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The Bioterrorism Preparedness and Response Early Aberration Reporting System (EARS)

Lori Hutwagner, William Thompson, G. Matthew Seeman,
and Tracee Treadwell

ABSTRACT *Data from public health surveillance systems can provide meaningful measures of population risks for disease, disability, and death. Analysis and evaluation of these surveillance data help public health practitioners react to important health events in a timely manner both locally and nationally. Aberration detection methods allow the rapid assessment of changes in frequencies and rates of different health outcomes and the characterization of unusual trends or clusters.*

The Early Aberration Reporting System (EARS) of the Centers for Disease Control and Prevention allows the analysis of public health surveillance data using available aberration detection methods. The primary purpose of EARS is to provide national, state, and local health departments with several alternative aberration detection methods. EARS helps assist local and state health officials to focus limited resources on appropriate activities during epidemiological investigations of important public health events. Finally, EARS allows end users to select validated aberration detection methods and modify sensitivity and specificity thresholds to values considered to be of public health importance by local and state health departments.

KEYWORDS *Aberration detection, Centers for Disease Control and Prevention, CUSUM.*

INTRODUCTION

Data from public health surveillance systems can provide meaningful measures of population risks for disease, disability, and death.[1–3] Analysis and evaluation of these surveillance data help public health practitioners react to important health events in a timely manner both locally and nationally. Statistical methods such as aberration detection algorithms are frequently used by epidemiologists to assist them in this task. Aberration detection methods allow for the rapid assessment of changes in frequencies and rates of different health outcomes and for the characterization of unusual trends or clusters.[4–6] In general, aberration detection algorithms are used to enhance the public health practitioner's ability to identify and characterize unusual trends or clusters in public health surveillance data.[4]

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Ms. Hutwagner, Mr. Seeman, and Dr. Treadwell are with the National Centers for Infectious Diseases, Bioterrorism Preparedness and Response, and Dr. Thompson is with the National Immunization Program, Immunization Safety Branch, Centers for Disease Control and Prevention, Atlanta, Georgia.

Correspondence: Lori Hutwagner, 1600 Clifton Road Northeast, Mail Stop C-18, Atlanta, GA 30333. (E-mail: Lhutwagner@cdc.gov or EARS@cdc.gov)

ration detection methods that have been developed for syndromic surveillance by CDC and non-CDC epidemiologists.[7–9] All of the aberration detection methods available through EARS have been tested and validated with several types of infectious disease data sources. The National Center for Infectious Diseases (NCID) Bioterrorism Preparedness and Response Program currently provides technical support and research and development for EARS activities.

EARS has been implemented throughout the United States in several state and local health departments and in health departments in several other countries. EARS has also been used for syndromic surveillance at several large public events in the United States, including the Democratic National Convention of 2000, the 2001 Super Bowl, and the 2001 World Series. Following the terrorist attacks of September 11, 2001, EARS was modified into a standard surveillance system for use by the New York City Department of Health and several health departments in the Washington, DC, metropolitan area.

For the purpose of this article, we define *aberration detection* as the change in the distribution or frequency of important health-related events when compared with historical (more than 3 years in the past) or recent (less than 9 days in the past) data. It is important to remember that data aberrations are not necessarily caused by an infectious disease outbreak, and more important, they may or may not be of public health importance.

Use of aberration detection algorithms allows the public health practitioner to readily identify and quantify variations in the expected distribution of selected health outcomes under surveillance. Once detected, a statistical aberration in the data must be evaluated by an epidemiologist or a public health practitioner to determine its epidemiological or clinical significance. Ideally, aberration detection algorithms should be applied to current public health surveillance data to facilitate the timely detection of previously difficult to recognize outbreaks and to enable the efficient and rapid implementation of effective prevention and control measures.

Several characteristics associated with bioterrorism syndromic surveillance aberration detection systems differ from traditional public health surveillance systems. Bioterrorism syndromic surveillance systems need to provide a real-time, rapid assessment of infectious disease outcomes reported by local health departments or health care facilities (hospitals, emergency departments, clinics, laboratories, etc.). The systems also tend to set relatively sensitive aberration detection thresholds because the cost to society of failure to detect a bioterrorism event could be extreme. The systems also require rapid dissemination of information and coordination of public health responses to identified aberrations of interest. From practical experience in implementing systems quickly and efficiently in several different situations, the most common benefit reported is the improvement in communication across health agencies.

During an actual bioterrorism event, local health practitioners may be the first to identify events of interest, but the significance of any given event may not be realized until data from several sources are collected and analyzed.

REVIEW OF THE LITERATURE

The literature divides aberration detection methods into two broad categories: case definition methods and pattern recognition methods (Fig. 1). Pattern recognition methods, which are not discussed in detail in this article, are useful for identifying symptoms (or sets of symptoms) that deviate from the expected baseline, but these

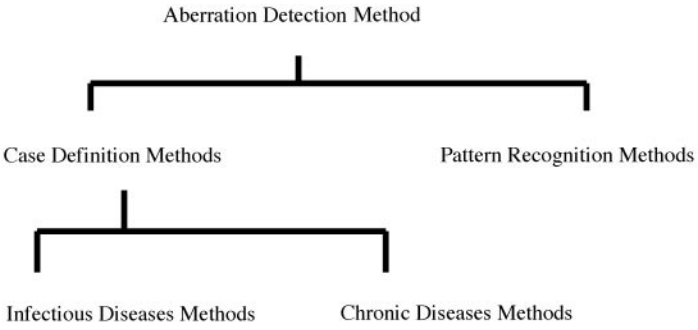

FIGURE 1. A review of aberration detection literature.

methods are likely to identify random aberrations that are not epidemiologically important. Case definition methods use epidemiological expertise to define an "event of interest" and thus track those syndromes considered of greatest importance, such as hepatitis A or influenzalike illness. The case definition methods can be subdivided into infectious disease methods and chronic disease methods. This report focuses primarily on infectious disease methods relevant to the detection of a bioterrorism event.

INFECTIOUS DISEASE METHODS

Infectious disease methods are categorized according to the length of time the surveillance system will be collecting data. Long-term implementation methods expect syndromic surveillance to last longer than 30 days (Table). For most long-term systems, we recommend that only the most recent 5 years of data be used for the baseline because significant changes occur in populations and in surveillance systems over time. For long-term systems with at least 3 years of baseline data, specific methods have been implemented for various types of diseases.[7,8,10–12]

If fewer than 3 years of baseline data are available, you need to consider alternative aberration detection methods,[4] referred to as long-term implementation methods with limited baseline data. Short-term implementation methods, often referred to in the bioterrorism surveillance literature as drop-in surveillance systems, are used when epidemiologists expect to conduct the surveillance for no more than 30 days. These types of systems are often implemented to deal with large public events such as national political party meetings and national sports events. In these situations, immediate feedback is required, and often only 1 to 6 days of baseline data are available.

TABLE. Infectious disease methods

Long-term implementation	Short-Term Implementation
Extended baseline methods (3–5 years)	Implementation expected for less than 30 days
Limited baseline methods (7 days–3 years)	No initial baseline available (1–6 days)

LONG-TERM IMPLEMENTATION METHODS WITH THREE OR MORE YEARS OF BASELINE DATA

We published an analysis of five infectious disease long-term aberration detection methods (for application with 3 or more years of baseline data) that are in use nationally or internationally, including the historical limits method, a log-linear regression model, a quality control model, a compound smoothing technique, and a cyclical regression model.[7,8,10–13]

Historical Limits Method

Most epidemiologists are familiar with the bar chart model presented as "Figure 1" in CDC's *Morbidity and Mortality Weekly Report* (*MMWR*). The results in this figure are based on application since 1989 of the historical limits method to infectious disease surveillance data in the United States by CDC.[8,14,15] The method is applied to incidence data for nine diseases (hepatitis A, hepatitis B, hepatitis C/non-A/non-B, legionellosis, meningococcal infections, measles, mumps, pertussis, and rubella) reported to the National Notifiable Diseases Surveillance System (NNDSS) maintained by CDC. The method compares the number of reported cases in the current 4-week period for a given health outcome with historical incidence data on the same outcome from the preceding 5 years and is based on a comparison of the ratio of current reports with the historical mean:

$$x_o/\mu > 1 + (2^*\sigma_x/\mu) \qquad (1)$$

where x_o is the current total for a 4-week interval, μ is the mean of 15 totals of 4-week intervals (including the same 4-week period, the preceding 4-week period, and the subsequent 4-week period over the preceding 5 years of historical data), and σ_x is the standard deviation of these 15 historical incidence data values.

Log-Linear Regression Model

Farrington et al.[10] developed a log-linear regression model that is used to analyze national-level infectious disease data reported to the Communicable Disease Surveillance Center (CDSC) in the United Kingdom. The log-linear regression model used by this center to assess different types of variation in communicable disease incidence data is represented as

$$\log \mu_i = \alpha + \beta t_i \qquad (2)$$

where μ_i is the mean of the baseline, α is the threshold value, βt_i is the systematic component of the model, and i is the week indicator. The exceedance score X is estimated as

$$X = (y_0 - \mu_0)/(Y - \mu_0) > 1 \qquad (3)$$

for counts considered epidemiologically significant (e.g., counts of 5 or more in the preceding 4 weeks), where y_0 is the current weekly count, μ_0 is the corresponding historical mean, and U is the expected acceptable shift based on a 2/3 power transformation.

Quality Control Cumulative Sums Methods

CDC statisticians routinely apply the quality control method cumulative sums (CUSUM) to laboratory-based *Salmonella* serotype data using the *Salmonella* Outbreak Detection Algorithm.[7] Because more than 2,000 *Salmonella* serotypes exist and outbreaks are typically serotype specific, the model is always applied to *Salmonella* isolate data by serotype. The method is based on the formula

$$S_t = \max(0,\ S_{t-1} + (X_t - (\mu_0 + k\sigma_{xt})/\sigma_{xt})) \qquad (4)$$

for counts of 5 or more with a decision value of $S_t \geq 0.5$, where X_t is the count for the current week, μ_0 is the 5-year weekly mean, σ_{xt} is the standard deviation of the 5-year weekly counts for a given week, k is the detectable shift from the mean, S_t is the current CUSUM calculation, and S_{t-1} is the previous CUSUM calculation.

Quality Control Compound Smoothing Technique

A quality control method called compound smoothing (4253H) was developed by Stern and Lightfoot.[12] This method was applied to serotype *Salmonella* and *Shigella* data in Australia at national, state, and specified geographic levels. Weekly data are collapsed into monthly data over 5 years for a total of 60 observations, and the compound smoothing technique is applied to the median for consecutive monthly values using 4-month intervals, 2-month intervals, then 5-month intervals, and finally 3-month intervals across the entire time series. The 60 smoothed values are then smoothed an additional time by summing the estimates of one fourth of the previous month ($t - 1$), the current month (t), and one fourth of the following month ($t + 1$). The 60 observations represent five smoothed estimates per month, 1 month per year. After the data are resmoothed, the median is taken of these monthly estimates and then divided by the appropriate number of weeks for each month to return the estimate to a scale based on weeks. The current count x_o is compared with a threshold

$$x_o > \beta + 2{*}\sigma_x \qquad (5)$$

where β is the smoothed baseline, and σ_x is the standard deviation calculated as the differences between the smoothed value and the raw value for each data point.

Cyclical Regression Models

To assess the relationship between influenza virus circulation and cause-specific morbidity and mortality, cyclical regression models have been applied to influenza mortality data and to administrative data on hospitalizations and outpatient visits associated with influenzalike illness. In the United States, pneumonia and influenza deaths are monitored using excess death models. Time series autoregressive integrated moving average (ARIMA) models have been applied to pneumonia and influenza deaths to detect outbreaks or increases in the number of reported cases.[11]

The cyclical linear regression model used by CDC to evaluate pneumonia and influenza mortality trends uses 5 years of weekly historical mortality data with epidemic periods removed to estimate a baseline curve of expected weekly deaths for the subsequent season. The cyclical linear regression model can be written as

$$y = \beta_0\ \beta_1{*}\mathrm{Time}\ \beta_2{*}\mathrm{Time}{*}{*}2 + \beta_3{*}\cos(2{*}\pi{*}\mathrm{Time}) + \beta_4{*}\sin(2{*}\pi{*}\mathrm{Time}) \qquad (6)$$

where y represents the pneumonia and influenza deaths for a particular week, β_0 is the intercept, β_1 and β_2 represent terms associated with the secular trends, and β_3 and β_4 represent cyclical terms associated with seasonal trends.

Comparisons of these five published methods found that several methods had similar flagging patterns. Therefore, we selected two methods to be included in EARS: the historical limits method and the seasonally adjusted CUSUM method. In addition, CDC has more than 5 years of experience in problem solving using these two methods. EARS plans to incorporate additional validated aberration detection methods.

LONG-TERM IMPLEMENTATION METHODS WITH LIMITED BASELINE DATA

For long-term implementation methods with limited baseline data, we use C1-MILD, C2-MEDIUM, and C3-ULTRA. All three methods are based on the CUSUM formula,[4] with S_{t-1}, the previous CUSUM, equaling zero for C1-MILD and C2-MEDIUM. For C1-MILD and C2-MEDIUM, a flag is produced if the current count is greater than the baseline mean plus three standard deviations.

The other difference among the methods is the baseline used for the mean and standard deviation. C1-MILD uses data 1 to 7 days in the past for calculating the mean and standard deviation, and C2-MEDIUM and C3-ULTRA use data from 3 to 9 days in the past for calculating the mean and standard deviation, with C3-ULTRA based on a CUSUM calculation with an average run length time of 3 days (Fig. 2).

EARS SHORT-TERM DROP-IN SURVEILLANCE METHODS

The short-term implementation methods, or drop-in surveillance, are represented primarily by traditional quality control methods such as the P Chart, the moving average, and CUSUM. We also calculate a 2 × 2 table, chi square since epidemiologists are more familiar with this summary statistic. For these methods, the average run length is usually 30 days. The length of time for the surveillance periods tends to be very short (approximately 21 days); therefore, seasonality factors are less important in the assessment of daily aberrations.

It is important to consider that industrial manufacturers spend billions of dol-

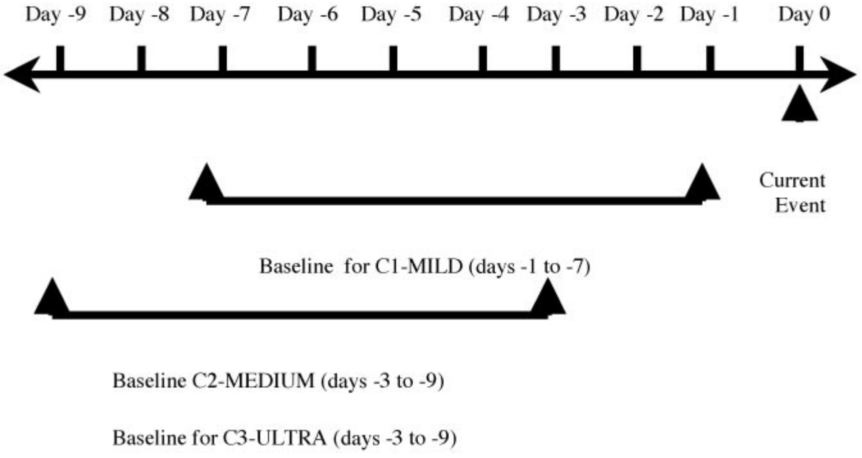

FIGURE 2. Baseline time line for C1-MILD, C2-MEDIUM, and C3-ULTRA.

lars on rather straightforward quality control methods because they successfully identify unusual or important aberrations and thus allow the companies to save significant amounts of money. Quality control methods are listed as one of the most important modern technologic inventions of the past century.[16] P charts were first developed in the 1920s and, as noted by Stoumbos et al.,[17] after 70 years of development, P charts and CUSUM methods are still among the most popular quality control methods used by industry. Quality control methods are currently used in a wide variety of industries, including manufacturing, engineering, environmental science, biology, genetics, epidemiology, medicine, finance, law enforcement, and athletics.

EXAMPLES USING THE EARS SHORT-TERM DROP-IN SURVEILLANCE METHODS

CDC has tested short-term, drop-in surveillance methods systems for identifying foodborne outbreaks, respiratory illnesses, and data entry errors. Unfortunately, following the September 11, 2001, attacks in New York City, we were unable to identify the cluster of anthrax cases in New York City in a timely manner. CDC was participating in the monitoring of hospital emergency departments, and individuals in six of the seven cases consulted private physicians.[18] Also, CDC and the New York City Department of Health were only monitoring for inhalation, not cutaneous, anthrax. Since then, CDC has modified the drop-in surveillance system and added monitoring for cutaneous anthrax cases.

SUMMARY

The CDC Bioterrorism Preparedness and Response Team continues to develop and expand its rapid assessment surveillance system (EARS). The main goal in the development and implementation of EARS is to provide local and state health departments with a tool to assist in the best application of often-limited resources during epidemiological investigations of important public health events.

EARS allows users to select validated aberration detection methods and modify sensitivity and specificity estimates to values considered to be of public health importance by local and state health departments. EARS can be used with a variety of data sources to produce outputs that enable the users to determine how many resources and personnel they can invest in investigating specific aberrations. This output can be viewed simultaneously by several different public health officials at different locations. EARS incorporates several different methods that have been validated using different data sources. If additional methods are validated and proven to be useful for identifying outbreaks important to epidemiologists, these methods will be incorporated into EARS, enhancing the information end users can receive and monitor.

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