

The ESSENCE II Disease Surveillance Test Bed for the National Capital Area

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Disease surveillance began in Europe in the 14th century to try to contain the spread of disease within communities. Since then, surveillance techniques have matured as new technologies and methods have evolved. Today, the threat of bioterrorism has placed ever-increasing demands on the need for early recognition of an outbreak. The Electronic Surveillance System for the Early Notification of Community-based Epidemics, version two (ESSENCE II), is being developed through a collaboration between the DoD Global Emerging Infections System and APL. ESSENCE II uses nontraditional health indicators in syndromic groupings coupled with advanced analytical techniques in an advanced information technology environment. It is the first system to integrate both military and civilian indicators into a test bed for the National Capital Area. This article provides a high-level description of ESSENCE II.

INTRODUCTION

One of the most insidious terrorist threats today is the widespread, clandestine release of a deadly pathogen on an unsuspecting population. Most pathogens available as bioweapons could cause high mortality and the potential collapse of the care delivery and emergency response systems in the area under attack. The contamination and closure of major medical centers, even if only temporary, could have an impact on the health of the populations they serve. To mitigate the consequences of such an event, an effective public health campaign must be launched early in the course of the outbreak.

Disease surveillance began in Europe in the 14th century as a means of controlling disease within communities. In the United States, disease reporting began in 1741 when Rhode Island passed an act requiring tavern

keepers to report patrons with contagious diseases. In 1743 a broader law was passed requiring the reporting of smallpox, yellow fever, and cholera. In 1925 all states began participating in a national morbidity reporting system following the severe poliomyelitis epidemic of 1916 and the influenza pandemic of 1918–1919.

Traditional disease surveillance requires the identification and reporting of certain diseases to the local health department, with the information subsequently making its way to the state and national level. However, reporting is typically not performed until a confirmatory result is obtained from a laboratory analysis of samples taken from patients with disease. For a widespread bioterrorism event, the delay introduced by this identification process may result in delayed implementation of preventive

measures. Figure 1 illustrates the impact of time on mortality for an anthrax weapon.

The red curve in Fig. 1a represents the cumulative probability of detection for a surveillance activity that relies on sick people presenting with acute symptoms in a clinic or emergency room and the recognition of that disease by the care providers. At this stage, anthrax is difficult to treat effectively. The blue curve represents a detection requirement that must be met in order for an effective response to be delivered. Anthrax is more readily treatable 2 or more days before it is normally recognized, when the symptoms may be only flu-like in nature. Figure 1b shows the impact of an effective public health response on mortality. This response would include identification of the disease, an estimate of the size of the infected population, administration of prophylaxis, and follow-up with the population at risk.

With the increased concern not only over bioterrorism, but also over the reoccurrence of deadly diseases from the past (e.g., malaria, highly virulent strains of influenza), and with the presence of diseases not previously found in this hemisphere (e.g., West Nile virus), new techniques are being developed to rapidly identify abnormal disease patterns in the population. These techniques include the use of nontraditional health care indicators and syndromic surveillance. This article addresses the use of such techniques in the Electronic Surveillance System for the Early Notification of Community-based Epidemics, version two (ESSENCE II). Other articles in this issue provide a more in-depth look at the analytical techniques and

information technology used in the system (see Happel Lewis et al. and Magruder, this issue).

ESSENCE I is a worldwide military syndromic surveillance system operated by the DoD Global Emerging Infections System (DoD-GEIS).^{1,2} ESSENCE II relies solely on the acquisition and processing of existing data from various sources. It is also unique in that it is the only known system to integrate both military and civilian health care indicators. This integration is possible because of the collaboration between DoD-GEIS and APL on ESSENCE II development.

ESSENCE II is being developed as a test bed for the National Capital Area (NCA). As such, it permits the implementation and evaluation of novel surveillance concepts.

The NCA is a complex, multi-jurisdictional region with a large military population. A significant portion of this population works and resides in different public health jurisdictions. Because pathogens do not honor jurisdictional boundaries, the sensitivity needed for the early identification of bioterrorism can be achieved only by the integration of information across the region. ESSENCE II is providing this capability in a syndromic surveillance format and making the system outputs available to all public health jurisdictions in the NCA region.

ESSENCE II

System Description

ESSENCE II comprises several modular components (Fig. 2) that are being developed in parallel. The systems architecture permits individual components to be upgraded in a nonproprietary environment with inexpensive off-the-shelf applications software.

The data and the telecommunications infrastructure for acquiring and transferring the information are external to the system. ESSENCE II modules implement the following:

- Policies to ensure the privacy of personal health care information
- Policies governing the exchange of information among other surveillance or reporting systems
- Data archive
- Processes for detection and alerting of abnormalities in the indicator data
- Processes for notifying users of special events or environmental conditions that warrant changes in detection parameters
- Processes that allow users to fully exploit the archive to identify

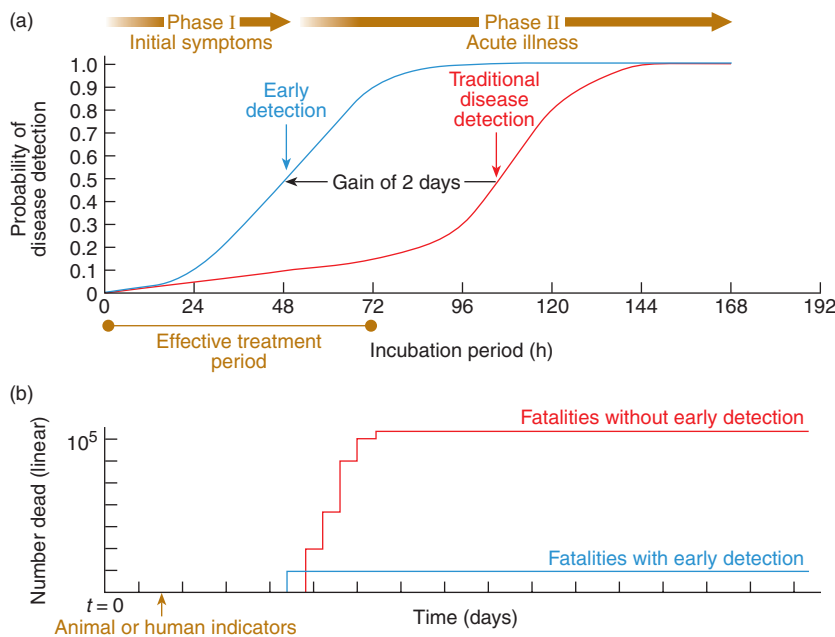


Figure 1. Impact of early recognition and an effective public health response on mortality for an anthrax weapon: (a) cumulative probability of detecting abnormal disease occurrence with and without aggressive surveillance, and (b) potential reduction in mortality due to aggressive surveillance. (Anthrax is noncommunicable; victims are exposed directly.)

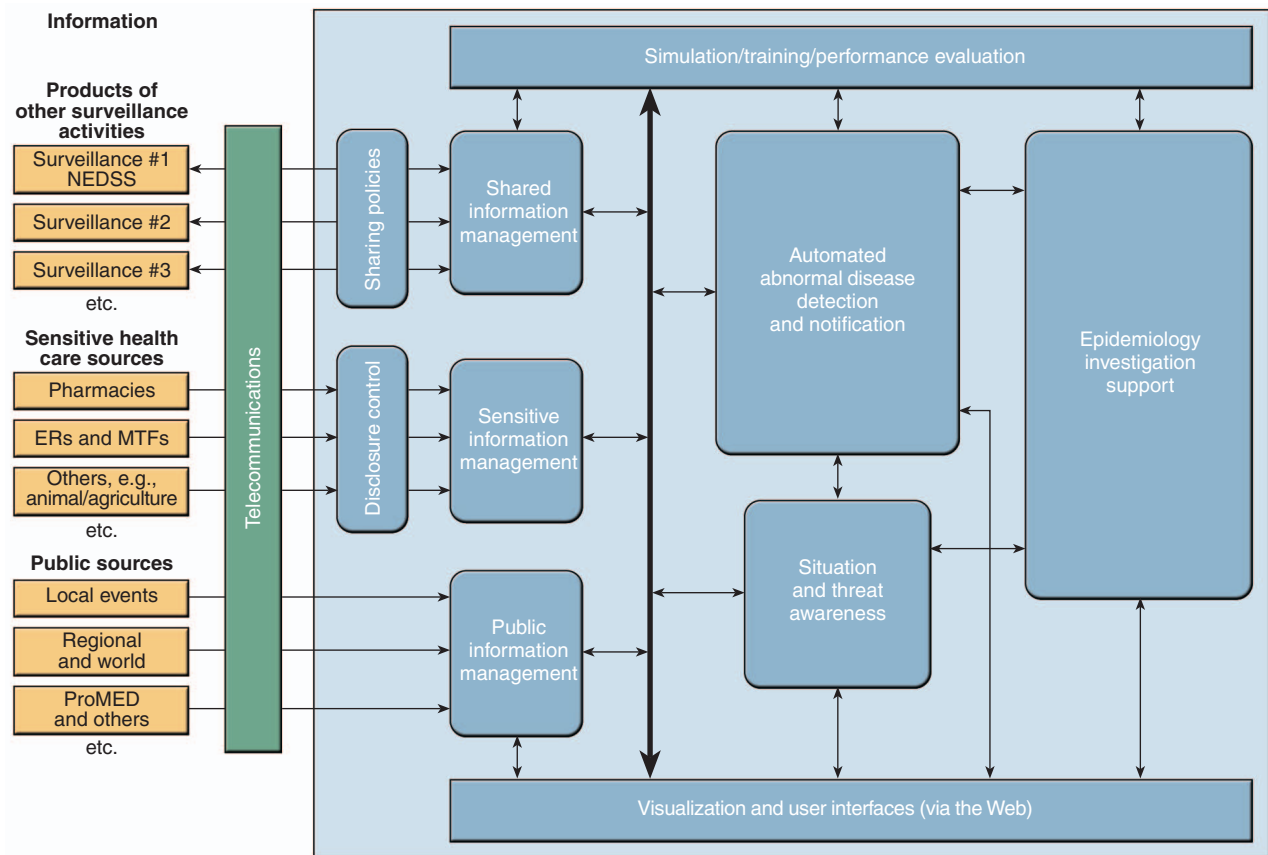


Figure 2. Functional view of ESSENCE II test bed components (MTFs = military treatment facilities, NEDSS = National Electronic Disease Surveillance System).

false positives or to obtain information about current or historical trends in the indicator data

- Visualization and user interfaces
- Processes for injecting simulated data for training and measuring the performance of ESSENCE II detectors and indicators

The data needed to effectively use and operate ESSENCE II fall into three distinct categories: sensitive health care information, publicly available information, and products of external surveillance.

The first category consists of basic information that implicitly contains the levels of disease activity in the population, e.g., chief-complaint data from hospital emergency rooms; International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) codes used for billing patient visits for private practice groups; over-the-counter (OTC) sales of pharmaceuticals that can be used for self-medication; nurse hotline calls; school absenteeism records; etc. We have grouped these data streams into the *sensitive health care* category because they may be acquired and used only in conformance with privacy laws, corporate policies, memoranda of agreements, etc. These data sources also have varying degrees of specificity associated with their use in surveillance. For example, laboratory tests are more spe-

cific indicators of public health issues than are sales of OTC medications. An increase in sales may be a result of sales promotions, the onset of the winter season, or stocking up in anticipation of need. Unless the uncertainties in the nontraditional data sources can be sufficiently resolved, their use must be given lower weighting in the anomaly detection process.

Providers of data in the sensitive health care category must maintain the privacy of individuals. Therefore, before ESSENCE II can use the sensitive data, identifiers must be removed.³ If the personal records cannot be made totally anonymous, their use must be limited, and other surveillance initiatives may not be able to share them. The process of ensuring anonymity ("anonymization") can be performed before the data are sent to the ESSENCE II test bed.

Supporting information needed to effectively use data with low specificity falls into the second category: *publicly available information*. For example, data about local endemic disease, sales promotions, and even weather events are important to support the use of OTC pharmaceutical sales data as an early indicator of the presence of disease. This information in most cases is available via electronic media. Likewise, the occurrence of high-profile events in the community may change detection and alerting thresholds.

The third category of information consists of the *products of external surveillance* activities in the NCA. Many of these activities generate results that could be useful for increasing the sensitivity, specificity, and timeliness of alerts from ESSENCE II. Agencies conducting the surveillance activities must agree on which data elements can be shared. Integral to the ESSENCE II test bed is a set of rules that implement the policies agreed to by the providers and recipients of sensitive data.

In summary, to ensure that sensitive information is not compromised, the ESSENCE II data archive is partitioned into three parts: public domain information, sensitive health care data, and data that are subject to the policies agreed upon by the providers and users of the data.

Sensitive Health Indicator Data Sources

For ESSENCE II to achieve the desired early warning performance, it must evaluate all reasonable data sources. Therefore, a primary objective of the ESSENCE II project is to identify sources of data that contain early indicators of abnormal disease in the population. Many of the data sources are unconventional when compared to past or present surveillance activities undertaken by public health entities. Data sources can be segmented into three categories: traditional, nontraditional clinical, and nontraditional nonclinical.

The traditional gold standard is a confirmed laboratory result, but this data source may not provide the timeliness needed to respond to a widespread outbreak caused by a covert attack with a weaponized disease. Nontraditional clinical data are obtained from encounters with health care professionals. These data are potentially crucial to early detection because the early presentation of diseases caused by a biowarfare attack, as noted in the previous anthrax example, is likely to resemble common illnesses such as influenza.⁴ Syndromic surveillance, using the ESSENCE II syndrome groups when possible, is applied to these data. Data sources in the nontraditional clinical category could include 911 calls, nurse hotline calls, poison center calls, visits to private practice physicians and military clinics, requests for laboratory work, emergency room visits, and prescription medications purchases.

Daily counts are grouped to the following syndromes:

- Death
- Gastrointestinal
- Neurological
- Rash
- Respiratory
- Sepsis
- Unspecified

Each group is defined by a specific set of ICD-9-CM codes. In conducting surveillance on symptoms that

occur in the early stages of disease, ESSENCE II monitors the occurrence of common diseases. The daily syndrome group counts usually reflect the normal background levels. The key to effectively identifying abnormalities in syndrome group levels is the ability to model and estimate normal background levels, which vary as a function of season and the normal evolution of endemic disease strains.

One problem with removal of all personal identifiers in nontraditional clinical data is that a single case of illness could show up in several of the data streams used for surveillance. For example, a call to a nurse hotline could result in a visit to a private practice physician, a request for a laboratory test, and a medication prescription. Without a way to link the data sources by individuals, these dependencies tend to degrade the performance of alerting algorithms. Patient records from military treatment facilities and many health maintenance organizations can be used to link data sources; however, since the data contain identifiers, these records can only be used internally. The other approach is to find data sources that are totally independent. Capturing surveillance data on zoonotic diseases (diseases communicable from animals to humans) provides an independent data source that can be used to reduce false positives. These independent sources may not always be available, however.

Nontraditional nonclinical data contain disease indicators that are not reported as the result of an encounter with a health care professional. Included in this category are absenteeism and the purchase of OTC medications. Such data cannot be easily grouped by syndrome. OTC medications can be grouped as anti-flu or anti-diarrheal, etc., but absentee records do not typically indicate the causes of absence. It is also difficult to determine from the data elements available how many independent occurrences of illness exist in these sources. Despite this drawback, on average, increases in OTC sales of anti-influenza medications have preceded increased activity in emergency rooms by up to 4 days. Figure 3 shows a typical example of this relationship (see also the article by Magruder, this issue). However, it is difficult to separate out the existence of actual illness represented by OTC sales versus stocking up for the upcoming cold and flu season. Several years of data are needed to understand the sales patterns of these medications.

The effective use of nontraditional data requires the understanding and modeling of confounders that result in normal increased levels of activity. For OTC medications, as noted earlier, these confounders include sales promotions, stocking up owing to the onset of seasonal changes, and socio-economic factors that limit the use of these medications. Florio⁵ has modeled the effect of these confounders, which has resulted in better utilization of OTC sales data in the detection process. Figure 4 represents the impact of the season, day of week, and sales promotions on daily sales of OTC flu medications.

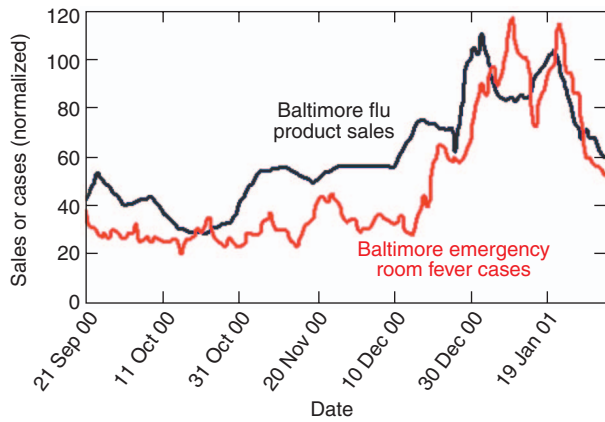


Figure 3. Flu product sales versus emergency room fever cases in Baltimore during the 2001–2002 influenza season. Curves were normalized by dividing the daily levels by their seasonal mean.

Electronic Data Collection and Formatting

Disease surveillance activities requiring daily feeds from several data sources must rely on modern information technology and telecommunications. Automated collection, transfer, formatting, processing, and visualization are needed to ensure continuous operations. In addition, the processes implemented must fit into the business rules and privacy policies of the organizations supplying the data.

Wojcik⁶ has defined methods for the electronic acquisition and formatting of sensitive health indicator data. Take, for example, automated hospital emergency room data. Chief-complaint text fields are typically captured and archived on an emergency room log. Scheduled queries can be made to this archive to generate an electronic report that includes a limited set of data fields, which satisfies privacy policies while capturing those fields needed to perform surveillance. The electronic report is encrypted, sent to a secure FTP site, and placed in a unique location set up for the hospital's data. The surveillance system continually polls the site for update

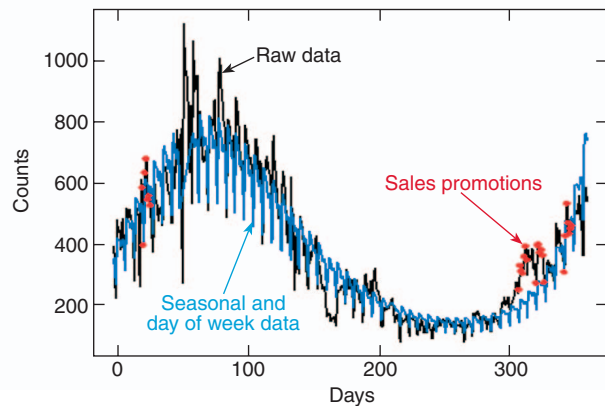


Figure 4. Comparison of raw data with model output for over-the-counter flu medication sales.

information and transfers the encrypted record into the surveillance archive. As soon as the new record is received in the archive, a natural language parsing program converts the chief-complaint text into syndrome groupings. Once converted to this common format, the information is available for use or for other surveillance activities. Within minutes of the query to the hospital emergency room's electronic log, the system can forward counts of the syndrome groups to the participating hospital, state, and county surveillance activities. Figure 5 illustrates the process.

Detection of Abnormal Health Conditions

ESSENCE II has been used to investigate several analytical processes needed to detect abnormal syndromic levels using heterogeneous data types. Abnormal disease patterns can be determined by constructing detectors that operate on the input data streams. The ESSENCE II program has investigated such statistical techniques as odds ratios,⁷ autoregressive estimates,⁸ cumulative summation⁹ techniques from industrial quality control, and matched filter techniques¹⁰ used in radar and sonar signal processing. Surveillance using purely temporal techniques depends on the choice of geographic regions whose counts are included in the time series. If the aggregate region is too small or not well chosen, the counts may be too small for accurate background representation, and outbreak cases may be excluded. Conversely, if the region contributing to the time series is too large, early cases of an outbreak may be lost in the noise. In practice, the temporal algorithms are usually run at the county level.

Spatial processing techniques are applied to avoid spatial preselection bias. Most data available to ESSENCE II can be resolved down to only the patient zip code. The Health Insurance Portability and Accountability Act of 1996 prohibits greater resolution because it specifies that local jurisdictions may limit the use of information that can identify the health care records of individuals. The primary spatial approach in ESSENCE II has been an enhanced use of the Kulldorff scan statistic^{11,12} as implemented in the Satscan software available from the National Cancer Institute. This method combines a likelihood ratio statistic developed by Kulldorff with a cluster analysis technique that finds clusters of maximum likelihood, regardless of location or extent. Several modifications have been necessary for application to the various data sets of ESSENCE II; e.g., because the spatial data are not generally proportional to the populations of the underlying zip codes, modeling or data history is used to calculate expected zip code counts. Substantial data analysis has been done to reduce the false cluster rate.

Burkom¹³ has applied the Kulldorff statistic to multiple data sources in ESSENCE II by treating them as covariates while using whatever spatial information is

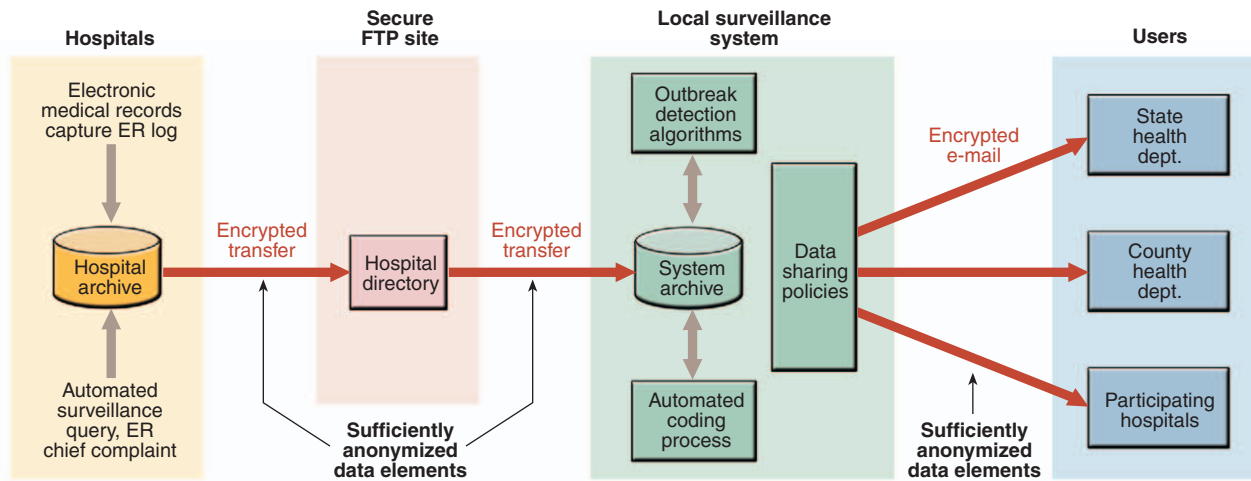


Figure 5. ESSENCE II process for capturing emergency room chief-complaint information.

available in each source. Figure 6 presents an example using two data sources: OTC sales of anti-flu medications and physician office visits with diagnosis codes in the respiratory syndrome group. The figure represents a test case where an insignificant cluster was found using the physician office visits alone (p -value indicates a 9.3% chance of random event), but when the OTC sales were added, a more significant cluster was formed (p -value indicates a 0.1% chance of random occurrence). The spatial information used for this analysis included patient zip codes and exact store locations. An advantage of this method is that additional sources or improved spatial information can be readily incorporated.

The modified scan statistic produces approximate clusters of space–time interaction. Its clusters may also be used to reduce the preselection bias in the temporal methods noted above or in more elaborate

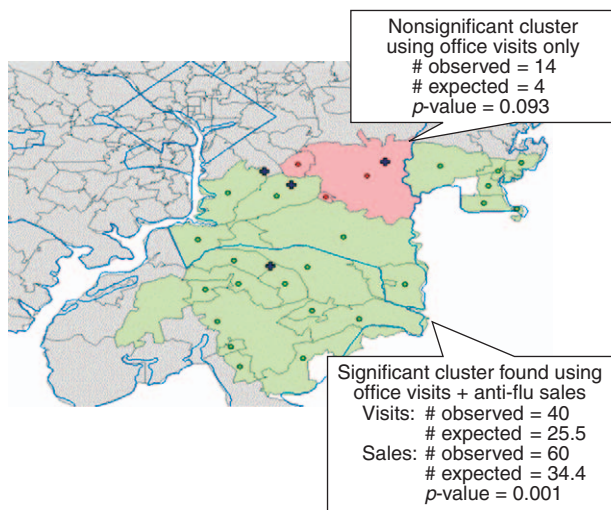


Figure 6. The effect of cluster formation using data on both physician office visits and over-the-counter pharmaceutical sales.

spatial–temporal alerting methods. Given the appropriate surveillance focus, a time-domain matched filter method¹¹ has shown the potential for excellent sensitivity as a regional anomaly detector.

Internet-Based Information Distribution

A basic function of ESSENCE II is to deliver alerts and surveillance information to civilian public health authorities in the NCA. The system provides detector outputs as well as the details of individual data streams via secure Web sites. Figure 7 shows an example from the ESSENCE II site.¹⁴ Data are provided in many separate information layers. Layering was implemented to facilitate distribution to the various users. Separate user names and passwords are provided so that ESSENCE II can recognize each authorized user and give only the data the user is authorized to view. For example, a user who logs on from an emergency room may be able to see only the emergency room data from his or her jurisdiction, whereas a user recognized as a director of epidemiology would have access to all the information within his or her jurisdiction as well as the shared information from the surrounding jurisdictions.

Each ESSENCE II layer is divided into sublayers. For many of the sensitive health care data layers, the sublayers are the ESSENCE syndrome groupings. Sublayers for OTC product groupings contain anti-influenza and anti-diarrheal medications. Sublayers for school absenteeism data are the sets of elementary, middle, and high school records. The cursor can be used to select one or several zip codes for temporal plotting of individual data elements. ESSENCE II contains lists of data indicators prioritized by the degree of the anomaly.

Various plotting formats are available for presenting archived data to help resolve false positives or initiate an investigation when needed.

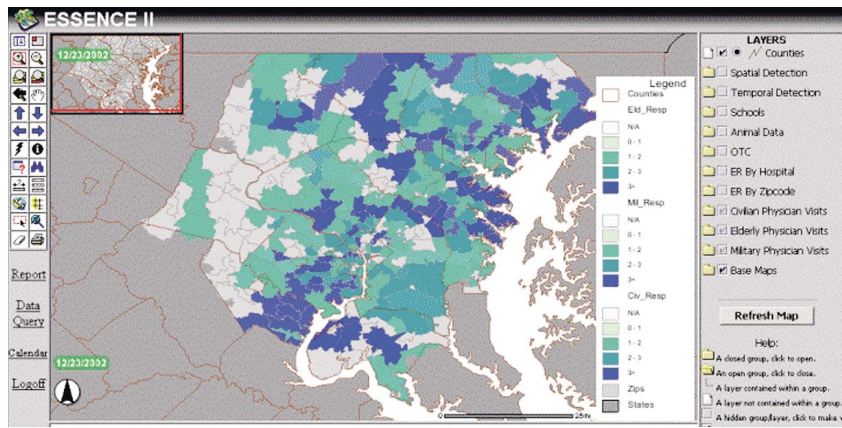


Figure 7. Screen shot showing incidence of respiratory counts in the National Capital Area based on military and civilian physician visits.

EVALUATION AND PERFORMANCE

A major difficulty in the development of a disease surveillance system for bioterrorism is lack of experience with authentic outbreak data with which to design the system. ESSENCE II has relied on two separate approaches for evaluating its early alerting capability. The first is its ability to identify unusual endemic disease events. Large seasonal events are relatively easy to detect (allergies, influenza, etc.) compared to smaller events that are more contained in time and space.

A second approach for determining performance is to simulate a variety of different bioterrorist events. This requires an understanding of susceptibility, infectivity, symptoms at onset, human behaviors, and many other physical parameters (see the article by Happel Lewis et al., this issue). Given an incomplete understanding of the effects of many possible pathogens, constructing an accurate outbreak model that includes estimates for indications in all of the ESSENCE II data streams is also very difficult. The validity of the actual estimates obtained can be questioned, but estimates are needed if a solution is to be found. These estimates can be refined as additional knowledge to properly model the parameters is obtained.

To assess the performance of the processing used in the ESSENCE II test bed, several outbreak scenarios were developed that consist of the following steps:

1. Select a time, location, pathogen, and mode of dispensing the material with a specific terrorist objective in mind.
2. Review the literature for previously published information on infectivity, incubation period, onset distribution, symptoms at onset, the change in symptoms in the acute phase of the disease, etc. ESSENCE II has relied on previous work performed by Sartwell¹⁵ to estimate the distribution of the onset of disease symptoms.

3. Estimate the percentage of the infected population fitting into socio-economic classes and age brackets.
4. Estimate the behaviors of economic classes and age brackets from analysis of behaviors during previous influenza seasons.
5. Using steps 3, 4, and 5, create a temporal and spatial model of the additional numbers of cases, products sold, absenteeism, etc.
6. Merge additional cases with actual data streams obtained previously during the same time of year as the simulated event.

The result of this method is a series of real data streams with a simulated outbreak superimposed. The alerting algorithms use these data streams as a test case for evaluation. The number of infected people and other units added to each data stream are treated as parameters, not only to test the performance of the algorithms but also to assess the value added of each data source. Figure 8 shows detector performance as a function of the number of infected and the number of data sources used in the detection process. The number of infected is varied to achieve a detector performance with a sensitivity of 0.95 and a specificity of 0.97.

The data set for this evaluation includes four data types: hospital emergency room respiratory syndrome counts, office visit respiratory counts, OTC influenza medication sales, and school absentee totals. Figure 8 is from a targeted surveillance scenario in which a

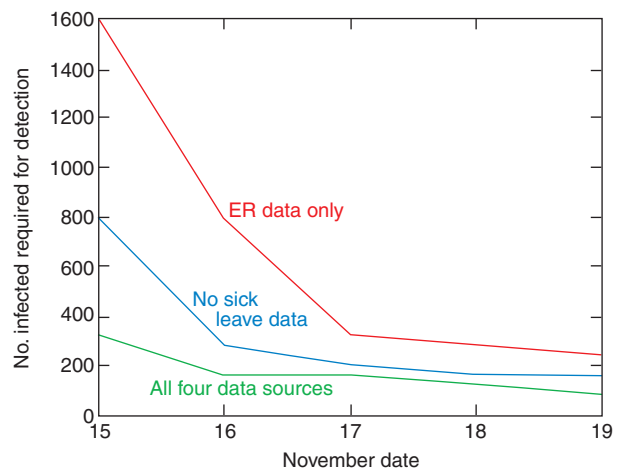


Figure 8. Wide-area detection performance as a function of the number of indicators used. In this case, indicators were sick leave, OTC medication sales, physicians' office visits, and emergency room visits. (Scenario based on the release of *Franciscella tularensis*, which results in tularemia; number of infected is varied to achieve detector performance with a sensitivity of 0.95 and a specificity of 0.97.)

matched filter algorithm was applied over a fixed geographic area. The scenario shown in the figure includes a large percentage of school-aged children in the infected population, with onset of the symptoms occurring during a week when these children would normally be at school.

For this scenario, absenteeism was a major contributor to the early detection of the abnormality. It permitted the abnormality to be identified with 300 infected when used in conjunction with the other data sources. Similar performance with only emergency room syndromic surveillance would require an infected population of 1600. Two days later, similar performance could be achieved with emergency room data alone.

The performance outcome is a direct result of the scenario chosen (time, location, incubation period, etc.). If the onset had occurred when school was not in session, this result could not have been achieved. A scenario with onset occurring on a weekend, in the inner city, or during the summer would favor the emergency room indicator. For a surveillance system to be effective, it must evaluate each indicator source in the context of a wide variety of scenarios.

STATUS

ESSENCE II has been developed as a tool for health department epidemiologists to support the early recognition of abnormal disease patterns within the NCA. This research test bed is being used to identify health indicators for early recognition of abnormal disease, as well as algorithms that can be used to detect those abnormalities. It also provides a user-friendly interface to permit a rapid investigation. Versions of ESSENCE II are being delivered to the Maryland, Virginia, and District of Columbia health departments to form a surveillance network for the NCA.

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