RESEARCH

National Survey of Laboratory Response Network Sentinel Laboratory Preparedness

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ABSTRACT

Objective: The Laboratory Response Network (LRN) is the United States' laboratory system for detecting, confirming, and reporting potential bioterrorism agents. The first tier—sentinel laboratories—is composed principally of hospital-based laboratories and is tasked with ruling out potential biological threat agents in clinical specimens or the identification of suspicious specimens for further testing in higher tiers of the LRN system. The aim of the present study was to broadly describe preparedness of the first tier of the hospital LRN, the sentinel laboratories, with a specific focus on training, personnel, and communications.

Methods: A semistructured cross-sectional survey of US sentinel laboratories was designed and conducted. Hospitals with greater than 250 beds and an emergency department were considered eligible for inclusion. A geographically weighted sample of 201 hospitals was selected for inclusion. The survey was administered by telephone to the microbiology managers (or designees) at the selected hospitals. The survey contained questions related to drill frequency, proficiency survey participation, personnel training, personnel responsibilities, procedures for biological threat response, and overall confidence in preparedness.

Results: Overall, 179 hospitals (89.1%) identified themselves as sentinel laboratories and participated in the survey; 11.7% reported that they had had an emergency alert within the last 2 years. Although rates of internal drills were low (20.7%), participation in some form of bioterrorism proficiency evaluation was high (79.9%). In all, 83.8% of laboratories reported that they had personnel designated to coordinate response to acts of bioterrorism. More than 73% of respondents indicated that they had sufficient personnel, equipment, and training to respond to a biological terrorism event. By multivariate analysis, sentinel laboratories were 3.4 times more likely to feel confident that they had sufficient personnel, equipment, and training to respond to a biological terrorism event if they had designated personnel for bioterrorism roles.

Conclusions: This pilot study of sentinel laboratory bioterrorism preparedness demonstrated that hospital laboratory personnel, training, and communication preparedness were not universal, despite designation as sentinel laboratories. A need for unified monitoring of sentinel laboratories exists, and efforts should be made to develop standardized metrics for sentinel laboratory preparedness. (*Disaster Med Public Health Preparedness.* 2009;3(Suppl 1):S17–S23)

The Laboratory Response Network (LRN) is the United States' laboratory system for detecting, confirming, and reporting potential bioterrorism agents. Founded through the collaborative efforts of the Centers for Disease Control and Prevention (CDC), the Association of Public Health Laboratories (APHL), the US Army Medical Research Institute of Infectious Diseases, and the Federal Bureau of Investigation, the LRN is a 3-tiered network, with each tier serving a discrete function in biological threat detection and response.[1] The first tier—sentinel laboratories—is composed of approximately 2300 laboratories (principally based in hospitals) that are embedded in the communities of the nation. As part of their daily routine of processing large numbers of patient samples for clinical purposes, sentinel laboratories are tasked with singling out suspicious biothreat specimens for further testing in higher tiers of the LRN system.[1] Workers responsible for this task are hospital and veterinary microbiology laboratory technologists, who receive basic sentinel clinical laboratory training (including rule-out testing, packaging and shipping of infectious agents, and biosafety), and use a variety of routine microbiological methods, such as staining, colony morphology, and various rapid tests, described in standardized

pathways.[2] Sentinel laboratories must operate using Biosafety Level 2 procedures and possess a class II certified biological safety cabinet.[3]

When suspected biothreat agents are identified, they are sent on to 1 of the nation's 150 second-tier LRN reference laboratories, which principally comprise local and state public health laboratories.[1] When a suspicious agent is confirmed by reference laboratories, the specimen is passed on to the third tier of the pyramid, the national laboratories, which are responsible for select agent handling, strain characterizations, and other highly specialized tasks such as bioforensics, specimen repository, and handling of highly infectious biological agents.[1] National laboratories are few in number, tightly regulated at the federal level, and staffed with highly trained and skilled personnel.

Reference laboratories, although much larger in number, are also moderately to highly regulated at the state level, and are staffed with personnel who receive specialized training. Direct monitoring of the reference laboratories is conducted via regular proficiency training overseen by the CDC Laboratory Response Branch. Additional monitoring is ensured via the CDC's Coordinating Office for Terrorism Preparedness and Emergency Response, which functions under the Public Health Emergency Preparedness Cooperative Agreement and is responsible for routine monitoring of reference laboratories across a variety of measurements, including outreach efforts to the sentinel laboratories. In addition, the APHL conducts annual assessments of state public health laboratories that focus on funding, workforce, laboratory connectivity, laboratory integration, sample intake, laboratory testing, and reporting capabilities.[4]

The LRN system is heavily reliant on the base of the pyramid—the numerous community-based sentinel laboratories—for the early recognition of suspicious organisms and the referral of samples for further analysis. This role is critical to the overall mission of early detection and rapid response to bioterrorism events. The effective operation of this complex, multilayered system requires robust and reliable methods for monitoring preparedness at all tiers, especially because individuals with varied degrees of expertise must integrate seamlessly to produce a coordinated response.

Although the sentinel laboratories serve as a pillar of the federal LRN system, the CDC largely delegates monitoring of these laboratories to the state and/or local reference laboratories. Because sentinel laboratories may be private, there are no formal requirements for them to participate in training and oversight, which is mandated for the publicly based reference and national laboratories. Although training is available to sentinel laboratories, few incentives for participation exist, and there are numerous uncompensated costs to hospitals for sending laboratory personnel to participate in training exercises. A careful search of the literature and a review of LRN-related materials revealed that there is no uniform approach to systematically evaluating interoperability and preparedness of sentinel laboratories. Although the College of American Pathologists distributes a biannual Laboratory Preparedness Exercise as an educational survey for the detection of emerging and biothreat pathogens, participation in this proficiency survey is voluntary and the survey largely focuses on detailed technical procedures (as opposed to structural/systemic components of preparedness).[5] No uniform assessment of readiness (including training, personnel, and communications) for sentinel laboratory preparedness exists, as is conducted by APHL for reference laboratories. This is a critical gap in bioterrorism preparedness that needs to be addressed.

The aim of the present study was to broadly describe the preparedness of hospital sentinel laboratories, with a specific focus on capacity (specifically training, personnel, and communications). To accomplish this goal, we undertook a survey of LRN designated hospital-based sentinel microbiology laboratories across the United States. Because this is the first survey of a national system, we chose to evaluate a representative sample, and the survey was necessarily broad in scope. The results of this study should provide the first national picture describing the level of preparedness of the first tier of the LRN system. It is intended that this initial survey will guide further in-depth analyses, provide a framework for developing measurements used to gauge sentinel laboratory preparedness, and inform policy makers regarding future resource allocation.

METHODS

This study was funded by the Department of Homeland Security as part of a Consortium Program Project (Center of Excellence for the Study of Preparedness and Catastrophic Event Response) aimed at establishing the scientific foundation and principles of the practice of homeland security in matters of preparedness and response to catastrophic events. This project was one of several from a study group focused on describing and evaluating methods of biothreat detection and surveillance. This study was deemed exempt by the Johns Hopkins University institutional review board.

A nationally representative cross-sectional survey of US sentinel laboratories was designed and administered. Because no publicly accessible list of sentinel laboratories was available for sampling, hospitals with more than 250 beds and an emergency department were considered eligible for inclusion. Hospitals with fewer than 250 beds were considered less likely to have the laboratory capacity required to be designated as a sentinel laboratory. A list of eligible hospitals was obtained from the American Hospital Directory (*www.ahd.com*). Sample size calculation estimated that a sample size of 196 hospitals would provide a power of 80% to detect 50% of sentinel laboratories with sufficient personnel/equipment/training to respond to a biological terrorism event (upper bound 60%, lower bound 40%, $\alpha = .05$, 2-tailed test). Considering potential nonresponders, we oversampled an additional 50% of hospitals, giving a sample size of 300 for

the survey. A stratified random sampling scheme selected by CDC-defined geographic regions (Northeast, Midwest, South, and West) was performed such that the number of hospitals sampled from each region was proportional to the total number of hospitals in the region. Surveys were completed by telephone or submitted by fax or e-mail, based on recipient request. Multiple attempts for telephone contact were made over a 4-month period (February–May 2008). Any hospital microbiology laboratory that was determined not to be a sentinel laboratory (by self-report) was excluded from the analysis (22 were excluded).

Survey content was adapted from the APHL Survey for Laboratory Preparedness for Bioterrorism, which has been distributed on an annual basis to state public health laboratories since 2002, and is widely accepted as a key tool for educating policy makers, scientists, and the public.[4] Several additional questions were included to directly address the unique role of sentinel laboratories in the LRN, based on expert input from representatives from various professional organizations in the field of laboratory science and preparedness. The final survey contained 31 fields, with specific questions related to drill frequency, proficiency survey participation, personnel training, personnel responsibilities, procedures for biothreat response, and overall confidence in preparedness. The survey was vetted and finalized with input from content experts in microbiology and laboratory preparedness from academia and professional organizations. Survey respondents also were given the opportunity to state their recommendations for improvement in laboratory bioterrorism preparedness.

Data Analysis

Descriptive data analysis was used to assess respondent characteristics with adjustment for sampling weights based on a stratified random sampling scheme. Bivariate analyses, followed by multivariate logistic regression analyses, were performed to identify significant factors ($P < .05$) associated with perceived confidence to respond to a biological terrorism event. SAS version 9.1 (SAS Institute, Cary, NC) was used to perform all data analyses.

RESULTS

Of 300 laboratories in the sample, 201 (67%) agreed to participate. Of the participants, 179 (89.1%) self-identified as LRN sentinel laboratories (Table 1). The following results pertain only to those laboratories identified as sentinel laboratories. Of those laboratories, 29% reported that they had a previous emergency alert experience, with 11.7% reporting that they had an emergency alert within the last 2 years (Table 2, Fig. 1A).

Rates of training exercises were reported as follows: 20.7% of laboratories reported that they conducted internal drills related to biothreat detection; 62.0% reported that they participated in drills with a local or state public health laboratory, an LRN laboratory, first responders, or another agency;

TABLE 1

General Questions Related to Sentinel Laboratory Status

	Yes, %
Are you a sentinel laboratory?*	89.1
Written algorithms in place for ruling out BT pathogens	99.4
If yes, are these algorithms reviewed annually?	97.2
Quality assurance protocols for ruling out BT agents	68.8
Sufficient personnel/equipment/training to respond to a BT event	73.8
If no, what could be improved?	
Training	51.4
Additional personnel	28.4

BT = biological threat.
*Asked of all 201 participants.

and 79.9% of laboratories reported that they participated in some form of a bioterrorism proficiency survey (with 90.1% of these laboratories participating in the College of American Pathologists Laboratory Preparedness Exercise; Table 2, Fig. 1B). Nearly all (97.2%) of the respondents stated that they had written methods/algorithms in place for ruling out biothreat pathogens that were reviewed annually, whereas 68.8% of laboratories stated that they had quality assurance protocols in place specifically for ruling out biothreat agents (Table 1).

With regard to personnel resources, 83.8% of laboratories reported that they have personnel designated to coordinate bioterrorism response, and 73.2% have a designated employee who serves as a liaison to their LRN reference laboratory. Of respondents, 81% reported that their institution had a bioterrorism advisory committee or equivalent group; 71.5% of these laboratories reported having a representative to the committee (Table 3, Fig. 1C). Figure 1D displays the percent of respondents with personnel trained to rule out specific bioterrorism agents.

In terms of communications preparedness, nearly all (99.4%) of the respondents stated that they had protocols in place to notify the appropriate LRN reference laboratory in the event that a biothreat agent could not be ruled out, and the same percentage of respondents maintained the contact informa-

TABLE 2

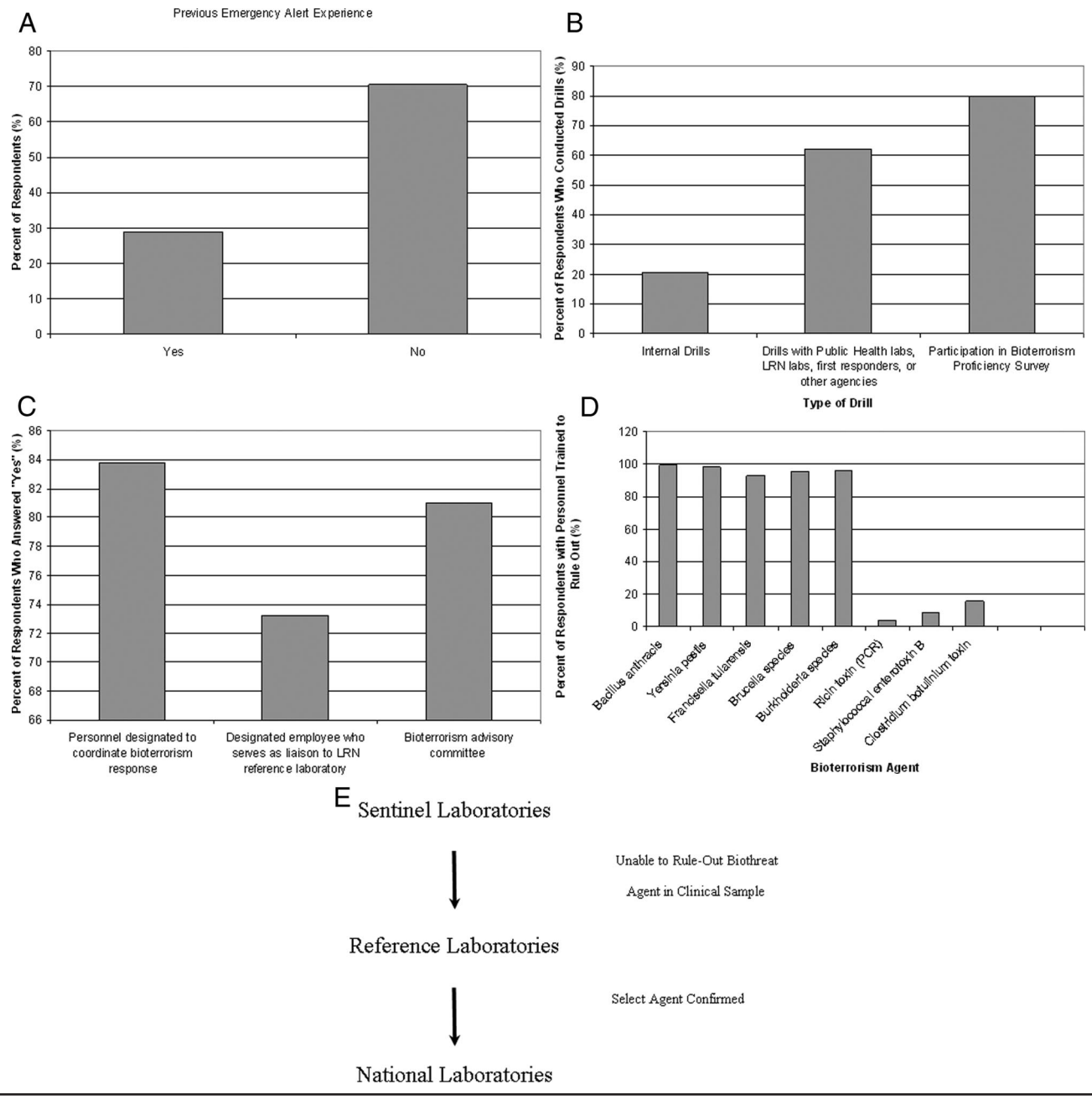
Survey Questions Related to Laboratory Training Practices

	Yes, %
Internal drills	20.7
Drills with PH/LRN laboratories or other agencies	62.0
Participate in BT proficiency survey	79.9
Previous emergency alert experiences	29.0

BT = biological threat; LRN = Laboratory Response Network; PH = public health.

FIGURE 1

A–D, LRN Sentinel Laboratory Survey Result Summary; E, schematic of LRN system.



tion for their LRN reference laboratory. Almost all (98.9%) of the laboratories reported having a laboratory information system (LIS)[6] in place, but only 28.4% of those reported that their LIS allowed them to send, create, and receive Public Health Information Network–compliant HL7v2.5 messages. Of laboratories with an LIS, 9.5% stated that their LIS has a component for biological terrorism testing data. When asked how they would communicate test results related to suspected biothreat agents to their LRN reference laboratory, 95.5% used telephone, 7.3% used online results reporting, 10.1% used fax, 3.4% used e-mail, and 1.7% used their LIS. All but 1 laboratory responded that they have an all-hours emergency contact system in place (Table 4).

Overall, 73.8% of laboratories indicated that they had sufficient personnel, equipment, and training to respond to a biological terrorism event (Table 1). By bivariate analysis, only the presence of personnel or organizational commitment to bioterrorism preparedness (personnel designated to coordinate bioterrorism response, personnel to act as liaisons to reference laboratories, or institutional presence of a bioter-

TABLE 3

Survey Questions Related to Laboratory Personnel

	Yes, %
Designated personnel to coordinate BT response	83.8
Designated liaison to LRN reference laboratory	73.2
Bioterrorism advisory committee	81.0
Laboratory liaison to BT committee	71.5
Representatives from local/state PH laboratory on BT committee	26.9
Laboratorian trained to rule out the following agents:	
Bacillus anthracis	99.4
Yersinia pestis	98.3
Francisella tularensis	92.8
Brucella sp.	95.6
Burkholderia sp.	96.1
Ricin toxin	3.9
Staphylococcal enterotoxin B	8.4
Clostridium botulinium toxin	15.7

BT = biological threat; LRN = Laboratory Response Network; PH = public health.

rorism advisory committee) was significantly associated with self-reported confidence in the ability to respond to a bioterrorism event. A much higher proportion of sentinel laboratories that had some personnel or organizational commitment to bioterrorism preparedness (vs those that did not) self-reported sufficient resources to respond to a bioterrorism event (76.2% vs 46.6%; $P = .044$). No other characteristics—either individually or collectively—were significantly associated with respondents' confidence in response capabilities.

TABLE 4

Survey Questions Related to Laboratory Communication Practices

	Yes, %
Protocols to notify the appropriate LRN reference laboratory	99.4
Maintain contact information for LRN reference laboratory	99.4
LIS in place	98.9
Send, create, and receive PHIN messages via LIS	28.5
LIS has a component for biological terrorism testing data	9.5
All-hours emergency contact system in place	99.4
Method of communicating BT test results to LRN reference laboratory	
Telephone	95.5
Paper mail	3.9
E-mail	3.4
Fax	10.1
Online results reporting	7.3
LIS	1.7
Other	6.7

BT = biological threat; LIS = laboratory information system; LRN = Laboratory Response Network; PHIN = Public Health Information Network.

By multivariate analysis, the odds of a sentinel laboratory feeling confident that they had sufficient personnel, equipment, and training to respond to a biological terrorism event were 3.4 times greater if they also had indicated by survey that they had significant personnel and institutional commitment to bioterrorism preparedness, as described above (95% confidence interval 1.1–10.3). Of respondents, 41.3% gave recommendations for improvement in bioterrorism preparedness. More than half (51.4%) of the comments cited training as an area in need of improvement, and 28.4% stated that the number of current personnel was insufficient to respond adequately to a bioterrorism event.

DISCUSSION

This pilot study of sentinel laboratory bioterrorism preparedness demonstrated a relatively low rate of prior emergency alert experience among sentinel laboratories and a moderate level of participation in bioterrorism drills or simulations. The fundamental capability of biothreat communications at the level of the sentinel laboratories—the referral of specimens to reference laboratories—was present in nearly all of the laboratories that responded to the survey. Laboratories with a commitment of personnel to bioterrorism coordination were 3.4 times more likely to feel overall confidence in response capability. Approximately one-fourth of respondents felt that they did not have sufficient personnel, equipment, and training to respond to a biological terrorism event.

The day-to-day tasks of sentinel laboratories revolve around routine processing and work-up of clinical samples for patient care. Given the shortages of medical technologists, many small hospitals may simply send isolates that are suspicious or cannot be easily identified by an automated identification system to a reference laboratory. Even though some of the organisms on the Select Agent list are zoonotic pathogens endemic to certain geographic locations of the United States, few laboratories have direct experience with recognizing and detecting them in practice. Training is one of the few means of obtaining the skills necessary to fulfill the function of the sentinel laboratory, and ideally this should be continuous and comprehensive, including case scenarios and hands-on training. Notably, the most common recommendation by survey respondents for bioterrorism preparedness was need for additional hands-on training. The fact that few sentinel laboratories have had real-life emergency alert experience underscores the importance of regular bioterrorism drills.

The designation of specific laboratory personnel to oversee bioterrorism preparedness is critical to ensuring that preparedness activities are integrated into the clinical activities of sentinel laboratories. Confidence in overall preparedness may be improved by making specialized training available to 1 or 2 representative laboratory personnel. This training could be provided by various methods, ranging from sending personnel to specialized workshops sponsored by professional organizations (such as the American Society for Microbiology or APHL), to sending trainers sponsored by the LRN to

local sites. Experience gained by such training could then be passed on to other technicians. The presence of a designated person in charge of preparedness in every microbiology laboratory would serve to integrate this preparedness function into daily laboratory activities.

The function of sentinel laboratories as the front line of the LRN is to rule out and refer specimens suspicious for being bioterrorism agents. Thus, the ability to effectively communicate concerns to higher tiers of the LRN system in a timely manner is crucial. Laboratories must establish notification protocols and identify point-of-contact personnel, often in coordination with hospital infection control.[7] Public health laboratories are mandated to communicate with sentinel laboratories, but there is no reciprocal legal requirement. This often results in less than effective participation of sentinel laboratories in preparedness and response plans at the local or state level. Although the generally high rates of participation across the various measures of preparedness assessed in this study are positive, there is still room for improvement. About 20% to 30% of respondents were lacking in fundamental areas of laboratory preparedness, including drills and personnel organization.

One of the central obstacles to monitoring preparedness of sentinel laboratories is the lack of a single organization for oversight. Various organizations, including the American Society of Microbiology, issue standards and recommendations,[6] but no specific organization governs bioterrorism preparedness of sentinel laboratories as does the APHL with the reference laboratories in the LRN system. Such administrative oversight could be assumed by the reference laboratories to whom the sentinel laboratories report; this supervision would be a valuable adjunct to national preparedness for early rapid detection of biothreat agents.

This study had several limitations, most notably the fact that the survey was a broad description of preparedness-related activities, and that no standard measures of effectiveness were available to which to compare the responses. The survey sought to identify possible areas for more in-depth assessment and to provide a basic framework for the measurements that may be constructed to assess sentinel laboratory preparedness. The basis for that framework is the definition of key preparedness gaps associated with multiple realms of sentinel laboratory preparedness, as identified by those most knowledgeable about the day-to-day working of this arm of the LRN. Measurements quantifying capability are not validated for sentinel laboratories, and the proper validation of these measurements would require national expert consensus. A preliminary study such as this is necessary to assess perceived strengths and weaknesses. This study describes the opinions of microbiology supervisors at sentinel laboratories as to weaknesses in preparedness, which is something not described elsewhere.

Another limitation was the decision not to include all US sentinel laboratories, which number more than 2000. We instead chose to restrict our study to hospital-based laboratories (these comprise the vast majority of sentinel laboratories) and sample a geographically representative subset, using bed count as a surrogate for identifying those with sentinel laboratory status. This narrower sampling method was chosen because there was no publicly available comprehensive list of all sentinel laboratories, and because our study was a pilot study. Notably, our sampling method proved to be high yield (89% of hospitals who agreed to participate were self-identified as sentinel laboratories) and was adequately powered to address our study question. Furthermore, there is no inherent reason to believe that hospital-based sentinel laboratories would have significant differences in preparedness from the non–hospital-based laboratories that were not included in the study.

Given the survey design of this study, the data collected also are limited by the fact that they rely on self-reporting. Future studies could address this limitation by using alternative methods, such as site visits or mock drills, to complement the survey approach described here.

CONCLUSIONS

This study provides the impetus and conceptual framework for the development, application, and evaluation of preparedness measurements used to gauge a quantifiable component at the level of sentinel laboratories. Accordingly, these data can guide the design of more detailed future surveys and provide an important baseline measure.

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Authors' Disclosures

The authors report no conflicts of interest.

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