strong concerns. When the number of reported cases reaches a fixed value, the system will generate warning signals. In CIDARS, the threshold defined for FDM is 1, i.e., early warning on single case. In CIDARS, this method is applied to 12 diseases, including plague, cholera, etc. (Table 7.1).

TEMPORAL MODEL

In CIDARS, methods the temporal models used include MPM and Cumulative Sum Control Chart (CUSUM) method. Specifically, MPM is applied to 17 infectious diseases including hepatitis A, rubella, etc., while CUSUM is applied to HFMD (see Table 7.1).

MOVING PERCENTILE METHOD

MPM is used to detect aberration of disease occurrence by comparing the reported cases in the current observation period to certain percentile in historical data. If the former is higher than the latter, a signal of aberration is indicated. In CIDARS, to account for the weekend effect and the stability of data, the most recent 7-day period is used as the current observation period and the previous 3 years as the historical period. The number of cases (C) in the current observation period is the sum of reported cases within the recent 7 days. The corresponding historical period included, for each of the previous 3 years, the same 7-day period, the two preceding 7-day periods and the two following 7-day periods that resulted in 15 historical 7-day data blocks (C_1–C_{15}) (Table 7.2). We set the percentile (P) of the 15 blocks of historical data as the warning threshold. If the number of cases in the current observation period exceeds the warning threshold ($C \geq P$), the system will generate a warning signal. The method is applied to calculation on a daily basis. The current observation period and historical data block are dynamically moved forward day by day, and the above calculation and determination are repeated.

	Table 7.2	**Baseline of Moving Percentile Method in China Infectious Diseases Automated-Alert and Response System (CIDARS)**			
Year	**Before current observation period (pre second 7 days)**	**Before current observation period (pre first 7 days)**	**Current observation period (recent 7 days)**	**After current observation period (post first 7 days)**	**After current observation period (post second 7 days)**
2008			C		
2007	C_1	C_2	C_3	C_4	C_5
2006	C_6	C_7	C_8	C_9	C_{10}
2005	C_{11}	C_{12}	C_{13}	C_{14}	C_{15}

Note: Assumes that the current year is 2008; C refers to the number of cases in the current observation period (last 7 days); C_1–C_{15} refer to the number of cases in the corresponding historical period for each of the previous 3 years, the same 7-day period, the two preceding 7-day periods and the two following 7-day periods.

To reduce duplicate signals, the calculation result of MPM must simultaneously meet two conditions for CIDARS to generate signal: (1) $C > 2$ cases (for Japanese Encephalitis and Meningococcal Meningitis) or $C > 3$ cases (for the other 15 diseases in CIDARS); and (2) C of the current date is larger than C of the previous date, or the percentile of C of the current date in the historical baseline is larger than that of the previous date.

In the initial phase of the system operation, the warning threshold for MPM was unanimously set to P_{50}, in order to raise the system sensitivity and maximize the early detection of all possible infectious disease outbreaks. In 2010, the research team thoroughly analyzed the actual operation and outcomes of CIDARS throughout China from Jul. 1, 2008 to Jun. 30, 2010, while outbreaks reported in the "public health emergency reporting and management system" were referred to as the reference standards for assessment, and the effectiveness of detection of MPM was assessed by using the indicators of sensitivity, rate of false warning and outbreak detection duration, etc. Based on results of the evaluation, the thresholds for diseases in CIDARS were changed as appropriate in Dec. 2010. Besides, and the various local regions were allowed to flexibly determine the warning thresholds for 13 diseases including infectious diarrhea, rubella, hepatitis A, etc. in the range of P_{50}–P_{80} according to their local situations. The changes made to the thresholds for MPM, can be found in Table 7.3.

Table 7.3	Thresholds Adjustments for MPM in Early Warning System	
Disease name	**Default threshold**	**Adjustable threshold range**
Other infectious diarrhea[a]	P_{80}	P_{60}–P_{80}
Mumps	P_{80}	P_{60}–P_{80}
Dysentery	P_{80}	P_{60}–P_{80}
Influenza	P_{80}	P_{60}–P_{80}
Scarflet fever	P_{80}	P_{60}–P_{80}
Typhoid and paratyphoid fever	P_{80}	P_{60}–P_{80}
Hepatitis E	P_{80}	P_{60}–P_{80}
Acute hemorrhagic conjunctivitis	P_{80}	P_{60}–P_{80}
Japanese encephalitis	P_{80}	P_{60}–P_{80}
Malaria	P_{80}	P_{60}–P_{80}
Epidemic hemorrhagic fever	P_{80}	P_{60}–P_{80}
Rubella	P_{80}	P_{50}–P_{80}
Hepatitis A	P_{70}	P_{60}–P_{70}
Typhus fever	P_{50}	P_{50}
Meningococcal meningitis	P_{50}	P_{50}
Leptospirosis	P_{50}	P_{50}
Dengue	P_{50}	P_{50}

[a]Other infectious diarrhea in addition to cholera, bacillary and amoebic dysentery, typhoid and paratyphoid.

CUSUM METHOD

MPM used by CIDARS needs to use 3-year historical data as the baseline, while HFMD was not incorporated as a notifiable infectious disease in China until May 2, 2008. By early 2010, the surveillance data has a history of merely 3 years, which is not adequate for detection by MPM. Therefore, another aberration detection method, EARS-3Cs, which does not rely on long-term baseline data, has been adopted. EARS-3Cs method is based on CUSUM formula and it calculates the expected value by date. According to the characteristics of HFMD incidence, CIDARS optimized the design of the method. Based on the method testing and effectiveness comparison of data on HFMD cases and incidents from May 2, 2008 to Mar. 20, 2010 in six provinces (Hebei, Liaoning, Guangdong, Shandong, Chongqing, and Gansu), EARS-C3 method (threshold value: 1.3) was selected for HFMD outbreaks early detection, and HFMD was officially incorporated into CIDARS in May 2010 throughout China.

Fig. 7.2 describes the early warning technical road map for the FDM and temporal model in CIDARS.

SPATIAL-TEMPORAL MODEL

Spatial-temporal model integrates MPM and spatial detection method. It first leverages MPM to detect abnormal changes in the current number of cases throughout the county/district over time, and then utilizes the spatial detection method to identify areas with possible clusters within the county/district. Among them, spatial detection model is built using spatial clustering detection method for infectious diseases, which is established on the basis of Kulldorff Spatial Scan Statistics. This method uses the area codes for the current residential addresses of the cases, and calculates the Spatial Scan Statistics for the search circle that covers
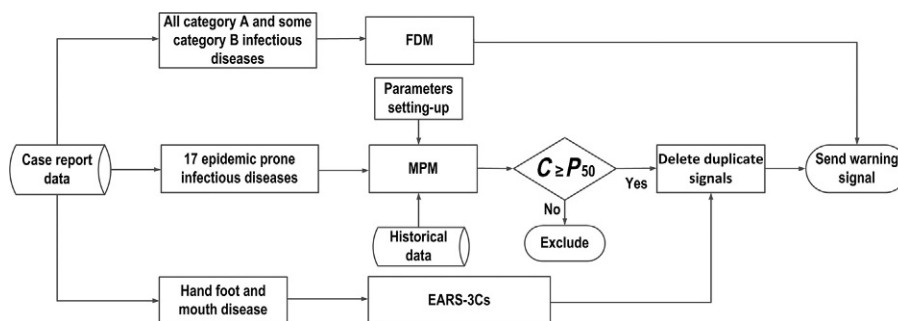
FIG. 7.2

The technical road map for the fixed-threshold detection method and temporal model in China Infectious Diseases Automated-Alert and Response System (CIDARS) (after Dec. 2010). *Note*: *C* denotes the number of cases in the current observation period; P_{50} is the 50th percentile of the historical data, the warning threshold for MPM, which can be according to Table 7.3; *FDM*, fixed-threshold detection method; *MPM*, moving percentile method.
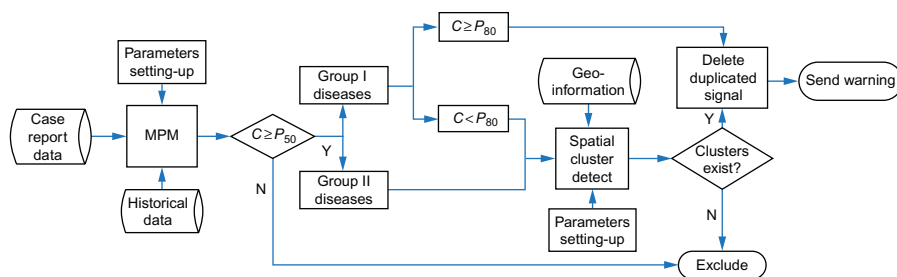
FIG. 7.3

The technical workflow for the spatial-temporal model in China Infectious Diseases Automated-Alert and Response System (CIDARS). *Note: C* denotes the number of cases in the current observation period; P_{50} is the 50th percentile of the historical data; P_{80} is the 80th percentile of the historical data; *MPM*, moving percentile method.

one or more towns/townships (maximum of six) in the individual county/district, while the search unit is town/township/sub district; Monte Carlo test method is used to screen case spatial clustering areas with statistical significance, and warning signal is sent to the county/district where the area is located. Spatial-temporal model groups 17 infectious diseases into two categories by the level of infectious disease morbidity, and performs calculations by using different technical road maps (Fig. 7.3): (1) category I diseases: infectious diseases with small number of cases and low morbidity, including seven infectious diseases, e.g., meningococcal meningitis, Japanese encephalitis, etc. For category I diseases, if $C \geq P_{80}$, warning signal will be generated directly; if $P_{50} \leq C < P_{80}$, spatial detection will be conducted and if there is spatial clustering, signal will be generated; (2) category II diseases: common infectious diseases with large number of cases and high morbidity, including 10 infectious diseases, e.g., hepatitis A, epidemic mumps, etc. For category II diseases, if $C \geq P_{50}$, spatial detection will be performed directly, and if there is spatial clustering, signal will be generated (Fig. 7.3).

The observation period and historical baseline for the spatial-temporal model are the same as the temporal model. There are two groups of parameter settings for warning thresholds: (1) temporal model only, using the 80th percentile as the warning threshold (P_{80}); (2) integration between temporal model and spatial clustering detection model; under P_{80}, the conditions for case spatial clustering should be met for the generation of signals. The specific parameters for spatial clustering detection model are as follows:

(1) Extension step length for spatial detection: 1/10 of the average distance to all townships/towns in the county/district;
(2) Extension ceiling for spatial detection: six townships/towns;
(3) Conditions for hotspot area screening: alert is generated if the number of cases throughout the county ≥ 10, and cases in the hotspot area ≥ 4, and cases in central townships/towns ≥ 3.

To avoid unnecessary duplicate signals generated by the early warning model for one particular aberration in the same area, signal to be generated by spatial-temporal model must conform to any of the following criteria:

(1) If there is no signal to be issued in the past 3 days, the current signal is issued;
(2) Signal is generated when $P_t \geq P_{t-1}$ and $C_t > C_{t-1} + C_0$ and $C_t > C_{t-2}$ and $C_t > C_{t-3}$;
(3) Signal is generated if $P_t < P_{80}$, and $H_t > H_{t-1}$ or $A_t > A_{t-1} + A_0$;
(4) Signal is generated if $C_{t-1} < C_{t-2} < C_{t-3}$, and $C_{t-3} - C_{t-2} > C_{t-1} - C_t$ and $B_{t-1} \geq \max(B_{t-8}, B_{t-2})$ and $B_{t-1} - B_{t-2} \geq 10$;
(5) If there was no warning signal issued in the past 6 days, the current warning signal is issued.

Where P is warning percentile, C is number of cases for warning; t is the date, H is the number of hotspot townships/towns, A is the number of cases in hotspot area, and B is the daily number of reported cases. C_0 is constant term— if $C_{t-1} < 30$ cases, then $C_0 = 1$; if $C_{t-1} \geq 30$ cases, then $C_0 = \text{INT}\left(\dfrac{C_{t-1}}{10} - 1\right)$, i.e., in the case of 30–39 cases, $C_0 = 2$; 40–49 cases, $C_0 = 3$; 50–59 cases, $C_0 = 4$; A_0 is the constant term—if $A_{t-1} < 30$ cases, then $A_0 = 1$; if $A_{t-1} \geq 30$ cases, then $A_0 = \text{INT}\left(\dfrac{A_{t-1}}{10} - 1\right)$, i.e., in the case of 30–39 cases, $A_0 = 2$; 40–49 cases, $A_0 = 3$; 50–59 cases, $A_0 = 4$.

7.4   DISSEMINATION OF EARLY WARNING SIGNALS

In order to timely, accurately disperse the signals generated by early warning model to the epidemiological surveillance staff at CDCs, CIDARS has developed a mobile phone SMS platform which maintains a list of mobile phone numbers of all epidemic staff at CDCs at national, provincial, city and county levels, and can automatically send signals to the specified mobile phones via SMS.

For the diseases for which FDM is applied, CIDARS performs real-time detection. Once any health facility reports a case, CIDARS can immediately recognize it and generate warning signal, which will be sent to staff at the local county CDC as well as staff at CDCs at national, provincial and city levels via SMS. For the diseases for which MPM or CUSUM method is applied, CIDARS performs model calculation on a 24-h basis, and automatically sends signals to local staff via SMS at 8:00 in the ensuing morning.

7.5   WARNING SIGNAL RESPONSE

The responses to signals are composed of two phases, which are signal initial verification and field investigation (Fig. 7.4).
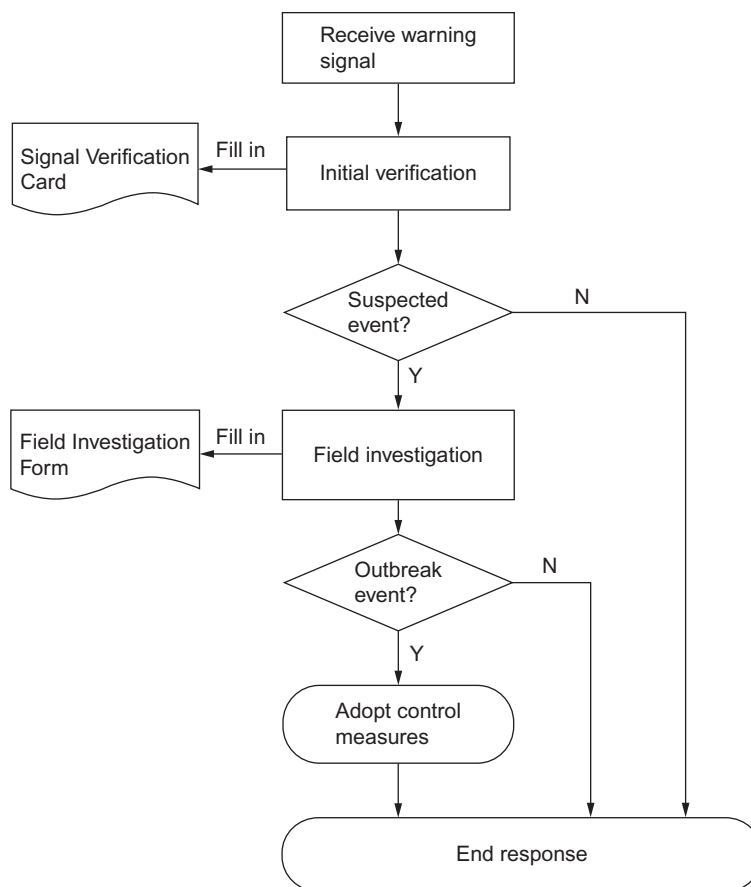
FIG. 7.4
The response process for warning signal of China Infectious Diseases Automated-Alert and Response System (CIDARS).

7.5.1 Signal Initial Verification

CDCs at the county level will be in charge of the initial verification of warning. Upon receipt of SMS warning signal, the local epidemiological surveillance staff will immediately perform initial verification of the signals, including logging onto the disease surveillance system to view the information of the cases, comparing against surveillance data from other sources, and verifying with the reporting agency or patients via phone calls, etc. The accuracy of the case information, the rationale for disease diagnosis, and the characteristics and development trend of case clustering, etc. will be verified. Signal which has been initially verified and has met any of the following criteria will be interpreted as suspected event (alert) that calls for field investigation: (1) possible spatial, temporal or population clustering of the cases covered by the signal; (2) the scope of disease incidence is expanding; (3) rare disease in the local area in the recent years; (4) disease subject to early warning by FDM.

Following signal initial verification, local epidemiological surveillance staff will log onto CIDARS and enter the basic results of signal verification on Signal Verification Card. CDCs at national, provincial and city levels can view the initial verification results for individual warning signals in CIDARS.

7.5.2 Field Investigation

When a warning signal is interpreted by the initial verification as a suspected event, the local CDCs at county level will rapidly launch field investigation. If the suspected event is confirmed as infectious disease outbreak, the health authority will carry out epidemic prevention and control as per the national and local emergency response protocol. If the possibility of outbreak is ruled out, the response to the warning signal will be concluded. Within 24 h after the completion of field investigation, investigators at CDCs at county level will log the basic investigation findings on CIDARS Field Investigation Form. According to the dynamics of the event, CDCs at county level will also fill in and update the form at any time.

7.6 FUNCTIONS FOR CIDARS MANAGEMENT

CIDARS offers a warning information management system that enables data processing and operation, warning signal generation and dissemination, signal response result feedback, signal query and sharing and other functions. Among these functions, data processing, early warning model operation and alert SMS sending are the background operations of the information system, which are invisible to the users; warning signal query, signal verification, investigation result reporting, and related statistical analysis functions are accessible to the users after they log onto the information system (for the system interface, see Fig. 7.5). The functions accessible to users are described in the following section.

7.6.1 Warning Signal Viewing

INFORMATION LISTING AND QUERY

System users can browse the list of issued warning signals on the target diseases in local area, including signal codes, areas involved, target diseases for early warning, number of cases involved, time of signal issued, percentile of historical data in the same period, number of cases in the spatial hotspot area, and number of townships/towns in the spatial hotspot area, etc.

TIME SERIES PLOT

The system can show the cumulative number of cases reported in the current observation period, and the 50th, 60th, 70th, 80th, and 90th percentiles of the historical data in the same period, in order to help public health workers determine the latest morbidity trend and the extent of exceeding historical percentiles (Fig. 7.6).
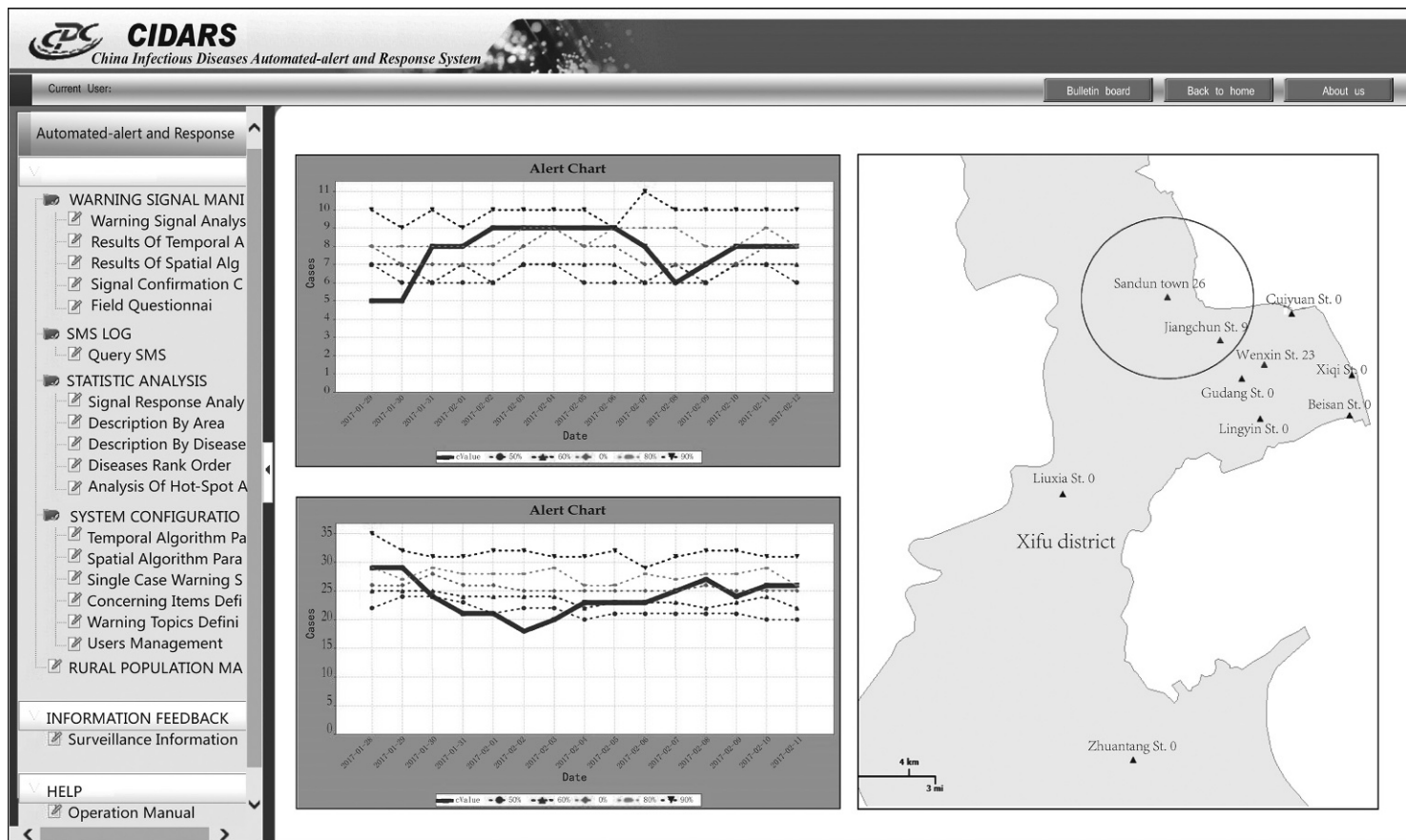
FIG. 7.5

Users interface of China Infectious Diseases Automated-Alert and Response System (CIDARS).
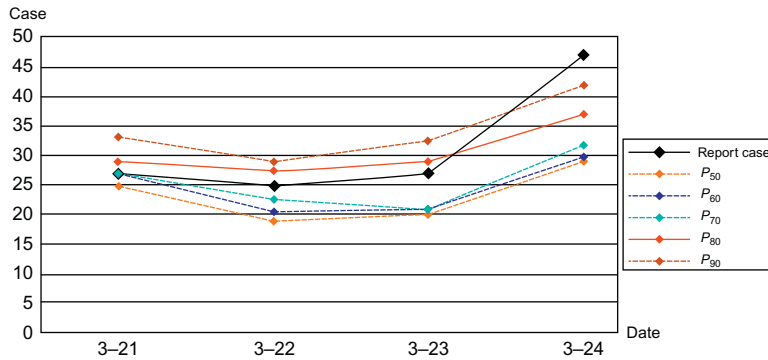
FIG. 7.6

Demonstration of time series chart in China Infectious Diseases Automated-Alert and Response System (CIDARS).

FIG. 7.7

Township hot spots of mumps of a county in China. *Note*: 7-day report cases are referred besides township names.

HOTSPOT AREA MAP

System users can view the locations of townships/towns/subdistricts for the target diseases for early warning, and the number of cases in the current observation period in the spatial hotspot townships/towns (Fig. 7.7).

7.6.2   Signal Response and Feedback

WARNING SIGNAL VERIFICATION

After logging into the information system, the user can view the information of cases covered by warning signals through the linkage between the system and the case database of "Disease surveillance reporting information management system," including the genders, ages, dates of incidence, date of reporting, current residential addresses, occupations and other information of the patients, in order to further determine whether it reveals suspected outbreak. System users can also view the trend of morbidity over time and the spatial clustering through the above-mentioned time series plot and hotspot area map, in order to facilitate verification of warning signals.

COMPLETION AND QUERY OF SIGNAL VERIFICATION CARD

After verifying the aberration information, local CDC staff can log into the information system and fill in the Signal Verification Card which contains warning signal code, target diseases for early warning, number of reported cases, reporting area, reporting agency, date and method of initial verification, whether any schools, kindergartens, or other institutions are involved, initial verification results (suspected event or exclusion), the rationale for the judgment, date of completion, person completing the card, and the contact phone number, etc. CDCs at national, provincial and city levels can understand the progress and outcome of signal response by checking the Signal Verification Card.

COMPLETION AND QUERY OF FIELD INVESTIGATION FORM

After a warning signal is interpreted as suspected event based on initial verification findings, field investigation will then be carried out, and the Field Investigation Form should be completed within 24 h after the completion of the investigation. The Form contains the reporting agency, warning information serial number, townships/towns involved in the event, cumulative number of cases, cumulative number of deaths, whether any schools or kindergartens are involved, date of initial onset, investigation conclusion (outbreak, to be followed up, or excluded), the duration of field investigation, the person completing the form and the contact phone number, etc. The form can be updated from time to time according to the progress of investigation, until the final investigation is completed. CDCs at national, provincial and city levels can learn about the progress and outcome of the field investigation by checking the Field Investigation Form.

SIGNAL STATISTICS AND SUMMARIZATION

In order to understand the response status of warning signals in the local area, the system automatically generates the statistical table of each signal response, including the list of signal generation and response timing, summary of signal responses by area, summary of signal response by disease, statistical table of ranking of signals on target diseases for early warning, and statistical table of ranking of signals in warning areas. Besides, users can also export signal data in order to carry out more in-depth analysis.

7.6.3   System Management

ADJUSTMENT TO EARLY WARNING METHODS

Users from CDCs at all levels can adjust the early warning method from spatial-temporal models to FDM for specific diseases prioritized by locality, so as to receive signals in a timely fashion after a case is reported.

QUERY OF ALERT SMS

Users can query warning signals to look at the sending time of SMS, content of SMS, recipient, mobile phone at the receiving end and result (success or failure), so as to understand the status of SMS. If SMS fails to be sent, the system will automatically send it again until SMS is sent successfully.

PERMISSION ASSIGNMENT FOR USERS

SMS users include system administrators at national, provincial, city and county levels, and general users. Specifically, system administrators designated by CDCs at all levels are responsible to assign accounts and permissions to general users at the same levels and subordinate system administrators. General users at national, provincial and city levels receive single-case signals and alert SMS of suspected infectious disease outbreak; check local warning information on a daily basis; track the investigation and management of suspected outbreaks in a timely fashion; and summarize, analyze, and report warning information on a regular basis. General users at the county level receive and verify signals of infectious diseases and feedback results.

7.7   ANALYSIS OF CIDARS APPLICATION OUTCOMES

By 2015, CIDARS covered all CDCs at the county level and above. System users mainly included infectious disease control and health emergency response staff at CDCs at all levels. By 2010, CIDARS had a cumulative total of over 12,000 system users across the country; and over 6000 from CDCs at national, provincial, city, and county levels could receive alert SMS via mobile phone. Until Apr. 2009, CIDARS (temporal model) was rolled out throughout the country. Meanwhile, 221 counties/districts from 22 provinces of all 31 provinces were selected to pilot CIDARS (spatial-temporal model) based on such factors as morbidity levels and geographical distributions of infectious diseases. These counties/districts also had favorable conditions for the pilot study of early warning temporal model. Additionally, six cities (i.e., Beijing, Shanghai, Tianjin, Qingdao, Shenyang, and Qinhuangdao) selected to host the events for 2008 Beijing Olympic Games were incorporated into the pilot study in order to strengthen the prevention and control of infectious diseases during the Olympic Games. Application outcomes of CIDARS (temporal model) throughout the country and CIDARS (spatial-temporal model) in some provinces are described in the following section.

7.7.1   Analysis of CIDARS Operation Outcomes

In 2011–2013, CIDARS generated a total of 960,831 signals, with a proportion of 98.9% (949,936 signals) responded by local staff and the median from sending

SMS to report initial verification results is 1.0 h; 91.9% of the signals received response within 24 h. The proportion of signal response rose year by year from 2011 to 2013, which was, 98.3%, 98.87% and 99.3%, respectively, and the time to report initial verification results decreased year by year, with the median of 1.1 h, 1.0 h, and 0.9 h, respectively.

The FDM generated a total of 242,355 signals, involving 3056 counties/districts. Specifically, the signals on measles (173,488 signals) and HFMD (56,274 signals) (serious and death cases) accounted for the largest parts, jointly accounting for 94.8%; the signals on plague were the least (only 37 signals) (Table 7.4).

Table 7.4	Signal Response With Fixed-Threshold Detection Method for China Infectious Diseases Automated-Alert and Response System (CIDARS) in the Year of 2011–2013									
		Confirmed	Response ratio (%)				Median response time (h)			
Disease name	Signals	cases[a]	2011	2012	2013	Mean	2011	2012	2013	Mean
Measles	173,488	43,966	95.1	98.6	99.4	98.1	1.6	0.9	0.8	0.9
Hand, foot, and mouth disease (severe and death)	56,274	51,219	98.9	99.1	99.8	99.1	1.0	0.7	0.7	0.8
Malaria[b]	8863	4713		97.8	99.1	98.8		1.0	0.8	0.8
Filariasis	878	0	99.3	97.3	99.7	98.8	1.0	0.7	0.8	0.8
Unexplained pneumonia	760	2	100.0	97.6	98.3	98.6	0.6	0.6	0.5	0.6
Cholera	709	152	93.5	98.2	99.6	97.3	0.5	0.4	0.5	0.4
Polio	523	21	93.3	99.5	98.4	97.3	0.9	0.5	0.6	0.6
Pulmonary anthrax	284	1	99.0	98.0	97.7	98.2	0.8	0.5	0.6	0.6
Human Infection with avian influenza virus (H7N9)[c]	183	143			99.5	99.5			0.5	0.5
Human infection with highly pathogenic avian influenza virus	168	4	98.0	98.1	98.5	98.2	0.6	0.5	0.6	0.6
Diphtheria	89	0	93.3	100.0	100.0	97.8	1.2	1.5	0.7	1.0
Severe acute respiratory syndrome	56	0	100.0	100.0	100.0	100.0	0.5	0.3	0.9	0.5
Acute schistosomiasis[d]	43	9		100.0	100.0	100.0		6.4	0.9	1.1
Plague	37	2	80.0	90.0	100.0	89.2	0.6	1.4	0.6	0.7
Total	242,355	100,232	96.4	98.8	99.4	98.4	1.3	0.8	0.7	0.9

[a]Confirmed cases refer to final report cases from National Infectious Disease Network, including clinical diagnosis cases and laboratory diagnosis cases.
[b]Early warning of malaria using a fixed threshold method from Aug. 2012.
[c]Early warning of human infection with avian influenza virus (H7N9) using a fixed threshold method from Apr. 2013.
[d]Early warning of acute schistosomiasis using a fixed threshold method from Oct. 2012.

In 2011–2013, the proportion of signal response was 96.4%, 98.8%, and 99.4%, respectively, while the median time to report initial results was 1.3 h, 0.8 h, and 0.7 h. Signal initial verification was performed mainly through surveillance data analysis for a total of 118,797 signals (49.8%), and 33,550 (14.1%) signals were verified via phone calls, and 86,105 (36.1%) signals were preliminarily investigated via both surveillance data analysis and phone calls.

The temporal model method (MPM and CUSUM) generated a total of 718,476 signals, involving 3008 counties/districts; averagely 1.53 signals were generated in each county/district per week. Specifically, signals on other infectious diarrhea, HFMD, epidemic mumps, bacillary and amoebic dysentery and influenza were the most, jointly accounting for 88.18%, while signals on leptospirosis were the least (only 128 signals) (Table 7.5). In 2011–2013, 98.9%, 98.9%, and 99.3% signals have been respond, respectively, with a median time was 1.1 h, 1.0 h, and 1.0 h.

The number of signals increased along with the increase in the number of reported cases. Overall, the ratio between number of reported cases and number of signals was 15.6:1. Specifically, the ratios for malaria (3.5:1) and Japanese encephalitis (2.1:1) were low, while the ratios for HFMD (32.7:1), dengue fever (15.9:1) and other infectious diarrhea (13.8:1) were relatively higher (Table 7.6).

Surveillance data analysis is the primary approach to the verification of signals under temporal model method. A total of 455,734 (64.1%) were verified; 101,069 (14.2%) signals were verified via phone calls; 154,681 (21.7%) signals were verified via both surveillance data analysis and phone calls. According to the initial verification findings, a total of 8155 signals were associated with suspected events, accounting for 1.1% of all signals (Table 7.6).

7.7.2 Comparison of Application Outcomes of Temporal Model and Spatial-Temporal Model in CIDARS

In 2011–2013, China CDC compared the outcomes of temporal model and spatial-temporal model for 16 infectious diseases in 20 pilot provinces of China, and evaluated the alert effectiveness of both methods under the CIDARS platform, in order to provide references for improving and applying early warning model in the next steps.

In the 3 years, temporal model generated a total of 57,662 signals; averagely 1.8 signals were generated in each county/district per week; 414 signals (0.7%) were associated with suspected events (Table 7.7). Spatial-temporal model generated a total of 24,007 signals; on average 0.7 signals were generated in each county/district per week; 444 signals (1.9%) were associated with suspected events. The gap in the number of signals between spatial-temporal model and temporal model was 33,655 (58.4%) signals. In 2011–2013, the pilot areas reported a total of 159 outbreaks (Table 7.8) involving 10 infectious diseases, and the sensitivity of temporal model and spatial-temporal model was 96.2% (153 outbreaks) and 90.6% (144 outbreaks), respectively; the false alarm rate of spatial-temporal model

Table 7.5	Signal Response With Temporal Model for China Infectious Diseases Automated-Alert and Response System (CIDARS) in the Year of 2011–2013								
		Response ratio (%)				Median response time (h)			
Disease name	Signals	2011	2012	2013	Mean	2011	2012	2013	Mean
Respiratory infectious disease	227,389	98.5	98.5	99.1	98.7	1.1	1.1	1.0	1.0
Mumps	148,589	98.7	98.5	99.2	98.7	1.1	1.0	0.9	1.0
Influenza	41,478	99.2	99.0	98.8	99.0	1.0	1.1	1.0	1.0
Scarlet fever	22,141	97.0	97.4	99.2	97.6	1.1	1.1	1.1	1.1
Rubella	15,044	98.6	98.7	99.1	98.7	1.1	1.1	0.9	1.0
Meningococcal meningitis	137	95.8	100.0	98.1	97.8	1.8	1.7	2.6	2.0
Intestinal infectious disease	466,479	99.1	99.1	99.4	99.2	1.0	1.0	0.9	1.0
Hand, foot, and mouth disease	171,693	99.3	99.3	99.6	99.4	1.0	1.0	0.9	1.0
Other infectious diarrhea[a]	198,679	99.2	99.2	99.4	99.3	1.0	1.0	1.0	1.0
Bacillary and amebic dysentery	73,133	98.5	98.4	98.9	98.6	1.0	1.2	1.0	1.0
Hepatitis E	9691	99.0	99.5	99.9	99.5	0.9	0.9	0.8	0.9
Hepatitis A	8010	98.5	98.3	97.5	98.2	1.6	1.7	2.1	1.7
Typhoid and paratyphoid fever	5273	99.6	99.8	99.1	99.4	1.0	1.1	1.1	1.1
Natural focal and insect-borne infectious diseases	11,039	99.5	99.1	99.2	99.2	1.0	0.9	0.9	0.9
Epidemic hemorrhagic fever	5546	99.4	99.5	99.5	99.5	0.9	0.8	0.8	0.8
Epidemic and endemic typhus	671	99.6	97.2	95.9	97.8	1.1	0.9	1.0	1.0
Malaria	1662		98.4	99.6	99.3		0.7	0.7	0.7
Japanese encephalitis	2695	99.5	98.8	99.6	99.3	1.1	1.0	0.9	1.0
Dengue	337	100.0	100.0	95.7	97.0	1.1	0.9	2.0	1.5
Leptospirosis	128	100.0	100.0	100.0	100.0	1.0	0.9	1.4	1.1
Other infectious diseases[b]	13,569	99.0	99.4	99.9	99.4	1.1	1.0	0.9	1.0
Total	718,476	98.9	98.9	99.3	99.0	1.1	1.0	1.0	1.0

[a]Other infectious diarrhea in addition to cholera, bacillary and amoebic dysentery, typhoid and paratyphoid.
[b]It includes only acute hemorrhagic conjunctivitis.

(0.6%) was lower than that of temporal model (1.6%); the median of outbreak detection duration of temporal model was 3.0 days, while that of spatial-temporal model was merely 1.0 days.

For the six category I diseases, spatial-temporal model generated 983 signals, which was 2.3% less than those generated by temporal model; the percent of

Table 7.6	**Signal Response With Spatial-Temporal Model for China Infectious Diseases Automated-Alert and Response System (CIDARS) in the Year of 2011–2013**				
		Early warning system			**Reported cases: warning signal number**
Disease name	**Reported cases**	**No. of all signal**	**No. of signal related to suspected event[a]**	**Confirmed outbreaks**	
Respiratory infectious disease	1,848,828	227,389	4014(1.77)	1468	8.1:1
Mumps	1,264,883	148,589	2690(1.81)	931	8.5:1
Influenza	314,769	41,478	622(1.50)	303	7.6:1
Scarlet fever	144,762	22,141	77(0.35)	20	6.5:1
Rubella	123,771	15,044	611(4.06)	209	8.2:1
Meningococcal meningitis	643	137	14(10.22)	5	4.7:1
Intestinal infectious disease	9,195,963	466,479	3888(0.83)	936	19.7:1
Hand, foot, and mouth disease	5,622,819	171,693	3365(1.96)	807	32.7:1
Other infectious diarrhea[b]	2,735,822	198,679	309(0.16)	74	13.8:1
Bacillary and amebic dysentery	634,950	73,133	131(0.18)	35	8.7:1
Hepatitis E	85,254	9691	12(0.12)	1	8.8:1
Hepatitis A	79,049	8010	39(0.49)	12	9.9:1
Typhoid and paratyphoid fever	38,069	5273	32(0.61)	7	7.2:1
Natural focal and insect-borne infectious diseases	61,706	11,039	196(1.78)	75	5.6:1
Epidemic hemorrhagic fever	37,150	5546	12(0.22)	3	6.7:1
Epidemic and endemic typhus	6465	671	0(0.00)	1	9.6:1
Malaria	5885	1662	17(1.02)	0	3.5:1
Japanese encephalitis	5643	2695	71(2.63)	4	2.1:1
Dengue	5357	337	95(28.19)	66	15.9:1
Leptospirosis	1206	128	1(0.78)	1	9.4:1
Other infectious diseases[c]	103,010	13,569	57(0.42)	11	7.6:1
Total	11,209,507	718,476	8155(1.14)	2490	15.6:1

[a]Data in "()" refer to the percentage of early warning signals of suspected event accounts for all kinds of warning signals of this disease.
[b]Other infectious diarrhea in addition to cholera, bacillary and amoebic dysentery, typhoid and paratyphoid.
[c]It includes only acute hemorrhagic conjunctivitis.

signals on suspected events generated by spatial-temporal model (6.1%) was slightly higher than that generated by temporal model (5.0%). Among the six infectious diseases, merely outbreaks of dengue fever and Japanese Encephalitis were reported. Both temporal model and spatial-temporal model detected all outbreaks of the two infectious diseases; the rate of false warning of both models was 0.1%, while the median of outbreak detection duration was 2.5 days and 3.0 days, respectively. See Table 7.8.

For the 10 category II diseases, spatial-temporal model generated a total of 23,024 signals, which was 59.36% less than those generated by temporal model. The percent of signals on suspected events generated by spatial-temporal model (1.7%) was higher than that generated by temporal model (0.6%). In the pilot areas, 151

| | Table 7.7 | Compare Early Warning Outcomes of Temporal Model and Spatial-Temporal Model in 208 Pilots Counties/Districts for China Infectious Diseases Automated-Alert and Response System (CIDARS) in the Year of 2011–2013 |

Disease classification	Temporal model			Spatial-temporal model			Warning signal number change (%)[b]	Suspected event signal ratio difference (%)[c]
	Signal number	Suspected event signal number	Suspected event signal ratio (%)[a]	Signal number	Suspected event signal number	Suspected event signal ratio (%)[a]		
Category I diseases	1006	50	5.0	983	60	6.1	−2.3	1.1
Epidemic hemorrhagic fever	692	6	0.9	672	7	1.0	−2.9	0.2
Japanese encephalitis	178	12	6.7	151	11	7.3	−15.2	0.5
Dengue	82	32	39.0	113	42	37.2	37.8	−1.9
Meningococcal meningitis	29	0	0.0	24	0	0.0	−17.2	0.0
Epidemic and endemic typhus	22	0	0.0	20	0	0.0	−9.1	0.0
Leptospirosis	3	0	0.0	3	0	0.0	0.0	0.0
Category II diseases	56,656	364	0.6	23,024	384	1.7	−59.4	1.0
Other infectious diarrhea[d]	16,719	22	0.1	9128	13	0.1	−45.4	0.0
Mumps	14,783	206	1.4	6490	227	3.5	−56.1	2.1
Dysentery	7479	5	0.1	2119	10	0.5	−71.7	0.4
Scarlet fever	5960	15	0.3	1783	21	1.2	−70.1	0.9
Influenza	3592	59	1.6	1625	55	3.4	−54.8	1.7
Rubella	2447	44	1.8	916	48	5.2	−62.6	3.4
Hepatitis E	1967	1	0.1	106	0	0.0	−94.6	−0.1
Acute hemorrhagic conjunctivitis	1622	4	0.3	614	1	0.2	−62.2	−0.1
Hepatitis A	1069	5	0.5	117	6	5.1	−89.1	4.7
Typhoid and paratyphoid fever	1018	3	0.3	126	3	2.4	−87.6	2.1
Total	57,662	414	0.7	24,007	444	1.9	−58.4	1.1

[a]Suspected event signal ratio=Suspected event signal number/Signal number × 100%.
[b]Warning signal number change=(Signal number of temporal model-Signal number of spatial-temporal model)/Signal number of temporal model × 100%.
[c]Suspected event signal ratio difference=Suspected event signal ratio of spatial-temporal model-Suspected event signal ratio of temporal model.
[d]Other infectious diarrhea in addition to cholera, bacillary and amoebic dysentery, typhoid and paratyphoid.

Table 7.8	Compare Outbreak Detection Outcomes of Temporal Model and Spatial-Temporal Model in 208 Pilots Counties/Districts for China Infectious Diseases Automated-Alert and Response System (CIDARS) in the Year of 2011–2013

		Temporal model				Spatial-temporal model			
Disease classification	Number of outbreaks[a]	Number of outbreaks detection[b]	Sensitivity (%)	False alarm ratio (%)	Median of outbreak detection duration (days)	Number of outbreaks detection[b]	Sensitivity (%)	False alarm ratio (%)	Median of outbreak detection duration (days)
Category I diseases	8	8	100.0	0.1	2.5	8	100.0	0.1	3.0
Dengue	7	7	100.0	0.0	2.0	7	100.0	0.0	3.0
Japanese encephalitis	1	1	100.0	0.1	15.0	1	100.0	0.1	15.0
Epidemic hemorrhagic fever	0	0	–	0.3	–	0	–	0.3	–
Meningococcal meningitis	0	0	–	0.0	–	0	–	0.0	–
Epidemic and endemic typhus	0	0	–	0.0	–	0	–	0.0	–
Leptospirosis	0	0	–	0.0	–	0	–	0.0	–
Category II diseases	151	145	96.0	2.5	3.0	136	90.1	1.0	1.0
Mumps	70	68	97.1	6.4	3.0	68	97.1	2.7	2.0
Influenza	34	33	97.1	1.6	2.0	28	82.4	0.7	0
Rubella	30	27	90.0	1.0	3.0	25	83.3	0.4	1.0
Other infectious diarrhea[c]	6	6	100.0	7.3	1.5	4	66.7	4.0	1.5
Hepatitis A	6	6	100.0	0.5	0	6	100.0	0.1	0
Dysentery	3	3	100.0	3.3	5.0	3	100.0	0.9	0
Scarlet fever	1	1	100.0	2.6	5.0	1	100.0	0.8	2.0
Acute hemorrhagic conjunctivitis	1	1	100.0	0.7	0	1	100.0	0.3	4.0
Hepatitis E	0	0	–	0.9	–	0	–	0.1	–
Typhoid and paratyphoid fever	0	0	–	0.5	–	0	–	0.1	–
Total	159	153	96.2	1.6	3.0	144	90.6	0.6	1.0

[a]Number of outbreaks refer to reported cases from outbreak of infectious diseases event reporting network.
[b]Number of outbreaks detection refer to number of outbreaks that warning system detected through temporal model and spatial-temporal model.
[c]Other infectious diarrhea in addition to cholera, bacillary and amoebic dysentery, typhoid and paratyphoid.

outbreaks were reported for eight category II diseases. The outbreak detection sensitivity of temporal model and spatial-temporal model was 96.0% and 90.1%, respectively; both models issued early warning signals on all events of hepatitis A, dysentery, scarlet fever and acute hemorrhagic conjunctivitis, but the sensitivity did not reach 100% for more common infectious diseases and for which outbreaks are reported more frequently, e.g., epidemic mumps, influenza, etc. Compared to temporal model, spatial-temporal model detected nine less events, but the number of signals on the various diseases and the rate of false warning of spatial-temporal model were both lower than those of temporal model. The average outbreak detection duration of spatial-temporal model for the various diseases was shorter than that of temporal model.

7.7.3 Evaluation of CIDARS to Detect HFMD Outbreaks

HFMD became officially a notifiable disease in China (Chinese Ministry of Health, 2008) since 2008, and has been included in the CIDARS since 2010. Li et al. conducted a study to evaluate the performance of CIDARS by analyzing the sensitivity, timeliness in the detection of HFMD outbreaks, and also evaluated the CIDARS' effectiveness by comparing the size and duration of HFMD outbreaks—and the timeliness in reporting such outbreaks—before and after HFMD was included in the CIDARS (Li et al., 2014).

The evaluation used the information on each laboratory-confirmed or clinically diagnosed case of HFMD that was reported to the Nationwide Notifiable Infectious Diseases Reporting Information System (NIDRIS) between May 1, 2008 and Apr. 30, 2012. Aberration detection of HFMD outbreak in the CIDARS is based on the C3 algorithm (Hutwagner et al., 2003, 2005; Fricker et al., 2008). Following advices of senior epidemiologists and statisticians in the CIDARS' research group, the HFMD outbreaks recorded in the public health emergency reporting system were used as the "golden" standard in our estimations of the CIDARS' sensitivity, specificity, and timeliness.

Between May 1, 2008 and Apr. 30, 2012, 5,471,108 cases and 1209 outbreaks of HFMD were reported in China (Table 7.9). The number of HFMD cases per month ranged from 7512 cases in Jan. 2009 to 353,104 cases in May 2010, with a mean value of 113,981. Over this period, HFMD incidence showed marked seasonality, with a major peak—comprising almost half of all cases—in Apr.–Jun. and a smaller secondary peak—comprising 18.0% of cases—in Sep.-Nov. Reported outbreaks, signals and alerts showed a similar seasonal pattern (Fig. 7.8).

The number of outbreaks reported per year ranged from 211 for the period May 1, 2008–Apr. 30, 2009 to 380 for the period May 1, 2009–Apr. 30, 2010. Between May 1, 2010 and Apr. 30, 2012, 106,005 signals in a total of 2608 counties were generated by the CIDARS for HFMD (Table 7.9). This represents a mean of 5.6 such signals every 100 days in each of the counties that had at least one signal. Initial verification indicated that 2361 (2.2%) of the signals merited being raised to alert status and field investigation. Field investigation of the CIDARS' signals led to 573 HFMD outbreaks being confirmed. The CIDARS received the initial verification results for 94,920 (89.5%) of the signals within 24 h.

Table 7.9	**Outbreaks of Hand, Foot, and Mouth Disease in China, 2008–2012**				
	Period				
Indicator	**May 1, 2008– Apr. 30, 2009**	**May 1, 2009– Apr. 30, 2010**	**May 1, 2010– Apr. 30, 2011**	**May 1, 2011– Apr. 30, 2012**	**Overall**
Cases					
Cases reported in the NIDRIS	757,141	1,256,320	1,576,918	1,880,729	5,471,108
Outbreaks recorded by the public health emergency reporting system	211	380	298	320	1209
Ratio of all reported cases to outbreaks recorded in the public health emergency reporting system	3588:1	3306:1	5292:1	5877:1	4525:1
No. of cases related to outbreaks	4077	7376	4795	4956	21,204
Ratio of all reported cases to cases related to outbreaks	186:1	170:1	329:1	379:1	258:1
Signals					
Warning signals generated by the CIDARS	–	–	48,916	57,089	106,005
Ratio of all cases to warning signal	–	–	32:1	33:1	33:1
Alerts recorded in CIDARS	–	–	1117	1244	2361
Ratio of warning signals to alerts	–	–	44:1	46:1	45:1
Detected outbreaks	–	–	278	295	573
Ratio of alerts to detected outbreaks	–	–	4:1	4:1	4:1

As 618 HFMD outbreaks were recorded in the public health emergency reporting system in the period when 573 such outbreaks were identified in the CIDARS, the overall sensitivity of the CIDARS in the detection of HFMD outbreaks was 92.7% (Table 7.10). The CIDARS' sensitivity was significantly higher for large outbreaks involving more than 20 cases than for small outbreaks that involved no more than 10 cases (99.3% versus 84.6%; $P<0.001$). In the detection of HFMD outbreaks, the overall specificity of the CIDARS was 95.0% and the overall mean time to detection was 2.1 days. The mean time to detection was 1.7 days for outbreaks that involved no more than 10 cases but 2.7 days for outbreaks that involved more than 20 cases. The mean time from detection to report in the public health emergency reporting system was 4.5 days.

Before HFMD was included in the CIDARS, the mean size ($P=0.982$), duration ($P=0.572$) and time to report ($P=0.358$) of the HFMD outbreaks detected between May 1, 2008 and Apr. 30, 2009 were similar to those of the outbreaks detected in the following 12 months. Similarly, after HFMD was included in the CIDARS, the mean size ($P=0.443$), duration ($P=0.370$) and time to report ($P=0.840$) of the HFMD outbreaks detected between May 1, 2010 and Apr. 30, 2011 were similar to those of the outbreaks detected in the following 12 months. The outbreaks recorded in the 2 years immediately after HFMD
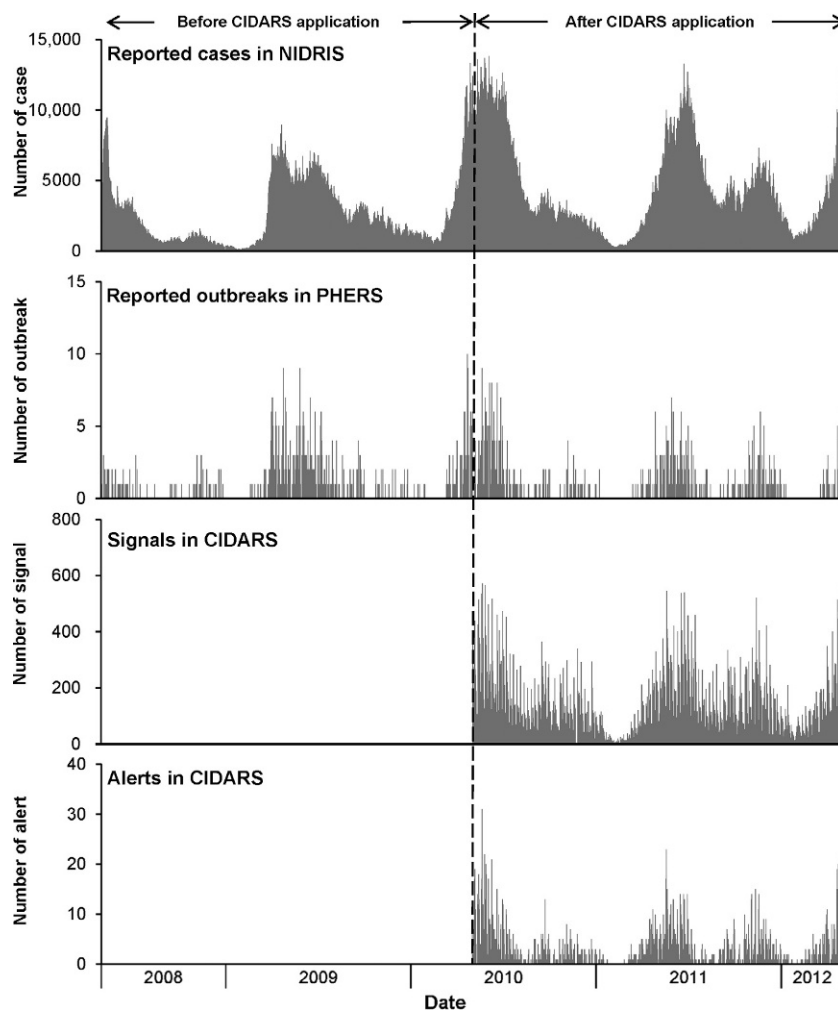
FIG. 7.8
The temporal distribution of reported cases, reported outbreaks, signals, and alerts of HFMD in China from May 2008 to Apr. 2012. *NIDRIS*, Notifiable Infectious Diseases Reporting Information System, *CIDARS*, China Infectious Disease Automated-Alert and Response System, and *PHERS*, Public Health Emergency Reporting System.

was included in the CIDARS were generally smaller than those recorded over the previous 2 years, with mean sizes of 15.8 and 19.4 cases, respectively (Table 7.11). The mean size of outbreaks that involved more than 20 cases was significantly less in the 2 years immediately after HFMD was included in the CIDARS than the corresponding value for the previous 2 years (29.2 versus 55 cases; $P = 0.015$).

Table 7.10	Detection of Outbreaks of Hand, Foot, and Mouth Disease in China, May 1, 2010–Apr. 30, 2012			
	No. of outbreaks		**Performance of CIDARS**	
No. of cases in outbreak	**Reported in public health emergency reporting system**	**Detected by CIDARS**	**Sensitivity[a] (%)**	**Mean time to outbreak detection, days[b] (95% CI)**
3–10	156	132	84.6	1.7 (1.3–2.1)
11–20	326	306	93.9	1.9 (1.7–2.2)
>20	136	135	99.3	2.7 (1.9–3.5)
Overall	618	573	92.7	2.1 (1.8–2.3)

[a]Values differ significantly according to size of outbreak ($P < 0.001$).
[b]The time between the reporting of the first known case of an outbreak and the CIDARS' generation of the first warning signal about that outbreak. Values do not differ significantly according to size of outbreak (one-way analysis of variance; $P = 0.28$).

Table 7.11	Size, Duration and Reporting Times of Hand, Foot, and Mouth Disease (HFMD) Outbreaks Before and After China Infectious Diseases Automated-Alert and Response System (CIDARS) Application, China, 2008–2012			
	Outbreaks of HFMD reported to public health emergency reporting system			
No. of cases before/ after inclusion of HFMD in CIDARS	**No. reported**	**Mean size, cases (95% CI)**	**Mean duration, days (95% CI)**	**Mean time to report, days (95% CI)**
Before inclusion[a]				
3–10	161	6.7 (6.3–7.1)	9.1 (8.2–10.0)	8.1 (7.4–8.7)
11–20	328	14.5 (14.2–14.8)	14.0 (13.1–14.9)	10.1 (9.5–10.7)
>20	102	55.0 (34.3–75.8)	28.7 (24.4–32.9)	12.7 (11.1–14.3)
Overall	591	19.4 (15.6–23.2)	15.2 (14.1–16.2)	10.0 (9.5–10.5)
After inclusion[b]				
3–10	156	6.4 (5.9–6.8)	8.4 (7.6–9.2)	7.3 (6.8–7.8)
11–20	326	14.7 (14.4–15.0)	14.0 (13.2–14.7)	9.4 (8.9–9.8)
>20	136	29.2 (27.2–31.1)[c]	26.0 (23.5–28.5)	10.5 (9.5–11.5)[d]
Overall	618	15.8 (15.0–16.5)	15.2 (14.4–16.1)	9.1 (8.7–9.5)[e]

[a]For the period May 1, 2008–Apr. 30, 2010.
[b]For the period May 1, 2010–Apr. 30, 2012.
[c]Significantly lower than corresponding value for the study period before HFMD was included in CIDARS ($P = 0.015$).
[d]Significantly lower than corresponding value for the study period before HFMD was included in CIDARS ($P = 0.020$).
[e]Significantly lower than corresponding value for the study period before HFMD was included in CIDARS ($P = 0.004$).

The overall mean duration of an HFMD outbreak was estimated to be 15.2 days for the study periods before and after HFMD was included in the CIDARS. However, the mean duration of outbreaks that involved more than 20 cases fell from 28.7 days in the 2 years before HFMD was included in the CIDARS to 26.0 days in the following 2-year period. The corresponding falls in the mean number of days taken to report an HFMD outbreak of any size—from 10.0 to 9.1 ($P=0.004$)—and an HFMD outbreak that involved more than 20 cases—from 12.7 to 10.5 ($P=0.020$)—were significant.

This case study indicates that the CIDARS had good sensitivity and specificity in the detection of HFMD outbreaks and could lead to a reduction in the eventual size of an outbreak—by shortening the reporting time and so permitting an earlier response. If well designed and operated, the automated early warning system for outbreaks of infectious disease can help local epidemiologists identify outbreaks rapidly, thereby facilitating the prevention of outbreak spread. The CIDARS' design framework and methods could provide a useful example for institutes of public health in many countries.

7.8   MAJOR FEATURES OF CIDARS

CIDARS has covered national, provincial, city and county levels and achieved automated detection and rapid response to aberration of 30 notifiable infectious diseases aberration. The system is highly automated and easily operated. It has been successfully incorporated into routine infectious disease surveillance and early warning within CDCs at all levels, and has become an important tool for epidemiological surveillance staff in early detection of disease outbreaks.

CIDARS has obvious advantages by using notifiable infectious diseases as outbreak detection data sources. Firstly, notifiable infectious diseases are subject to powerful legal support and administrative binding effect, health facilities and medical workers at all levels are highly aware of diagnosing and reporting infectious diseases, and the stability of surveillance systems and the quality of data are more assuring than other sources. Secondly, notifiable infectious diseases are directly reported via Internet in China, which has significantly shortened the duration from diagnosis of infectious diseases to Internet-based reporting to less than 1 day on average and has created a favorable condition for early detection of infectious disease outbreaks. Additionally, surveillance data of notifiable infectious diseases contain the demographical and geolocation data of each patient. After receiving warning signals, local epidemiological surveillance staff can quickly check information related to individual patients, so as to verify warning signals and identify and track patients in a timely fashion.

CIDARS has achieved rapid and automatic analysis of surveillance data, and is capable of sending warning signals to relevant staff via SMS. Different types of SMS are sent to staff at different levels. Compared to previous manual analysis

of surveillance data, CIDARS significantly increases the frequency of data processing and analysis, and potentially reduces the workload of local staff in data analysis and aberration judgment. CIDARS also leverages international concept and framework for the design of alert system, and has completed and standardized work flow, including data processing and quality control, data aberration detection model operation, signal generation and sending, signal response and result feedback. Moreover, epidemiological surveillance staff at all levels adopt common procedures to implement early warning and response, enabling more standardized detection, identification and response to infectious disease outbreak warning signals. In addition, initial verification of warning signals is very simple. Most signals can be quickly excluded just by browsing surveillance data or verifying them via phone calls.

By using Internet-based information system framework, CDCs at county level can log on CIDARS via Internet to give timely feedback on initial verification and field investigation result for each warning signal. CDCs at national, provincial and city levels can track and monitor signal response at the first time, which will promote information communication among CDCs at all levels during the response to infectious disease surveillance, achieve synergic response to infectious disease outbreaks, and provide timely and effective technical guidance and support. Moreover, the information system has been developed, centrally managed and maintained by China CDC. As system users, CDCs at provincial, city and county levels only need to receive alert SMS via designated mobile phones and don't need to create network hardware environment or develop extra software systems. Expenses for sending alert SMS are also covered by China CDC, substantially reducing the input of financial and human resources at grassroots levels.

CIDARS is open and flexible to some extent. CDC staff submit applications to system administrators at higher levels and can access the system after obtaining permission system users can adjust threshold parameters of the MPM according to their actual needs. They can also include locally prevalent diseases in CIDARS or adjust the early warning method for some diseases from MPM to FDM. Overall, CIDARS has a complete work flow; is highly operable; and has taken into account of the repeated warning and other issues. CIDARS has been set as the exemplary in applying early warning models and methods in daily practice.

Nevertheless, there are still some limitations for CIDARS. For example, suspected event signals from the MPM only account for a small proportion of all signals, indicating the need to further improve the specificity of signals and reduce false positive signals. The MPM is more accurate in early warning of infectious diseases subject to frequent outbreak, prevalence or case clustering, but is less accurate in early warning of infectious diseases subject to rare outbreaks. Therefore, warning thresholds of existing early warning methods can be optimized for individual diseases according to their respective geographic distribution, morbidity level and infectivity.

7.9   CHALLENGES AND THE FUTURE DIRECTIONS

The development of CIDARS has fully taken into account the technical features of international surveillance alert systems (Bradley et al., 2005; Mandl et al., 2004), and is closely aligned to the characteristics and needs of infectious disease prevention and control in China. It has been a significant exploration and practice in Chinese public health arena. Certain achievements have been made, but exploration and research are still needed to further develop the infectious disease early warning system.

Quality surveillance data are the basis for effective early warning. The current CIDARS is mainly based on notifiable infectious diseases surveillance information. Its application outcomes are directly affected by the quality of infectious disease surveillance data reported. If the diagnosis accuracy, report timeliness and integrity of surveillance data are not ensured, the timeliness, sensitivity and specificity of the alert system will be undermined. The management of surveillance should be constantly enhanced, and effective actions should be taken in order to ensure the accuracy, integrity and timeliness of surveillance data and avoid wrong data reported, missing report and delay in reporting.

The existing infectious disease surveillance systems in China are mostly based on post-diagnosis case information. One of the important approaches to enhancing the timeliness of infectious disease early warning is to constantly expand the sources of surveillance data, including the development of surveillance on the risk factors for infectious disease, information retrieved from the Internet, results of laboratory test, symptoms of patients, and other sources of information, in order to enhance the performance of infectious disease early warning.

Due to the lack of criteria and indicators, the evaluation of actual operation of the alert system, balancing the sensitivity and specificity, and the selection of appropriate methods and parameters for different diseases in different areas become the challenges for research on infectious disease early warning. In the future, survey on users of the early warning system can be conducted in order to further understand the responses made by grassroots staff towards signals, the acceptability and tolerance against false positive signals, and the defects in warning response work flow and system user functions. Besides, the public health implications and value of early generation of signals by the system should be explored in depth, as well as the cost-effectiveness of early warning, in order to constantly improve the early warning protocol and provide users with more convenient, practical system operation functions.

CIDARS has realized the automated linking of warning signals to NIDRIS that reports notifiable infectious diseases and the report cards of related disease reporting systems, so that users can directly retrieve and view the related case information in the alert system and analyze and use the surveillance data. However, the current alert system cannot directly link the events reported on the Field Investigation Form to the relevant events in a "Public Health Emergency Reporting and Management Information System." Therefore, it is necessary to further

explore how to match and link signals related to emergencies reported, and to avoid generating duplicate signals for events for which warning has been issued so that the early-warning system can be integrated with surveillance and event reporting systems and become an organic, coordinated system.

References

Bradley, C.A., Rolka, H., Walker, D., Loonsk, J., 2005. BioSense: implementation of a National Early Event Detection and Situational Awareness System. MMWR 54 (Suppl.), 11–19.

China CDC, 2008a. National Protocol for Piloting Infectious Diseases Automated-alert (Temporal Model).

China CDC, 2008b. Protocol for Piloting Infectious Diseases Automated-Alert (Spatial-Temporal Model).

Chinese Ministry of Health, 2008. The Declaration of Hand, Foot and Mouth Disease as a Notifiable Disease in China (Online). Available from: http://www.chinacdc.cn/jkzt/crb/szkb/jszl_2275/200805/t20080506_24699.htm (accessed 01.02.13).

Hutwagner, L., Browne, T., Seeman, G.M., Fleischauer, A.T., et al., 2005. Comparing aberration detection methods with simulated data. Emerg. Infect. Dis. 11 (2), 314–316.

Hutwagner, L., Thompson, W., Seeman, G.M., et al., 2003. The bioterrorism preparedness and response Early Aberration Reporting System (EARS). J. Urban Health 80 (1), i89–i96.

Fricker Jr., R.D., Hegle, B.L., Dunfee, D.A., 2008. Comparing syndromic surveillance detection methods: EARS' versus a CUSUM-based methodology. Stat. Med. 27 (17), 3407–3429.

Kulldorff, M., 1997. A spatial scan statistic. Commun. Stat. Theory Methods 26 (6), 1481–1496.

Li, Z., Lai, S., Zhang, H., et al., 2014. Hand, foot and mouth disease in China: evaluating an automated system for the detection of outbreaks. Bull. World Health Organ. 92 (9), 656–663.

Mandl, K.D., Reis, B., Cassa, C., 2004. Measuring outbreak-detection performance by using controlled feature set simulations. MMWR 53 (Suppl.), 130–136.

Wang, L., Wang, Y., Jin, S., et al., 2008. Emergence and control of infectious diseases in China. Lancet 372 (9649), 1598–1605.