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Regionalization of Bioterrorism Preparedness and Response

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-Based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. This report on Regionalization of Bioterrorism Prepaaredness and Response was requested and funded by AHRQ's Center for Primary Care, Prevention, and Clinical Partnerships. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review prior to their release.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome written comments on this evidence report. They may be sent to: Director, Center for Outcomes and Evidence, Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850.

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Structured Abstract

Context: No single community can prepare fully, nor respond completely, to a large-scale bioterrorism event. Regionalization of some aspects of preparedness planning for bioterrorism may facilitate a timely and effective response.

Objectives: The purpose of this project was to first identify the key tasks of responders during a bioterrorism response and the resources required to perform them, and then to evaluate the evidence about the potential effectiveness of existing regional systems for the delivery of these resources and services for bioterrorism preparedness and response.

Data Sources: We searched the medical, emergency management, and supply chain management literatures and government documents. For each literature, we searched databases (e.g., MEDLINE®), Web sites, prominent journals, and bibliographies of retrieved articles.

Study Selection: We sought articles describing the key tasks during responses to bioterrorism or bioterrorism-related events, the resources required for these responses, and existing regional systems for delivery of these resources. We included articles describing regionalized responses to the 2001 anthrax attack, naturally occurring outbreaks, and disasters; we also included articles describing regionalized systems for trauma care, bioterrorism surveillance, and the bioterrorism response supply chain.

Data Extraction: From articles meeting the inclusion criteria, we extracted information about the type of regionalized response system described in the article, whether it had been evaluated, and any evaluative results reported.

Data Synthesis: We reviewed 9542 publications and more than 500 Web sites. Of these, 396 articles, 61 government reports, and 75 Web sites met our inclusion criteria. We found numerous existing regionalized systems for the delivery of goods and services relevant to bioterrorism preparedness and response; however, these systems are not well coordinated and few have been evaluated for their ability to facilitate a response to bioterrorism or a bioterrorism-relevant event. For example, we found that the regionally organized Laboratory Response Network provided laboratory surge capacity during the 2001 anthrax attack and that an international research network rapidly identified the pathogen during the SARS outbreak. In several instances, mutual aid agreements successfully facilitated the regional provision of emergency goods and services; and regionalization of trauma care has reduced costs and improved patient outcomes. How well these regional systems would perform during a large-scale bioterrorism event remains untested.

Simulations: Because we found no evidence describing regionalization of bioterrorism surveillance, we developed a simulation model to evaluate the tradeoffs in sensitivity and specificity when analyzing surveillance data locally as opposed to regionally. We found that warning thresholds may need to be modified to prevent increases in false positives when pooling data. Because we found no evaluations of regionalized inventory management for resources for bioterrorism responses, we developed a simulation model to address the costs and benefits of differing strategies for pre-attack stockpiling and post-attack distribution of antibiotics. Preliminary results indicate that the number of deaths resulting from an anthrax-like attack is

sensitive to the number of people seeking prophylactic antibiotics and to the time required for dispensing. Maintaining local inventories is only effective when the probability of bioterrorism is relatively high.

Conclusions: Numerous regional systems exist for responding to bioterrorism; however, few have been evaluated. Efforts to coordinate them are ongoing and would likely benefit from evaluations of regionalized information management systems; of strategies to rapidly distribute and dispense pharmaceuticals and other response resources; and of plans to specify response roles, remuneration, and chain of command.

Contents

Evidence Report

Chapter 1. Introduction 3
Background 3
The Purpose of the Evidence Report 3

Chapter 2. Methods 5
Technical Expert Advisory Panel 5
Target Audience and Population .....
Key Questions 5
Development of an Analytic Framework 6
Development of Inclusion and Exclusion Criteria 6
Development of Search Strategies 7
Identification of Literature Sources 8
Preliminary Searches 10
Preliminary Medical Literature Database Searches 10
Preliminary Emergency Management Database Searches 13
Preliminary Supply Chain Management Database Searches 14
Preliminary Government Documents Database Searches 14
Focused Searches 15
Abstract Review 17
Data Abstraction 17
Determination of Methodologies for Evaluating Relevant Regional Systems 17
Evaluation Concepts from the Medical Literature 17
Evaluation Concepts from the Emergency Management Literature 18
Evaluation Concepts from the Supply Chain Literature 19
Evaluation Concepts from Government Documents 25
Simulation Model: Regionalization of Surveillance 26
Simulation Model: Inventory Management 26
Reviews and Revisions of Draft Evidence Report 27

Chapter 3. Results 29
Synthesis of Evidence about Regionalization of Supply Chains 29
Lessons Learned from the Supply Chain Literature 31
Existing Infrastructure for Local and Regional Responses to Bioterrorism 36
Summary of the Evidence of Existing Infrastructure for Local and Regional Responses to Bioterrorism 36
Infrastructure of U.S. Public Health System 37
The National Disaster Medical System 40
Disaster Medical Assistance Teams 41
The Metropolitan Medical Response System 42
The Department of Homeland Security 43
Department of Veterans Affairs 45

Bioterrorism Preparedness Programs Sponsored by the Department of Defense..... 46
Lessons Learned from the Literature on the Existing Infrastructure for Local and Regional Responses to Bioterrorism..... 47
Synthesis of Evidence about Responses to the 2001 Anthrax Bioterrorism..... 48
Summary of the Evidence of Regionalization of the Response to the 2001 Anthrax Bioterrorism..... 49
Application of Evaluation Criteria to the 2001 Anthrax Bioterrorism Literature 49
Lessons Learned from the Regional Response to the 2001 Anthrax Cases..... 53
Synthesis of Evidence about Regionalization of Responses to Naturally Occurring Outbreaks..... 54
Summary of the Evidence of Regionalization of Responses to Naturally Occurring Outbreaks..... 55
Application of Evaluation Criteria to the Responses to Naturally Occurring Outbreak Literature..... 55
Lessons Learned from the Responses to Naturally Occurring Outbreaks..... 61
Synthesis of Evidence about Regionalization of Responses for Disasters..... 63
Summary of the Evidence of Regionalization of Disaster Responses..... 64
Application of Evaluation Criteria to the Disaster Response Literature..... 64
Lessons Learned from the Disaster Literature for the Regionalization of Services for Bioterrorism Preparedness..... 74
Synthesis of Evidence about Regionalization of Emergency Trauma Care..... 76
Regionalization of Trauma Care..... 76
Summary of the Evidence of Regionalization of Trauma Care..... 77
Application of Evaluation Criteria to the Trauma Literature..... 79
Lessons Learned From Regionalization of Trauma Care..... 81
Synthesis of Evidence about Regionalization of Surveillance Systems for Bioterrorism 85
Summary of the Evidence of Regionalization of Surveillance Systems for Bioterrorism..... 85
Application of Evaluation Criteria to the Surveillance Literature..... 88
Lessons Learned From Regionalization of Surveillance Systems..... 92
Simulation Model Results: Regionalization of Surveillance..... 94
Changing Thresholds When Pooling Surveillance Data..... 94
The Effect of Inter-Regional Correlation on Pooled Surveillance Data..... 96
Lessons Learned for Regionalization of Analysis of Surveillance Data..... 97
Simulation Model Results: Inventory Management..... 97
Summary of Inventory Management Simulation Model..... 97
Summary of Preliminary Results of an Inventory Management Simulation Model 99
Lessons Learned from the Inventory Management Simulation Model..... 100
Summary Synthesis of Evidence about Regionalization for Bioterrorism Preparedness and Response..... 100

Chapter 4. Discussion..... 109
Future Research..... 112

References and Included Studies 113

Listing of Excluded Studies……143

Tables

Table 1. Literature Sources 9
Table 2: MEDLINE® Searches to Identify Potentially Relevant Systems and Organizations 10
Table 3: Search Terms and Citations for Cochrane Databases 13
Table 4: Search Terms and Citations for Emergency Management Databases 14
Table 5. Search Terms and Citations for Supply Chain Databases 14
Table 6: Search Terms and Citations for Government Databases 14
Table 7. List of Potentially Relevant Systems for Focused Searching by Primary Task 15
Table 8. Evaluation Concepts from the Supply Chain Literature and their Relevance to Regionalization of Bioterrorism Preparedness 23
Table 9. Lessons Learned From the Traditional (Manufacturing) Supply Chain Literature 32
Table 10. Regionalization of Outbreak Response 62
Table 11. Lessons Learned From Regionalized Responses to Disasters 74
Table 12. Selected Evaluations of Regionalized Trauma Care Systems 82
Table 13. Syndromic Surveillance Systems 92
Table 14. Examples of Tasks, Subtasks, and Resources Required for a Bioterrorism Response 101

Figures

Figure 1. The Bioterrorism Response Supply Chain 20
Figure 2. Regionalization of Public Health Departments in Texas and Alabama 39
Figure 3. The Metropolitan Medical Response System 43
Figure 4. Regions as Definined by FEMA, HHS, HRSA, and Others 44
Figure 5. The 23 VA Veterans Integrated Service Networks 46
Figure 6. Office of Emergency Services Mutual Aid and Administrative Regions 65
Figure 7. Homeland Security Advisory System 72
Figure 8. Thresholds for Detection of Outbreaks in Two Regions 95
Figure 9: Illustration of Pooled and Individual Thresholds for Detection of Outbreaks in Two Regions 96

Appendixes are provided electronically at
http://www.ahrq.gov/clinic/epcindex.htm

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Number 96

Regionalization of Bioterrorism Preparedness and Response

Summary

Introduction

The anthrax attacks of 2001, the outbreak of severe acute respiratory syndrome (SARS), and weapons of mass destruction tabletop exercises have made it clear that no single community can prepare fully, nor respond completely, to a large-scale bioterrorism event. Policymakers recognize the need to forge relationships and coordinate preparedness planning efforts at the local, state, national, and international levels.[1] However, there is little consensus about the optimal level of localization or regionalization for each of the resources and services that must be operationalized during a bioterrorism response.

We sought to evaluate the evidence regarding the effectiveness of existing regional systems that facilitate a response to bioterrorism. We sought evidence regarding the tasks that would need to be performed during a bioterrorism response (such as triage, provision of emergency medical care, transportation, and surveillance) and regionalized organizations that would likely contribute personnel, material, and information required to perform these bioterrorism response tasks.

Methods

Key Questions

The Key Questions addressed in this Report are:

1. What are the key tasks of local responders—such as local public health officials, clinicians, and emergency medical personnel—during a bioterrorism event?
2. What resources do local responders require to perform the tasks identified in Key Question 1?
3. Which existing regional systems for delivery of goods and services could be relevant to supplying the resources identified in Key Question 2?
4. Can regionalization of bioterrorism preparedness planning facilitate supplying needed resources to local responders during a bioterrorism event?
5. How do geographic variations in the affected population (e.g., urban as opposed to rural), special populations, and the interplay of private and public sector players affect regionalized systems?

Literature Searches

We sought relevant articles in four primary literature sources: the medical, emergency management, and supply chain management literatures, and government documents. We sought articles describing bioterrorism preparedness plans, vaccination strategies, evaluations of regionalized health care delivery systems, case studies of emergency responses, disaster preparedness plans, evaluations of responses to disasters, case studies about regional practices to increase the efficiency of manufacturing and distribution services, descriptions and evaluations of government programs responding to the 2001 anthrax cases, and bioterrorism-relevant events (e.g., naturally occurring outbreaks and disasters).

We developed separate search strategies for each of our four primary literature sources. In general, for each literature source we searched databases such as MEDLINE®, indices of key journals and conference proceedings, and the Web sites of relevant organizations. At least one investigator screened titles, abstracts, and articles, as necessary, to determine if they met inclusion

criteria. From each included article, we abstracted the following data: information describing the regional system, methods and results of evaluations of the system, information about the quality of the study, as well as references in the bibliography that might meet inclusion criteria.

Methodologies for Evaluating Relevant Regional Systems

From each of the four literature sources, we sought evaluative information about:

- Clinical outcomes: morbidity and mortality
- Financial outcomes: costs associated with the event or responses to it
- Process outcomes: timeliness of the response; adherence to clinical protocols; measures of cooperation, coordination, and communication among responders; information about the incident command structure that was used and how it affected the regionalized response; and iterative application of lessons learned from prior bioterrorism-relevant responses
- Outcomes associated with the efficiency of the bioterrorism response supply chain including considerations of: the design of the supply chain network, inventory management, postponement (which refers to the concept of customizing a product late in the supply chain), modularization (which refers to the use of standard parts that can be used in multiple end products), supply chain coordination, management of incentives, and management of information.

Supplemental Analyses

Because we found no evidence about regionalization of two key bioterrorism response tasks—bioterrorism surveillance and the stockpiling of medical supplies required for a bioterrorism response—we performed simulations of regionalization of these tasks, using estimates derived from the published literature. In our surveillance simulation, we explored the tradeoffs in sensitivity and specificity caused by analyzing surveillance data locally versus regionally. In our simulation of regionalization of inventories of bioterrorism-relevant medical supplies, we evaluated the costs and benefits of differing strategies for pre-attack stockpiling and post-attack distribution of antibiotics.

Results

We reviewed 8536 citations, more than 500 websites, 1006 government reports, and numerous texts for potential inclusion in this Evidence Report. Of these, 396 articles, 61 government reports, and 75 Web sites met our inclusion criteria.

Synthesis of the Literature Describing the Existing Infrastructure for Bioterrorism Response

We included 22 articles, 25 government reports, and 14 Web sites on systems and organizations with existing infrastructures likely to contribute to a regionalized bioterrorism response. This literature describes numerous systems including, but not limited to, public health departments at local, state, national, and international levels (e.g., CDC, World Health Organization); the National Disaster Medical System (a federally coordinated program that provides medical and mental health assistance including the evaluation of patients and provision of hospital care when local capabilities are overwhelmed); Disaster Medical Assistance Teams (voluntary specialty medical teams that can be deployed to provide a wide range of disaster medical services and resources); the Metropolitan Medical Response System (which expands municipal bioterrorism preparedness through grants that provide pharmaceuticals and other supplies and requires detailed preparedness planning by recipient cities); and the Department of Homeland Security (which has oversight responsibilities for many of the key bioterrorism response agencies and programs such as the Federal Emergency Management Agency and the Strategic National Stockpile). This literature suggests that numerous response agencies with regional organizations could contribute to a bioterrorism response. However, most of these agencies were designed either independently or for purposes besides bioterrorism response, and efforts to coordinate them for bioterrorism preparedness are only now emerging or under development.

Synthesis of Supply Chain Case Studies Relevant to the Bioterrorism Response Supply Chain

A traditional supply chain is the integrated network of entities involved in all aspects of the manufacture of goods, including the procurement of raw materials, their assembly into the manufactured product, transportation of the product to distributors, and distribution to final customers.[2] The bioterrorism response supply chain has several related components: suppliers of raw materials, manufacturers of goods (e.g., product manufacturers such as drug and device manufacturers), purchasers, providers who distribute the products, customers/payors (e.g., the government, employers, and individuals), and the transportation systems that connect these components.[3] Supply chain management concepts are directly relevant to those elements of a bioterrorism response that require the purchase, inventorying, distribution, and rapid dispensing of supplies. We included 22 articles and one Web site describing innovations relevant to the bioterrorism supply chain. From this literature we synthesized four key lessons:

1. Strategies to improve supply chain network designs, including regionalization of some elements of the supply chain (such as pooling of inventories at regional warehouses), can reduce inventories, improve the capacity to serve target populations, and save money. Some bioterrorism response supplies have limited shelf lives, so minimizing inventory may be important from economic and logistics perspectives.
2. Several supply chain case studies demonstrated that redesigning final products to be assembled from a limited number of common component parts, even if those component parts are costly, can result in overall cost savings for the supply chain (modularization). Similarly, postponing final customization of end products can reduce total inventories and costs. For bioterrorism, this supports the practice used by the Strategic National Stockpile of pre-packaging antibiotics and medical supplies for use in multiple localities, for a variety of bioterrorism events, and for use by a variety of patient populations.
3. Coordination of activities of heterogeneous bioterrorism response supply chain members, with specific consideration of the incentives of all stakeholders in the supply chain, can increase efficiency and reduce costs.
4. For the bioterrorism response supply chain, information systems that can accurately characterize the available supply of goods and personnel and the ongoing needs of the community affected may benefit the response.

Synthesis of the Literature Describing Responses to the 2001 Anthrax Attacks

We included 30 articles, 14 government reports, and 22 Web sites describing regionalized aspects of the response to the anthrax bioterrorism of 2001. None of these were evaluations; rather, most described particular aspects of the response to the anthrax attacks. From these articles, we synthesized five key lessons.

1. Cooperative agreements and regionalized response plans are needed for effective response to bioterrorism events. Pre-event regionalized planning and asset sharing agreements among local public health agencies and hospitals may facilitate enhanced surge capacity and coordinate responses during a bioterrorism event.
2. Incident command must be well defined and accepted by all relevant responders.
3. Information systems for communication among responders and with the public must be implemented and tested prior to an event.
4. The costs and benefits of acquiring, storing, and maintaining local inventories of medical supplies have not been established.
5. The Laboratory Response Network significantly enhanced regional laboratory surge capacity. Whether the surge capacity provided by the Laboratory Response Network will be adequate for a bioterrorism event of larger magnitude remains untested.

Synthesis of the Literature Describing Responses to Naturally-Occurring Outbreaks

We included 177 articles, 10 government reports, and 33 Web sites about responses to natural outbreaks including SARS, pandemic influenza, meningococcal meningitis, smallpox, and West Nile virus. From our review of this largely descriptive literature, we synthesized three main lessons regarding a regional response to outbreaks resulting from bioterrorism.

1. Communication and cooperation between health authorities of neighboring regions are needed for adequate and rapid responses. Rapid communication can be difficult to achieve through interim agreements. Thus, cooperation during a bioterrorism response may benefit from pre-event development and routine use of shared communication systems.
2. In the event of a bioterrorism attack, international cooperation to detect, report, and respond may reduce associated morbidity or mortality, as it did during the SARS outbreak.
3. During a bioterrorism event, strategies to protect responders and their families may be an essential component of maintaining a robust work force.

Synthesis of the Literature Describing Disaster Responses

We included 41 articles, 21 government reports, and 12 Web sites that described regionalized responses to natural or manmade disasters or described regionalization of disaster response systems. From these articles, we synthesized three key lessons, though evaluative evidence is limited.

1. Information management is essential for assessing the needs of the local community and the resources available to them, and for coordinating responses from regional agencies.
2. A key component of effective regional responses to disasters includes mutually agreed upon pre-event protocols that establish chain of command structures, including plans for how the chain of command changes as regional and federal response agencies become involved.
3. Mutual aid agreements (such as the Master Mutual Aid agreement in California and the Emergency Management Assistance Compact in the rest of the United States)[4, 5] are key components in providing surge capacity for regional response to disasters. These agreements ensure that every locale does not have to be staffed and prepared for a

maximal intensity event. They enable risk to be spread among several locales, and provide cost-sharing of disaster preparedness. Mutual aid agreements for bioterrorism are likely to benefit from careful pre-event consideration of liability issues, remuneration, and licensing.

Synthesis of the Literature Describing Regionalization of Trauma Care

We included 80 articles and government reports that described regionalization of trauma care; 40 of these reported the results of evaluations of regionalization of trauma care. From these, we synthesized four key lessons, based on the evaluative evidence.

1. Pre-event hospital designation contributes to lower costs and improved patient outcomes. The evidence from trauma care regionalization suggests that a key component of high quality, cost-effective care is limiting high-cost specialty care to specifically designated hospitals with increased experience in treating severely injured patients. A bioterrorism response system may benefit from the pre-event designation of hospitals.
2. Formalized protocols for pre-hospital and hospital care contribute to improved patient outcomes. A regionalized bioterrorism response may benefit from similar protocols so that first responders know where and how to rapidly transport exposed patients.
3. An established communication network is essential to the coordinated regionalization of trauma care. Such a system could play an important role during a bioterrorism response.
4. Correctly aligned incentives, particularly sufficient funding, are critical to maintaining the participation of designated trauma hospitals. The included articles suggest that regionalized trauma care systems do not provide sufficient incentives for some hospitals to remain in the system. A bioterrorism response system is likely to benefit from incentives for hospital participation.

Synthesis of the Literature Describing Regionalization of Surveillance for Bioterrorism

Our search identified 36 articles, two government reports, and one Web site describing regionalization of surveillance systems for bioterrorism. From these, we draw four key lessons.

1. Evaluations of regionalization of surveillance data collection and analysis are needed. Although numerous syndromic surveillance efforts in local areas are promising, no study has evaluated the tradeoffs in terms of costs and benefits of regionalizing bioterrorism surveillance.
2. If a regionalized surveillance system uses local data collection with regional analysis, considerations of means to reduce costs of data collection and to share relevant analyses with local data collectors may enhance local participation.
3. A common technology platform may facilitate the collection and analysis of surveillance data.
4. Privacy issues are a key concern: collection and analysis of surveillance data need to protect individual privacy while containing sufficient detail to detect new outbreaks.

Simulation Model Results

The results of our surveillance model suggest that whereas large outbreaks can be relatively easy to detect using either unpooled (i.e., local) or pooled (i.e., regionalized) data analysis methods, small outbreaks can be difficult to detect by either method. Additionally, we found that pooling strategies may improve detection capabilities, but the circumstances under which pooling strategies are consistently more effective or cost effective than using unpooled data remain poorly characterized.

Our inventory logistics simulation model yielded three results. First, the mortality associated with anthrax bioterrorism may be highly sensitive to the number of people seeking prophylactic antibiotics. This is a critical finding given that for many types of bioterrorism responses it will be difficult to determine whether an individual has been exposed to the biothreat agent. Second, strategies that deliver multiple Push Packs to the site of the attack, until the regional Vendor Managed Inventory has been delivered to these areas, may reduce mortality. Finally, increasing the availability of local inventories may be cost effective only if the annual probability of attack is high.

Summary of Answers to Key Questions

Key Question 1: What are the key tasks of local responders during a bioterrorism event? The literature describes nine main bioterrorism response task categories: preparedness planning, field assessment and triage, diagnosis, management of the acutely ill, prevention of the spread of disease, surveillance, outbreak investigation, communication, and emergency management. For each of these main tasks, we considered the subtasks that responders are required to perform. For example, subtasks of surveillance include collection, analysis, and reporting of surveillance data.

Key Question 2: What resources do local responders require to perform the tasks identified in Key Question 1? For each task described above, we abstracted information about four broad categories of resources required for that task: personnel, material, information, and financial. For example, for the key task of "prevention of the spread of disease," numerous personnel, material and information resources are required, including: clinicians, public health officials, logisticians and

pharmacists (personnel); pharmaceuticals, isolation facilities, sites for mass vaccination, and supplies for mass care (material); prevention guidelines, home-care instructions for patients, and information regarding characteristics of the infectious agent to aid decisionmaking about quarantine, isolation, and evacuation (information); and the financial support for each of these.

Key Question 3: Which existing regional systems of delivery of goods and services could be relevant to supplying the resources identified in Key Question 2? We found numerous systems and organizations with regionalized infrastructures engaged in the timely delivery of bioterrorism-relevant material, personnel, and information. Specifically, we found systems and organizations responsible for each of the response tasks described in our answer to Key Question 1: for preparedness planning (e.g., the Joint Commission on the Accreditation of Healthcare Organizations), field assessment and triage (e.g., US trauma care system), diagnosis (e.g., Laboratory Response Network), management of the acutely ill (e.g. Medicins Sans Frontieres), prevention of the spread of disease (e.g., Strategic National Stockpile), surveillance (e.g., Electronic Surveillance System for the Early Notification of Community-based Epidemics), outbreak investigation (e.g., Epidemic Intelligence Service), communication (e.g., ProMed), and emergency management (e.g., Emergency Management Assistance Compacts).

Thus, we conclude that numerous existing systems and organizations could contribute to a regionalized bioterrorism response. Many of these have long histories of successful participation in bioterrorism-related events such as infectious disease outbreaks and natural disasters. However, most of these systems were designed independently, typically to facilitate particular response tasks. Ongoing efforts to coordinate such systems have not been evaluated.

Key Question 4. Can regionalization of bioterrorism preparedness planning facilitate supplying needed resources to local responders during a bioterrorism event?

Our evidence synthesis produced six main results about regionalization of services for bioterrorism preparedness and response.

1. There have been few evaluations of whether regionalization has benefited a particular response organization or task. Efforts to develop a regionalized infrastructure for bioterrorism responses will likely benefit from careful evaluations of the numerous tasks involved in a bioterrorism response and the alternative strategies for providing the necessary resources to perform these tasks.
2. Regionalization has benefited response capability in disaster situations. Our review of the responses to natural and manmade disasters found that during large-scale disasters, local response capacity can be quickly overwhelmed. The key method of organizing regionalized disaster responses is by mutual aid agreements. The elements of successful mutual aid agreements include pre-event ratification of legislation by all signatories to resolve issues of compensation, liability, and insurance, and uniform information systems to track needs and resources. Bioterrorism responses are likely to benefit from mutual aid agreements in all states (including agreements with neighboring regions of Mexico and Canada), which will provide surge capacity for public health services.
3. Regionalization efforts have successfully expanded surge capacity for laboratory services. During the anthrax attacks, the Laboratory Response Network successfully provided laboratory surge capacity. Whether there is sufficient transportation infrastructure to facilitate the delivery of laboratory specimens from a bioterrorism attack location to Laboratory Response Network facilities during a larger bioterrorism event has not been evaluated.
4. Information technologies facilitate accurate determination of response needs and available resources, effective application of the chain of command, communication among responders and with the public, and surveillance. Our review of evaluations of supply chains emphasized the importance of accurate information for coordination of all elements of the supply chain. Additionally, the evaluations demonstrated that investments in information technologies often resulted in net cost savings for the supply chain while improving service. The disaster response literature provided examples of how inadequate information infrastructures led to delays in responses. Regionalization of bioterrorism preparedness and response efforts will likely benefit from careful consideration of the information technologies that can facilitate sharing of information by different response organizations and by responders at local and regional levels.
5. The disaster and outbreak response literatures emphasize that local responders are often at risk of personal injury during a response. Because local responders will be the first on a scene during an emergency, bioterrorism responses may benefit from careful consideration of the incentives of local personnel to participate in a response and from first responder training that emphasizes personal safety, triage, diagnosis, and outbreak management tasks.
6. Few included articles specifically articulated lessons learned from their bioterrorism-related preparedness or response experiences. Our review of government documents, particularly responses of military personnel, found that organizational commitment is a key factor in implementing a 'lessons learned' approach to ensuring that knowledge gained from both good and bad experiences is maintained in institutional memory. Plans to regionalize services for a response to a large-scale bioterrorism event could benefit from the experiences of responses to small bioterrorism events and relevant naturally occurring outbreaks if the lessons learned from these experiences were documented and used to improve planning efforts. Given the complexity of a bioterrorism response, the iterative

application of lessons learned from one experience to the next requires commitment from all relevant response organizations to institutionalize a 'lessons learned' approach.

Key Question 5: How do geographic variations in the affected population, special populations, and the interplay of private and public sector players affect regionalized systems? In the United States, special populations including children, the elderly, the disabled, and pregnant women account for about 134 million people.[6-9] Thus, bioterrorism preparedness planning requires consideration of these special populations. However, we found little evidence that specifically addressed variations in regionalized responses on the basis of geography, population, or public-private cooperation.

Discussion

Given the complexity and cost of training, staffing, equipping, and mobilizing an adequate bioterrorism response infrastructure, no single community can be expected to develop and maintain the necessary capacity for a large-scale bioterrorism response. Instead, regionalization may benefit some bioterrorism preparedness and response capabilities. Our extensive search of four literature sources relevant to bioterrorism responses found that the response infrastructure for a bioterrorism event includes numerous agencies with regionalized organizational structures. However, most of these agencies have been developed independently or for purposes other than bioterrorism response, and efforts to coordinate them for bioterrorism preparedness are underway but not yet widespread. Specifically, the Department of Homeland Security, which has oversight and coordination responsibilities for many of the agencies that would contribute to regionalized bioterrorism responses, is currently reorganizing its regional structure.

We conclude that regionalization is likely to benefit elements of a bioterrorism response including the provision of surge capacity in essential response services such as triage, the provision of medical care, distribution and dispensing of prophylactic therapies, outbreak investigation, security management, and emergency management. Additionally, regionalization may be a cost effective strategy for developing teams of trained response personnel and maintaining inventories of response equipment. Numerous response organizations with regionalized infrastructures will serve key functions during a large-scale bioterrorism response. Coordination of these organizations may benefit from implementation of information management strategies and pre-event agreements that specify response roles, remuneration, and chain of command.

Future Research

Despite the large number of studies and articles we reviewed, we found very few evaluations of systems relevant to bioterrorism preparedness, and even fewer evaluations of the regionalization of a system relevant to bioterrorism preparedness. Future research is needed to fill this gap in the literature. Specifically, evaluations are needed for a better understanding of the costs and benefits of regionalization of surveillance, inventory management and distribution systems, and information management.

Availability of the Full Report

The full Evidence Report from which this summary was taken was prepared for the Agency for Healthcare Research and Quality (AHRQ) by the Stanford–UCSF Evidence-based Practice Center under Contract No. 290-02-0017. Printed copies may be obtained free of charge from the AHRQ Publications Clearinghouse by calling 800-358-9295. Requesters should ask for Evidence Report/Technology Assessment No. 96, *Regionalization of Bioterrorism Preparedness and Response*. Additionally, the report and this summary will be available online through AHRQ's Web site at www.ahrq.gov.

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Evidence Report

Chapter 1. Introduction

The best we can do is to realize nobody can save his own skin alone. We must all hang together.
—Eleanor Roosevelt, April 5, 1938. [1*]

Background

The anthrax attacks of 2001, the severe acute respiratory syndrome (SARS) outbreak of 2003, and numerous weapons of mass destruction drills of the past few years have made it clear that no single community can prepare fully, nor respond completely, to a large-scale bioterrorism event. Policy makers, including elected officials, public health officials, emergency management professionals, clinicians, and leaders from the first responder communities, recognize the need to forge relationships and coordinate preparedness planning efforts at the local, state, national, and international levels.[2] However, there is little consensus about the optimal level of localization or regionalization for each of the resources and services that must be operationalized during a bioterrorism response.

The Agency for Healthcare Research and Quality (AHRQ) determined that a comprehensive review of preparedness planning efforts, and response tasks and capabilities at local, state, national, and international levels could provide insights about ways to coordinate response efforts and maximize available resources for a bioterrorism response. The literature revealed widely disparate systems, reflecting the frequently individualized preparedness planning efforts of each group of response personnel (e.g., public health officials, clinicians, first responders, and emergency management professionals). There is little direct evidence as to whether regionalization either benefits or impairs bioterrorism preparedness planning or responses. Ongoing efforts to regionalize bioterrorism preparedness and response planning could be greatly advanced by rigorous evaluation and synthesis of the lessons learned from the 2001 anthrax response; ongoing bioterrorism surveillance efforts; regional responses to naturally occurring outbreaks and disasters; regional systems for the provision of specialty medical care, such as trauma care; and regionalization of the bioterrorism response supply chain.

The Purpose of the Evidence Report

The purpose of this Evidence Report is to evaluate the evidence regarding the effectiveness of existing regional systems that facilitate a response to bioterrorism. Because of the limited evidence about regionalized systems specific to bioterrorism preparedness and response, we evaluated evidence from relevant bioterrorism-related fields that bear on the question of whether regionalization of goods and services is likely to benefit a bioterrorism response. Specifically, we searched four primary sources: the medical, supply chain, and emergency management

[*] Throughout this Report, the references referred to in the text can be found on pages 113 to 142 in the section entitled References and Included Studies. Note that pages 143 to 166 contain a Listing of Excluded Studies, not references.

literatures and government documents. From these sources we sought three types of articles: those describing agencies with regionalized organizational structures that would likely contribute to a bioterrorism response, those describing bioterrorism-related events such as infectious disease outbreaks resulting from bioterrorism and natural causes and disasters, and those describing tasks routinely performed during a bioterrorism response such as triage, provision of emergency medical care, transportation, and surveillance. We analyzed the included articles for evidence that regionalization either benefited or impaired responders' performance of key tasks and whether it effected a more rapid delivery of the resources essential to performing these tasks.

The dearth of evidence regarding regionalization of two key tasks, bioterrorism surveillance and the timely delivery of pharmaceuticals and medical supplies to local dispensing sites, prompted us to develop simulation models of regionalization of these tasks. In our surveillance simulation, we explored the tradeoffs in sensitivity and specificity when the analysis of surveillance data includes pooling of data over a region. In our simulation of regionalization of stockpiles of pharmaceuticals, we investigated the costs and benefits of various strategies of maintaining local as opposed to regional inventories of antibiotics for a large-scale anthrax attack.

Chapter 2. Methods

Technical Expert Advisory Panel

For advice on the scope of the project, refinement of the Key Questions, and preparation of this Evidence Report, we consulted technical experts in the following fields: bioterrorism/biodefense, public health, supply chain management, surveillance, disaster epidemiology, disaster logistics, and emergency management (Appendix A).

Target Audience and Population

The decisionmakers addressed in this Evidence Report are clinicians, emergency preparedness officials, public health officials, and policymakers. For the purpose of this Report, clinicians include all clinical health providers such as physicians, nurses, respiratory technicians, and community health workers. First responders include paramedics, fire, police, and hazardous materials professionals. Public health officials and policymakers include those at the local, state, federal, and international levels.

The ultimate target population of this Report is the U.S. population at risk for morbidity or mortality resulting from bioterrorism. We are interested in systems and organizations relevant to regionalized bioterrorism preparedness plans that affect the entire U.S. population at risk for bioterrorism, including those of all racial and ethnic backgrounds, all ages, and both genders.

Key Questions

We developed the Key Questions in collaboration with AHRQ and our Technical Expert Advisory Panel.

The Key Questions addressed in this Report are:

1. What are the key tasks of local responders such as local public health officials, clinicians, and emergency medical personnel during a bioterrorism event?

2. What resources (e.g., laboratory supplies and services, vaccines and pharmaceuticals, hospital capacity, training, and information) do local responders require to perform the tasks identified in Key Question 1?

Note: Appendixes are provided electronically at http://www.ahrq.gov/clinic/epcindex.htm

3. Which existing regional systems for delivery of goods and services could be relevant to supplying the resources identified in Key Question 2? Which elements of these systems have been critically evaluated? What are their strengths and limitations?

4. Can regionalization of bioterrorism preparedness planning facilitate supplying needed resources (including personnel, material, and information) to local responders during a bioterrorism event?

5. How do geographic variations in the affected population (e.g., urban as opposed to rural), special populations (e.g. children, elderly, or disabled), and the interplay of private and public sector players affect regionalized systems?

Development of an Analytic Framework

The analytic framework for this Report advanced logically from our 2002 Evidence Report for AHRQ titled, "Information Technologies and Decision Support Systems for Bioterrorism Preparedness."[3] In that 2002 Report, we evaluated the potential utility of 217 information technologies and decision support systems designed to support the tasks and decisions of clinicians and public health officials during a bioterrorism response. For the current project, our analytic framework focuses on the decisions and tasks of local responders and the resources (i.e., material, trained personnel, and information) they require to perform their key tasks. We considered how these tasks changed depending upon whether they were performed by local, state, or federal responders (i.e., depending on the unit of regionalization). To inform our analytic framework, we sought published guidelines describing relevant tasks associated with robust bioterrorism response planning, such as those published by government and professional organizations,[4-8] the Institute of Medicine,[9] individual state plans,[10-15] the Joint Commission on Accreditation of Healthcare Organizations' list of potential hospital criteria,[16-28] guidelines published by the American Hospital Association,[29, 30] and input from our Expert Advisory Panel. We describe the development of the specific evaluation criteria in the "Determination of Methodologies for Evaluating Relevant Regional Systems" section of this chapter.

Development of Inclusion and Exclusion Criteria

Based on input from our expert advisors, our conceptual model, and practical considerations, we developed inclusion and exclusion criteria to identify potentially relevant systems of regionalization for bioterrorism preparedness and response. Two types of articles potentially met our inclusion criteria. First, we sought articles describing systems specifically designed for regional bioterrorism or related disaster preparedness or response (e.g., the Strategic National Stockpile, the Metropolitan Medical Response System, the Disaster Medical Assistance Teams, and the Laboratory Response Network). We searched for articles that described the design,

implementation, or evaluation of these systems at local, state, federal, and other regional levels (i.e., multi-county, multi-state, international). Second, we sought articles describing systems that have regionalized the key tasks and decisions outlined in our conceptual model (e.g., evaluation of triage methods used in trauma care) and articles describing the regionalization of the distribution of bioterrorism-relevant material, trained personnel, and information (e.g., case studies from supply chain management that describe cost-effective design of manufacturing, distribution, and warehousing networks).

We excluded articles describing regionalization of medical services for chronic conditions or other services that do not necessitate a rapid response. We excluded articles about specific bioterrorism-preparedness material (e.g., descriptions of personal protective equipment or rapid diagnostic tests) unless those articles discussed the use of such equipment as part of a bioterrorism response or preparedness plan. Because training, exercises, and bioterrorism preparedness drills for hospital personnel and other first responders has been the topic of other Evidence Reports prepared by the Johns Hopkins University Evidence-Based Practice Center,[31] we did not include systems principally intended to support responder training or exercises and drills.

Development of Search Strategies

The objective of our search strategy was to identify systems and regional organizations that perform tasks relevant to a bioterrorism response, as identified in our conceptual framework. The heterogeneity of these tasks necessitated a search strategy that differs in two significant ways from traditional systematic reviews of health care topics. First, many relevant systems are described in non-medical sources such as the supply chain management and emergency management literatures. Because these literatures have not been cataloged in comprehensive databases like MEDLINE®, they cannot be systematically searched using keywords. Thus, it was necessary for us to seek bibliographic recommendations from our Expert Advisors in order to perform manual searches of the tables of contents of relevant journals and conference proceedings, as well as to conduct Web searches for information disseminated by relevant organizations.

Second, because of the many types of potentially relevant systems and regional organizations, and the diverse literature on each relevant system, we did not attempt to collect all published reports of any included system. Instead, we adopted an iterative search strategy of preliminary searches to identify potentially relevant systems, followed by focused searches to evaluate the relevance of such systems to regionalization of bioterrorism preparedness. We performed the preliminary searches of each relevant literature source in a hierarchical manner: we searched for systems specifically related to regionalization of bioterrorism preparedness, planning, and response prior to searching for systems associated with less specific bioterrorism-related events (e.g., infectious disease outbreaks, natural disasters, and man-made disasters). For example, we performed focused searches to identify published reports of the responses of the American Red Cross to bioterrorism-relevant events, particularly those that discuss the effects of regionalization on such a response. We did not include descriptions of Red Cross responses to non-bioterrorism-relevant events. Similarly, we did not attempt to evaluate the preparedness plans and capabilities of every public health and emergency management jurisdiction in the

United States. Instead, we sought a general understanding of local and state public health approaches by reviewing a representative sample of geographically distributed and organizationally diverse public health infrastructures.

Identification of Literature Sources

Published work on bioterrorism preparedness planning and on regional systems for delivery of goods and services is found in four primary literature sources: the medical, emergency management, and supply chain management literatures, and government documents. We developed separate search strategies for each of these literature sources. Details of our literature sources are presented in Table 1.

From the medical literature, we sought articles describing bioterrorism preparedness plans, vaccination strategies, and evaluations of regionalized health care delivery systems. For this literature we searched two databases (MEDLINE® and Cochrane), bibliographies of relevant articles, Web sites of relevant organizations (e.g., American Hospital Association, the National Association of County and City Health Officials), and reference lists provided by our Expert Advisors (Table 1).

From the emergency management literature, we sought case studies of emergency responses, descriptions of disaster preparedness plans, and evaluations of disaster responses. For this literature, we searched six databases (e.g., HazLit), reviewed the past five years of articles from four prominent journals in the field of emergency management (e.g., *Disasters*), and searched Web sites of relevant organizations (e.g., the Natural Hazards Center at the University of Colorado at Boulder). We also reviewed reference lists provided by our expert advisors and bibliographies of included articles.

From the supply chain management literature, we sought case studies and articles about regional practices to increase the efficiency of manufacturing and distribution services and methods for evaluating supply chains. For this literature, we searched seven databases (e.g., databases of case studies at prominent graduate business schools), reviewed the past five years of articles from five prominent journals in the field of supply chain management (e.g., *Interfaces* and *Harvard Business Review*), and searched Web sites of relevant associations (e.g., the Institute for Operations Research and Management Science and the Fritz Institute). We also reviewed reference lists from our expert advisors and bibliographies of included articles.

Finally, from relevant government documents we sought local and regional bioterrorism preparedness plans, descriptions and evaluations of government programs responding to bioterrorism events (e.g., 2001 anthrax cases), and bioterrorism-relevant events (e.g., naturally occurring outbreaks and disaster responses). For this literature, we searched three government databases (i.e., GrayLit, the National Technical Information Services, and the National Academies Press), reviewed the past five years of articles from *Military Medicine*, and searched the Web sites of relevant government agencies (e.g., the Centers for Disease Control and Prevention and the Federal Emergency Management Agency), including those named as primary or support agencies in the Federal Response Plan.

Table 1. Literature Sources

Literature	Databases for published material (articles, books, reports, and Websites)	Key journals and conference proceedings	Examples of Relevant Organizations (for Web-based searches)
Medical	MEDLINE® Cochrane	Conference proceedings for the last two years (2001-2) for: American Medical Informatics Association Medical Decision Making Infectious Disease Society of America American Public Health Association American Pharmaceutical Association	American Hospital Association Joint Commission on Accreditation of Healthcare Organizations Council of State and Territorial Epidemiologists ProMED-mail National Association of County and City Health Officials National Professional Society of Pharmacists American Pharmaceutical Association Center for Civilian Biodefense Strategies
Emergency Management	Fire Academy (FEMA) HazLit (UC Boulder) Disaster! Finder (NASA) Global Emergency Management System Health and Safety Sciences Abstracts Risk Abstracts	*Disasters* *Prehospital Disaster Medicine* *Disaster Prevention and Management* *Disaster Recovery Journal*	Center for Excellence in Disaster Management and Humanitarian Assistance Natural Hazards Center (University of Colorado, Boulder)
Supply Chain	Harvard Business School case database Stanford Graduate School of Business case database Darden School of Business Administration (University of Virginia) case database Institute for Operations Research and Management Science (INFORMS) bibliographic database	*Interfaces* *Operations Research* *Management Science* *Harvard Business Review* *Manufacturing and Service Operations Management*	Institute for Operations Research and Management Science Fritz Institute American Red Cross
Government Documents	GrayLit National Technical Information Service National Academies Press	*Military Medicine*	Centers for Disease Control and Prevention (CDC) Federal Emergency Management Agency (FEMA) Metropolitan Medical Response System National Disaster Medical System (NDMS) Department of Veterans Affairs (VA) Health and Human Services (HHS) National laboratories U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) Global Emerging Infections System, Department of Defense (DoD) U.S. General Accounting Office (GAO)

Preliminary Searches

This section describes our preliminary searches for potentially relevant response organizations, bioterrorism-related and naturally occurring outbreaks, responses to natural disasters, and supply chain management cases.

Preliminary Medical Literature Database Searches

To identify potentially relevant articles in the medical literature, we searched MEDLINE® and Cochrane databases and references provided by our Expert Advisors.

MEDLINE® search strategies. We searched MEDLINE® (January 1966 to February 15, 2003) using the search terms described in Table 2.

Table 2: MEDLINE® Searches to Identify Potentially Relevant Systems and Organizations

Search	Search Terms	Citations reviewed	Articles retrieved
Bioterrorism-relevant Events			
Anthrax attack, 2001	"anthrax"[MESH] AND bioterror* AND 2001	219	25
Salmonella bioterrorism , The Dalles, Oregon, 1984	"food contamination"[MESH] AND "disease outbreaks"[MESH] AND Oregon AND salmonella	2	2
Natural Outbreaks			
Smallpox, New York City, 1947	"smallpox"[MESH] AND "New York City"	7	0
Smallpox, Boston, 1903-4	"smallpox"[MESH]AND Boston AND 1903	2	2
Hantavirus pulmonary syndrome	"hantavirus"[MESH] AND "Disease Outbreaks"[MESH]	90	30
Meningitis, Minnesota, 1995	"meningitis"[MESH] AND "disease outbreaks"[MESH] AND Minnesota	4	2
Meningitis, other	"disease outbreaks"[MESH] AND "meningitis"[MESH] AND "North America"[MESH]	112	49
West Nile Virus (WNV)	"West Nile Virus"[MESH]AND "North America"[MESH]	198	46
Cryptosporidiosis, Wisconsin, 1993	"cryptosporidium"[MESH]AND Milwaukee	22	9
Severe acute respiratory syndrome, 2002-3	“severe acute respiratory syndrome” OR “SARS virus”[MESH]	140	29
Natural Disasters			
Disaster planning	“Natural Disasters”[MESH] AND “Disaster Planning”[MESH]	525	87
Hurricane Andrew	"Natural Disasters"[MESH] AND "Hurricane Andrew"	92	43
Hurricane Hugo	"Natural Disasters"[MESH] AND "Hurricane Hugo"	48	12
Hurricane Iniki	"Natural Disasters"[MESH] AND "Hurricane Iniki"	12	4
Loma Prieta earthquake	"Natural Disasters"[MESH] AND "Loma Prieta"	27	13
Northridge earthquake	"Natural Disasters"[MESH] AND "Northridge"	34	3
Mass Gatherings			
Olympics	Olympic* AND (surveil* OR “disaster planning”[MESH])	43	33
Political conventions	“Disaster Planning”[MESH] AND “Politics”[MESH]	64	21
Sporting events	"sports"[MESH] AND "disaster planning"[MESH]	32	29
Hajj-related	"disease outbreaks"[MESH] AND hajj	13	7
Man-made disasters			
Bombings	(“Terrorism”[MESH] OR bombing) AND “Oklahoma City”	85	24

Search	Search Terms	Citations reviewed	Articles retrieved
Sarin attacks, Tokyo, 1995	“Tokyo”[MESH] AND “Sarin”[MESH]	24	9
Plane crashes	"Disasters"[MESH] AND plane AND crash	20	7
Nightclub disasters	Nightclub AND (fire OR stampede)	1	1
Bhopal chemical spill	"Disasters"[MESH] AND Bhopal	95	12
Chernobyl nuclear disaster	"Disasters"[MESH] AND Chernobyl	44	9
Preparedness Plans for Bioterrorism			
General preparedness plans	Bioterror* AND “disaster planning”[MESH]	385	155
Hospitals plans	"disaster planning"[MESH] AND "hospitals"[MESH] AND bioterror*	18	17
Public health department plans	"public health"[MESH] AND "disaster planning"[MESH] AND bioterror*	213	81
Government plans	"Government"[MESH] AND "disaster planning"[MESH] AND bioterror*	74	61
Laboratories plans	"laboratories"[MESH] AND (bioterror* OR "disaster planning"[MESH])	55	21
Bioterrorism-relevant Tasks			
Planning and Preparedness			
Relationship development	"disaster planning"[MESH] AND ("relat*"[TITLE/ABSTRACT] OR "partner*"[TITLE/ABSTRACT])	3	3
Warning systems	“warning system” AND “disaster planning”[MESH]	6	4
Resource stockpiling	stockpile AND (disaster[MESH] OR bioterror*)	15	9
Field Assessment and Triage			
Rescue and stabilization of victims	("emergency treatment"[MESH] OR "emergency medical services"[MESH]) AND bioterror*	94	77
Rescue and stabilization of victims	("Regional Medical Programs"[MESH] OR "regional health planning"[MESH]) AND ("trauma centers"[MESH] OR "burn units"[MESH])	240	115
Transportation of victims	transport* AND bioterror*	14	7
First responder protection	("safety management"[MESH] OR "first responder"[TITLE/ABSTRACT] OR “personal protect*”) AND bioterror*	13	12
Field assessment	“Emergency Medical Services”[MESH] AND bioterror*	100	78
Triage	“triage”[MESH] AND bioterror*	9	6
Hazard assessment	(hazard OR danger) AND assess* AND bioterror*	4	3
Diagnosis			
Diagnosis and agent identification	("diagnostic equipment"[MESH] OR "laboratories"[MESH]) AND bioterror*	42	19
Management			
Decontamination of victims	"decontaminat*"[TITLE/ABSTRACT] AND bioterror*	20	9
Definitive medical care	("critical care"[MESH] OR manag*) AND clinic* AND bioterror*	24	12
Definitive medical care	("regional health planning"[MESH] OR "Regional Medical Programs"[MESH]) AND "Intensive Care Units, Neonatal"[MESH]	79	40
Distribution of supplies, equipment, pharmaceuticals	(“equipment and supplies”[MESH] OR pharmacy*) AND distribut* AND bioterror*	20	13
Prevention			
Immunization and prophylaxis	("mass immunization"[MESH] OR prophylax*) AND bioterror*	74	48
Isolation and quarantine	("quarantine"[MESH] OR "patient isolation"[MESH]) AND bioterror*	16	12
Surveillance			
Surveillance	(“epidemiology”[MESH] OR surveil*) AND bioterror*	135	103
Detection	Detection AND bioterror*	58	32
Outbreak Investigation			

Search	Search Terms	Citations reviewed	Articles retrieved
Outbreak investigation	“Contact Tracing”[MESH] AND bioterror*	0	0
Evaluation of responder, caregiver and victim health	"epidemiologic methods"[MESH] AND bioterror*	268	81
Communication			
Communication system development	("communication"[MESH] OR "communications media"[MESH]) AND bioterror*	81	46
Addressing the information needs of the public/media	("telecommunications"[MESH] OR "persuasive communication"[MESH] OR "Information dissemination"[MESH] OR "mass media"[MESH] OR "Hotlines"[MESH]) AND bioterror*	33	19
Emergency Management			
Command and control	(“incident command” OR “command and control” OR command control”) AND bioterror*	5	5
Volunteer utilization and control	("international agencies"[MESH] OR volunteer*) AND bioterror*	38	13
Mental health services for responders, victims, caregivers and families	("mental health"[MESH] OR counsel*) AND bioterror*	7	6
Fatality management	("coroners and medical examiners"[MESH] OR "fatality management") AND bioterror*	5	2
Mutual aid agreements	“mutual aid”	143	11
Bioterrorism-relevant Resources			
Material			
Pharmaceuticals and related equipment (syringes, gloves, etc.)	pharm* AND bioterror*	32	15
Communications equipment	Communicat* AND equipment AND bioterror*	3	3
Patient transportation equipment, including helicopters and ambulances	"Transportation of Patients"[MESH] AND bioterror*	2	2
Laboratory	"laboratories"[MESH] AND bioterror*	44	15
Trained personnel			
General personnel	Personnel AND bioterror*	157	48
Medical: physicians, nurses, hospital administrators, pharmacists	(doctor*[TITLE/ABSTRACT] OR nurs*[TITLE/ABSTRACT] OR physician*[TITLE/ABSTRACT] OR pharmacist*[TITLE/ABSTRACT] OR administrator*[TITLE/ABSTRACT]) AND bioterror*	92	66
Public health: local, regional, state and national officials; epidemiologists	"public health"[MESH] AND ("local"[TITLE/ABSTRACT] OR "state"[TITLE/ABSTRACT] OR "epidemiolog*"[TITLE/ABSTRACT]) AND bioterror*	65	58
Emergency response	("Emergency Medical Technicians"[MESH] OR firefighter*) AND terror*	35	10
Total		4669	1852

The use of the asterisk expands search terms such that all combinations of terms with the phrase preceding the asterisk will be returned in the search (e.g., bioterror returns searches for bioterrorism, bioterrorist, bioterror, etc.).
MESH = Medical Subject Heading

Cochrane search strategies. We searched the Cochrane databases from January 1, 1990 through May 1, 2003 (Ovid, Evidence Based Medicine Reviews Multifile) using the search terms described in Table 3.

Table 3: Search Terms and Citations for Cochrane Databases

Search terms	Citations reviewed	Articles retrieved
Anthrax	7	0
Bioterrorism OR bioterrorist OR terrorism OR terrorist	1	0[†]
Salmonella AND outbreak	4	0
Outbreak	137	4
Smallpox	38	1
Hantavirus	4	0
Meningitis AND outbreak	11	1
West Nile Virus	2	0
Cryptosporidiosis	22	0
SARS OR severe acute respiratory syndrome	9	0
Disaster	31	1
Hurricane	3	3
Earthquake	6	4
(Olympic OR Olympics) AND (sport OR game)	3	0
national convention AND politic*	0	0
Hajj	2	0
Bhopal	0	0
Chernobyl	10	0
Emergency AND prepare*	13	0
AND government	2	0
AND hospital	73	0
AND public health	13	1
AND laborator*	19	3
Regional trauma	8	1
Regional burn	1	0
First responder	6	2
Triage	126	1
Mass immunization	7	1
Quarantine	7	0
Coroner OR medical examiner	1	0
Media and public and communication	28	4
Hospital capacity	2	0
Laboratory capacity	0	0
Disease surveillance	7	0
MMRS OR Metropolitan Medical Response System	0	0
DMAT OR Disaster Medical Assistance Team	1	0
National Pharmaceutical Stockpile	0	0
Total	613	27

The use of the asterisk expands search terms such that all combinations of terms with the phrase preceding the asterisk will be returned in the search (e.g., bioterror returns searches for bioterrorism, bioterrorist, bioterror, etc.).
[†]This reference discusses clinical aspects of the anthrax vaccine but does not address regionalization.

Preliminary Emergency Management Database Searches

We searched six emergency management databases, using a similar search strategy for each (Table 4). Two databases (NASA's Disaster! Finder and FEMA's Global Emergency Management System) were eliminated after we searched them using terms similar to the terms

listed below and determined that they did not contain reports or articles meeting our inclusion criteria.

Table 4: Search Terms and Citations for Emergency Management Databases

Search Terms	Fire Academy (FEMA)		HazLit (UC Boulder)		Health and Safety Sciences Abstracts		Risk Abstracts	
	Reviewed	Retrieved	Reviewed	Retrieved	Reviewed	Retrieved	Reviewed	Retrieved
Mutual aid AND (health* or medicine)	16	6	2	1	0	0	0	0
Bioterror*	123	23	0	0	43	7	33	11
Regionalization	45	14	6	2	13	1	0	0
Total	184	43	8	3	56	8	33	11

The use of the asterisk expands search terms such that all combinations of terms with the phrase preceding the asterisk will be returned in the search (e.g., bioterror returns searches for bioterrorism, bioterrorist, bioterror, etc.).

Preliminary Supply Chain Management Database Searches

The search strategy used for supply chain case databases (e.g., Harvard Business School's case database and the Stanford Graduate School of Business case database) and for other supply chain management databases (e.g., databases maintained by the Institute for Operations Research and Management Science (INFORMS)) is presented in Table 5.

Table 5. Search Terms and Citations for Supply Chain Databases

Search Terms	Harvard Cases		Stanford Cases		Darden Cases		Bibliographic INFORMS	
	Reviewed	Retrieved	Reviewed	Retrieved	Reviewed	Retrieved	Reviewed	Retrieved
Bioterror	0	0	0	0	0	0	0	0
Supply chain	65[†]	11	31	7	6	0	69	7
Disaster	12	1	0	0	7	1	8	2
Logistics	67	7	3	0	8	2	34	2
Terror	5	0	0	0	0	0	1	0
Total	149	19	34	7	21	3	112	11

[†]Note that these search terms were often duplicative; for example, not surprisingly, the supply chain and logistics searches in any given database often returned the same articles.

Preliminary Government Documents Database Searches

The search strategy employed for government databases is presented in Table 6.

Table 6: Search Terms and Citations for Government Databases

Search Terms	GrayLit		NTIS**		NAP[††]	
	Reviewed	Retrieved	Reviewed	Retrieved	Reviewed	Retrieved
Bioterror*	80	35	89	29	15	7
Disaster AND "preparedness plan*"	39	1	0	0	15	6
Laboratory AND region*	201	2	10[†]	0	15	2
Disaster AND (manage* OR	213	48	100[§]	29	15	2

Search Terms	GrayLit		NTIS**		NAP††	
	Reviewed	Retrieved	Reviewed	Retrieved	Reviewed	Retrieved
respon*)						
All Hazards AND "preparedness plan*"	50	2	0	0	15	5
All Hazards AND (manag* OR respon*)	148	1	0	0	15	4
Total	731	89	185	58	90	26

The use of the asterisk expands search terms such that all combinations of terms with the phrase preceding the asterisk will be returned in the search (e.g., bioterror returns searches for bioterrorism, bioterrorist, bioterror, etc.).
†laboratory AND regionaliz* ; §disaster AND management AND response; **National Technical Information Service; ††National Academies Press

Focused Searches

Having reviewed the citations obtained in our preliminary searches, we identified systems and organizations that performed one or more of the tasks identified in our conceptual framework or facilitated the timely distribution of relevant material, personnel, and information. We then performed focused searches of these systems and organizations for articles describing their participation in regionalized responses to bioterrorism-relevant events (Table 7).

Table 7. List of Potentially Relevant Systems for Focused Searching by Primary Task

Main Task	Example System or Organization
Planning and preparedness	Systems for training (e.g., National Laboratory Training Network; State fire training centers (FEMA); National Emergency Training Center (Federal Emergency Management Agency); Metropolitan Fire and Emergency Medical Services Training Program (Department of Justice); Public Health Training Network) Organizations for hospital preparedness (e.g., Joint Commission for the Accreditation of Healthcare Organizations, the American Hospital Association) National Domestic Preparedness Consortium National Domestic Preparedness Office (Federal Bureau of Investigation) Office of Emergency Preparedness Office of Public Health Preparedness Domestic Preparedness Program (DoD) Bioterrorism Preparedness and Response Program (HHS)
Field assessment and triage	Castro Halloween Party Emergency Management System (San Francisco) Aeromedical Evacuation System U.S. trauma care system
Diagnosis	Laboratory Response Network
Management of the acutely ill	Systems for tracking capacity (e.g., BEDTRACK, HERIS) Systems that regionalize trained personnel (e.g., *Medicins Sans Frontiers,* Medical Reserves Corps, Disaster Medical Assistance Teams (DMAT), National Pharmacists Response Team, National Nurses Response Team, Metropolitan Medical Strike Teams, National Medical Response Teams) Systems that regionalize delivery of specialized medical care (e.g., trauma care, burn units, neonatal intensive care systems) Rapid delivery of essential medical supplies (e.g., America's Blood Centers, American Association of Blood Banks, Organ Procurement and Transplantation Network, United Network for Organ Sharing) Hospital Emergency Response Data System Emergency Management Strategic Healthcare Group (VA)

Main Task	Example System or Organization
	Modular Emergency Medical System (i.e., Neighborhood Emergency Help Center and Acute Care Center) from U.S. Army Soldier and Biological Chemical Command Modular Assistance Medical System Metropolitan Medical Response System
Prevention of the spread of disease	Strategic National Stockpile
Surveillance	Influenza systems (e.g., FluNet, FluWatch, Worldwide Influenza Surveillance Program [DoD], EuroGROG) Syndromic surveillance systems (e.g., ESSENCE, BioSTORM, RODS) Surveillance for food borne illness (e.g., FoodNet, PulseNet) Healthwatch (U.S. Army) DARPA Biosurveillance Project National Electronic Disease Surveillance System National Weather Service Smallpox vaccine related surveillance systems (e.g., Smallpox Vaccine Adverse Events Monitoring and Response System, Hospital Smallpox Vaccine Monitoring System, Vaccine Adverse Event Reporting System) Global Outbreak Alert and Response Network Biowatch ProMed
Outbreak investigation	Epidemic Intelligence Service (EIS)
Communication	Among public health systems (e.g., Health Alert Network, Epi-X) Communication to the public (e.g., Amber Alert, FCC Public Safety Program, Emergency Alert System, Disaster News Network, Cable News Network (CNN), National Communications System, Homeland Security Advisory System, Farm Disaster Helpline) Warning systems for military responders (e.g., LERTCON system) Public Safety Radio Pool Rapid Response Information Center (FEMA) Warning systems for emergency medical services (e.g., FirstWatch)
Emergency management	Mutual aid agreements (e.g., California Master Mutual Aid Agreement, Emergency Management Assistance Compacts) Federal Response Plan Charitable organizations (International Federation of Red Cross and Red Crescent Societies, Red Cross, USAID) Federal Emergency Management Administration (FEMA) National Association for Search and Rescue Transportation systems (e.g., U.S. Postal Service, Federal Express) Global Expeditionary Medical Systems Chemical and Biological Rapid Response Teams (DoD), National Guard Weapons of Mass Destruction Civil Support Teams, Civilian Support Teams (National Guard), Emergency Response Team (EPA), Technical Escort Units (DoD), Strike Teams (Coast Guard), Chemical and Biological Response Teams (National Guard), DMORTs, Community Emergency Response Team Incident Management Systems (e.g., Unified Command System, National Interagency Incident Management System, Hospital Emergency Incident Command System) Enhanced Consequence Management, Planning and Support System Specially trained military responders (e.g., Soldier's Biological and Chemical Command, Chemical and Biological Immediate Response Force) Biological and Chemical Weapons Improved Response Program Joint Forces Command: Force Packages (DoD) Joint Programs Office for Biological Defense (DoD) U.S. Government Interagency Domestic Terrorism Concept of Operations Plan Bomb Data Center (DOJ)

Abstract Review

To identify potentially relevant articles for focused searching, at least one investigator reviewed each article. For the MEDLINE® search, two investigators reviewed a random selection of titles to ensure consistent application of the inclusion and exclusion criteria. Discrepancies in inclusion were resolved by discussion and re-review. An expert in the field of supply chain management research reviewed titles of potentially relevant cases from the supply chain literature.

Data Abstraction

All retrieved articles were reviewed by one or more investigators to determine if they met inclusion criteria. From each description or evaluation of a system, we abstracted the following data: information describing the regional system, methods and results of evaluations of the system, information about the quality of the study, as well as references in the bibliography that might meet inclusion criteria (Abstraction Form, Appendix B).

Determination of Methodologies for Evaluating Relevant Regional Systems

From each of the four literature sources (i.e., medical, emergency management, and supply chain management literatures, and government documents), we sought methods for evaluating the effectiveness of relevant systems. Specifically, we sought methodologies for evaluating whether a regional system would assist the key decisions and tasks required for effective bioterrorism preparedness and response. The following sections describe the relevance of each of the literatures to regionalization of bioterrorism preparedness planning, and describe our rationale for selecting the evaluation criteria from this literature. For each included article we abstracted information about only those evaluation concepts relevant to that article.

Evaluation Concepts from the Medical Literature

Evaluation concepts from the medical literature are relevant to considerations of bioterrorism preparedness because a major component of the response to bioterrorism includes the evaluation, treatment, and prevention of illness resulting from biothreat agents. Studies of health-related interventions vary with respect to outcomes and processes under evaluation. For example, evaluations of medical interventions (e.g., treatments for bioterrorism-related illness) may be designed to determine whether the intervention is effective, cost-effective, or safe. Such evaluations may directly measure clinical and financial outcomes (e.g., morbidity, mortality, or cost). Some evaluations of health care interventions consider process outcomes rather than

clinical outcomes. For example, evaluations of diagnostic decision support tools for bioterrorism may study whether the decision support tool increases the likelihood that a clinician makes the correct diagnosis, or orders an appropriate diagnostic test. From each included article we abstracted information about any evaluative outcomes of interest, including clinical, financial, and process outcomes such as morbidity, mortality, cost of the intervention, adherence to clinical protocols, and timeliness of administration of definitive medical care.

High volume has been associated with better health-related outcomes for numerous health interventions. Often the volume-outcome association is described in terms of "practice makes perfect," although there is the related phenomenon that physicians and hospitals with demonstrated excellence in clinical outcomes tend to receive more referrals and thus accrue larger volumes.[32] For example, as we will describe in greater detail in Chapter 3, sub-section "Application of Evaluation Criteria to the Trauma Literature," regionalized systems for the delivery of trauma care have achieved cost savings and improved health outcomes by concentrating the treatment of severely ill patients at trauma centers.[33-38] Because bioterrorism is a rare event, clinicians, public health officials, hospitals, and others have little opportunity to practice some bioterrorism-related response tasks (e.g., medical treatment of highly contagious, critically ill patients; and mass vaccination of an exposed population). By regionalizing services, some responders may gain sufficient skills for managing bioterrorism-related events. Thus, from each included article we abstracted information about how regionalization of bioterrorism-related services may increase the volume or expertise of response organizations, and thus potentially improve clinical or financial outcomes.

Evaluation Concepts from the Emergency Management Literature

Bioterrorism requires rapid responses characterized by the deployment of trained personnel (e.g., first responders, medical personnel, hazardous materials experts, and emergency management professionals), mobilization of supplies, and an effective command structure. Thus, evaluation concepts from the emergency management literature are relevant to considerations of bioterrorism preparedness. The emergency management literature largely comprises case studies (i.e., descriptions) of responses to particular events such as fires, hurricanes, and earthquakes. Occasionally, authors compare responses across similar types of disasters. The outcomes of interest in emergency management studies include morbidity and mortality associated with an event and responses to it;[*39, 40] the timeliness of the response; measures of cooperation, coordination, and communication among responders; and costs resulting from the disaster and/or the response.[41-45] The emergency management literature emphasizes the importance of a clear chain of command for efficient decision making and execution of response tasks, and repeatedly recommends the use of the Incident Management System when managing an emergency.[44] This system, developed in the 1970s in California for firefighting, is based on military command and

[*] Numerous articles about disaster responses describe injuries sustained by responders attempting to aid victims. For example, during the 1995 Tokyo sarin attack, 135 paramedics (9.9% of the total affected population), became ill after they were exposed to sarin from the clothes of victims. Similarly, following the 1985 earthquake in Mexico City, volunteers served a large role in rescuing victims trapped in collapsed buildings. However, the cost was considerable: 800 people were saved but 100 volunteers were killed during attempts to save victims. The enormity of the impact of this disaster on untrained volunteers stimulated several programs to train community members for natural disasters as described in greater detail in Chapter 3, sub-section "Lessons Learned from the Disaster Literature for the Regionalization of Services for Bioterrorism Preparedness."

control models, and has been expanded to an "all-hazard/all-risk" system routinely used in the management of a wide array of emergencies.[44] It includes "organization, unity of command, incident planning, integrated logistics and other key operational command and control elements."[46] From each included article, we abstracted information about any evaluative outcomes of interest, including emergency- and response-related morbidity, mortality, timeliness, costs, and information about the incident command structure used and how it affected the regionalized response.

Evaluation Concepts from the Supply Chain Literature

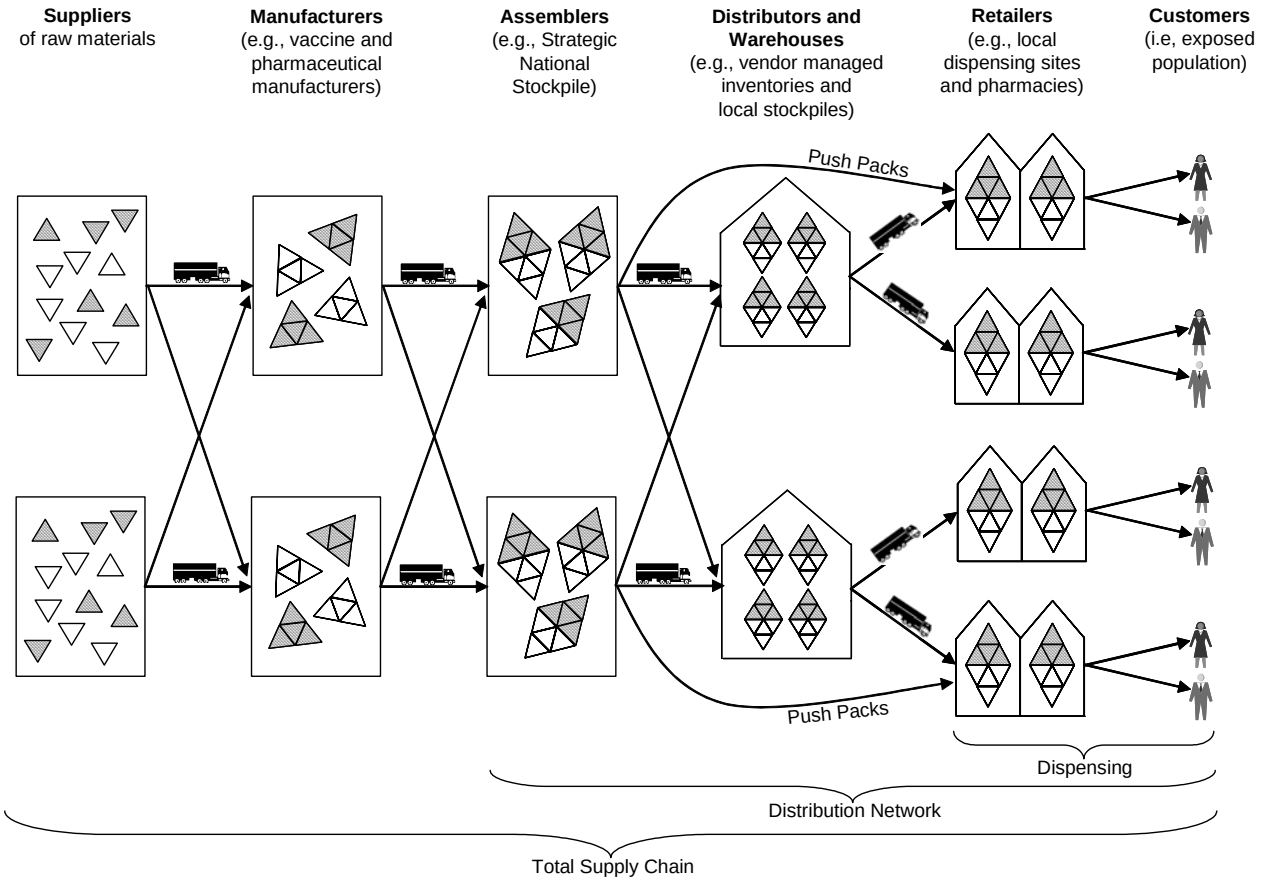
Supply chain management concepts are directly relevant to those elements of a bioterrorism response that require the purchase, inventorying, distribution, and rapid dispensing of medical supplies (e.g., antibiotics, vaccines, and equipment) to remotely located users (e.g., hospitals, pharmacies, and local dispensing sites). A traditional supply chain is the integrated network of entities involved in all aspects of the manufacture of goods, including the procurement of raw materials, their assembly into the manufactured product, transportation of the product to distributors, and distribution to final customers.[47] The bioterrorism response supply chain has several key components: suppliers of raw materials, manufacturers of goods (e.g., product manufacturers such as drug and device manufacturers), purchasers (e.g., group purchasing organizations, wholesalers, mail-order distributors, and federal and local government agencies), providers who distribute the products (e.g., clinicians, hospitals, pharmacies, integrated delivery networks, and dispensing sites), customers/payors (e.g., the government, employers, and individuals), and the transportation systems that connect these components.[48] The bioterrorism response supply chain is a particular type of health care supply chain. We direct interested readers to a recent comprehensive review of the health care supply chain by researchers at the Wharton School, University of Pennsylvania.[48]

Figure 1 presents the key components of the bioterrorism response supply chain. The supply chain entities labeled in bold (e.g., suppliers, manufacturers, and retailers) refer to the elements of a traditional supply chain (such as for the manufacture of pharmaceutics for routine health care delivery). Examples of the components of the bioterrorism response supply chain corresponding to the traditional supply chain are provided. Although all elements of the supply chain are essential, during a response to bioterrorism, until all antibiotics and medical supplies available through local stockpiles and the Strategic National Stockpile have been consumed, the last three elements of the supply chain—also known as the distribution network—are the most critical. The establishment and coordination of the distribution network is currently the focus of considerable planning by local, state, and federal officials.

To determine criteria for evaluating the bioterrorism response supply chain, we sought descriptions and evaluations of innovations in supply chain management. Evaluations of traditional (manufacturing) supply chains often include considerations of four logistical issues: *strategic* issues, *structural* issues, *functional* issues, and *implementation* issues.[49] Briefly, *strategic* issues involve determining customers' needs and the strategies used to meet them. For example, how should sufficient prophylactic antibiotics be acquired, stored, distributed, and dispensed to a population exposed to bioterrorism? *Structural* issues involve determining which functions need to be performed to achieve a desired level of service and which elements of the supply chain should perform them.[49] For example, how many distribution sites are needed to

supply an exposed population? Which customers and products will be served from each facility or antibiotic/vaccine stockpile? How much inventory should be held in each facility? *Functional* issues involve determining how various tasks will be carried out (e.g., transportation carrier selection, fleet management, warehousing, and inventory management).[49] *Implementation* issues involve creating the information systems to support the supply chain, and installing and maintaining facilities, equipment, and personnel.

Figure 1. The Bioterrorism Response Supply Chain



The literature is inconsistent in its use of the terms *dispensing* and *distribution*. In general, dispensing refers to the end of the supply chain when medical supplies are given to patients—it is the terminal component of the distribution network.

From each supply chain case study, we abstracted information about the supply chain innovation described, and the outcomes of interest. We now describe the five specific concepts from evaluations of supply chains that are relevant to the bioterrorism response supply chain about which we abstracted information from each included article: **network design**, **inventory management**, **postponement and modularization**, **supply chain coordination and management of incentives**, and **management of information**. (We present details of the data abstracted from the supply chain case studies in Chapter 3 under the section "Synthesis of Evidence About Regionalization of Supply Chains".)

Network design. Network design broadly encompasses decisions about the number and location of physical elements of a supply chain (e.g., manufacturing plants and dispensing sites), and relationships between them (e.g., transportation networks). Network design evaluations typically determine whether the number and location of manufacturing and distribution facilities are ideal for achieving strategic goals of the supply chain. The outcomes of interest in evaluations of network designs of traditional supply chains include costs saved, percentage of customer orders that can be filled immediately, and customer satisfaction. For example, an evaluation of network design may find that eliminating redundant distribution centers results in reduced total costs for the supply chain.[50-54]

For bioterrorism preparedness, the key elements of network design include the manufacturers and wholesalers of resources such as antibiotics and vaccines, regional distribution centers, warehouses, hospitals, pharmacies, and other local dispensing sites, and the transportation networks among them. For the bioterrorism response supply chain, the network design outcomes of interest are reductions in morbidity and mortality, and time to provide treatment and prophylaxis. For example, an evaluation of the network design of the bioterrorism response supply chain might determine whether local plans for distributing materials from the Strategic National Stockpile result in reduced response times and reduced bioterrorism-related morbidity and mortality.

Although many supply chains are designed with the minimal numbers of elements to create cost efficiencies, for some industries (particularly service industries), redundancies in the supply chain are essential to making the supply chain robust. This is particularly true for the bioterrorism response supply chain. For example, eliminating redundant distribution centers certainly reduces costs, but if that center should be attacked or otherwise incapacitated, the entire response supply chain could be compromised. Table 8 presents the key evaluation concepts associated with network designs of traditional (manufacturing) supply chains and bioterrorism response supply chains.

Inventory management. Evaluations of inventory management address the costs and benefits associated with maintaining numerous, small local stocks of needed resources, as opposed to regionalizing these into larger centralized inventories. The outcomes of interest in evaluations of the inventory management of traditional supply chains include costs of holding inventories, time to fill customers' requests, and timeliness and accuracy of inventory information. In general, evaluations of traditional supply chains demonstrate that the smaller the number of distribution centers, the lower the costs of holding inventory.[54, 55] However, some evaluations have found that, when delivery times are critical, increasing the number of distribution centers or locally held inventories improves customer satisfaction.[45] Typically, minimizing inventories while maintaining the ability to meet customers' demands requires accurate and timely information about supplies of raw materials and finished products, inventories available locally, and customer demands.[50, 56, 57]

The Strategic National Stockpile* (which will be discussed in greater detail in Chapter 3 in the context of responses to the 2001 anthrax incident) has been developed to regionalize the

*The Strategic National Stockpile maintains 12 Push Packs containing antibiotics, vaccines, and other medical supplies, which are stored in undisclosed locations around the country for deployment to emergency sites. Once ordered, a Push Pack is designed to arrive anywhere in the United States in 12 hours. The Strategic National Stockpile also maintains Vendor Managed Inventories, designed to arrive after the Push Packs (about 36 hours later). These are tailored according to the specific needs of the requester. The Strategic National Stockpile, formerly under primary CDC control, was previously called the National Pharmaceutical Stockpile and now operates under the control of the Department of Homeland Security.

inventories of resources such as antibiotics and vaccines for a bioterrorism response. For the bioterrorism response supply chain, the outcomes of interest in evaluations of inventory management are the costs of maintaining and storing inventories (including considerations of pharmaceuticals' shelf lives), time to supply the demands of the exposed population, and timeliness and accuracy of inventory information.

For example, an evaluation of a bioterrorism inventory management strategy might assess the costs and benefits of maintaining local inventories of antibiotics and vaccines as opposed to increasing the inventory maintained by the Strategic National Stockpile.

Postponement and modularization. Postponement refers to the concept of customizing a product late in the supply chain (i.e., closer to customer delivery). Modularization refers to the use of standard parts that can be used in multiple end products (so that less customization is required). Evaluations of traditional supply chains have found that product costs and inventories can often be reduced by delaying the customization of products and designing final products that can be assembled from common component parts.[58-61] For example, different countries' electrical standards require different plugs on appliances. Thus, electronic equipment manufactured for use in different countries can be designed with a base unit that carries several different plugs, allowing the appropriate plug to be attached, depending on the purchaser's needs. Designing the supply chain to postpone a part of the manufacturing or assembly process can reduce the cost of specifically customizing end products for each target market.[58, 59] Similarly, automotive manufacturers who design their new models to be built out of shared components have been able to reduce inventories of parts and increase profits.[59]

For bioterrorism preparedness, postponement and modularization are relevant for the efficient distribution and dispensing of antibiotics and other essential medical supplies. For example, the TOPOFF exercise demonstrated the importance of having pre-packaged antibiotics in assemblages of materials for use against numerous weapons of mass destruction attacks in the first hours and days after an attack.[62] Push Packs from the Strategic National Stockpile contain antibiotics, vaccines and other medical supplies necessary to respond to bioterrorism. These supplies are pre-packed for rapid dispensing. Recipients of the Push Packs dispense only those items required to combat their particular event. Later, Vendor Managed Inventories (customized inventories containing outbreak-specific resources), are sent to the dispensing site. The outcomes of interest in evaluations of the postponement strategies of traditional supply chains include costs of inventories and time to fill customer requests. Similarly, for the bioterrorism response supply chain, the outcomes of interest in evaluations of postponement strategies are the costs of inventories and time to supply the demands of the exposed population.

Supply chain coordination and management of incentives. Evaluations of supply chains have found that the diverse purchasing, manufacturing, and distribution organizations in a supply chain often operate independently and may have their own (often competing) objectives.[47, 53] Efforts to coordinate the activities of supply chain members may involve better management of information, inventories, and incentives. Explicit evaluation of the incentives offered to each member of a supply chain, and efforts to align these incentives, have resulted in significant cost savings and improvements in customer satisfaction. For example, a cash bonus may be offered to a supplier who modifies his information system to better integrate with the other members of the supply chain, thereby improving the overall efficiency of the supply chain.

For bioterrorism preparedness, incentives might include monetary payments, additional supplies, additional power to respond to potential bioterrorist events, and for some organizations (such as the Red Cross) positive media exposure. (The flows of money associated with the health care supply chain are highly complex. A detailed analysis of these is outside the scope of this project; we direct interested readers elsewhere.[*48])

Management of information. Evaluations of supply chains demonstrate that accurate and up-to-date information about the level of raw materials, finished products and their locations, and customer demands are essential to keeping inventories low and supplying customers in a timely manner.[49, 52] Sophisticated supply chain management information systems—in addition to real-time tracking of products through the supply chain—include decision support tools that optimize routing and scheduling and minimize costs of component parts and inventories.[48, 57] In the health care industry, during the process of ordering goods, clinicians, pharmacists, and other customers submit purchase requests to a procurement officer who identifies the requested items in a distributor's catalog (often paper-based) and submits the order to the group purchasing organization and to the distributor.[48] These orders are communicated to the manufacturer for shipment. The industry is increasingly adopting a common electronic data platform for the direct electronic transmission of standard business forms (e.g., purchase orders, shipping notices, and invoices); however, this protocol is far from universal.[48]

For bioterrorism, management of information about the needs of local responders and the availability of regional inventories is an essential component of a coordinated response.

Table 8. Evaluation Concepts from the Supply Chain Literature and their Relevance to Regionalization of Bioterrorism Preparedness

Key Concepts and Evaluation Criteria For Traditional (Manufacturing) Supply Chains	Key Concepts and Evaluation Criteria For Bioterrorism Response Supply Chains
Network Design	
Entities: • Suppliers and manufacturing plants • Warehouses • Distribution facilities • Customers • Transportation network	*Entities:* • Antibiotic and vaccine manufacturers and wholesalers • Antibiotic/vaccine stockpiles (e.g., Strategic National Stockpile and local inventories) • Hospitals, pharmacies, and local dispensing sites • Exposed population • Transportation network

[*] The Wharton review of the health care supply chain describes some money flows among supply chain members as follows.[48] Products are sold by manufacturers—at prices set by them—to distributors. Distributors sell products to providers, typically at discounted prices resulting from contracts negotiated by a group purchasing organization. Distributors issue credits or rebates to the manufacturer for the difference between the list price that it paid for the goods and the discounted price (plus a handling fee) that it received from the purchaser. In general, the fees paid to distributors for shipping, marketing, and tracking products is about 1-2% of sales. Group purchasing organizations receive contract administration fees from the manufacturer, which typically amount to 2-3% of the sales contract. Depending on the purchasing organization, these fees are sometimes returned to its purchaser members. It is estimated that 40-67% of hospital supplies (approximately $25.1 billion) are purchased through contracts negotiated via national purchasing organizations. The remaining items are purchased via regional and local contracts.

Key Concepts and Evaluation Criteria For Traditional (Manufacturing) Supply Chains	Key Concepts and Evaluation Criteria For Bioterrorism Response Supply Chains
Considerations: • Determining the number and location of manufacturing and distribution facilities • Determining an appropriate distribution network for finished goods • Iterative improvement of an existing supply chain	*Considerations:* • The number and location of stockpiles of necessary resources such as pharmaceuticals, medical supplies, and equipment • Appropriate distribution network for these necessary resources • Iterative improvement of a bioterrorism response supply chain
Evaluation criteria: • Profit • Order fulfillment (percentage of customer requests that can be filled immediately from stock on hand)	*Evaluation criteria:* • Reduction in morbidity, mortality, timeliness of treatment/prophylaxis • Cost
Inventory Management	
Entities: • Inventories of raw materials and finished goods • Information systems that monitor inventories and customer demands	*Entities:* • Inventories of equipment and drugs • Information systems that monitor inventories of needed resources
Considerations: • The fewer distribution centers that serve a region, the less product they must stock to provide the same level of customer service • Fewer distribution centers can often provide the same level of service to customers with reduced total inventory • Marketing affects demand and subsequent inventory (e.g., advertisements for products may enhance demand and require changes in inventory management)	*Considerations:* • Resources required for a bioterrorism response can be held in regional stockpiles rather than in individual local communities • Regionalization of inventories of bioterrorism resources requires accurate and timely information about demands for these resources and the availability of local and regional stockpiles • Communication of information about a suspected or actual bioterrorism event may affect the behavior of the public to seek medical attention
Evaluation criteria: • Time to fill customers' demands • Costs of inventories • Timeliness and accuracy of inventory information	*Evaluation criteria:* • Time to supply the demands of the exposed population • Costs of inventories • Timeliness and accuracy of inventory information
Postponement and Modularization	
Entities: • Subassemblies (i.e., components of the final product) and final products	*Entities:* • Resources required for treatment and prophylaxis of bioterrorism-related illness (e.g., prophylactic antibiotics could be assembled into a variety of products of distribution including individual packages containing multiple days of adult or pediatric therapy)
Considerations: • Products are customized for a specific market late in the supply chain • Products are designed in modular parts that can be used in a variety of end products • Postponement and modularization can minimize inventory while still providing a high level of customer service	*Considerations:* • Individualized packets of supplies can be prepared regionally to reduce the preparation time required at the local dispensing site to divide up and repackage the antibiotic arriving in 500+ tablet shipments. (The Push Packs have pre-packaged antibiotics in 10day regimens and the Vendor Managed Inventories provide pre-packed 25-day regimens.)
Evaluation criteria: • Time to fill customers' demands • Costs of inventories	*Evaluation criteria:* • Time to supply the demands of the exposed population • Costs of inventories

Key Concepts and Evaluation Criteria For Traditional (Manufacturing) Supply Chains	Key Concepts and Evaluation Criteria For Bioterrorism Response Supply Chains
Supply Chain Coordination and Management of Incentives	
Entities: • Partners in the supply chain: suppliers, manufacturers, distributors, retail outlets	*Entities:* • Partners in the supply chain: pharmaceutical companies, medical supply manufacturers, pharmacies, transportation companies, clinicians, hospitals, governmental agencies responsible for the storage and distribution of antibiotics, vaccines, and medical supplies
Considerations: • Coordination of activities of supply chain members results in lower cost and improved customer service • All partners in the supply chain are incentivized to work toward the same final goal • Different members of the supply chain have different financial incentives	*Considerations:* • Coordination of activities of all relevant bioterrorism responders results in quicker response and improved clinical outcomes • All relevant bioterrorism responders are incentivized to work to protect the public health • Different elements of bioterrorism response (e.g., clinicians vs. pharmaceutical manufacturers) have highly heterogeneous financial and legal responsibilities
Evaluation Criteria: • Profits for the overall supply chain • Satisfaction of supply chain partners	*Evaluation criteria:* • Speed and effectiveness of response to bioterrorism events • Clinical outcomes
Management of Information	
Entities: • Partners in the supply chain: suppliers, manufacturers, distributors, retail outlets • All relevant data	*Entities:* • All relevant bioterrorism response partners • All relevant data
Considerations: • Accurate information on inventory and parts made available in a timely manner to plan for resources required • Centralized database to manage the data, thus making all information readily available in one place	*Considerations:* • Accurate and timely information on inventories of pharmaceuticals, vaccines, medical supplies • Accurate information on number of infected cases and exposed individuals, and availability of personnel and supplies made available in a timely manner to allow for planning of resources required
Evaluation Criteria: • Data completeness and accuracy • Date timeliness (up-to-date)	*Evaluation Criteria:* • Data completeness and accuracy • Date timeliness (up-to-date)

Evaluation Concepts from Government Documents

Because a major component of the response to bioterrorism includes government agencies, evaluation concepts from the military, emergency response agencies, and other governmental responders are relevant to considerations of bioterrorism preparedness. In our review of government documents, in particular those from the military, we found that emergency responses often benefited from a clear chain of command and from careful review of the lessons learned from previous related responses. For example, in its report to NASA, the Columbia Accident Investigation Board described the Navy as having "institutionalized their 'lessons learned' approaches to ensure that knowledge gained from both good and bad experiences is maintained in corporate memory. This has been accomplished by designating a central technical authority

responsible for establishing and maintaining functional technical requirements as well as providing an organizational and institutional focus for capturing, documenting and using operational lessons to improve future designs."[63] From each included article, we sought to abstract information describing lessons learned from each response to bioterrorism-relevant events. In addition, for each broad category of included articles (responses to the 2001 anthrax cases, responses to naturally occurring outbreaks, and responses to natural disasters) we summarize the lessons learned relevant to a regionalized response to bioterrorism.

Simulation Model: Regionalization of Surveillance

Because of the importance of surveillance and the limited evaluative information available in the literature, we conducted supplemental analyses. These analyses were informed by the results of our previous review of the literature of syndromic surveillance systems for bioterrorism-related illness,[3] and additional information abstracted to specifically consider issues relating to the regionalization of surveillance.[64-77] In disease surveillance systems, surveillance data are analyzed to determine whether the number of observed cases exceeds a threshold for an expected number of cases. Locally collected surveillance data can be pooled in several ways to determine whether this threshold has been crossed (e.g., data from multiple hospitals or regions could be pooled, or data for several related syndromes could be pooled). Because each method for pooling surveillance data results in tradeoffs in terms of sensitivity and specificity, we used simulation to explore the effects of various strategies for regionalizing the analysis of surveillance data on the system's detection characteristics. The research questions that we addressed with this simulation model are an extension of Key Question 4. They are:

1. How does regionalization (i.e. pooling) of surveillance data change the probability of detecting an outbreak related to bioterrorism? How does it change the probability of false positives (i.e., false alarms)? Strategies that we considered for analyzing surveillance data were: analysis of local data alone, analysis of pooled data alone, and analysis of both local and pooled data.

2. How do the characteristics of the surveillance data (i.e., correlations in data among local sources) and the disease outbreak (i.e., small as opposed to large outbreaks) effect the pooling of surveillance data?

To answer these research questions, we simulated syndromic surveillance data for two regions (e.g., neighboring counties). We briefly describe this model and the assumptions we used to develop it in Chapter 3 in the section on "Simulation Model Results." We direct readers interested in the details of our simulation elsewhere.[78] Briefly, for each simulated day, we calculated an expected number of patients with syndromes of interest. We assumed that the correlations of disease incidence between the two local sources would be similar to that typically found in surveillance data. We varied the attack size to represent different sizes of bioterrorism events. We considered that an attack had been detected if the surveillance data exceed the thresholds used to distinguish between an expected number of cases and a larger than expected number of cases.

Simulation Model: Inventory Management

The literature is insufficient to evaluate another critical area of bioterrorism preparedness planning and regionalization: inventory management. Thus, we developed a simulation model to address the costs and benefits of differing strategies for pre-attack stockpiling and post-attack distribution of necessary pharmaceutical supplies such as antibiotics. Specifically, we developed a simulation model to evaluate the effects of changes in distribution capacity and policy on health outcomes following anthrax bioterrorism. The simulation model was informed by the results of our review of the literature of inhalational anthrax in the United States (these results are presented in Chapter 3). The research questions that we addressed with this simulation model are an extension of Key Question 4. They are:

1. What are the costs and benefits associated with maintaining local, limited inventories of material to be distributed before the arrival of a shipment from the Strategic National Stockpile? Costs include those of acquiring, maintaining, and storing the inventories; costs of durable and consumable goods; costs associated with the labor to manage and distribute the inventories; and costs associated with treatment of victims of an attack and deaths. Benefits include reduced time to distribute material, lives saved, and access to immediate prophylaxis by emergency responders.

2. What are the costs and benefits of increasing or decreasing the numbers of Push Packs maintained by the Strategic National Stockpile?

To answer these questions, we simulated an aerosol exposure to *B. anthracis* in an urban area of 5 million people. We briefly describe this model and the assumptions we used to develop it in Chapter 3. We direct readers interested in the details of our simulation elsewhere.[79] Briefly, this simulation model incorporates a model of anthrax disease progression in the exposed population and includes the effects of prophylaxis and treatment on disease progression and mortality. We considered scenarios in which the number of people exposed to an anthrax attack was different from the number of people who request prophylactic antibiotics. We used the simulation model to assess the outcomes associated with changes in the size of local inventories, as well as changes in the times required for distribution and dispensing of the Push Packs and regional Vendor Managed Inventories. We performed extensive sensitivity analysis to validate the output of the simulation.

Reviews and Revisions of Draft Evidence Report

In October 2003, we sent a draft of the Report to our expert advisors and to additional reviewers with expertise in bioterrorism/biodefense, public health, supply chain management, surveillance, disaster epidemiology, disaster logistics, and emergency management (Appendix A). We solicited comments on all aspects of the Report, using a structured comment form. The submitted Report incorporates the reviewers' input.

Chapter 3. Results

This chapter presents the results of our systematic review and simulations. We reviewed 9542 articles and reports, more than 500 Web sites, and numerous texts recommended by our expert advisors for potential inclusion in this Evidence Report. Of these, 396 articles, 61 government reports, and 75 Web sites met our inclusion criteria. Most rejected articles did not report on regionalization of a bioterrorism-relevant response, or did not report an application of relevant supply chain management concepts (see Alphabetical Listing of Excluded Studies).

The first section of this chapter reviews the 22 included articles and one Web site describing supply chain management innovations used to inform our evaluation criteria. The second section reviews the 20 articles, 16 government reports, and 12 Web sites describing the key infrastructure elements of the organizations that would be primarily responsible for a regional response to bioterrorism (e.g., local and state health departments; local, state, and federal emergency management agencies). Subsequent sections synthesize the evidence about regionalization of responses to the 2001 anthrax bioterrorism (30 articles, 14 government reports, and 16 Web sites were included), to naturally occurring infectious disease outbreaks (181 articles, ten government reports, and 33 Web sites included), to natural disasters (37 articles, 17 government reports, and 12 Web sites included), for trauma care (74 articles and two government reports included), and for bioterrorism surveillance (32 articles, two government reports, and one Web site included). We also provide the results of our two supplemental analyses: simulations for regionalization of surveillance data analysis and regionalization of inventories for the treatment of non-communicable bioterrorism-related illness. Finally, the summary synthesis of evidence about regionalization for bioterrorism preparedness and response section of this chapter presents our answers to the Key Research Questions.

Synthesis of Evidence about Regionalization of Supply Chains

We reviewed 316 articles and cases studies reporting innovations intended to improve supply chain performance; 22 articles and one Web site are relevant to the bioterrorism supply chain and are included in our report.[*] Ten of these articles specifically evaluated supply chain innovations.[†] The remaining 12 articles described implementations of supply chain modifications, but did not provide detailed analyses of the effects of these modifications in terms of costs saved, timeliness of orders filled, or customer satisfaction.[‡] Table 9 presents the lessons learned from the 22 included articles and one Web site which describe 27 supply chain case studies (i.e., several articles describe more than one supply chain).

[*] We had hoped to include case studies of the pharmaceutical supply chain, given its enormous relevance to the bioterrorism response supply but found none that met our inclusion criteria.
[†] References[50-56, 58-60]
[‡] References[45, 48, 57, 61, 80-87]

From our review of the traditional (manufacturing) supply chain literature we identified five practices that are consistently associated with improved outcomes: improved **network design**,[*] careful attention to **inventory management**,[†] **postponement and modularization** (postponement of product customization and modularization of product components),[50, 58-61] **supply chain coordination and management of incentives**,[52, 58] and appropriate **management of information**.[56, 57, 84, 85] We used these lessons learned to inform our evaluation criteria (see Chapter 2).

The supply chain for Hewlett-Packard, a company that manufactures and distributes computers and computer peripherals such as printers, has been subjected to extensive evaluation (Table 9).[58, 59] Several concepts from the evaluation and redesign of Hewlett-Packard's supply chain are relevant to considerations of regionalization of the bioterrorism response supply chain. For example, Hewlett-Packard adopted a **network design** that incorporates "design for localization:" local distribution centers, rather than remotely located factories, customize products for local countries. This allows factories to hold less inventory and allows demand uncertainty to be managed at both the local and factory levels. Redesign of Hewlett-Packard's European distribution network saved the company $8 million annually.[58] This redesign required careful **supply chain coordination and management of** the sometimes competing **incentives** of the numerous members of the supply chain including manufacturers, distributors, and retailers.[58] Design for localization is a relevant consideration for regionalization of the bioterrorism response supply chain to the extent that local decisionmakers, who have a greater understanding of the needs and resources of their communities, could participate with state and national organizations to acquire, assemble, store, and distribute resources during a bioterrorism response. Similarly, considerations of supply chain coordination and management of incentives is highly relevant to the ongoing efforts to facilitate cooperation among the heterogeneous members of the bioterrorism response supply chain.

Evaluations of the Hewlett-Packard supply chain also illustrate the benefits of **postponement** to delay product differentiation. The company sells products in many countries, each of which has different national languages and electrical circuits. It used postponement strategies to design its products to include manuals printed in all relevant languages and to include a variety of electrical plugs that can be attached by customers based on their needs. This obviated the need for distant factories to pre-assemble multiple combinations of products specific to each country. The result was a 187% decrease in material handling cost and a 47% reduction in storage space.[59] Postponement is relevant to regionalization of bioterrorism because resources delivered to local responders during a bioterrorism response will need to be customized for the local population and suspected bioterrorism agent. For example, as regional planners evaluate alternative strategies for the packaging of antibiotics for local dispensing, they may want to consider pre-packaging antibiotics in doses appropriate for both adult and pediatric populations with labels available in several languages. The regional center could send all components so that the local site could more easily customize distribution locally (i.e., **modularization**). Alternatively, the regional center could pre-pack most of the shipment but delay adding the labels until the location and bioterrorism threat were known. In this case, the regional center would add, just prior to shipment, the appropriate labels (e.g., languages needed by the receiving site, treatment instructions for specific biothreat situation). In advance, the regional center would

[*] References[50-54, 56, 58, 80, 82, 83, 86, 87]
[†] References[45, 50, 52, 55, 56, 59]

need to estimate how many of each type of label would be required for each major city in the country, and have the locale-specific packing lists available.

IBM, another manufacturer of personal computers and servers, has also been the subject of rigorous supply chain evaluations (Table 9). IBM improved **inventory management** by pooling inventories at regional warehouses. By consolidating multiple smaller inventories into larger regional inventories, IBM significantly reduced its overall inventory stock while maintaining the same level of customer service.[57] Specifically, IBM improved its **information management** systems to obtain up-to-date customer demand information from retailers to optimize inventories for its configure-to-order operations. This resulted in a 50% reduction in inventory levels, improved customer service, and $20 million in annual savings.[50, 56] Information and inventory management are essential components of plans to regionalize inventories of materials and trained personnel for bioterrorism responses, and for providing decisionmakers with information about changing supply and demand of resources during a bioterrorism response.[3]

Lessons Learned from the Supply Chain Literature

From our review of the supply chain literature, we synthesized five key lessons learned.

1. *Strategies to improve supply chain network designs, including regionalization of some elements of the supply chain, can reduce inventories, improve service, and save money.* A number of traditional (manufacturing) supply chains have benefited from network redesign that balance the needs of local customers with the objectives of the overall supply chain (which typically include reducing inventories, maintaining high levels of customer service, and reducing overall costs). Appropriate design of the bioterrorism response supply chain network that facilitate effective and timely response to a bioterrorism event needs to balance considerations of adequate redundancy (to maintain adequate capacity in the event of a large-scale attack) while reducing excessive costs. The key elements of the bioterrorism response supply chain currently receiving considerable attention from policymakers are the distribution networks that dispense the materials from the Strategic National Stockpile.

2. *For any given network design, effective inventory management, such as pooling of inventories at regional warehouses, can reduce levels of held stock, improve service, and save money.* Regionally held inventories of supplies needed for a bioterrorism response may allow for less inventory to be held overall while still being available to local regions in a timely manner. This is the philosophy behind the Strategic National Stockpile. Because, some bioterrorism response supplies have limited shelf lives, minimizing (and/or rotating) inventory may be important from economic and logistics perspectives. This is a key consideration for locally held inventories.

3. *Postponement of product customization and reliance on component modularization can reduce supply chain costs while improving manufacturing and delivery times.* Several supply chain case studies demonstrated that redesigning final products to be assembled from a limited number of common component parts, even if those component parts are costly, can result in overall cost savings for the supply chain.

For bioterrorism, "components" include antibiotics and medical supplies packaged in local and regional inventories, teams of trained personnel available for deployment to the affected locality, and protocols such as clinical practice guidelines for the diagnosis and management of populations exposed to a biothreat agent.

4. *Coordination of activities of supply chain members, along with specific consideration of the incentives of all stakeholders in a supply chain, can improve service, increase efficiency, and reduce costs.* The bioterrorism response supply chain is highly complex with numerous stakeholders. Specific delineation and alignment of their (sometimes competing) incentives may benefit programs to coordinate response efforts.

5. *Timely and accurate information about customer demands facilitates inventory management and rapid delivery of products.* For the bioterrorism response supply chain, information systems that can accurately characterize the available supply of goods and personnel and the ongoing needs of the community affected may benefit the response.

Table 9. Lessons Learned From the Traditional (Manufacturing) Supply Chain Literature

Reference	Company/supply chain under evaluation	Key lessons learned from the supply chain case study
Lee, Billington[58]	**Hewlett-Packard** (HP) manufactures and distributes computers and computer peripherals such as printers.	The authors describe evaluations of several changes in the HP supply chain **network design** including "design for localization" which requires that local distribution centers customize products for local countries, rather than relying on a distant factory to perform this step. This allows factories to reduce total inventory and allows demand uncertainty to be managed both at the local and factory levels. The authors describe the strategy of **postponement** of product customization. This allows the greatest possible flexibility to respond to changing customer demands. These supply chain initiatives enabled HP to reduce inventory levels by 10-30%; redesign of HP's European distribution network saved the company $8 million annually; product postponement saved the company money and improved service. Supply chain management strategies such as "design for localization" and postponement increased order fulfillment (the percentage of customer orders that can be filled immediately) and contributed to the company's profits directly (by decreasing inventories) and indirectly (by increasing customer satisfaction).
Ernst, Kamrad[59]	**Hewlett-Packard**	HP adopted **postponement** and **modularization** principles in its production of the company's popular DeskJet printers, allowing different models to share manuals, software and accessories. The result was a 187% decrease in material handling cost and a 47% reduction in storage space.

Reference	Company/supply chain under evaluation	Key lessons learned from the supply chain case study
Lin, et al.[50]	**IBM** manufactures personal computers (PCs) and servers.	Changes in IBM's supply chain **network design,** including reductions in the number of assembly facilities, resulted in a 6% improvement in customer service and a 5% reduction in inventories. **Postponement** of computer customization cut costs by 12% while improving service. Improved i**nventory management** (specifically, pooling of inventories at regional warehouses) resulted in a 50% reduction in inventory levels, while maintaining the same level of customer service. IBM's supply chain redesign resulted in $650 million in annual savings.
Nahmias[56]	**IBM**	IBM optimized **inventory management** in its supply chain. This resulted in improved service and $20 million in annual savings.
Cheng, et al.[57]	**IBM**	IBM used **information management and inventory management** to cut costs. IBM used customer demand information from retailers to optimize inventories for its configure-to-order operations. IBM employed risk pooling strategies to significantly reduce inventories: when inventories are consolidated, less inventory can be held while still providing the same level of customer service.
Arntzen, et al.[51]	**Digital Equipment Corporation** (DEC) manufactures computers.	DEC optimized its supply chain **network design**. By reducing the number of manufacturing plants from 33 to 12 and service facilities from 34 to 17, DEC saved $300 million in operating costs, $80 million in service facility costs, and $70 million in inventory costs.
Davis[52]	**General Electric** (GE) Transportation Systems manufactures railway locomotives and motors for other off-highway vehicles.	GE examined its supply chain **network design**. Network redesign resulted in fewer purchasing entities. Remaining entities achieved improved **coordination**, resulting in an estimated total savings to GE of $4 million.
Mohammed, Hammond[53]	**Polaroid** manufactures a variety of instant photographic products.	Polaroid examined its supply chain **network design**. Polaroid changed its European distribution system from 12 local warehouses to a single centralized inventory location. Operating costs were reduced by $5 million annually (due to inventory pooling and reduced warehouse operation costs) and customer service improved. However, local managers required **incentives** to move to a regional warehousing system.
Graves, Willems[55]	**Eastman Kodak** manufactures cameras and camera accessories.	Kodak examined its supply chain **network design** and **inventory management** in its warehouses. Regionalization of warehouses for safety stock (inventories of component parts) for their high-end digital camera division minimized inventories by as much as 30% and improved delivery times. (The authors describe a free software and optimization algorithm for the placement of strategic inventories they applied to the Eastman Kodak supply chain [available at: http://web.mit.edu/lfmrg3/www/]. [88])

Reference	Company/supply chain under evaluation	Key lessons learned from the supply chain case study
Sery, et al.[54]	**BASF Group** manufactures a range of chemicals and chemical related products.	After examining its supply chain **network design**, BASF regionalized its distribution network, moving from 86 distribution centers to 12 centers. As a result, service improved and costs decreased. Cost savings were about 6% of original transportation, facility and inventory costs. Some savings came from improved network design; other savings resulted from improvements in **inventory management.**
Karabakal, et al.[80]	**Volkswagen** (VW) of America imports and distributes Volkswagen and Audi vehicles in the United States.	VW of America examined its supply chain **network design**. The company increased its distribution centers from 5 to 12. This resulted in improved service and reduced costs for dealers in the Midwest region of the United States. However, the 12 distribution centers could not maintain sufficient inventory of certain very popular models to remain financially viable.[*]
Ernst & Kamrad[59]	**Suzuki** is an automotive manufacturer.	**Modularization** of new car design, so that cars share as much as 70% of their parts with other models, allowed Suzuki to minimize inventory levels of component parts.
Brown, et al.[60]	**Xilinx** manufactures semiconductors.	**Postponement** of product customization helped Xilinx reduce its inventory by 23%.
Maniscalco & Christen[45]	**EMS Incident Management System** (IMS) provides logistical support and command and control for emergency medicine professionals.	IMS is partly a system for **inventory management**. Push-packs (inventories) of emergency supplies can be regionally stored for rapid response following an emergency that requires a major EMS response.
Burns[48]	**OmniCell.com** manufactures "smart cabinets" that automate the dispensing of medical supplies and pharmaceuticals. These cabinets require users to enter a code before removing supplies and the product facilitates tracking of supplies and provides information used automated reordering of supplies.	OmniCell.com has a web-based procurement platform (called OmniBuyer) for **inventory management** and **management of information**. OmniBuyer offers a customized multisupplier catalogue that automates the approval and workflow process. This purchasing program links to all automated supply cabinets so that suppliers can automatically replenish depleted stocks. Users of OmniBuyer report savings in personnel costs, inventory costs, and greater compliance with negotiated purchasing contracts. However, the system is not widely used throughout the health care supply chain, and even in facilities where it is used, it is not universally used in all departments. Many users remove items without pressing the buttons required for the inventory management system to log the transaction.
Hahn, et al.[81]	**Hyundai** Motor Company is an international car manufacturer based in South Korea.	Supply chain **coordination** led to improved customer service (cars were delivered to dealerships more quickly). Improvement in customer service not quantified by the authors.
Thonemann, Brandeau[61]	An unnamed major **automobile manufacturer**.	The auto manufacturer incorporated **modularization** into the design of automobile components. The company found that designing products using common components, even if those components are more expensive than customized components, can save money. An appropriate balance must be struck between no commonality and full commonality.
Ernst & Kamrad[59]	**Magnero-Marelli** is an international automotive component manufacturer.	The company streamlined and reorganized its French manufacturing facilities, resulting in simplified material flow and minimized inventories. Specific savings from **inventory reduction** not reported by the authors.

[*]Volkswagen was able to reduce costs and improve customer service by *increasing* the number of its distribution centers, but several other companies found that *decreasing* the number of distribution centers achieved the same result. Each supply chain is unique, so the appropriate number of entities in each level of the supply chain (e.g., suppliers, manufacturers, warehouses, distribution centers) depends on the nature of the particular supply chain.

Reference	Company/supply chain under evaluation	Key lessons learned from the supply chain case study
Rao, et al.[82]	**Caterpillar, Inc.** manufactures construction and mining equipment, diesel and natural gas engines, and industrial gas turbines.	Managers at Caterpillar, Inc. developed a system to design a rapid-response supply chain and to determine the most cost-effective level of regionalization. This modeling system recommended modifications in supply chain **network design,** that resulted in cost savings for Caterpillar, Inc. Dollar amount of cost savings not reported by the authors.
Nahmias[56]	**Dell Computer** manufactures made-to-order personal computers (PCs).	Dell Computer was able to dominate the PC market through innovations in **inventory management** and supply chain **network design**. For example, Dell builds every computer to order, allowing the company to hold no finished products as stock, limiting inventory to component parts.
Hoyt, Lee[83]	**Lucent Technologies** provides networking systems and software to local and long distance telephone companies and cable companies.	Lucent examined its supply chain **network design**. Redesign of its network resulted in reduced costs and improved customer service. Cost savings and improvements in customer service not quantified by the authors.
Chen, et al.[84]	**Instill Corporation** provides electronic commerce and information services to the foodservice industry.	Instill Corp. created and marketed products to assist in the implementation of Efficient Foodservice Response (EFR), resulting in more efficient **information management** and product flows in the food service industry.
Ernst, Kamrad[59]	**Texas Instruments** manufactures electronic equipment.	Texas Instruments employs **postponement** to enhance its capacity to manufacture distinct products, giving Texas Instruments "a strategic edge". [59] Benefit to Texas Instruments not otherwise quantified by the authors.
Takeda, Matsuo[85]	**7-11**, **York Mart** and **Yokado** retail perishable goods such as fresh-baked bread, morning-harvested vegetables and sushi in Japan.	For timely and coordinated distribution of perishable products, Japanese companies rely on real-time **management o**f **information**, hourly logistics **coordination**, and **coordination** between members of the supply chain.
Nahmias[56]	**Wal-Mart** is an international discount retailer.	Wal-Mart was able to dominate the competitive discount market largely through its supply chain **network design** and through effective **management of information**. For example, Wal-Mart invested in information technologies that link cash registers in retail stores directly to company headquarters, keeping inventory records and demand forecasts as accurate as possible. Wal-Mart also invests heavily in distribution centers in order to keep stores supplied in a timely fashion.
Lockamy, et al.[86]	**3M** manufactures over 60,000 products marketed worldwide.	3M examined its supply chain **network design** and its processes for **management of information**. Redesign of 3M's distribution system and the introduction of electronic data interchange led to improved service and reduced costs.
Ghemawat, Nueno[87]	**Zara**, a Spanish clothing retail chain, produces and distributes fashion items.	Zara remained competitive with its supply chain **network design**, specifically its supplier and distribution network. The company maintains a single distribution center and no warehouses, allowing inventory levels to remain low and eliminating the "bullwhip" effect (wildly fluctuating order sizes placed to suppliers caused by inadequate logistics information and improper resupply procedures at intermediate-level distribution facilities). A carefully configured network of suppliers and internal manufacturers also contributes to the company's ability to respond quickly to demands from individual stores.

Existing Infrastructure for Local and Regional Responses to Bioterrorism

From each of the included articles we abstracted information about organizations that could contribute to a bioterrorism response. The evidence about the systems is drawn from focused searches about each included organization and from descriptions of each organization's participation in the responses to the 2001 anthrax attack, naturally occurring outbreaks, and natural disasters. In the following sections we present information from 20 articles,[*] 16 government reports,[†] and 12 Web sites[‡] on systems with existing infrastructures that would likely contribute to a bioterrorism response. We present the information that we abstracted from these articles about the tasks of local responders and the resources they required during responses to bioterrorism-relevant events in the "Summary Synthesis of Evidence about Regionalization for Bioterrorism Preparedness and Response" section of this chapter (answers to Key Questions 1 and 2).

A comprehensive review of all of the local, state, and federal agencies relevant to a bioterrorism response is outside the scope of this project. For discussion of each of the national response agencies, we direct interested readers to reviews of the Federal Response Plan.[106, 117, 137, 138] For a review of bioterrorism preparedness drills, we direct interested readers to the systematic review by the Johns Hopkins Evidence-based Practice Center (one of many projects to enhance bioterrorism preparedness sponsored by AHRQ).[139] AHRQ sponsors a portfolio of bioterrorism preparedness research including evaluations of bioterrorism response technologies, pharmaceutical and vaccine distribution plans, clinician training initiatives, and assessments of preparedness drills and exercises.[140] Because several key organizations with existing infrastructures would perform essential roles during a regional bioterrorism response, we sought to identify these systems and synthesize the evidence evaluating their responses to bioterrorism-relevant events. In this section, we briefly describe these organizations, their regional infrastructures, and how their regional infrastructures affect regional responses for bioterrorism. Throughout the rest of this Report we will discuss the role of these and other organizations in response to specific outbreaks and disasters. This section addresses Key Question 3.

Summary of the Evidence of Existing Infrastructure for Local and Regional Responses to Bioterrorism

Numerous existing systems could play a key role during a bioterrorism response. These systems can be broadly categorized in two ways: by the level at which they primarily operate (e.g., local as opposed to regional) and by the type of response tasks they perform (e.g., systems to protect the public health, to increase hospital capacity, to increase the number of trained and equipped response teams, and to provide inventories of pharmaceutical and medical supplies).

The term "regionalization" has been used describe two phenomena—to describe the process of breaking down a centralized system into component regions and to describe the inverse process of collecting local systems into an overarching region. For the purposes of this Report,

[*] References[89-108]
[†] References[109-124]
[‡] References[125-136]

we define a local response to bioterrorism as occurring under the jurisdiction of the local public health officer. However, we recognize that many relevant local responders and response organizations (such as clinicians, first responders, hospitals, and emergency management professionals) may not organize themselves in relationship to the local public health jurisdiction. Thus, if an included article defined a local response in another way, we supply the authors' definition in our description of the evidence.

Regional responses fall into three broad categories: sub-state, multi-state, and federal. Most states utilize sub-state regions (often drawn according to county lines) for disaster planning. For example, in California these regions are an integral organizational element of the state's mutual aid agreements. (Mutual aid agreements are described in further detail in the section on "Synthesis of Evidence About Regionalization of Emergency Trauma Care".) Multi-state regions are typically defined by one or more federal agencies. For example, there are ten Federal Emergency Management Agency (FEMA) regions, each made up of between four and eight states (described in greater detail below). These same regional designations are also used by other federal agencies, such as the Health Resources and Services Administration (HRSA)[*] and the Department of Health and Human Services (HHS). Other federal agencies divide multi-state regions differently: the Department of Veterans Affairs (VA) and the Indian Health Service distribute medical care according to unique geographical designations.

Infrastructure of U.S. Public Health System

The mission of the U.S. Public Health system is "to promote physical and mental health and prevent disease, injury, and disability."[125] During a bioterrorism event, public health officials have numerous responsibilities, including outbreak investigation; laboratory testing; provision of treatment and infection control guidelines to clinicians; development and implementation of plans for mass prophylaxis, treatment, isolation and quarantine; assessment of hospital/clinical resources; and communication with the public via the media. The organization and legal mandates of public health departments vary significantly across the United States. We briefly review the effects of these differences on chain of command, outbreak investigation, and the institution of epidemiologic control measures such as quarantine during a bioterrorism response. In subsequent sections, we review additional specific CDC programs such as the Laboratory Response Network, Strategic National Stockpile, and Epidemic Intelligence Service. We direct interested readers elsewhere for comprehensive reviews of the public health system.[142]

Regionalization of Public Health Departments. Generally, eastern states such as New York, Connecticut, and Massachusetts with their large urban areas, define the local public health official jurisdiction by municipal boundaries. In contrast, western states typically define the local public health jurisdiction at the county level.[143] Overall, 60% of the nation's local public

[*]HRSA administers more than $500 million in grants that are awarded to states for programs to enhance bioterrorism preparedness, principally invested in hospital preparedness and bioterrorism preparedness training and curriculum development.[141] The CDC also has grant programs in bioterrorism preparedness training and curriculum development. State officials responsible for bioterrorism preparedness planning often treat these grants and these granting regions separately, as they have historically been separate grants (this will change in 2004).

health departments are defined by county boundaries,* 25% are defined by municipal boundaries (e.g., New York City), 7% are defined by overlapping city-county boundaries (e.g., San Francisco city/county), and 8% serve several counties/districts (e.g., Texas).[143]

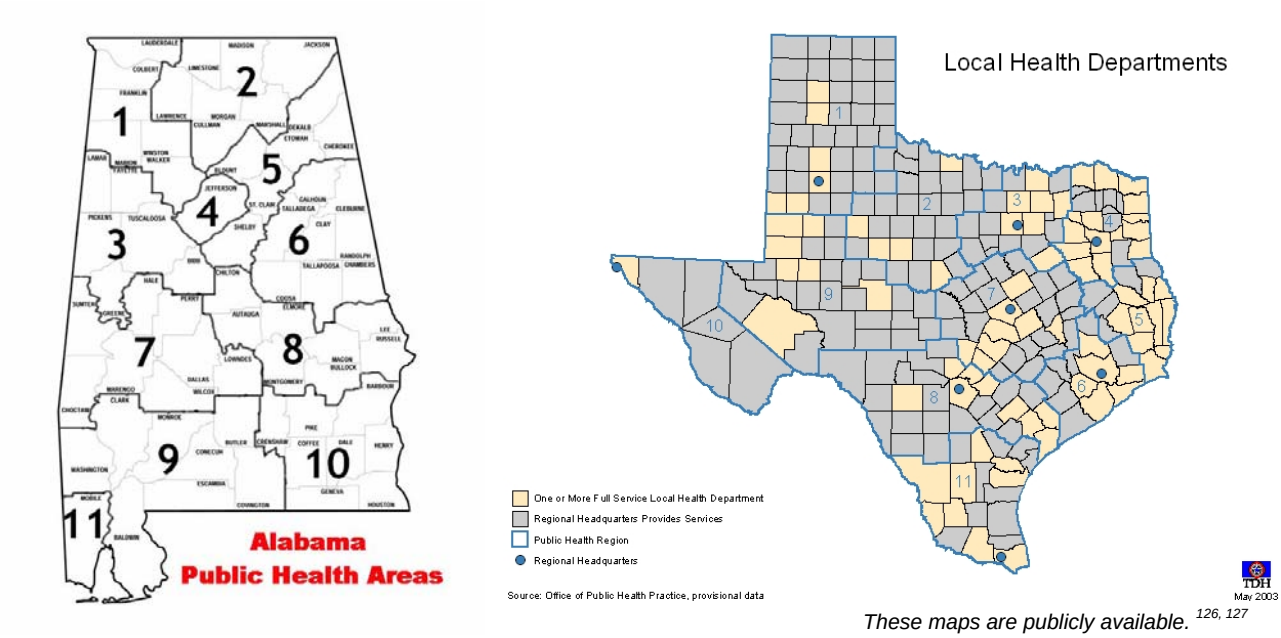
Local public health departments also differ according to whether public health services are provided within the context of a larger health department that provides other health services (e.g., direct patient services such as operating hospitals) and by the degree of autonomy given to the local departments. Centralized systems, such as those in Arkansas and Florida, retain a large degree of control at the state health department.[109] In contrast, decentralized systems such as those in Arizona and Colorado, direct authority to the city or county health department.[109] Some state health departments offer a "hybrid" approach—centrally coordinating some services while allowing local departments broad latitude in the provision of other services.[109] In several states, local health departments are grouped by the state departments of public health into regions (often with the borders of these regions drawn along county lines) with leadership provided by regional health directors and/or regional headquarters. Texas and Alabama are examples of this kind of regionalization (Figure 2).

These differences in organizational infrastructure are likely to affect bioterrorism preparedness and response planning in three ways. First, to the extent that neighboring states have public health departments with different organizational structures, and thus different chains of command, identification of key public health decisionmakers with whom to coordinate response planning may be complex. Second, numerous Federal Response planning efforts (such as the Strategic National Stockpile) are managed through state health departments that are given responsibility for planning the distribution and dispensing of the Stockpile (and, often, associated funds and other resources), which they then pass on to local health officials. The local implementation of these federal programs will differ depending on the organizational relationships between state and local health departments. Third, because a bioterrorism response requires cooperation among public health officials and other first responders, coordination of these services may be complex if one group of first responders (e.g., fire/police) is organized at the municipal level whereas public health personnel are organized at the county level.†

*For example, in California most local public health offices are associated with counties. The state has 58 counties, 55 county public health departments, three city-county health departments (San Francisco, Napa and Siskiyou), and four city health departments (Berkeley, Long Beach, Pasadena, and Vernon).[144]

†The fragmentation between state and local jurisdictions also has implications for the integration of preparedness activities. For example, in states where multiple local jurisdictions have independent authority the state agency may have difficulties in assuring the same level of preparedness and coordination in all local jurisdictions.

Figure 2. Regionalization of Public Health Departments in Texas and Alabama



These maps are publicly available. [126, 127]

Public Health Legislation Affecting Bioterrorism Planning and Responses. A comprehensive review of the heterogeneous municipal, state, and federal legislation that directly affects the decision making responsibilities of public health officials, clinicians, and emergency management officials during a bioterrorism event is outside the scope of this Report. Moreover, many relevant laws are currently under revision following the recent national attention to the tradeoffs between personal privacy, civil liberties, and national security. For reviews of the salient legal issues, we refer interested readers elsewhere.[89, 90]

In our brief review of the laws affecting key public health and clinical decisionmakers, we found two issues that may affect regionalization during a bioterrorism response. First, for some highly controversial policies such as quarantine, the legal authority to implement the policy may be inadequate for its practical implementation and enforcement.[*91, 92] For example, in many states the legal authority to institute a quarantine lies with the local health officer (and if local and/or state laws are inadequate for implementation of necessary quarantine or isolation, local

[*] In his article on the legal issues raised by the 1999 West Nile Virus outbreak, attorney Wilfredo Lopez of the New York City Department of Public Health wrote: "In modern society, public health initiatives, no matter how justified and necessary, are likely to be scrutinized and challenged, both in the media and in the courts. The proliferation of federal, state, and local agencies since the 1960s, and the laws and regulations that go along with them, means that there is much more jurisdictional overlap among governmental entities than ever before. Perhaps the most fundamental lesson of the W[est] N[ile] V[irus] experience is the reaffirmation of the fact that today's public health practitioner cannot implement public health policy and interventions without sound legal advice that is cognizant of not only the nuances of traditional public health law but also of the law that governs kindred agencies. In effect, public health law is broader and more complicated than in the past."[91]

public health officials may apply relevant federal laws).[93, 110] In the event that local control is deemed inadequate, CDC's domestic quarantine regulations provide that CDC may institute appropriate quarantine or isolation.[110] However, implementation of such authority during a bioterrorism event requires enforcement cooperation from police, elected officials, and other responders. In some jurisdictions, the relevant statutes do not obligate these responders to enforce quarantine decisions. Thus, the implementation of public health laws requires coordination with the laws governing related response organizations and personnel.

The second legal issue is that clinicians who are employed by a hospital are required to report to that hospital during a disaster or bioterrorism event. (However, even if clinicians do not report for work—as some have refused to do during responses to naturally occurring infectious disease outbreaks—it is not clear what repercussions they should expect.) For clinicians employed by more than one hospital, or who are members of more than one response unit (e.g., clinicians who are members of both their local Disaster Medical Assistance Team and the Army National Guard), it may be unclear where their primary obligation for service resides. This raises the related conflict of double counting—when, for purposes of preparedness planning, each of these organizations counts the same individual as part of its team during a bioterrorism response.

The National Disaster Medical System

Background. The National Disaster Medical System is a federally coordinated program whose primary purpose is to provide medical and mental health assistance in the event of mass casualties, when local capabilities are overwhelmed.[94, 95, 128] The National Disaster Medical System program falls under the auspices of the Department of Homeland Security and is co-managed by four federal agencies: HHS, VA, DoD, and FEMA. The three primary roles of the National Disaster Medical System are: to provide a rapid medical response through Disaster Management Assistance Teams, to evacuate patients through the military Aeromedical Evacuation System, and to provide hospital care to evacuated patients.[95, 96] We describe Disaster Medical Assistance Teams in more detail in the next section. The Aeromedical Evacuation System, operated by the DoD, has a "specialized airlift mission supporting patient movement on any mobility airlift platform" to safely transport patients to a hospital for definitive care.[111] Hospital participation in the National Disaster Medical System is voluntary; however, hospitals that participate during a mass casualty event are reimbursed by the federal government. The resources available to the National Disaster Medical System are coordinated by 64 centers around the country.[94] The National Disaster Medical System program also supports Disaster Mortuary Teams to assist with mortuary needs, Veterinary Medical Assistance Teams to administer care to animal victims of disasters, and National Medical Response Teams who receive special training and equipment to respond to weapons of mass destruction terrorist attacks—although this training has traditionally emphasized hazardous materials/chemical weapons preparedness.[*]

Regionalization of the National Disaster Medical System. The National Disaster Medical System is managed federally with coordination of available resources provided by 64 centers around the country. The ability of the National Disaster Medical System to respond to local

[*]References[94, 97, 98, 128, 145]

events is based in large part on two factors: a robust communication system, and voluntary participation of hospitals and individual members of the various response teams. The National Disaster Medical System relies on a communication system that tracks available resources, facilitates the timely deployment of National Disaster Medical System teams, and coordinates ongoing resource demands and availability. The National Disaster Medical System has typically responded to isolated mass casualty incidents (although in 1999 it did respond to four different disasters concurrently).[94] Thus, the ability of the National Disaster Medical System to coordinate a response to a bioterrorism event that spans several geographic regions remains largely untested.

Disaster Medical Assistance Teams

Background. Disaster Medical Assistance Teams are voluntary specialty teams designed to provide medical care to victims during a mass casualty incident when local medical resources have been overwhelmed.[*] Teams are organized and sponsored locally, and team members operate on a volunteer basis during training exercises and planning meetings. Local sponsors may provide considerable financial support to their Disaster Medical Assistance Teams, since the federal stipend for team organization is minimal.[99] Other team members provide their own funds for training and equipment (often these teams are incorporated as non-profit organizations to aid in fundraising).[99] Teams typically have about 35 members and include physicians, nurses, emergency medical personnel, and logisticians, among others.[100] Disaster Medical Assistance Teams are designated Level I, II or III depending on their capabilities and experience. To receive a Level I designation, a team must be self-sufficient for up to three days (provide food, water, energy, and other basic services to team members and patients in the event that local services are temporarily disabled by the disaster) and have between three and five people that can serve each Disaster Medical Assistance Team role (e.g., surgeon, logistician, etc.). Level II teams are not required to be self-sufficient, and are required to have two people for each team role. Level III teams are still in the developmental phase and may be deployed to assist a Level I or II team.[99] Teams may also have a specialty designation: currently, the program supports trauma, mental health, burn, pediatric, and weapons of mass destruction specialty teams. Disaster Medical Assistance Teams can be mobilized to provide support anywhere in the United States. When teams are mobilized, their members are paid as Federal employees, and their licenses and certifications are recognized by all the states during the activation period.

Regionalization of Disaster Medical Assistance Teams. Disaster Medical Assistance Teams are staffed, organized, and managed at a local level and deployed regionally. Disaster Medical Assistance Teams differ widely in terms of number of volunteers, types of expertise of the volunteers, level of experience of the volunteers under emergency circumstances, and equipment and supplies. Because members are volunteers, they can require as little as 24 to 72 hours to be ready for deployment, although times were much longer for some responses when the program was new.[95] This lag in time to deployment could significantly affect the utility of a Disaster Medical Assistance Teams during a bioterrorism response. (In some cases, Disaster Medical Assistance Teams have arrived at the scene of a disaster as many as five days after the

[*] References[94, 99-106, 129-132, 145]

disaster struck and for this reason have not been considered to be a completely reliable resource by some disaster planners.)[104]

The Metropolitan Medical Response System

Background. In the event of a large-scale bioterrorism event, it may take considerable time for regional responders to arrive. During this initial response period, local responders will be primarily responsible for the management of the response. Recognizing the need to enhance the capacity of local responders, the Metropolitan Medical Response System* was designed in 1996 as part of a coordinated national response to bioterrorism, providing preparedness plans and funds to purchase the equipment and supplies specifically required for bioterrorism preparedness and response.[133] Public Law 104-201 provided funding through HHS for 125 local emergency medical systems of the Metropolitan Medical Response System in selected cities in the United States (Figure 3).[96] The Metropolitan Medical Response System, now under the auspices of the Department of Homeland Security, provides funding to U.S. cities to create and enhance local capacity to respond to a covert release of chemical, biological, radiological, nuclear, and explosive weapons. In exchange for initial funds† to purchase medical equipment, pharmaceuticals, and supplies, the Metropolitan Medical Response System program requires detailed plans from participating cities regarding preparedness for chemical and biological attacks.[107, 108, 112] For a more detailed review of the Metropolitan Medical Response System, which is presently under expansion, and for an evaluation of the system, we direct interested readers elsewhere.[9, 133]

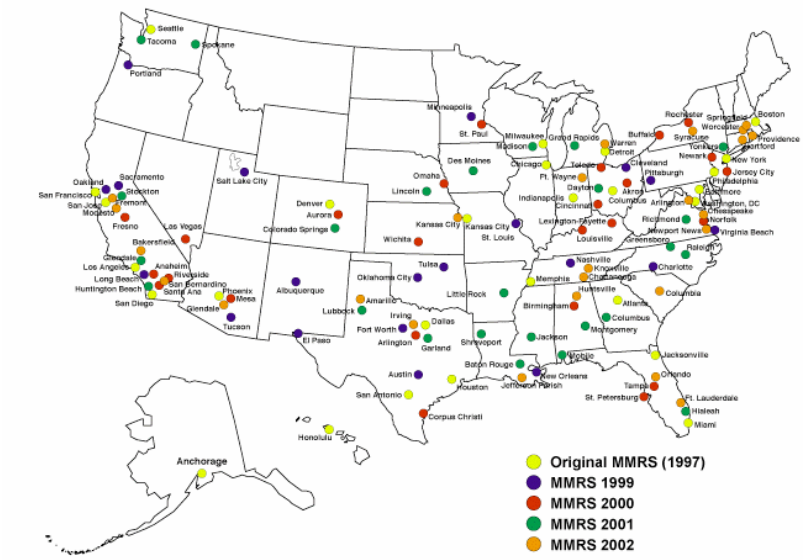
Regionalization of the Metropolitan Medical Response System. The Metropolitan Medical Response System is a local program designed to enhance the preparedness of municipalities; however, a large-scale bioterrorism event may necessitate regional coordination of efforts among municipalities. A lack of regional planning by Metropolitan Medical Response System members may complicate a bioterrorism response. For example, individual cities each write their own preparedness plans and there is no formal mechanism for exchange of information between Metropolitan Medical Response System cities during the preparation phase or during a response. Thus, cities may not have the capacity to readily determine the needs or the capacity of their neighbors. Also, most Metropolitan Medical Response System plans involve participation from numerous organizations, such as local public health departments, hospitals, and emergency personnel, which tend to have different organizational infrastructures across cities. A coordinated response among cities may be complicated by these organizational differences. Cities responding to bioterrorism also must work with the National Disaster Medical System to organize the evacuation of patients and the deployment of Disaster Medical Assistance Teams (and other response teams). Thus, an efficient bioterrorism response will require coordination of services between affected Metropolitan Medical Response System cities

*The Metropolitan Medical Response System evolved from the Metropolitan Medical Strike Teams that were originally trained to enhance local capacity to respond to mass casualty events (primarily hazardous materials/chemical weapons attacks) in large metropolitan areas in the United States.

†Subsequent funding was not provided until 2003, meaning that the original cities had to rely exclusively on local funding sources for three years.

and non-Metropolitan Medical Response System cities, other federal programs (such as National Disaster Medical System, Medical Reserve Corps, Public Health Service's Commissioned Corps Readiness Force, the National Guard's weapons of mass destruction Civil Support Teams), and other regional response providers.*

Figure 3. The Metropolitan Medical Response System



This map is publicly available.[133]

The Department of Homeland Security

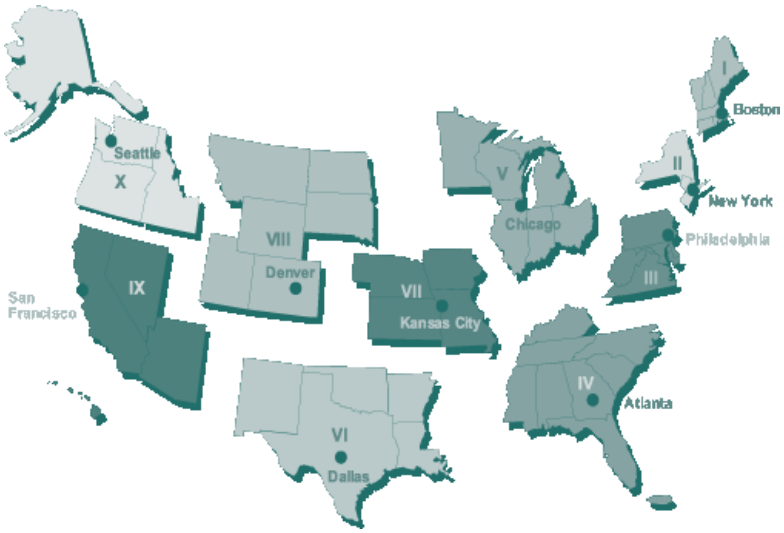
Background. The Department of Homeland Security was established by Congress under the Department of Homeland Security Act of 2002,[134] to integrate and coordinate the leadership, assets, personnel, and functions of the numerous federal agencies involved in all aspects of homeland security, including bioterrorism preparedness and response.[113-116] The establishment of Department of Homeland Security required an enormous reorganization of the federal government, including the transfer of several programs in their entirety (e.g., U.S. Coast Guard, FEMA, U.S. Secret Service, and Metropolitan Medical Response System) and the selective transfer of key defense programs from other departments (e.g., from HHS the Office of Emergency Preparedness and the Strategic National Stockpile).[134] Ongoing efforts by these agencies (such as the use of surveillance technologies to monitor cargoes coming into the United States for weapons of mass destruction) represent promising initiatives in preventions efforts against bioterrorism. The Department of Homeland Security is organized into four main directorates: Border and Transportation Security, Emergency Preparedness and Response, Science and Technology, and Information Analysis and Infrastructure Protection. The role of the

*Some cities in FEMA region IX, such as San Jose, California, serve as a model for coordination between the Metropolitan Medical Response System and other regional responders known as the Metropolitan Medical Task Force.

Emergency Preparedness and Response directorate is to "oversee domestic disaster preparedness training and coordinate government disaster response."[135] This directorate coordinates efforts of FEMA, the Strategic National Stockpile, National Disaster Medical System, the Nuclear Incident Response Team (DOE), and the Domestic Emergency Support Teams (DOJ).

FEMA, the agency responsible for coordinating federal responses to disasters, created the Federal Response Plan,* which identifies the essential emergency response functions of the 27 participating federal departments and agencies, and the American Red Cross.[117] The 12 essential emergency response functions include communications, medical services, and search and rescue.[117] FEMA does not have its own response materials or equipment but does have emergency response professionals who advise and coordinate the requesters and providers of disaster relief. FEMA has coordinated successful regional relief efforts to hurricanes, earthquakes, tornadoes and volcanic eruptions; specific responses are described in the section on "Synthesis of Evidence About Regionalization of Emergency Trauma Care". FEMA has four main responsibilities for disaster preparedness: preparedness, response, recovery, and mitigation.[117] Since the September 11th attack, FEMA has been designated as the lead agency for incident management.[118]

Figure 4. Regions as Definined by FEMA, HHS, HRSA, and Others



This map is publicly available. [119]

Regionalization of the Department of Homeland Security. At the time of writing this Report, the organization of Department of Homeland Security is underway. Once this reorganization is completed, it is expected that Department of Homeland Security will have a significant role to play in a regionalized response to bioterrorism. Currently, Department of

*The Federal Response Plan will soon be replaced by the National Response Plan which will utilize the National Incident Management System.

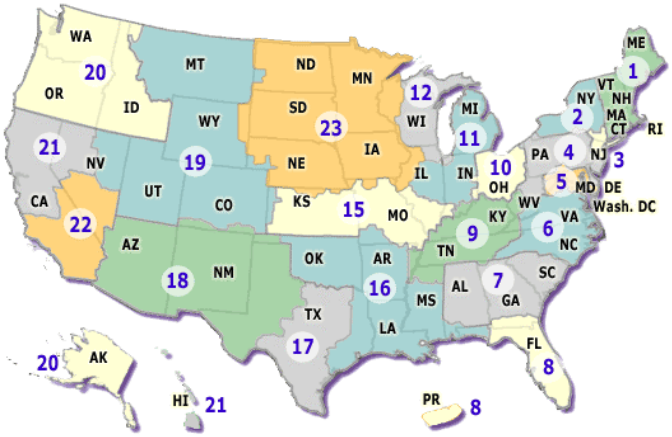
Homeland Security has adopted a regional structure previously used by FEMA, HHS, and HRSA (Figure 4 depicts the ten organizational regions). For bioterrorism preparedness, Department of Homeland Security responsibilities include working with local preparedness planners to develop strategies to receive and distribute the Strategic National Stockpile (this effort is primarily directed through state coordinators rather than the ten regions). Because the reorganization of programs into Department of Homeland Security is ongoing, there is no published evidence regarding the effects of the developing regional infrastructure on a regional bioterrorism response.

Department of Veterans Affairs

Background. The Department of Veterans Affairs (VA) has more than 1100 health care facilities across the country and maintains four mobile clinics that have been deployed in natural disasters. Under the Federal Response Plan, the VA is held responsible for "backup medical support for military personnel in wartime and the general public during natural, manmade, or technological emergencies."[117] In addition, the VA Emergency Management Strategic Healthcare Group plans and coordinates five other emergency management functions: 1) development of VA hospital emergency plans for disasters and coordinated mutual aid agreements for patient transfers, 2) backup of the military health care systems, principally through the 69 VA medical centers designated as primary receiving centers for DoD casualties, 3) joint administration duties of the National Disaster Medical System, 4) participation in the Federal Radiological Emergency Response Plan to respond to accidents at nuclear power plants and acts of terrorism, including training and support of the Medical Emergency Radiological Response Team (which consists of physicians and nuclear physicists), and 5) activities to support the continuity of federal government functions during a national emergency.[96] As Kenneth Kizer described in his report on the VA's role in federal emergency management, "A number of VA facilities are well equipped to handle decontamination and patient staging, and these capabilities could be expanded to additional VA medical centers. Enhancing and maintaining this capability at VA hospitals may well be easier, in many cases, than it would be in the private sector where managed care, market forces, and the effects of the Balanced Budget Agreement may make it impossible to sustain support for disaster contingency efforts over time."[96]

Regionalization of the VA Healthcare system. The VA is divided into 23 Veterans Integrated Service Networks across the county (Figure 5). Each Veterans Integrated Service Network includes certain states in its network and provides care to veterans in the regions it covers. Since each Network covers distinct geographic areas, the relationships of Veterans Integrated Service Networks with the local and state health departments in their areas may differ. The effectiveness of the VA in providing medical support during a bioterrorism event will likely depend on these types of relationships.

Figure 5. The 23 VA Veterans Integrated Service Networks



This map is publicly available [136]

Bioterrorism Preparedness Programs Sponsored by the Department of Defense

The DoD has sponsored several programs that translate its military expertise in preparedness and response to bioterrorism for civilian use. We direct interested readers to a recent evaluation by the U.S. General Office of Accounting of federally sponsored information technologies that could be used during a bioterrorism response (including several sponsored at least in part by the DoD).[120] This section briefly describes two military programs that would likely play a key role during a regionalized civilian response.

National Guard. During a bioterrorism event or other disaster, governors can mobilize the Army and Air National Guards of their state. Often these guardsmen and women provide security, medical treatment, debris clearing, transportation, shelter construction, and other services.[146-148] Under mutual aid agreements (described in greater detail in the "Synthesis of Evidence About Regionalization of Emergency Trauma Care" section), governors can also direct the use of their state National Guard units in a neighboring state. If the magnitude of the disaster has exceeded the capacity of local responders and state's National Guard, the governor can request federal assistance from the President of the United States.[146] Depending on the type of support required, FEMA, as coordinator of all federal assistance through the Federal Response Plan, may send active U.S. military forces to provide disaster relief.

Emergency response decisionmakers (such as the head of each state's National Guard and governor) differ with respect to the role that they envision for the National Guard during a bioterrorism response. For example, the DoD has developed National Guard Weapons of Mass Destruction Civil Support Teams* to "assist local and state authorities in assessing the situation surrounding a weapons of mass destruction emergency; advise these authorities regarding appropriate actions; and facilitate requests for assistance to expedite the arrival of additional state

*National Guard Weapons of Mass Destruction Civil Support teams were formerly known as Rapid Assessment and Initial Detection (RAID) teams.

and federal military assets."[121] The 1999 GAO Report on the use of National Guard response teams noted that whereas some states have integrated Weapons of Mass Destruction Civil Support Teams into their statewide preparedness plans, "the Federal Bureau of Investigation and the Federal Emergency Management Agency do not see a role for the [Weapons of Mass Destruction Civil Support Teams] in the federal response."[121] There have also been concerns that reductions in the size of the U.S. military and engagement of U.S. forces in operations abroad have restricted the availability of U.S. military personnel to respond to a domestic bioterrorism event or other disasters.[146]

Biological Weapons Improved Response Program. The Biological Weapons Improved Response Program was developed by the DoD to assist with mass casualty care at the local level.[122, 123] A key component of this program is the development of the Modular Emergency Medical System, which is intended to expand local hospital capacity, and integrate with other disaster medical resources.[124] The Modular Emergency Medical System has two components: Acute Care Centers that serve as mass inpatient care facilities for incident victims, and Neighborhood Emergency Help Centers that are designed for high-volume triage and dispensing of prophylaxis and information.[124] The Modular Emergency Medical System is designed to use the Incident Management System and communication links between local hospitals, Acute Care Centers, and Neighborhood Emergency Help Centers to coordinate patient care. For example, as an incident unfolds, the Modular Emergency Medical System might be used as follows: the initial victims are triaged in the usual manner to available hospitals until local hospitals have no additional capacity, at which point the city could mobilize the Modular Emergency Medical System and establish Neighborhood Emergency Help Centers and Acute Care Centers (at predetermined locations such as schools for the Neighborhood Emergency Help Centers and outpatient clinics for the Acute Care Centers), each of which is linked to a local hospital. The Acute Care Centers would accept non-critical patients from the local hospital. The Modular Emergency Medical System has been tested in full-scale operational evaluations but has not been deployed for an actual disaster response.[124]

Lessons Learned from the Literature on the Existing Infrastructure for Local and Regional Responses to Bioterrorism

We derived three key lessons from our synthesis of the literature on the existing infrastructure for local and regional responses to bioterrorism.

1. *Numerous response agencies with regional organizations could contribute to a bioterrorism response.* Many of the agencies described in this section have successfully contributed to regionalized responses to bioterrorism and bioterrorism-related emergencies (e.g., infectious disease outbreaks and disasters). The literature suggests that numerous response agencies with regional organizations could contribute to a bioterrorism response including public health departments at local, state, national, and international levels; the National Disaster Medical System (a federally coordinated program that provides medical and mental health assistance including the evaluation of patients and provision of hospital care when local capabilities are overwhelmed); Disaster Medical Assistance Teams (voluntary specialty medical teams that can be

deployed to provide a wide range of disaster medical services and resources); the Metropolitan Medical Response System (which expands municipal bioterrorism preparedness through grants that provide pharmaceuticals and other supplies and requires detailed preparedness planning by recipient cities); and the Department of Homeland Security (which has oversight responsibilities for many of the key bioterrorism response agencies and programs such as the Federal Emergency Management Agency and the Strategic National Stockpile).

2. *Most of these agencies were designed independently. Efforts to coordinate them are ongoing or under development.* Most of the agencies described in this section were developed to provide specific resources (e.g., trained personnel) or facilitate particular tasks during a response to different situations. The Department of Homeland Security has ongoing efforts to coordinate many of these response agencies.

3. *Given the demonstrated ability of personnel to participate in more than one of the key response agencies, decisionmakers must be aware of the potential for double-counting.* Double-counting can become an issue for responders who are members of more than one response organization (e.g., one person who is simultaneously a member of the Army National Guard, their local Disaster Medical Assistance Team, and a key part of the local response). A single database or coordinated information system to record all response personnel and resources could address this issue.

Synthesis of Evidence about Responses to the 2001 Anthrax Bioterrorism

On October 2, 2001, a 63-year old photo editor in Florida was hospitalized with high fever and altered mental status.[149] On the day of his admission, his physician performed a lumbar puncture, examined a gram stain of his cerebral spinal fluid, and suspected anthrax on the basis of the gram stain appearance.[149] He notified the Palm Beach County Health Department and the Florida Department of Health who initiated an epidemiological investigation.[149] Within seven hours, both CDC and Florida Department of Health confirmed *B. anthracis* via spinal fluid culture and immediately initiated concurrent epidemiological investigations in Florida and North Carolina (where the patient had traveled three days prior to onset of illness).[150] Between October 3 and November 16, 11 of 23 cases of bioterrorism-related anthrax reported in Florida, New York, New Jersey, Connecticut, and the District of Columbia were confirmed as inhalational anthrax.[151] Of these 11 cases, five individuals died, resulting in a case fatality rate of 45% (considerably lower than had been previously observed).[152-154] The source of this epidemic was eventually traced to the intentional delivery of anthrax spores via the U.S. postal service.[155] The response to these cases included the testing of more than 121,700 laboratory samples for anthrax,[156] the initiation of prophylactic antibiotics for 30,000 exposed patients,[157] and the decontamination of numerous buildings.[158]

The September 11th terrorist attacks and the subsequent cases of inhalation anthrax heightened awareness of the vulnerability of the United States to bioterrorism and the need for enhanced bioterrorism response capacities.[159, 160] The GAO in its 2003 report to Congress on

bioterrorism stated that "state and local response organizations need to have several basic capabilities, whether they possess them directly or have access to them through regional agreements."[*] [161] Despite this recommendation, many local preparedness plans are lacking. After the 2001 terrorist attacks, the U.S. General Accounting Office surveyed seven U.S. cities and found that none of the cities had sufficient training, equipment or communication systems for a response to bioterrorism.[161] The following section synthesizes the evidence about the 2001 anthrax bioterrorism event, the regional nature of the response to it, and the preparedness gaps highlighted by the attack.

Summary of the Evidence of Regionalization of the Response to the 2001 Anthrax Bioterrorism

Our search identified 373 citations regarding the 2001 anthrax attack and subsequent evaluation and response. Of these, we included 60 citations that described regionalized aspects to the response to bioterrorism: 30 articles, 14 government reports and 16 Web sites.[†] None of the included articles provided a comprehensive evaluation of the response to the 2001 anthrax bioterrorism. Rather, most focused on a particular aspect of the response, such as the laboratory response.

Application of Evaluation Criteria to the 2001 Anthrax Bioterrorism Literature

In this section we discuss our application of the four evaluation criteria relevant to the 2001 anthrax bioterrorism literature: network design, inventory management, management of information, and incident command. We found no articles that specifically described efforts to employ postponement or modularization, coordinate the bioterrorism response supply chain, or manage the incentives of the numerous relevant responding agencies. Nor did we find articles analyzing volume-outcomes associations.

Network design. A loosely connected network of organizations, each member of which is responsible for a portion of a bioterrorism response in the United States includes national, state and local agencies. Regional coordination and mutual aid agreements between these agencies are designed to facilitate the rapid and efficient deployment of equipment and expert personnel to a local area that may lack resources or be overwhelmed by surge-capacity requirements.[183]

***National Response Organizations*.** Although the GAO has identified over 20 federal departments and agencies that have responsibilities during a bioterrorism event,[168] only four agencies, the FBI, CDC, HHS' Office of Emergency Preparedness, and FEMA, have primary

[*]The term "response organizations" as defined by GAO-03-373 report to Congress are, "any organization or individual that would respond to a bioterrorist incident. These include physicians, hospitals, laboratories, public health departments, emergency medical services, emergency management agencies, fire department and law enforcement agencies."

[†]References[9, 13, 143, 149, 152, 153, 155, 156, 160-211]

responsibility to provide regionalized assistance to state and local agencies during a bioterrorism event.[169] The following paragraphs summarize the evidence about the role of three of these key federal agencies in a regionalized bioterrorist response and review their actions during the 2001 anthrax attack.

Centers for Disease Control. CDC has the responsibility "to provide national leadership in the public health and medical communities in a concerted effort to detect, diagnose, respond to, and prevent illnesses, including those that could occur as a result of bioterrorism."[170] Prior to the 2001 attacks, CDC defined several regional priorities in preparing for response to a bioterrorism event, including disease surveillance, public health networks, medical consequence management, and the Strategic National Stockpile (then the National Pharmaceutical Stockpile).[171] Thus, CDC developed the Laboratory Response Network, awarded grants to all 50 states and four major metropolitan health departments, and funded several communication programs such as Health Alert Network and the Epidemic Information Exchange System.[172]

The Laboratory Response Network was developed in 1998 as a tiered system of laboratories across the United States with a hierarchy of capacity to handle specimens during a bioterrorism response.[172] The Laboratory Response Network includes CDC's Rapid Response and Advanced Technology Laboratories, charged by Congress as having responsibility for rapidly identifying an infectious agent during a bioterrorism event. During the 2001 outbreak, the Laboratory Response Network's laboratories processed more than 121,000 samples for *B. anthracis* providing surge capacity for local laboratories.[156, 173]

Communication was a key role of CDC during the anthrax attack.[177] Unfortunately, no single integrated information system connects all health departments with one another, nor health departments with local hospitals and first responder communities.[174] However, the included articles described two systems that facilitated some information sharing among members of the public health community during the 2001 anthrax bioterrorism: the Health Alert Network and the Epidemic Information Exchange System. The Health Alert Network is an electronic communications system that enables sharing of information by public health professionals nationwide during an infectious disease outbreak.[172] During the 2001 bioterrorism events, the Health Alert Network allowed local public health agencies to request information from CDC, and provided general information such as how to handle suspicious letters and packages.[175] Because the Health Alert Network is limited to public health personnel, hospitals, infection control professionals, and first responders, physicians had no access to these essential reports.[162, 165*] The Epidemic Information Exchange System, is a Web-based communications network that provides a format for state, local and national health officials to share preliminary information regarding potential disease outbreaks.[172] During the 2001 attack, the Epidemic Information Exchange System provided 90 reports to public health decisionmakers including state epidemiologists, local CDC investigative teams, and other public health officials.[176] However, one survey of the health response to the 2001 attack noted that no public health official cited the Epidemic Information Exchange System as a source of information.[162] Thus, the likely utility of these systems to clinicians, public health officials, and the public during a large-scale bioterrorism response remains uncertain.

[*]During the anthrax attacks, the national news media often had relevant information before it was available through the Health Alert Network—limiting the utility of the Network to public health officials.

Office of Emergency Preparedness. At the time of the 2001 Anthrax attacks, the National Disaster Medical System was organized under the auspices of the Department of Health and Human Services' Office of Emergency Preparedness into 44 Disaster Medical Assistance Teams and four National Medical Response Teams. These included 7,000 volunteer health and support personnel to assist local response organizations.[172] On October 21, 2001, units from the U.S. Public Health Service, including a Disaster Medical Assistance Team, established a clinic in the Washington, DC area to educate and provide prophylactic antibiotics to persons exposed at the Brentwood U.S. Postal Facility.[181] Over a 14-day period, this clinic operated 14 hours per day, seven days per week with a total staff of 136 persons, and dispensed medications to over 18,000 persons. The productivity of this clinic (in terms of numbers of staff relative to numbers of patients served) has now become a reference standard for planning efforts for dispensing medications and providing immunizations during a future bioterrorism event.

Federal Emergency Management Agency. FEMA is the lead agency for consequence management following a bioterrorism event.[186] Due to the September 11, 2001 terrorist attacks, FEMA had fully activated the Federal Response Plan and all ten of FEMA's regions prior to the anthrax incidents.[187] Our review found no assessment of FEMA's actions during the 2001 anthrax attack. This is most likely because FEMA had a limited role in responding to the anthrax attack (they were involved in the World Trade Center disaster management at the time) and because no Emergency or Major Disaster Declarations were made by FEMA for the sites involved in the anthrax attacks.[188] Since the 2001 attacks, FEMA has been instrumental in providing assessments of state and local preparedness for future bioterrorism events.[167]

State and Local Response Organizations. In the years prior to the 2001 anthrax attacks, several initiatives appropriated resources for state and local preparedness programs. The National Defense Authorization Act of 1997 appropriated $97 million for "domestic emergency assistance programs, including the implementation of programs providing advice, training, and the loan of equipment to state and local emergency response agencies and assistance to major cities in establishing medical strike teams."[169] In 1999, CDC received Congressional funding "to enter into multi-year cooperative agreements aimed at upgrading state and local health department preparedness and response capabilities relative to bioterrorism."[190] However, despite this funding, at the time of the 2001 anthrax attack, many of the state and local programs were operated independently, without significant regional coordination.[166, 192]

The United States has more than 2900 local public health agencies.[*143] Prior to the 2001 anthrax attack, there were few efforts to regionalize local public health agencies through cooperative agreements within and among states.[161, 192] Since the 2001 anthrax incident, some regionalized systems have evolved. For example, in New Jersey, a cooperative agreement to share resources during a bioterrorism event has been organized into three regions, each representing approximately ten counties, linked together via the Local Information Network and Communication System.[193] However, to date there have been no evaluations to assess the readiness of such regionalized plans and no evidence to suggest that particular methods of

[*]The National Association of City and County Health Officials defines a local public health agency as, "an administrative or service unit of local or state government concerned with health, and carrying some responsibility for the health of a jurisdiction smaller than the state."

regionalization benefit the ability to respond to naturally occurring or bioterrorism-related illness.[174]

Coordination Among National, State and Local Response Organizations. During the initial stage of the 2001 anthrax attack, local agencies worked closely with CDC and other federal agencies to rapidly confirm the diagnosis of anthrax and to initiate an epidemiological investigation.[162] As the scope of the attack increased, so did the challenges to the available systems for coordinating local, regional, and federal response efforts.[162, 165, 194, 195] For example, during the 2001 anthrax attack, the three separate health departments in the Washington, DC region (Maryland, Virginia, and the District of Columbia) had no established mechanism for coordination of information regarding epidemiologic assessments or medical recommendations.[194] Since the 2001 attack, these three local health departments have agreed to "coordinate disease surveillance, alerts, evacuation, and other emergency preparedness efforts" for future bioterrorist incidents.[162]

Inventory Management. During the 1990s, Congress authorized establishment of the National Pharmaceutical Stockpile, which was renamed the Strategic National Stockpile after it came under the broader umbrella of the Department of Homeland Security. The Strategic National Stockpile provides a national repository of medical resources, including antibiotics that can be deployed at the local level during a bioterrorism event.[196] During the initial stages of an attack, 12-hour Push Packs from the Stockpile could be deployed. These consist of antibiotics, antidotes, and other medical supplies necessary to treat a wide range of possible biological or chemical agents over a short period of time.[197] If the attack requires "a larger or multi-phased response," the second component, the Vendor Managed Inventory, could be shipped within 36 hours.[198] The Vendor Managed Inventory is a "tailored" supply of pharmaceuticals and medical supplies intended to treat a specific biological agent in a larger population over a prolonged period of time. After the 2001 World Trade Center attack, CDC was able to deliver a Push Pack to New York City within seven hours after it was requested.[178] During the 2001 anthrax attacks, the pharmaceutical stockpile team made 143 sorties to nine states and delivered 3.75 million antibiotic tablets between October 8, 2001 and January 11, 2002.[156]

Since the anthrax attacks, some state and local agencies have obtained their own inventories of medical supplies. In 2002, the U.S. Medicine Institute for Health Studies forum on surge capacity during a bioterrorism event recommended that hospitals have 48 hours worth of antibiotics to treat or prophylax staff and other first responders, but did not recommend that individual communities stockpile pharmaceuticals.[199] However, the 2000 weapons of mass destruction tabletop exercise in Spokane, Washington suggested that local communities need to be self sufficient for at least 24 hours and, "if financially feasible, [to have] some local stockpiling of certain antidotes, like antimicrobials."[200] Currently, most local hospital and pharmacy inventories of antimicrobials are inadequate for a large-scale bioterrorism response. A survey in New Mexico found that, on average, local communities had four doses of ciprofloxacin on hand per 1000 persons.[201] A study in New Jersey noted that hospitals had an average of 289 doses of ciprofloxacin, which roughly equaled three doses per 1000 persons.[13] No published evidence specifically evaluates what should be included in a local inventory or the costs and benefits of procuring and maintaining such inventories.

Information Management. Regional management of information needs during the anthrax attacks of 2001 fell broadly into three categories: management of information relating to epidemiological investigations, communication among responders, and communication with the public.[208] Detection of the index case of inhalational anthrax occurred at the local level in a timely manner.[156] Six days later, when a coworker of the initial case became ill and was ultimately diagnosed with inhalation anthrax, the investigation then focused on the work environment of these two patients and administration of prophylaxis to potentially exposed coworkers. Subsequent to the Florida case, response times were markedly shorter: On October 15, 2001 a letter containing a powdery substance was opened in Senator Daschle's office with preliminary tests suggesting anthrax within 15 minutes.[209] Approximately 45 minutes after the letter was opened, the ventilation system was shut down, potentially exposed persons had nasal swabs performed, and an initial 3-day supply of antimicrobial prophylaxis was distributed.

The included articles did not describe information systems that facilitated communication among responders or with the public.[162, 210] Several untested but promising information systems have recently been deployed to facilitate local responder communication (e.g., San Diego County's Emergency Medical Alert Network, the Rochester Area Community Healthcare Information System, and the New Jersey Local Information Network and Communication System).[211]

Incident Command. Effective command and control is a required component of a successful response to a bioterrorism event. The included articles report that during the 2001 anthrax attack, incident command was complicated by three factors: 1) no single organization led the response across the nation, 2) no hierarchy of authority became clearly established or accepted among the numerous response organizations, and 3) there was no single system for effective information processing to facilitate incident command.[165, 177]

Lessons Learned from the Regional Response to the 2001 Anthrax Cases

Five key lessons regarding a regionalized bioterrorism response system can be learned from the evidence about the 2001 anthrax attacks.

1. *Cooperative agreements and regionalized response plans are needed.* Pre-event regionalized planning and asset sharing agreements among local public health agencies and hospitals may facilitate enhanced surge-capacity and coordinate responses during a bioterrorism event.

2. *Incident command must be well defined and familiar to responders*. The chain of command during a bioterrorism event may benefit from pre-event planning, practice, and widespread acceptance by relevant response agencies.

3. *Information systems for communication among responders and with the public must be implemented and tested prior to an event*. A bioterrorism response is likely to benefit from a coordinated effort to provide and share accurate information at all levels: local,

state, and federal. There is little evidence regarding current efforts to facilitate sharing of information across types of response professionals (i.e., among clinicians, public health officials, and criminal investigators) or with the public—critical gaps in the literature.

4. *The costs and benefits of acquiring, storing, and maintaining local inventories of medical supplies have not been established*. The federal government has spent millions of dollars to acquire and maintain the Strategic National Stockpile and to develop tested strategies for deploying the Stockpile to a local population within a few hours of an event. However, local and state organizations are creating their own inventories. No published evidence describes the costs and benefits of establishing these local inventories.

5. *The Laboratory Response Network significantly enhanced regional laboratory surge capacity*. Although most local and state public health laboratories were highly taxed, the Laboratory Response Network was able to offset many surge capacity requirements at the local level during the anthrax attacks. Whether the logistical framework exists to support transportation of samples from local clinical laboratories to regional Laboratory Response Network laboratories for processing during a bioterrorism event of larger magnitude remains untested.

Synthesis of Evidence about Regionalization of Responses to Naturally Occurring Outbreaks

> "Is the epidemic getting out of hand?" Rambert asked.
>
> Rieux said it wasn't that; indeed, the death-graph was rising less steeply. Only, they lacked adequate means of coping with the disease.
>
> "We're short of equipment. In all the armies of the world a shortage of equipment is usually compensated for by man-power. But we're short of man-power, too."
>
> "Haven't doctors and trained assistants been sent from other towns?"
>
> "Yes," Rieux said. "Ten doctors and a hundred helpers. That sounds a lot, no doubt. But it's barely enough to cope with the present state of affairs. And it will be quite inadequate if things get worse."
>
> —Albert Camus[212]

Naturally occurring outbreaks provide opportunities to design, deploy, and evaluate preparedness and response strategies for outbreaks resulting from bioterrorism. Often outbreaks cross geographic boundaries, requiring regional, even international, response coordination. Between July 1998 and August 2001, the World Health Organization (WHO) verified 578 outbreaks in 132 countries.[213] Of particular importance is the 2003 international outbreak of severe acute respiratory syndrome (SARS), which has been repeatedly cited as a model for a large-scale outbreak resulting from either pandemic influenza or a bioterrorism event.[214-216] SARS emerged in a manner that was suggestive to some experts of bioterrorism, and because the response to this international outbreak was unprecedented in scale and speed, the outbreak presents an opportunity to learn lessons for bioterrorism preparedness. This section synthesizes the evidence about the regionalized approach used to prepare for and respond to SARS and other naturally occurring infectious disease outbreaks.

Summary of the Evidence of Regionalization of Responses to Naturally Occurring Outbreaks

We reviewed 296 articles about the response to ten naturally occurring outbreaks involving SARS, Hantavirus Pulmonary Syndrome, pandemic influenza, meningococcal meningitis, smallpox (two outbreaks and the 2003 pre-event vaccination campaign), cryptosporidiosis, West Nile virus, and monkey pox. Of these, we included 181 articles, 10 government reports, and 33 Web sites that described one or more outbreaks and the regional responses to them.[*] We found no specific evaluations of regionalization of responses to outbreaks. Table 10 presents the lessons learned from articles describing regionalized responses to the nine outbreaks. From each of the included articles, we abstracted information about the tasks that responders performed during outbreak responses, and the resources required to perform these tasks. We present those data in our answer to Key Questions 1 and 2 in the "Summary Synthesis of Evidence About Regionalization for Bioterrorism Preparedness and Response" section and Table 14.

Application of Evaluation Criteria to the Responses to Naturally Occurring Outbreak Literature

In this section we discuss our application of the six relevant evaluation criteria to literature describing responses to naturally occurring outbreaks: network design, inventory management, postponement and modularization, coordination of outbreak response and management of incentives, management of information, and incident command. We found no article that specifically described volume-outcome associations. The following sections describe our application of the evaluation criteria to the literature describing regionalized outbreak responses.

Network Design. The effectiveness and timeliness of an outbreak response system is influenced by how key components of the system respond to the outbreak. Key components in the system (i.e., network) include field personnel, public health agencies, healthcare providers, laboratory professionals, and other governmental agencies. The included articles describe five key elements of regionalized outbreak responses performed by these response groups including: mobilization of trained personnel, the epidemiological response (including outbreak investigation and implementation of policies to reduce the spread of disease), the hospital responses, laboratory responses, and coordination of the response. This section synthesizes the available literature on how these five outbreak response tasks have been regionalized during responses to SARS and other outbreaks.

Mobilization of Trained Personnel. Response to an outbreak often requires pooled regional resources (throughout this section we regional responders include those at the state and federal levels). When local communities possess insufficient trained personnel to respond to a disease outbreak, trained personnel such as clinicians and epidemiologists can be mobilized from other

[*] References[2, 77, 91, 213-433]

communities or from national or international resources. In the United States, infrastructure exists to provide local communities with regional and national resources when necessary. For example, many leading outbreak investigation professionals have been trained through two-year assignments with the Epidemic Intelligence Service, which was established in 1951 by CDC as an early warning system against biological warfare and man-made epidemics. Each year, the 60 to 80 Epidemic Intelligence Service officers have played a key role in numerous outbreak investigations, eradication programs, and development and deployment of surveillance efforts.*

Trained personnel mobilized during outbreaks may be supplied by national or regional organizations that recruit both paid and volunteer professionals. For example, during the 1918 swine/Spanish flu pandemic, nurses were in drastically short supply because more than one third of U.S. nurses were supporting the war effort overseas. The American Red Cross responded to this shortage by developing a network of professional and volunteer nurses (including retired nurses, student nurses, and eventually, women with even minimal nursing experience). Although these nurses were recruited from a national pool, they were often deployed to specific regions by the U.S. Public Health Service or state public health officials.[218]

Deployment of regional resources can also occur on an international scale. During the SARS outbreak, the WHO, CDC, Institut Pasteur, Medecins Sans Frontieres, and National Health Service, among others, sent supplies and teams of experts to China, Vietnam, Singapore and Hong Kong.[216, 219] Once in the field, WHO and related international teams performed a variety of tasks, including the review of medical records. These teams played a critical role in determining that the cases of atypical pneumonia in Guangdong Province, China, were "clinically and epidemiologically" related to later outbreaks in Vietnam and Hong Kong.[220] During a bioterrorist attack, the ability to deploy highly trained personnel to the affected area may contribute significantly to the local response capacity.

Epidemiological Response. Epidemiological response to an outbreak by local, state, and regional public health agencies includes surveillance, case investigation, contact tracing and follow-up, issuing guidance to healthcare facilities, implementation of infection control measures a well as instituting public health policy such as issuance of travel advisories, isolation and quarantine. Epidemiological policy and legislation are often framed at the state, national, or international levels; however, epidemiological action often occurs at the local level and is performed by local and/or state responders. Thus, coordination of efforts among federal, state, and local officials is key to effective epidemiological responses. Conversely, differences in epidemiological approaches (and political will) between federal and state policymakers and local public health officials can complicate epidemiologic responses to outbreaks. For example, China's local responses to SARS may have been slowed by delays resulting from Beijing-based officials who discouraged clinicians and hospital administrators from fully disclosing the extent of the outbreak.[221, 223, 434] Specifically, early in the outbreak, most hospitals were not reporting cases on a daily basis, and even as late as April 2003, two months after the outbreak was reported to have begun, contact tracing was not performed reliably.[224] As the outbreak continued, China demonstrated dramatic improvement in its responses.[225] For example, in Hong Kong, officials instituted a policy of heightened travel surveillance for one year, to immediately detect any resurgence in SARS cases.[226] Hong Kong border screeners used infrared temperature scanners

*For example, EIS officers were deployed to New York City in 1999 following the detection of West Nile Virus (WNV) in a cluster of patients suffering from encephalitis, and contributed significantly to the outbreak investigation.[217]

and required health declarations from all travelers.[226] Similarly, local Hong Kong health officials quarantined all known contacts of SARS patients at home. These local responders, working in collaboration with their colleagues in the Department of Immigration, prevented quarantined patients from leaving the country and spreading the disease. China's improved epidemiological response was largely credited to changes in the attitude of high-ranking officials, and in two prominent situations, to the change of the officials themselves.[434]

Hospital Responses. Hospital responses to infectious disease outbreaks include provisions for definitive medical care, infection control, emergency management, and communication. Hospital responses may be organized locally at a single hospital facility or regionally within the context of a hospital network. During the SARS outbreak, several infection control practices were effectively instituted on a multi-hospital basis. For example, a team from the Taiwanese Center for Disease Control visited each of the 15 hospitals in Taiwan treating suspected or confirmed SARS cases.[227] This team audited charts and implemented strict infection control measures, including education of health care workers and distribution of personal protective gear. Additionally, the infection control nurses at these 15 hospitals undertook surveillance of staff absenteeism.[227]

There are ongoing efforts in U.S. hospitals to pool their resources to prepare more efficiently for a bioterrorism event.[*] For example, the MediSys hospital network includes three large hospitals in New York City (in Flushing, Jamaica, and Brookdale).[228] These hospitals share a network-wide Nuclear, Biological, and Chemical Incident Task Force charged with providing assessments of and recommendations for pharmaceutical preparedness at both the individual hospital and network levels. This Task Force recommends that each hospital pharmacy retain a specified inventory, with a mutual aid understanding that needed supplies can be borrowed within the network, as available. Each pharmacy stocks supplies to treat staff and patients for three days, should drugs from the Strategic National Stockpile be delayed.[228]

Laboratory Responses. Laboratory responses to outbreaks have been regionalized for two primary purposes: to provide surge capacity for diagnostic testing of specimens during a large outbreak that overwhelms local laboratories, and to serve as the reference laboratory capable of testing for rare pathogens. The Laboratory Response Network, which serves both of these functions, was described in the sub-section "Application of Evaluation Criteria to the 2001 Anthrax Bioterrorism Literature". During the 1999 West Nile virus outbreak in New York City, the primary laboratory with capacity for diagnosing West Nile virus was CDC's Division of Vector-Borne Infectious Diseases, in Fort Collins, Colorado. While the outbreak was developing in the New York City area, laboratory samples had to be mailed to Colorado using commercial mail carriers and express mail service for testing. Significant delays in diagnoses resulted from laboratory services not being available on the weekend[228] and the lack of surge capacity to handle the large number of specimens requiring analysis (more than 2000 in three months).[217] As a result of this outbreak, the capacity to perform diagnostic analysis for West Nile virus has been expanded to other laboratories around the country—a critical step given the concerns about this agent becoming endemic in more geographic regions of the United States.[228]

[*] Several of regional initiatives have been sponsored by HRSA, whose hospital bioterrorism preparedness cooperative agreement places emphasis on regionalization.

Coordination of the Outbreak Response. The included articles describe several regional and international networks developed for coordination of disease surveillance, laboratory support, and outbreak response efforts.[*] For example, a number of affected Asian nations came together during the SARS outbreak to sign an agreement that they would screen all incoming and outgoing international travelers, create an international emergency SARS hotline, freely exchange epidemiological information, cooperate on research and training, plan and attend meetings to devise other countermeasures to combat the outbreak, and commit to complete transparency where the outbreak was concerned.[230]

One of the most recognized efforts was the WHO-sponsored network of research laboratories established during the SARS outbreak.[231] Eleven laboratories in ten countries were invited to participate in the effort to identify the causative agent and to develop a diagnostic test for SARS. All accepted the offer, choosing to cooperate rather than compete.[232, 233] Networked participants communicated via daily teleconferences and used a secure WHO Web site to post results and questions and to access research tools, such as polymerase chain reaction primers. Samples were shipped around the world within hours of a request.[233] Such cooperation contributed greatly to the timely worldwide response to SARS. The laboratories announced the conclusive identification of the novel coronavirus responsible for SARS just one month after the creation of the network.[231] This rapid success can be attributed in large part to the design of the international network that enabled research to progress 24 hours per day with laboratories in every time zone. Also, laboratories had access not only to local strains of SARS, but also to samples from around the world.

During the SARS outbreak, WHO also erected parallel networks of epidemiologists and clinicians.[234] The epidemiologists worked in all local areas with documented transmission of SARS and collaborated to resolve several key issues of epidemiological concern, including the transmissibility of SARS among asymptomatic individuals and during the incubation and acute illness phases of the disease.[234] The clinicians' network included 80 clinicians from all 13 countries with SARS cases. This network compared the efficacy of different treatment regimes and reported on the results of clinical trials with ribavarin.[234] This type of collaboration would be particularly relevant for a bioterrorism event occurring with a novel infectious agent, or a previously recognized biothreat agent with antibiotic/antiviral resistance.

Inventory Management. Inventory management for outbreaks requires the acquisition of material resources such as antibiotics and vaccines, as well as their distribution to responders or members of the public. These tasks can be logistically challenging when resources are in short supply or when large numbers of people must receive prophylaxis or treatment. For example, during the 1947 smallpox outbreak in New York City, city leaders decided to vaccinate all six million residents but initially had only 250,000 individual doses of smallpox vaccine on hand. City workers quickly repackaged 400,000 bulk doses, and additional doses were made available from military stockpiles. However, these were still insufficient to meet the demand. The mayor responded to the shortage by calling an emergency meeting between vaccine manufacturers and the New York City health department. In response, manufacturers agreed to undertake a 24-hour

[*]Occasionally, networks designed for other purposes support outbreak responses. For example, prior to the 1993 outbreak of Hantavirus Pulmonary Syndrome in the Four Corners region of the southwestern United States, the primary care physicians of the regionally integrated Indian Health Service (who were geographically dispersed) frequently consulted among themselves about challenging or unusual cases. The regional organization of the Indian Health Service facilitated this collaboration, which led to the more timely recognition of the disease outbreak.[229]

per day schedule for packaging existing bulk vaccine and to divert all available vaccine to New York City.[235]

Postponement and Modularization. The concepts of postponement and modularization apply to two key aspects of regionalized planning for outbreaks. First, the distribution of pre-packaged antibiotics in unit doses rather than bulk packaging, which facilitates their dispensing to a wider variety of target populations, is an important example of modularization. If antibiotics are packaged in short course dose packs (e.g., seven-day supplies), public health officials uncertain about whether their current inventory of antibiotics will meet the demands of patients seeking prophylaxis, may choose to dispense an abbreviated course of antibiotics rather than a full course, allowing additional time for regional inventories to arrive. Second, public health recommendations and protocols for outbreak management can be generated at the state or national level and communicated to local users who may further customize these protocols for their use. This approach reduces the need for local officials to prepare their own materials and increases the likelihood that protocols within a region are concordant. CDC is working with professional organizations to educate responders about smallpox: CDC provides educational materials to organizations such as the Infectious Disease Society, the Dermatology Society, the Emergency Medicine Society, the Nursing Association, and the American Medical Association. These organizations repackage the information and distribute it to their members. [237] Although there have not been evaluations of the costs and benefits of postponement or modularization techniques for bioterrorism preparedness, the available evidence suggests that the use of these methods may facilitate the timely communication of essential outbreak response information to relevant organizations for further local customization.

Outbreak Response Coordination and Management of Incentives. For an infectious disease outbreak to be contained as quickly and efficiently as possible, it is necessary that responders at local and regional levels, including clinicians, government agencies, and members of the public, have incentives to work together to contain the outbreak.

For communicable diseases, the incentives of clinicians must be considered if a stable, well-trained work force is to be maintained. One devastating feature of the SARS outbreak was its effect on health care workers: as of April 14, 2003, 46% of SARS cases in Hong Kong and 63% of cases in Hanoi were among health care workers.[227] Because SARS infected such a high number of health care workers, many quit or did not come to work, resulting in reduced capacity just as health care systems were struggling to serve infected populations.[2, 238, 239] In Toronto, officials reported difficulty finding physicians to staff the SARS clinics. To combat the problem, the Toronto health ministry issued a call for volunteer infectious disease specialists from the United States to serve temporarily in Toronto. The Infectious Diseases Society of America e-mailed its members advertising the need for U.S. physicians to work in Canada. Although compensation was $2000/day plus expenses, and Canada provided malpractice and temporary licenses and work permits, many American clinicians "were afraid to go."[239] Thus, without carefully addressing the incentives for responders, regionalized systems for enhancing local responder capacity, particularly during communicable infectious disease outbreaks, may be compromised.

Management of Information. During a regionalized outbreak response, three flows of information are critical: flows between responders and the public, horizontal flows among responders (between regional responders which include information systems for logistics management), and vertical flows among responders (from local responders to national responders or vice versa).

To prevent the spread of disease, outbreak-related information from responders to the public must be accurate, timely, and complete. The included articles describe several simple yet effective strategies to communicate to the public during the SARS outbreak. WHO used international press briefings and global videoconferences for healthcare workers. CDC sponsored regular conference calls with medical professional associations and state and local health departments and laboratories.[2] During a two-week period early in the outbreak, CDC hosted nine telephone press conferences to keep the media informed and to ensure that the information presented on television and in print was accurate and complete. Travel health alerts were made available in eight languages for more than 60,000 travelers returning from East Asian countries.[2, 240]

Horizontal information flow among responders is also important. The day the WHO issued a global health alert for countries with documented local transmission of SARS, the director of the Los Angeles county health department issued a notice to all 81 hospitals in the county, informing them of the symptoms and requesting to be notified immediately of suspected cases. Similarly, during the 1999 outbreak of West Nile virus in New York City, the local health department used media releases, a public hotline, and printed materials in eight languages to teach an anxious public how to protect against the virus with considerable success: In two months of operation, the hotline received more than 150,000 calls.[217] Whether these methods of communication will adequately serve the needs of responders or the public during a large-scale bioterrorism response has not been evaluated.

Finally, outbreak responses require vertical information flow among regional and local responders. Technology can play an important role in this vertical information flow. [3] For example, Web-based communication technologies served a key role during the SARS outbreak. Internet technology was used by the international network of laboratories to facilitate the isolation of the causative agent for SARS. Also, California's Health Alert Network was used to send SARS-related e-mails to local health departments and to many hospitals.[2*] Electronic versions of SARS case reports and related information were available to worldwide subscribers to the New England Journal of Medicine one month before they were available in print.[241]

Other outbreaks have demonstrated the limitations of available communication systems. The 1999 outbreak of West Nile virus in New York City was multijurisdictional: patients lived and were treated in several cities and states. No agreements were in place regarding information sharing for outbreak tracking and surveillance before the outbreak occurred. Interim arrangements were unable to produce effective data management strategies.[217] Additionally, the health departments needed better integration with animal health agencies. In a GAO evaluation of the response to the 1999 West Nile virus outbreak, it was noted that, "the length of time it took to connect the bird and human outbreaks of West Nile virus signals a need for better coordination among public and animal health agencies."[242] This outbreak stimulated ongoing efforts to coordinate collection and reporting of surveillance data for zoonotic and other naturally occurring and bioterrorism-related outbreaks.[69, 435]

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[*] As with the Health Alert Network during the anthrax cases, some of the information provided about the SARS outbreak was insufficiently rapid and could already be obtained through the international news media and other public sources.

Incident Command. The included articles suggest that clear chain of command facilitates effective, expeditious containment of infectious disease outbreaks and communication of the ongoing epidemiological efforts to the public. The included articles described the emergency operations centers that were established worldwide during the SARS response to bring together local EMS, police, and community planners; however, most of these centers were not coordinated regionally or nationally.[2] CDC activated its Emergency Operations Center for which 800 "medical experts and support personnel" were available around the clock to coordinate a U.S. SARS response.[2] The Emergency Operations Center has only been activated twice before: for the 1999 West Nile virus outbreak and for the 2001 anthrax attack.[243] The WHO's contribution to the SARS response was facilitated by its event management information system which "generates a dynamic picture of operations, aids organization of logistics, and provides a systematic way to…manage resources."[244]

Lessons Learned from the Responses to Naturally Occurring Outbreaks

From our review of the outbreak response literature, we drew three main lessons regarding a regional response to outbreaks resulting from bioterrorism.

1. *Communication and cooperation between health authorities of neighboring regions are needed.* Infectious diseases can spread quickly and communication and cooperation among neighboring communities can facilitate a response. Rapid communication can be difficult to achieve through interim agreements. Thus, cooperation during a bioterrorism response may benefit from pre-event development and routine use of shared communication systems.

2. *International surveillance and reporting may be required to combat infectious disease outbreak.* The SARS response benefited from international efforts of disease surveillance and reporting of suspicious cases to the WHO. In the event of a bioterrorism attack, international cooperation to detect, report, and respond may reduce associated morbidity or mortality.

3. *During a response to an outbreak resulting from an emerging or communicable biothreat agent, it is essential to carefully consider and address responder incentives.* During bioterrorism event, strategies to protect responders and their families is an essential component of maintaining a robust work force.

Table 10. Regionalization of Outbreak Response

Disease	Time and place	Scope of outbreak	Lessons learned
Smallpox[235, 363]	New York City, 1947	12 cases and 2 deaths (case fatality rate of 17%); 6 million residents of New York City vaccinated in less than a month (5 million were vaccinated in two weeks).	• Benefit of consistent, accurate and calming communication from top officials (Mayor of NYC) • Successful distribution and administration of millions of doses of vaccine using volunteer clinicians at police precincts
Smallpox[364, 365]	Boston, 1901-3	1596 cases and 270 deaths (case fatality rate 17%).	• Benefit of teams of clinicians going out into the community to vaccinate at-risk people who might not otherwise seek vaccination (e.g., homeless men) • Problem of incentivizing public to be vaccinated against smallpox given difficulty estimating the probability of smallpox bioterrorism • Benefit of disease-designated hospitals for infection control
Smallpox pre-event vaccination campaign[237, 408-433]	Acute care hospitals and public health departments across the United States, 2003	Phase 1 of the vaccination campaign intended to vaccinate 500,000 civilian responders; fewer than 30,000 actually vaccinated as of March 16, 2003.	• Problem of incentivizing responders to be vaccinated against smallpox without compensation in place for adverse events • Problem of identifying of personnel to serve on teams of local responders
Severe Acute Respiratory Syndrome (SARS)[2, 214-216, 219-221, 223-227, 230-234, 238-241, 243-306, 434, 436]	International outbreak with the majority of victims in China, Hong Kong, Singapore and Canada, 2003.	As of 11 July 2003, 8427 patients infected with SARS in 29 countries; 813 died.	• Importance of timely, accurate disease reporting internationally • Benefit of internationally networked laboratory response • Benefit of disease-designated hospitals for infection control and volume outcome associations
West Nile Virus[77, 91, 217, 228, 236, 242, 311, 366-386]	New York City, 1999	59 cases hospitalized and seven died. No more cases reported after initiation of vector mosquito measures.	• Better interjurisdictional agreements for information sharing should be in place before an outbreak • Public must be educated and incentivized to perform key public health functions, such as reporting dead birds • Information sharing between agencies (e.g., between public health and animal health agencies) should be in place before an outbreak to perform more complete surveillance for zoonotic illness • More than one laboratory in the United States should possess the capability to perform diagnostic tests for a pathogen
Pandemic Influenza[213, 218, 305, 338, 387-407]	Worldwide, 1918-1919	International outbreak of swine flu, possibly of Spanish origin. 500,000 people dead in the United States; estimated worldwide deaths 20-40 million.	• Problem of educating and incentivizing public to follow infection control recommendations • Critical shortage of caskets and mortuaries • Networks of nurses and physicians formed by the ARC and the U.S. Public Health Service from a pool of personnel not able to serve as part of the overseas war effort

Disease	Time and place	Scope of outbreak	Lessons learned
Hantavirus Pulmonary Syndrome[320, 323-339, 341-347, 437]	Four Corners region of the U.S. southwest, 1993	By October 1993, 42 cases and 25 dead.	• Benefit of unofficial networks of clinicians who communicate and consult with each other for the detection of geographically dispersed outbreaks (Indian Health Service) • Effective use of aeromedical resources to link community and regional hospitals
Meningococcal meningitis[348-362]	Mankato, Minnesota, 1995	Seven cases and one death; 30,000 people vaccinated.	• Need for standardized forms for obtaining informed consent to give prophylactic antibiotics (in multiple languages)
Cryptosporidiosis[307-319]	Milwaukee, Wisconsin, 1993	403,000 people made sick; the illness contributed to at least 100 premature deaths in immuno-compromised people.	• Benefit of prospective surveillance of water supply

Synthesis of Evidence about Regionalization of Responses for Disasters

> It is necessary that all of the resources and facilities of the State, its various departments and agencies, and all its political subdivisions, municipal corporations, and other public agencies be made available to prevent and combat the effects of disasters which may result from such calamities as flood, fire, earthquake, pestilence, war, sabotage, and riot; and it is desirable that each of the[se] parties… should voluntarily aid and assist each other in the event that a disaster should occur, by the interchange of services and facilities, including but not limited to, fire, police, medical and health, communication, and transportation services and facilities, to cope with the problems of rescue, relief, evacuation, rehabilitation, and reconstruction which would arise in the event of a disaster.
>
> —Earl Warren, Governor of California, November 15, 1950[438]

The International Federation of Red Cross and Red Crescent Societies defines a disaster as an event that causes more than ten deaths, affects more than 100 people, or leads to an appeal by those affected for assistance.[439] Excluding droughts and war, approximately 500 such disasters occur annually worldwide, killing 50,000, injuring an additional 74,000, and displacing 5 million. More than 80 million people are affected by disasters in some way each year.[439]

Much of the U.S. response infrastructure designed for disasters would be activated during a bioterrorism response. Additionally, many of the primary response tasks necessitated by disasters are identical to the tasks required for a bioterrorism response. These include declarations of emergency; evacuation; quarantine; crowd and traffic control; emergency provision of mental health services for responders, victims, caregivers and their families; and volunteer utilization and control. Because earthquakes, hurricanes, floods, and volcanic eruptions tend to recur in specific geographic areas, elements of the U.S. planning and response infrastructure for disasters have been regionalized. As a result, in 1997, when FEMA was required by Congressional mandate to assess states' level of disaster readiness, the Agency concluded that states generally do have the ability to respond to disasters without significant federal assistance.[440] The following sections describe the regionalization of disaster management preparedness and response programs, present the results of evaluations of these regionalization

efforts, and summarize the evidence for and against regionalization of disaster services, as it relates to bioterrorism preparedness and response.

Summary of the Evidence of Regionalization of Disaster Responses

We found 155 articles that described responses to natural disasters, including hurricanes (i.e., Andrew, Iniki, and Hugo), earthquakes (e.g., Loma Prieta and Northridge), tornadoes, and floods, and to manmade disasters (e.g., the Tokyo sarin attack, the Keystone chairlift collapse, the destruction of the Alfred P. Murrah Federal Building in Oklahoma City, airline crashes, and the terrorist attacks of September 11, 2001). Of these, we included 37 articles[*] and 17 government reports and 12 Web sites.[†] None of the included articles specifically evaluated the effects of regionalization on disaster management services. Table 11 presents the evidence of lessons learned from articles on natural and manmade disasters that can be applied to bioterrorism preparedness. For reviews of disaster epidemiology and response, we refer interested readers elsewhere.[42, 441, 442]

Most included articles describe response organizations or responses to particular disasters. Although our review found no specific evaluation studies, it highlighted issues regarding regionalization of disaster preparedness and response, which we synthesize in the next section.

Application of Evaluation Criteria to the Disaster Response Literature

This section discusses our application of the evaluation criteria to the disaster response literature: network design, inventory management, supply chain coordination and management of incentives, management of information, volume-outcome associations, and incident command. Use of these evaluation criteria facilitates an assessment of the structure, timeliness, and capacity of regionalized disaster response systems. None of the included articles presented information relevant to postponement and modularization.

Network Design. The key elements of regionalized disaster responses include mutual aid agreements, available hospital capacity, available trained personnel, and available morgue capacity. Procurement and placement of relevant material is also a key component of a well-designed network for disaster response; material and supplies will be discussed under Inventory Management and Volume-Outcome Associations.

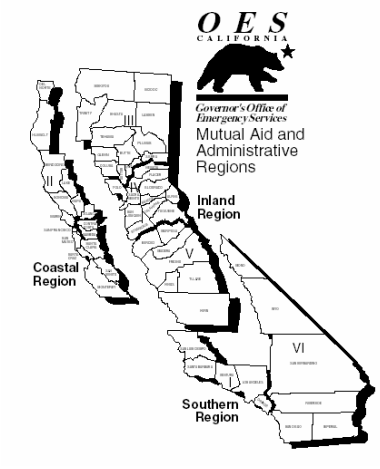
Mutual Aid Agreements. Mutual aid agreements are the primary method of regionalizing disaster responses.[438, 443-446] These agreements provide surge capacity to local jurisdictions when basic services such as law enforcement, firefighting, and health services are overwhelmed. Mutual aid agreements enable localities to expand surge capacity at minimal cost, as each individual locale does not have to maintain inventories of supplies and personnel at maximal-preparedness levels. In addition, such agreements facilitate multi-region involvement if a

[*] References[40, 42, 438, 441-477]
[†] References[39, 104, 478-501]

disaster becomes too large for a single area to manage alone or if a disaster encompasses multiple regions.

Having started as a statewide agreement among California fire and law enforcement agencies in the 1950s (Figure 6), statewide mutual aid systems now exist in many U.S. states.[438] Under mutual aid, local jurisdictions who expect to exhaust their own resources call on neighboring jurisdictions for assistance, according to mutually agreed upon rules for deployment and reimbursement. If the resources of a mutual aid region are expected to be overwhelmed, the region may also request state assistance. Several states have developed information systems that link members of the mutual aid regions. For example, California's Response Information Management System (RIMS) is a secure Web-based system (with access limited by user type) designed to coordinate and manage the State's response to disasters and emergencies.[502*]

Figure 6. Office of Emergency Services Mutual Aid and Administrative Regions



Map publicly available. [450]

Whereas mutual aid agreements are typically within states, neighboring states have developed regional agreements for disaster management (particularly important for states like Tennessee with multiple neighboring states). In 1992, the 19 members of the Southern Governors' Association, responding to the massive destruction caused by Hurricane Andrew in Florida and Louisiana, developed the Emergency Management Assistance Compact.[447, 448] The design of the Emergency Management Assistance Compact was complicated by the heterogeneity in participating states' constitutional and statutory laws. Party states independently resolved legal questions associated with the compact such as "whether a governor, absent specific statutory authorization, had the power to grant good faith immunity to relief workers from another state or to spend money out of state on interstate assistance."[447] The Emergency Management Assistance Compact has been highly effective, and since being

[*] An example of a mutual aid disaster response that could have been facilitated by more robust information management occurred following the 1989 Loma Prieta earthquake in the San Francisco Bay Area. Three counties (Marin, San Mateo, and Santa Clara) sent ambulances to San Francisco County in response to a mutual aid request, increasing San Francisco's ambulance capacity by 300%. However, radio frequencies used by these three ambulance organizations were not compatible, so dispatch centers were unable to track all units under their control. The result was that some ambulances idled, awaiting instructions, while others struggled to respond to multiple calls simultaneously.[478]

approved by Congress in 1996, has been adopted by all states and U.S. territories except for California and Hawaii.[447, 449]

The Emergency Management Assistance Compact is currently working to develop a 50-state database of available assets sorted according to standardized categories for each type of disaster (standardized aid packages describe the number and types of personnel and equipment needed for a given disaster response).[448] A barrier to the comprehensive utility of the Emergency Management Assistance Compact during a bioterrorism response (i.e., its ability to serve as the nation's mutual aid agreement) is that it is not in effect nationally. California, with its own long-standing agreements, has legislation and mutual aid contracts in place that conflict with the Emergency Management Assistance Compact.[448] Despite this, those states that have ratified the Emergency Management Assistance Compact are using it.

There are numerous examples of the Emergency Management Assistance Compact partnerships resulting in expedited regionalized disaster responses. In September 1998, as Hurricane Georges, having devastated Puerto Rico and the Caribbean, headed north to the Florida Keys, officials knew from prior hurricane experience that they would not be able to evacuate patients with special medical needs from the Keys to the mainland on the single highway connecting the two. Florida officials requested use of Emergency Management Assistance Compact partner North Carolina's medical evacuation aircraft, which were immediately dispatched and effected a rapid rescue of this vulnerable population. The Emergency Management Assistance Compact also provides interstate aid for disasters other than hurricanes. In response to ten Emergency Management Assistance Compact states sending help to Florida during its 1998 wildfires, Florida Governor Lawton Chiles stated, "Thanks to our compacts with other states through our Emergency Management Assistance Compact program, we got the help we needed. The coordinated effort during the fires is proof of the value of these compacts."[447, 449]

Regionalization of response for disasters often requires a coordinated international response with Canada or Mexico, particularly in cities close to the U.S. border. Extensions of mutual aid agreements have also developed between U.S. cities and states and their neighboring communities in Canada and Mexico. The La Paz Agreement, signed in 1983 by Presidents Ronald Reagan and Miguel de la Madrid Hurtado, identified 14 pairs of cities along the United States-Mexico border in need of joint response plans for disasters.[451] An analysis of the disaster response plans, personnel and equipment covered by a mutual aid agreement between El Paso, Texas and Juarez, Chihuahua, Mexico highlighted key problems in developing a joint plan: the development of written plans was complicated by conflicting international laws, worker's compensation, insurance, and cross-border communication frequencies; and lack of international incident command structures, bilingual databases and community notification systems.[451]

The mutual aid agreements that have been developed for disasters serve as a framework for regional agreements for bioterrorism preparedness and response. The literature on mutual aid for disasters highlights key considerations relevant to regional mutual aid for bioterrorism. First, the establishment of these agreements requires careful pre-event consideration of liability issues, remuneration, and licensing. Second, design of international mutual aid agreements with Canadian and Mexican regions require consideration of international law, multi-lingual information technologies, and heterogeneity of disaster resources.

Hospital Capacity. Following a disaster, hospitals must provide immediate care to injured victims, continue providing primary care to the populations they serve, and may themselves be

the victims of the event (either directly through plant and equipment damage or indirectly through loss of staff who are victims themselves or who are caring for family members). Similar to a bioterrorism event, both natural and manmade disasters can rapidly generate large numbers of casualties requiring urgent medical attention.[479-481] Hospital response systems have been designed to assist victims of disasters in the hours and days following an event. For example, the Medical Disaster Response Model is designed to mobilize local clinicians to provide immediate medical care in a carefully planned, regionalized system where clinicians initially provide care to injured victims in the field then move to pre-designated disaster medical aid centers, finally converging on pre-designated regional casualty collection points.[482]

A critical component in effective triage during a disaster is having real-time data on regional hospital capacity and bed availability. For example, immediately after the Loma Prieta earthquake, California's Emergency Medical Services Administration began a statewide bed and resources inventory. Before it could be completed, the bed count was discontinued, as it was clear by then that hospital capacity in the Bay Area would be sufficient to meet the needs of victims injured in the quake. However, 2000 available beds had been identified in unaffected regions of the state.[483] Similar activities occurred following other major disasters: after the September 11 attacks on the World Trade Center, the Greater New York Hospital Association worked to amass bed availability information and tracked patients so they could be located by families.[484]

These systems that track hospital capacity, numbers and locations of patients, and estimate the need for additional beds could serve a key role during a local or regional response to bioterrorism. However, none of the included articles specifically evaluated various strategies for estimating available surge capacity or for methods of enhancing local hospital capacity for bioterrorism-related events.

Response Personnel. Disaster responses often require large numbers of personnel. Response personnel typically consist of local responders, who are usually first to the disaster scene, and regional response teams, which may be activated once news of the disaster spreads. Local response personnel include trained professionals such as fire, police, and emergency medical personnel and trained volunteers, as well as untrained volunteers. Trained local responders are often sufficient for key response tasks, even following a major disaster. For example, following the 1994 Northridge earthquake in Southern California, the Los Angeles County public health department created 12 interdisciplinary assessment teams that were sent primarily to "high-risk" areas to provide public health education, environmental health assessment, mental health counseling, and first aid to victims of the earthquake.[485] Trained volunteers can augment the professional response. For example, prior to the 1989 Loma Prieta earthquake, the local American Red Cross chapter in one devastated Bay Area community had established close links to a local amateur (Ham) radio club. Immediately following the earthquake, when this community sustained extensive damage, the Red Cross chapter was able to leverage the pre-existing personal and professional relationships to provide emergency communication among its responders, even when telephones were not operating.[486]

Community members without specialty training can also contribute significantly to a local response. For example, taxis and taxi drivers played an important role following the 1995 Tokyo sarin attack because, unlike the EMS system, their communication and dispatch system was not overloaded. As a result, 25% of sarin victims were transported to the hospital by taxi. However, because the taxi dispatch system had no way to direct drivers to those hospitals able to accept

patients, many taxi-transported patients arrived at hospitals lacking capacity. For future Tokyo disasters, an informal taxi surveillance system has been implemented in which taxi drivers now report disasters to their dispatch center as soon as they are observed. However, this system offers no protection to taxi drivers responding to chemical or biological attacks, as drivers have not been given protective equipment or training.[39]

Other programs have invested more significantly in training and equipping community members for disaster response. For example, the Community Emergency Response Team Program originated in Los Angeles following the 1987 Whittier Narrows earthquake, and has since been promoted and supported by FEMA. Community Emergency Response Team trains community members to offer "immediate help to victims until professional services arrive."[452] Residents are trained to extinguish small fires, provide basic medical aid, rescue victims safely, and collect disaster intelligence.[40] Community Emergency Response Team members are often organized into neighborhood response teams.[40] Forty-eight states and six foreign countries currently have Community Emergency Response Team programs.[40]

Programs like Community Emergency Response Team underscore an important strength of local responders: they generally can arrive before regional responders. This timeliness of response may be critical during the response to a bioterrorist event. For example, following the Singapore Airline disaster in 2000, a contingency plan indicated that a Site Medical Team would be called to treat victims at the scene. However, the team did not arrive until 30 minutes following the crash—a delay that was concordant with planning and practice.[487] When the team arrived, members discovered that all critically injured patients had already been triaged and transported by local emergency transport vehicles. These vehicles had arrived within 15 minutes of the crash, and their quick response was credited with saving numerous lives.[487]

In addition to local responders, regional response teams with expertise in emergency management are often deployed to disaster sites. Numerous organizations, including the federal government, military, and professional volunteer organizations sponsor and support such teams. For example, the International Federation of Red Cross and Red Crescent Societies have participated in many of the responses described in Table 11. Recent regional restructuring has allowed the Red Cross's Field Assessment and Coordination Teams to save money and better coordinate response efforts among local, regional, and international responding organizations.[489] An international pool of approximately 200 trained Field Assessment and Coordination Team members with expertise in disaster assessment and response are on call at any given time. From this group, teams of six or seven members are typically deployed from the international Red Cross headquarters in Geneva within 12 to 24 hours following a disaster.[488] This team makes a report that can be used to coordinate the response efforts of each local Red Cross organization (this is compared with earlier practices of numerous response organizations each performing their own needs assessment prior to mobilizing response personnel and equipment).[489] Field Assessment and Coordination Teams have been augmented by Regional Intervention Teams that provide integration with regional responders who are often more familiar with the host country's language and culture.[488]

The federal government also deploys trained response teams to U.S. disaster scenes. For example, following severe hurricanes, Disaster Medical Assistance Teams are typically deployed and provide primary care services or augment overloaded local medical service providers.[104] Ten Disaster Medical Assistance Teams were placed on "standby alert" following a hurricane watch for Hurricane Andrew in 1992. A total of 16 Disaster Medical Assistance Teams were deployed to assist in the response and recovery following Andrew, which caused unprecedented

destruction in southern Florida and Louisiana. Teams deployed later in the response also served as replacements for exhausted teams that had been deployed earlier.[490]

In addition to civilian government responders, various branches of the U.S. military also train and maintain regional response teams for disaster preparedness. Such teams may be deployed to assist civilian communities following a major disaster. Some teams receive specific training to respond to bioterrorist events. For example, the Army National Guard maintains a Weapons of Mass Destruction Civil Support Team in each federal region.[453] These teams (also described in the "Bioterrorism Preparedness Programs Sponsored by the Department of Defense" section) consist of 22 Guard members, trained and ready for domestic deployment to either a chemical or biological incident.[453] Following deployment, teams may fall under either state or federal control.[454]

There are two key advantages to regional response teams for disasters and bioterrorism. First, regional placement allows for fewer responders to be trained, since one team can serve a broad area. Additionally, teams may benefit from more consistent deployment, adding to responders' experience and reducing the risk that training will decay if not reinforced. The section below on volume-outcome associations discusses this concept in greater detail. However, we found no specific evidence that describes optimal strategies for regionalization of highly trained personnel for bioterrorism or disaster preparedness (e.g., evaluation of the number of highly trained response teams required for a region), alternative methods for enhancing the cross-training of local personnel (e.g., local pharmacists used for triage functions during a bioterrorism response), or for the best methods of coordinating the activities of local and regional response personnel.

***Morgue Capacity*.** Due to their ability to cause a large numbers of deaths in a very short time, disasters can seriously strain morgue capacity. For example, in the case of the Loma Prieta earthquake, 57 of 63 deaths occurred within two minutes of the earthquake, and 42 of these deaths were in one small geographic area.[479] Bioterrorism events have a similar potential: recent estimates suggest that a smallpox attack on a major U.S. city could cause as many as 100,000 deaths.[455] However, we found no information regarding emergency preparedness or disaster response at morgues and other facilities for fatality management.

Inventory Management. Disaster responses can require enormous quantities of supplies, which are often needed immediately. Inventory management plays a critical role in ensuring that such needed supplies arrive in a timely fashion. While we found little discussion of inventory management in connection with disaster response in our literature review,* three key inventory management issues are relevant to regionalized approaches to disaster response. First, a needs assessment must be performed for each locale to determine the amount and type of resources required for a disaster response.[488, 489] Most often, this occurs after an event; however, for areas that are subject to annual or seasonal events (e.g., hurricanes), pre-event planning for expected disasters can take place. Second, determinations as to which organizations are responsible for purchasing, inventorying, and delivering different resources must be transparent and shared with all responders.[488, 489, 500, 501, 503] Finally, inventory distribution plans must be developed.

* We direct interested readers to the Fritz Institute (www.fritzinstitute.org), an organization whose mission is to "strengthen the infrastructures of humanitarian relief organizations by mobilizing logistics and technology expertise and resources from the corporate and academic communities." The Fritz Institute has developed software, currently in use by the International Federation of the Red Cross, to facilitate tracking of needs and resources during a disaster response.

Inventories can be pre-placed so that they are readily available during a disaster or can be transported to affected regions after an event occurs.[488, 489, 500, 501, 503] Alternatively, some humanitarian aid agencies have developed software systems, such as the Pan American Health Organization's Humanitarian Supply Management System (SUMA), to track the arrival and distribution of humanitarian supplies as they arrive following a disaster. [504]

Following its 1998 response to Hurricane Mitch, the International Federation of Red Cross and Red Crescent Societies determined that pre-positioned supplies were necessary to facilitate a timely response to victims' needs. Thus, the Red Cross established agreements with local vendors in hurricane prone areas.[488] These agreements specified the price to be paid for relief supplies and stipulated that the supplies would be stored in the vendors' own warehouses. Such warehouses are consistently stocked at a certain inventory level according to Red Cross needs.[488] According to these agreements, vendors assume the cost of warehousing and of stocking additional supplies, not the Red Cross.[489] The Red Cross also maintains its own regional warehouses and logistics units for further pre-positioning of supplies.[488] We found no specific evidence that evaluates key questions with respect to inventory management for disasters including assessments of methods to determine the size, location, or contents of pre-placed inventories.

Disaster Response Coordination and Management of Incentives. The included articles addressed the incentives of mutual partners, but did not specifically address the incentives of other responders. Since the establishment of California's comprehensive mutual aid agreements, numerous conflicts have occurred over payment for assistance provided, and liability insurance covering responders.[450] The California master mutual aid agreement specifies that responding jurisdictions retain control of their own personnel and facilities and that no party is required to deplete its resources to a point that endangers its ability to manage a local response. However, mutual aid is mandatory during "conditions of extreme peril or declared disaster." In some cases, mutual aid partners have resisted providing mutual aid, principally for economic reasons, despite being called on to do so.[450] In contrast to California's intrastate system of mutual aid, states requesting help under the Emergency Management Assistance Compact are responsible for "reimbursement of all out-of-state costs and accept tort liability for out-of-state personnel."[449] "States ask for out-of-state assistance only when they need it and can cover the costs. States know sending aid will not be a financial or legal burden."[449]

Management of Information. Management of information can affect every aspect of a disaster response. Some information about a disaster may be available before it occurs, allowing planners and the public extra time for coordination and planning. For example, because hurricanes are somewhat predictable, information from preceding years can inform future disaster preparations. The most critical information management and communication challenges often occur during the immediate post-event and disaster response phases, when infrastructure is likely to be overloaded and may be damaged or even destroyed. During these phases, effective communication among decisionmakers, responders, and the public is crucial.

Communication Among Decisionmakers and Responders. During a disaster, decisionmakers and responders have three main information requirements. First, decisionmakers require continuously updated information about local needs and available local and regional resources. Second, the information required to maintain a clear chain of command must be

readily available to decisionmakers and to the responders under their command. Finally, information about response task performance and response outcomes is essential for iterative improvements of disaster responses.[44]

Numerous commercial systems are available to facilitate disaster communications (e.g., California's Response Information Management System (RIMS). For example, most counties in the San Francisco Bay Area use the very high frequency Hospital Emergency Administrative Radio system in a disaster.[456] This system links all hospitals in a single county to a dispatch system. The system is organized at the county level, which also controls the EMS, and allows overloaded hospitals to divert ambulances to other hospitals with excess capacity.[456] However, such systems do not always function in a large-scale disaster. For example, following the 1995 Tokyo sarin attack, EMS communication systems lost contact with physicians at the Tokyo Metropolitan Ambulance Control Center. Because paramedics in Japan are prohibited from performing certain advanced life support activities without case-by-case permission from a physician, this loss of communication resulted in delayed treatment for victims.[39]

Communication with the Public. Systems for communication with the public can be grouped broadly in two categories: alert/warning systems intended to provide generalized alerts and to notify the public of an increased risk of a bioterrorism event, as well as news and information outreach systems that provide detailed information about particular events.

Among the included articles, we found one evaluation of a public alert/warning system.[457] This study evaluated the use of sirens as tornado warning systems. The study found that although people in communities served by a tornado siren are more likely to get their initial warning of an imminent tornado from a siren than from television or radio news, these residents are no more likely to seek shelter than those not served by tornado sirens (only about 30% of people in either group reported seeking shelter after receiving a tornado warning).[457]

A warning system of particular relevance to bioterrorism is the Homeland Security Advisory System. Created by presidential directive in March of 2002, this system uses five colors to represent perceived levels of threat to national security ranging from Red (severe threat) to Green (low threat) (Figure 7).[458] The perceived threat levels are assigned by the Attorney General in consultation with the Secretary of the Department of Homeland Security and others based on intelligence information. Since its inception, this system has remained primarily at Yellow Alert (elevated). As of August 10, 2003, the system has gone to Orange Alert four times.[458] The Advisory System requires the executive branch of the federal government to comply with a system of "Protective Measures" corresponding to each threat level. Additionally, the presidential directive that created the system encourages other departments and branches of government at every regional level to create their own list of "Protective Measures" to be instituted should the nation be placed under increased alert.[459, 460] The Advisory System is also intended to integrate with other alert systems used by decisionmakers in other federal agencies (e.g., the Department of Transportation, the Department of Agriculture) as well as officials at the state and local levels. The Advisory System aims to provide a "common language" for each of the nation's alert systems, allowing responders and the public to more easily interpret risks and threats.[*] However, according to the recent State of America's Cities survey conducted by the League of Cities, only 20% of American cities currently use the National Homeland Security Advisory System (although 71% of large cities either use the system or are working to

[*] The Advisory System was designed for communications from the federal government to other regional and local agencies—it was never designed to communicate with the public (although it is now being used that way).

implement it).[461, 462] The system continues to be developed, and may benefit from providing more specific alerts to localities rather than issuing a warning for the nation as a whole (thus avoiding unnecessary spending by localities unaffected by the perceived threat), and from providing responders with more information about appropriate measures to take in response to a given threat.[458]

Figure 7. Homeland Security Advisory System

Figure publicly available.[464]

During an emergency, the public can also receive information via disaster-specific media channels. After the 1994 Northridge earthquake, victims were kept updated by an extensive FEMA media effort that included "reports, memos, summaries and updates."[463] Six days after the earthquake, FEMA established the Recovery Channel, which was shown by local television stations and in disaster response centers such as shelters and disaster relief application centers. The following week, FEMA began publishing the Recovery Times, a newsletter with specific information for victims, updating them about the status of the recovery and providing information about where and how to apply for assistance.[463]

Volume-Outcome Associations. The included articles support the concept that increased disaster response experience is associated with better response outcomes.[486] After the 1989 Loma Prieta earthquake, residents of one community who had responded to many disasters, including mudslides and wildfires, contributed significantly to a high-quality response.[486] The ongoing risk of natural disasters increased the experience of local responders and compelled the community to plan and participate in disaster training exercises.[486]

Conversely, lack of experience has negatively impacted disaster responses. For example, during the 1990 Texas floods, one community's Red Cross chapter had only a single paid employee who was relatively new to the job and had no experience planning for or responding to disasters.[486] As a result, the quality of the local response was inadequate, prompting deployment

of national Red Cross volunteers who stayed for three weeks, providing the "backbone" of the local chapter's response.[486]

Such findings have important implications for regionalization of disaster and bioterrorism preparedness. First, personnel with experience in disaster response are often few in number. Staffing them at a regional level ensures wider availability of this scarce resource and allows local areas to spend their money elsewhere. (However, redundancy in the system through the allocation of some resources locally can enhance capacity when a large region is affected.) Second, because regional staffing models cover a wider geographic territory, they are therefore more likely to encounter disasters, thus improving their experience.

Incident Command. The 1900 Great Hurricane in Galveston, Texas resulted in more than 1000 casualties and led to the development of the modern approach to city management.*[491] The broader lesson of the Great Hurricane remains: the more complicated a response becomes, the more necessary it is to have a strong chain of command. This is particularly true when the response involves a large region and many diverse responders (especially regional responders who may never have previously worked together). This chain of command must be established and agreed upon before the event occurs. The chain of command must be integrated to include all responders and must allow resources to be rapidly deployable.[14, 454]

During a regionalized disaster response, it is essential to establish whether a local, regional, or federal agency is in command. Typically, incident command begins with local responders, as they are usually the first to the scene. Understanding when and how command changes as additional resources are called in is important to maintain an effective response to a disaster. Protocol should be defined prior to an event, and should clearly lay out changes in command. Lack of such protocols might lead to difficulties such as those experienced during the response to the 1989 massive Exxon *Valdez* oil spill off the coast of Alaska.[492] Following the spill, some time-sensitive cleanup actions, such as the application of dispersing agents and the burning of oil, were delayed due to competing contingency plans and a confused chain of command.[492] There was no established authority under which Exxon could assume control of the cleanup from local port authorities. After Exxon assumed control, it became clear that the corporation had no standing contingency plan for the geographic area where the spill had occurred, and that all response logistics would have to be created *de novo.* Ultimately, the response and cleanup were controlled by a triumvirate consisting of the president of Exxon Shipping Company, a Rear Admiral of the U.S. Coast Guard, and the Commissioner of the Alaska Department of Environmental Conservation. However, this command structure was not in place until more than two days after the tanker ran aground.[492]

For efficient disaster response, chain of command must be established as quickly as possible following the occurrence of the disaster. The Incident Command Center of the New York City Department of Health was activated only 32 minutes after the first plane crash on September 11, 2001.[484] The New York City Department of Health was aided by previous disaster planning and drills. The disaster literature provides compelling evidence that emergency management, including that which would be required for a bioterrorism response, is facilitated by a clear chain of command.[505, 506]

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*In response to the disaster, the mayor of Galveston assigned each essential response task to a single individual. This system worked so well that it became the basis of a new city charter and Galveston was the first in the country to be governed by a core team of commissioners.[491]

Lessons Learned from the Disaster Literature for the Regionalization of Services for Bioterrorism Preparedness

From our review of the disaster response literature, we synthesized three key lessons learned.

1. *Information management, using common technology platforms, is essential for assessing the needs of the local community and the resources available to them, and for coordinating responses from regional agencies.* The disaster literature emphasizes the need for updated information so that response resources can be dispatched to those in need in a timely manner. Bioterrorism responses may benefit from a common technology platform. These may be as simple as a common radio frequency or as complicated as multiple computer networks from different regions communicating with each other to exchange information on resource placement and availability.

2. *A key component of effective regional responses to disasters includes mutually agreed upon pre-event protocols that establish chain of command structures.* The evidence suggests that these protocols are most effective when they delineate the chain of command for an event at several levels: a chain of command utilizing only local responders should be established, as should plans for how the chain of command changes when regional and federal response agencies become involved.

3. *Mutual aid agreements are key components for providing surge capacity for regional response to disasters.* These agreements ensure that every locale does not have to be staffed and prepared for a maximal intensity event. They enable risk to be spread among several locales, and provide cost-sharing of disaster preparedness. Mutual aid agreements for bioterrorism are likely to benefit from careful pre-event consideration of liability issues, remuneration, and licensing.

Table 11. Lessons Learned From Regionalized Responses to Disasters

System	Description of System and its Regionalization	Lessons Learned
The Homeland Security Advisory System[459-462]	Uses colors to describe the level of terrorist threat from Red (severe threat) to Green (low threat) (Figure 7). Threat level set by the Secretary of Homeland Security, in coordination with other officials. Most alerts are given on a national basis and not regionalized or otherwise limited to geographic areas or specific terrorist targets.[459, 460]	A warning system benefits from specifying actions to be taken for a particular alert.
Emergency Alert System[465-467, 507]	General alert system used to issue warnings about weather emergencies and other natural disasters. Fully integrated with the National Weather Service and FEMA. The system includes the Radiological Emergency Preparedness Program, which requires all broadcast media to purchase and maintain equipment for the automated broadcasting of emergency messages. The Radiological Emergency Preparedness Program additionally designates 30 National Primary Stations (both radio and television), which are required to automatically broadcast presidential messages.	Pre-event designation of communication resources facilitates the timeliness of alerts issued to the public.

System	Description of System and its Regionalization	Lessons Learned
Aviation Incident Response (AIR) Team[468]	AIR Team members are mental health professionals with special aviation incident/grief counseling training and experience. Sponsored by the American Red Cross, AIR Teams are drawn from a pool of 400 trained mental health professionals deployable immediately following a domestic aviation disaster. Members of the AIR team are positioned near every major U.S. airport, allowing for timely deployment following a disaster.[468]	Regionally organized and localized groups of highly trained professionals can be rapidly deployed to augment services available locally.
Renal Disaster Task Force[493]	Maintained by the International Society of Nephrologists for disaster response, an advance team of nephrologists performs a needs assessment, after which additional assistance in the form of equipment, logistic support, transportation, and personnel are delivered. In the case of the 1988 Armenian earthquake, the Task Force established a presence in Armenia within 24 hours of the disaster and provided dialysis to nearly 500 people suffering from acute renal failure following crush injuries. The Task Force is internationally organized in three regions. Each region maintains rosters with the names of volunteers who can be deployed on short notice, as well as stocks of hardware and supplies to facilitate a response to a major earthquake requiring renal intervention.[493]	Regionally organized groups of highly trained professionals can be rapidly deployed to provide services unavailable locally.
Medecins Sans Frontieres (MSF)[469-473, 494]	The mission of MSF is to provide "emergency medical assistance to populations in danger." MSF operates under a formal hierarchy that includes four international regions with operations in 80 countries to which it dispatches over 2500 volunteer medical personnel.[473]	Highly trained volunteers can be rapidly deployed to augment a local response.
Urban Search and Rescue (USAR) Teams[495]	Maintained by FEMA, the 28 regionally located USAR teams are highly trained and equipped to travel to disaster scenes to rescue victims from collapsed buildings. Following the 1995 bombing of the Alfred P. Murrah Federal Building in Oklahoma City, FEMA deployed 11 USAR teams.	Regionally established teams with training and equipment can provide essential services unavailable locally.
Marine Corps' Chemical and Biological Incident Response Force (CBIRF)[474, 475]	This team is trained in weapons of mass destruction mitigation services including security, medical aid, decontamination, and search/rescue. Based in North Carolina, the 350-person team is designed to be deployed anywhere in the United States in response to a known incident, or can be pre-positioned at a high-risk mass gatherings such as the Olympic Games or a political inauguration.[476]	A single, highly specialized team may contribute to local responses.
Mental Health Community Response Coalition (MHCRC)[496]	Created by mental health responders following the September 11, 2001 attack on the Pentagon, it includes representatives from a variety of response organizations such as the American Red Cross, the Virginia Disaster Response Network, and the Capitol Area Crisis Response Team to manage the long-term mental health needs of those affected by the attack on the Pentagon. The group met regularly for months following the attack to avoid duplication of efforts, prevent any single agency from becoming overwhelmed, identify victims with unmet needs (e.g., non-English speakers, friends of victims), and facilitate collaboration and referral.[496]	Response agencies with similar or related purposes can effectively coordinate disaster response services in a geographic area.
World Food Program (WFP)[477]	The principal United Nations agency responsible for famine relief. In 1999, the WFP fed 89 million people in 82 countries organized according to the seven regional bureaus. To facilitate its logistics, the WFP partners extensively with governments, other UN agencies, and with non-government organizations. The non-government organizations are largely charged with the transport, storage, and distribution of food on behalf of the WFP.	The regional organization of the WFP facilitates famine surveillance, the establishment of relationships between WFP and local governments, and more consistent logistical support.
Veterans' Affairs (VA) mobile health clinics[497-499]	Deployable to the scene of national disasters to provide primary care to victims (including non-veterans).[497] Following the Northridge earthquake, the VA hospital in Spokane, Washington sent mobile outpatient medical clinics to the LA area.[499] Mobile health clinics have also assisted in the aftermath of Hurricane Andrew and 1993 Midwest flooding.[498]	Regional resources can be deployed to provide ongoing services (as opposed to disaster-related services) to reduce the effect of the disaster on the population.

System	Description of System and its Regionalization	Lessons Learned
International Federation of Red Cross and Red Crescent Societies (IFRC)[488, 489]	IFRC coordinates relief efforts of individual National Societies according to a regional plan: The IFRC has 14 regional offices, 63 country field offices, six sub-delegations, and two regional logistics centers. This regional structure allows for graded levels of disaster response: National Societies respond to small emergencies, regional offices respond to mid-size emergencies, and the IFRC in Geneva responds to large disasters.[488] This plan required providing training to local responders at the National Society level and pre-positioning supplies at the regional level.[489]	The regional organization of the IFRC has developed through iterative application of lessons learned from prior responses.
United Nations Joint Logistics Centre (UNJLC)[500, 501]	Coordinates logistics (particularly transportation needs) among UN organizations operating in a single geographic area.[500, 501]	Expert logistical support can be coordinated and may improve cost-efficiencies for numerous agencies working in the same region.

Synthesis of Evidence about Regionalization of Emergency Trauma Care

We searched the medical literature for examples of regionalization of the delivery of specialized medical care (e.g., care for the severely burned, neonatal intensive care, and trauma care). We found that regionalized trauma care was the most extensively evaluated. Thus, we reviewed the literature in this area in more detail to identify lessons that could be applied to regionalization of bioterrorism responses.

The purpose of the trauma care system in the United States is to provide rapid, coordinated medical services to injured patients by matching "a facility's resources with a patient's needs so that optimal and cost-effective care is achieved."[508] This purpose is achieved through a coordinated system in which pre-designated trauma hospitals work with emergency medical personnel to expedite the delivery of specialized trauma care. Trauma systems are relevant to regionalization of bioterrorism preparedness and response for two reasons: trauma systems have adopted regional approaches that can serve as models for regionalization of components of bioterrorism preparedness and response, and elements of the trauma system such as hospitals, emergency response personnel, management of patients, and communication systems are essential components of a bioterrorism response. The following sections describe the regionalization of trauma systems, present the results of evaluations of these regionalization efforts, and summarize the evidence for and against regionalization of trauma-related services relevant to bioterrorism preparedness and response.

Regionalization of Trauma Care

A regionalized trauma system includes classification of hospitals within the region according to the services that they can provide, protocols for pre-hospital trauma care and transportation by emergency medical personnel, and coordination of these pre-hospital and hospital-based services.[509] Regionalization of trauma care efforts in the 1980s and 1990s was spurred by a

report from West et al. documenting significant differences in the preventable death rates between San Francisco county, which had a regionalized system of care, and Orange County, which did not.[510] Regionalizing U.S. trauma care was further enabled by legislation such as the Emergency Medical Services Act in 1973 and the Federal Trauma Care Systems Planning and Development Act in 1990, which provided assistance to states to "plan, implement, and monitor organized trauma care systems."[511] Currently in the United States, five states have systems that meet all the criteria for a regional trauma care system. Only 24 states have trauma care systems that function across the entire state.[512]

Depending on the state, trauma care hospitals in the United States are designated by one of four or five levels (Level I through IV or V). The criteria for designation of hospitals, established by the American College of Surgeons,[508] are based on the type and amount of equipment, resources, and trained personnel available to the hospital.[508, 511] Level I hospitals (also referred to as tertiary care centers) provide the most extensive trauma care. A region within the trauma care system is typically defined as a geographic area that is served by at least one Level I center. Rural areas are more likely to be served by a Level III or IV center that collaborates with the nearest Level I center located in a more urban area. Urban areas are more likely to have Level I and II centers. Regionalization of trauma care is based on the principle that injured patients will be appropriately transported to the nearest hospital that can provide the best possible care to the patient. The destination hospital is determined by emergency medical personnel according to the severity of injury. The most severely injured patients are transported directly to the nearest Level I center, bypassing the closest hospital if it is not a Level I center. Less severely injured patients are transported to the closest hospital capable of meeting the needs of the patient. [508]

Summary of the Evidence of Regionalization of Trauma Care

We reviewed 98 articles and reports on trauma care. Of these, 74 articles and two government reports described regionalization of trauma care.[*] Thirty-nine of these articles presented evaluations of regionalization of U.S. and Canadian trauma care systems.[†] Table 12 presents the evidence from the 16 evaluations of trauma care regionalization with the greatest relevance to bioterrorism preparedness and response.

Most evaluations of regionalization of trauma care either compare patient outcomes before and after implementation of a regionalized trauma care system,[‡] or compare outcomes between trauma care centers and non-trauma care centers.[§] Mann and colleagues published a systematic review of the published evidence regarding trauma system effectiveness and found that most of the studies had systematic biases depending on the methodology used to assess trauma care effectiveness.[523] For example, panel studies could lead to biased results depending on the quality of data available or whether assessments of preventability of death were made by individual physicians or in a group setting.[523, 551] Other studies relied on data registries of questionable reliability due to incomplete data, data collected for another purpose, or outdated data used for comparison purposes.[37, 521, 523]

[*] References[33-38, 509, 511-579]

[†] References[34-38, 509, 515, 516, 519-525, 527-530, 532, 533, 536, 539, 541, 544, 545, 547, 551, 554, 556, 557, 560, 562, 566, 569, 571, 574, 576, 579]

[‡] References[34-38, 509, 516, 519-521, 524, 527, 529, 532, 533, 536, 539, 544, 545, 554, 569, 571, 574]

[§] References[36-38, 521, 525, 528, 530, 532, 544, 566, 580]

Despite these potential sources of methodological bias, 29 evaluation studies reported improved outcomes associated with regionalization, including reduced mortality,[*] pre-hospital time,[†] costs of treatment,[‡] and improved appropriateness of patient care.[§] The reviewed evidence is comprised mostly of retrospective cohort studies or observational studies where the comparison group differed by location or time period. Additionally, the published literature mostly relied on hospital survival as an outcome measure, and restricted patient inclusion criteria by injury severity or geographic location.[523] Despite the limitations of the published data, the results of evaluations of trauma care consistently favor regionalization. For example, a systematic review of nine regionalized trauma systems[37] reported a 15%-20% improvement in trauma-associated mortality after the implementation of regionalized trauma care.[37, 523] Miller and Levy reported 15.5% lower costs per injury episode and $1,025 average per case savings in states with regionalized trauma care.[37]

Four key elements of trauma care regionalization are primarily credited with these improved outcomes: 1) formal designation and accreditation of hospitals at the appropriate level,[508, 532] 2) implementation of protocols specifying patient triage and transportation to appropriate trauma centers, 3) use of communication networks between pre-hospital care givers and hospital personnel, and 4) availability and ongoing training of medical personnel to assess, triage, and treat patients. In a prospective evaluation of mortality and pre-hospital time during the regionalization of a trauma care system, Sampalis and colleagues reported a decrease in mortality from 52% to 18%, with a decrease in mortality for each year of the study since the initiation of the regionalization process.[509] The regionalization stages were classified as: initial designation of hospitals, establishment of triage and transfer protocols, and integration of hospital and emergency services.[509] A regression model of the stage of regionalization and the risk of death showed significant decreases in the adjusted odds ratio for the risk of dying at each advanced stage of regionalization (i.e., each stage was significantly associated with decreases in mortality). The study also reported a 30% reduction in pre-hospital time, a critical factor in reducing morbidity and mortality.[509, 574] In a systematic review of effectiveness of regionalized trauma systems, the elements contributing to improved mortality were the designation of trauma centers,[37] the development and implementation of appropriate patient triage and transfer protocols,[34-37] and improved pre-hospital care.[37]

Two other systematic reviews of effectiveness of regionalized trauma care systems provide some evidence as to the importance of designation of hospitals in improving survival.[521, 551] Simons and colleagues compared mortality rates between trauma centers that had been designated and accredited to those that had only been designated without formal accreditation, and found significantly improved outcomes in the center that met all the criteria for accreditation.[556] Voeller and colleagues reported a relative risk of dying before establishment of a regional trauma center to its establishment of a regional trauma center of 2.7 ($p < 0.03$). The researchers suggested that the improved outcomes they observed were most likely due to the designation of a tertiary care center, the establishment of triage protocols, improved pre-hospital care through a communications network, and the availability of dedicated and specialized personnel.[533]

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[*] References[34-38, 509, 515, 516, 519, 521, 524, 527, 529, 530, 532, 533, 544, 545, 551, 566, 569, 571, 574]

[†] References[37, 509, 529, 545, 569]

[‡] References[525, 536, 539]

[§] References[520, 529, 530, 533, 536, 541, 551, 562, 569]

The evidence suggests that geographic variations do not affect the importance of the key components of regionalized trauma care systems. Communication, designation, triage, and transportation protocols still play an important role in establishing regionalized trauma care systems in rural areas.[532] However, it might be important to tailor particular components according to the location of the system.[516] For example, for regional systems in a primarily rural or remote area of the country, designation of hospitals may concentrate on Level IV or V hospitals rather than Level I hospitals, or protocols for patient triage and transfer might focus on patient treatment and stabilization before transport to a tertiary care center rather than reduction in pre-hospital time.[516, 532]

Application of Evaluation Criteria to the Trauma Literature

The following section presents results of applying the relevant evaluation criteria to the trauma literature: network design, coordination of trauma services and management of incentives, management of information, volume-outcome associations, and incident command. None of the included articles presented information relevant to inventory management or postponement and modularization.

Network Design. The design of a regionalized trauma system provides for the designation of centers with highly specialized trauma care capabilities, including highly specialized personnel, surgical capacity, and specialized resources and equipment in urban areas, with less advanced centers in rural areas. This designation of hospitals, and the number and levels of centers, varies for different geographic regions. To achieve improved quality of trauma care at decreased cost, a trauma system requires a carefully determined number of hospitals at each level in the system. The number and level of centers established within a given area depends on the number of trauma patients expected in that area, the size of the population, and the population density. One report estimated that "75 to 90 macro-trauma/EMS regions would be appropriate for the nation."[574] Eastman and colleagues estimated that one trauma center could serve 500,000 to two million people, based on an estimate of 0.5 to 1 major trauma patients per 1,000 people per year.[518] They further calculated that in an urban area, with a population density of 10,000 people per square mile, one center could serve people in a 5.6 mile radius, whereas in a suburban area, with a population density of 1,000 people per square mile, the center could serve people in a 17.8 mile radius.[518] Some authors have suggested that the number of Level I centers serving a particular geographic region be limited to enable Level I centers to achieve a certain level of experience. Implementation of this policy led to a decrease in Level I centers in Oregon's statewide trauma system from five to two.[36, 37] However, we found no evidence that specifically evaluates variations of the number and level of trauma centers within a geographic region. Efforts to regionalize bioterrorism preparedness will need to consider the character of the area served and the population density.

Coordination of Trauma Services and Management of Incentives. The included articles highlight two key motivators of regionalization of trauma care: legislative mandates and funding and reimbursement issues.

Regionalization of trauma systems in the United States occurred primarily due to legislative mandates (such as the Emergency Medical Services Act in 1973 and the Federal Trauma Care

Systems Planning and Development Act in 1990).[518] Despite these legislative mandates, the government has provided limited financial support for the development and support of trauma systems,[33] an oversight that has been strongly criticized.[33] Eastman and colleagues estimated that the reimbursement for trauma patients on average results in a loss to the hospital of 19% of costs per patient.[511] Economic disincentives, including inadequate reimbursement for medical care, lack of governmental assistance, high operating costs, and high levels of uncompensated care, have led to closures of trauma centers.[33] One study reported that 95 hospitals had dropped their trauma designations.[581] Furthermore, the specialized personnel providing care at trauma centers are inadequately reimbursed.[511]

Funding and reimbursement issues will play an important role in decisions regarding regionalization of bioterrorism preparedness. At this time it is not clear how hospitals participating in these efforts will be reimbursed. The primary payers of trauma care reimbursement, including private insurance companies, Medicare, and Medicaid, will have to engage the federal government and hospitals in dialogue, so that the incentives for hospitals to provide specialized bioterrorism care are clearly understood.

Management of Information. A key feature of effective regionalized trauma care is the implementation and maintenance of trauma care data registries that facilitate the ongoing evaluation of regionalized performance, and the identification of areas for performance improvement.[518, 531, 574] Hospitals participating in statewide trauma registries can regularly audit their performance and compare it with that of similar hospitals in the system. This quality improvement process enables hospitals to identify gaps in care and target areas for focus. Iterative quality improvement processes are also relevant to bioterrorism preparedness because bioterrorism response systems will need to regularly monitor and update their plans and protocols.

Volume-Outcome Associations. Regionalized trauma care systems achieve cost savings and improved outcomes by concentrating the treatment of severely ill patients at trauma centers.[33-38] The premise underlying this volume-outcome association is that limiting the number of tertiary care centers, according to community need, leads to increased experience in treatment of severely injured patients, and thus improved outcomes. Cost savings are achieved by limiting the provision of expensive medical services to selected centers. The Oregon Trauma System, considered a model for a regionalized statewide system, specifically limits the number of tertiary care centers to achieve this level of experience.[37] Nathens and Maier concluded that the "limited direct evidence coupled with the extensive indirect evidence…[showed that] experience improves outcomes and that volume plays a critical role in the accrual of experience" for trauma care centers.[38] In a review of the Portland Trauma System, Mullins and colleagues reported that patient survival increased when the number of severely injured patients treated at each tertiary care center exceeded 350 patients annually.[34] Guidelines from the American College of Surgeons provide information as to the number of patients in different injury categories that should be treated at Level I centers for these centers to be cost-effective and maintain proficiency.[508]

Efforts to regionalize bioterrorism preparedness should take into consideration the volume-outcome association. It may be that restricting the hospitals providing care to patients during a bioterrorism event will result in those hospitals having better protocols and more experience in providing such care.

Incident Command. An established and centralized system for command and control is a key factor of trauma care regionalization. Because responders are often in the field or other disparate locations, communication systems form the foundation for command and control in trauma care.

An emergency communication system, like an emergency 911 system,[515] enables emergency medical personnel to reach the site of the accident in a timely manner. Furthermore, a centralized communications network permits the coordination of care in the field. It also serves as a link between hospital personnel and field personnel, thereby enabling hospital personnel to be informed of the status of injured patients, and to prepare for their arrival.[533] It can also be used in areas with more than one appropriate destination hospital to check for availability of beds and to triage patients to that hospital. This centralized communication system could play a similar key role in a bioterrorism response.

Lessons Learned From Regionalization of Trauma Care

The evidence we reviewed suggests that regionalization of trauma care has led to decreased morbidity and mortality among severely injured patients. The literature further implies that these improved outcomes may be due to the large volume of patients seen at specified trauma centers as a result of the regionalization process. This association is highly relevant for bioterrorism response planning since the availability of skilled, specialized care could impact the outcome of exposed patients. Five issues from the process of trauma care system regionalization might be considered during the planning of a regionalized bioterrorism response system.

1. *Pre-event hospital designation contributes to lower costs and improved patient outcomes.* The evidence from trauma care regionalization suggests that a key component of high quality, cost-effective care is limiting high-cost specialty care to specifically designated hospitals with increased experience in treating severely injured patients. A bioterrorism response system may benefit from the pre-event designation of hospitals. Such designation may allow facilities to ensure that they have all the resources and personnel they need for a bioterrorism response, ensure that emergency medical personnel know where to take exposed patients, and may allow the public to be directed to the appropriate hospitals in case of a bioterrorism event. Furthermore, a hospital designated prior to a bioterrorism event could have the various infection control equipment in place (e.g., negative pressure control rooms) which could be used during a bioterrorism response but which could also be used routinely for treatment of other communicable diseases. The designation of hospitals allows a clear understanding among all medical services personnel about the role of each hospital and the services it will provide. Such designation also allows planners to determine the number of hospitals at each level that will be required to serve a specific geographic area. Hospital designation is likely to be relatively easy for non-contagious diseases; however, hospitals may be hesitant to be designated as specialty care hospitals for more contagious diseases.

2. *Formalized protocols for pre-hospital and hospital care contribute to improved patient outcomes.* Formalized protocols in the regionalized trauma care system for patient triage

and transportation of patients to appropriate trauma care centers are directly relevant to the field assessment and triage that will need to be conducted during a bioterrorism response. A regionalized bioterrorism response may benefit from similar protocols so that first responders know where and how to transport exposed patients in a timely manner so as to contain exposure and ensure rapid delivery of definitive care to the patients.

3. *An established communication network is essential to the coordinated regionalized provision of trauma care*. It is likely that an established communication network such as that used by trauma care systems could also be used during a bioterrorism event. The existing traumacommunications network enables emergency medical personnel to reach the site of an accident in a timely manner and permits ongoing communication between the field and the destination hospital. Such a system could play an equally important role during a bioterrorism response. It could serve as a centralized command and control system to assist in managing the flow of patients to regional network hospitals that have the capacity to care for them.

4. *Correctly aligned incentives, particularly sufficient funding, are critical to retaining the participation of designated trauma hospitals.* The included articles suggest that regionalized trauma care systems do not provide sufficient incentives for some hospitals to remain in the system. A bioterrorism response system is likely to benefit from clearly outlined mechanisms for reimbursement to hospitals designated to care for patients within a given regional network so that hospitals are less likely to refuse to participate or to drop their designations.

5. *Data registries contribute to continuous evaluation and improvement of trauma systems.* Ongoing evaluation of trauma care systems is important to identify areas for performance improvement. One source of data to conduct such evaluations is a standardized data registry. Such a registry allows comparison of one system's performance with similar systems, and facilitates identification of areas for improvement. A bioterrorism response system may benefit from periodic, region-wide evaluations. Such evaluations could be facilitated by the use of data registries.

Table 12. Selected Evaluations of Regionalized Trauma Care Systems

Study	Study Design	Components of Regionalization	Outcomes Evaluated	Special Population
Sampalis, et al.[509]	Prospective study evaluating trauma care effectiveness during each stage of the regionalization process (pre-during-post)	Designation of hospitals; triage and transport protocols; communication network; pre-hospital care through improved EMS training	Mortality rate during each stage of regionalization: Pre-implementation: 52%, Stage 1: 32%, Stage 2: 19%, Stage 3: 18%, (p<0.0001). Pre-hospital time decreased from 62 to 44 minutes (p<0.001); mean time to admission after arrival decreased from 151 to 128 minutes (p<0.001). A multivariate analysis showed that treatment at a Level 1 center, decreased pre-hospital time and direct transport to the tertiary center contributed to the decreased mortality	Not stated

Study	Study Design	Components of Regionalization	Outcomes Evaluated	Special Population
Mullins & Mann[37]	Systematic review of population-based studies evaluating the effectiveness of regionalized trauma care systems	Designation of hospitals; triage and transport protocols	15%-20% improvement in survival rate; early transfer from rural to tertiary centers; favorable volume-outcome association (>350 patients treated annually) and restricted number of Level I centers.	Rural areas
Nathens, et al.[38]	Review of literature to evaluate volume-outcome association for trauma care	None stated	Adjusted mortality: OR 1.3 times greater at low volume centers (<140 patients/two yrs) compared with high volume centers (>200 pts/two yrs); predictor of outcome was annual number of seriously injured patients per surgeon and the threshold needed was 35 pts/yr. Length of stay was lower in centers with high volume. Studied the relationship between volume and outcome in 31 academic trauma centers across the United States and found that there was a benefit in mortality rate when hospital volume exceeded 650; however, volume-outcome association benefit was restricted to severely injured patients	Not stated
Jurkovich & Mock[521]	Systematic review of studies that evaluated regionalized trauma care system effectiveness by studying registry-based data	Designation of hospitals	Improved survival after trauma center designation and improved infrastructure in trauma centers. Important to have standardized data registries to enable comparisons across different systems	Rural areas
MacKenzie[551]	Systematic review of panel studies evaluating regionalization of trauma care systems. Panel studies determine the preventable death rate where preventability is defined by physician review.	Designation of hospitals	The preventable death rate ranged from 22% to 86% before designation of hospitals, which dropped to between 10% and 40% after designation. There was a decrease in the percent of errors after implementation of regionalized trauma care systems	Not stated
Mann, et al.[523]	Systematic review of population-based studies, registry-based studies and panel studies evaluating regionalized trauma care effectiveness.	None stated	The findings consistently support regionalization of trauma care systems; although the quality of evidence considered to be relatively poor.	Not stated
Hulka[544]	Systematic review of studies evaluating pediatric trauma care systems	Designation of hospitals	Decreased risk-adjusted logistic odds of death in seriously injured children: Odds Ratio: pre-trauma system vs. post-trauma system: 1.17 vs. 0.68 respectively, p<0.01	Pediatric
Nathens, et al.[527]	Pre-post implementation study. Assessed change in motor vehicle crash mortality over time after the initial designation of trauma centers	Designation of hospitals; triage and transport protocols; pre-hospital care through improved EMS training.	Mortality decreased from 16.2 to 11.6 per 100,000 person-years. There was an overall 8% decrease in motor vehicle crash mortality 15 years after trauma system implementation.	Not stated
Miller & Levy[525]	Assessed the impact of regionalization on costs by comparing states with and without established trauma systems. Conducted multivariate regression analysis to account for potential confounding variables	Designation of hospitals; triage and transport protocols; pre-hospital care through improved EMS training	15.5% lower costs per hospital injury episode in states with trauma care systems. Analysis showed a savings average of $1025 per case. Also observed a high mortality rates in hospitals with low volume of trauma cases.	Rural areas

Study	Study Design	Components of Regionalization	Outcomes Evaluated	Special Population
Smith[532]	Review of published articles that evaluated patient outcomes after trauma care regionalization	Designation of hospitals; triage and transport protocols; communication network; pre-hospital care through improved EMS training	Found high mortality rates in hospitals with a low volume of trauma cases	Not stated
Abernathy, et al.[536]	Pre-post implementation study. Assessed outcomes after the implementation of a voluntary trauma care system	Designation of hospitals; centralized communications center	Lower mortality rates: OR 0.48 (95% CI: 0.32-0.71); Shorter length of stay: 16.5 days vs. 19.5 days, (p<0.05); Decreased mean costs: $29,795 vs. $34,983, ($p$<0.05) after implementation of system	Not stated
West, et al.[571]	Pre-post implementation study. Reviewed autopsy records to determine the preventable death rate where the rate was determined by physician review	Designation of hospitals; triage and transport protocols	The preventable death rate decreased to 9% after implementation of system compared with 71% and 73% before implementation. The rate of appropriate care after implementation was 89% compared with 20% and 14% before implementation	Not stated
Mullins, et al.[36]	Compared outcomes between two states with trauma centers at different stages in the implementation of system. Also had a pre-post implementation comparison within a state. Conducted multiple logistic regression models to determine effect of a regionalized trauma system	Designation of hospitals; triage and transport protocols	Adjusted mortality rate OR=0.80 (0.7-0.9). An overall 20% reduction in mortality after implementation compared with another state in pre-implementation period.	Rural areas
Mullins, et al.[34]	Assessed change in mortality rates during the pre-implementation, early implementation and established phase of a regionalized trauma care system	Designation of hospitals; triage and transport protocols	Adjusted risk of death: in adults: OR 0.65 (95% CI: 0.51-0.81) and in children: 0.47 (0.26-0.84) after establishment of trauma system	Not stated
Mullins, et al.[35]	Pre-post implementation design. Assessed adjusted risk of death	Designation of hospitals; triage and transport protocols; pre-hospital care through improved emergency medical services training.	Adjusted risk of death: OR 0.82 (95% CI: 0.73-0.92) after implementation of regionalized system	Rural areas
Cales[569]	Pre-post implementation design. Assessed the preventable death rate. Preventability determined by physician review of records.	Designation of hospitals; triage and transport protocols; pre-hospital care through improved emergency medical services training.	The preventable death rate decreased from 34% to 15% after implementation. Average prehospital time increased one minute and transport time to hospital increased two and a half minutes after implementation; Appropriate pre-hospital care increased from 34% to 75%; Appropriate emergency department care increased from 38% to 90% after implementation.	Not stated

Synthesis of Evidence about Regionalization of Surveillance Systems for Bioterrorism

In response to the 2001 anthrax attacks, SARS, and the ongoing threat of bioterrorism, surveillance systems designed to detect both bioterrorism and emerging infectious diseases have been deployed throughout the United States and abroad. A systematic review of these systems through April 2002 is available elsewhere.[3, 582] That review identified 115 systems including nine syndromic surveillance systems, 20 systems collecting bioterrorism detector data, 13 systems collecting influenza-related data, and 23 systems collecting laboratory and antimicrobial resistance data that could be used for bioterrorism surveillance.[582] While syndromic surveillance systems have been deployed for both event-based and ongoing bioterrorism surveillance, none has been formally evaluated to determine its accuracy or timeliness.[582] Additionally, efforts to regionalize data collection or analysis were not described for any of the 115 surveillance systems. Understanding the effects of regionalization on the design and implementation of effective surveillance systems for bioterrorism is critical, as this determines the systems' detection capabilities, geographic scope, operations, and organizational structure. Many current syndromic surveillance systems have been implemented locally. Discussions are ongoing to determine how to integrate these systems at the state and national levels. Specifically, CDC is working to create an integrated surveillance system that combines data collected through several of its existing laboratory and clinical surveillance efforts.[583] Understanding the effects of regionalization on the data collection, analysis, and decision making processes of surveillance is essential to these efforts.

Our review of the recent surveillance literature focused on identifying articles that described currently active surveillance systems for bioterrorism and emerging infectious diseases, and understanding the effects of regionalization on these systems. This section presents our results updating the previous literature review of surveillance systems for bioterrorism and emerging infectious diseases, and evaluates current efforts to regionalize surveillance data.

Summary of the Evidence of Regionalization of Surveillance Systems for Bioterrorism

Our search identified 117 articles on surveillance systems. Of these, 32 articles, two government reports, and one Web site described regionalization of surveillance systems.[*] None of the included articles specifically evaluated the effects of regionalization on surveillance processes. CDC has proposed a draft framework for evaluating syndromic surveillance systems with some components that cover aspects of regionalization; however, an application of this framework to an existing surveillance system has yet to be published.[584] Few surveillance systems have been evaluated for their detection capabilities (e.g., sensitivity, specificity, or timeliness).[435] Thus, several ongoing evaluative efforts have focused on optimizing surveillance algorithms and comparing surveillance data with other routinely collected data (e.g., correlating surveillance data with seasonal influenza outbreak data).[74] Some systems have been compared to

[*]References[64-77, 435, 584-603]

simulated outbreaks in weapons of mass destruction exercises, but not with respect to issues of regionalization.[585]

Table 13 presents the evidence from 14 articles about 13 regionalized surveillance systems. Typically, surveillance requires three key processes: data collection, data analysis, and decision making/response. In the following section, we present evidence concerning the regionalization of each of these surveillance processes.

Data Collection. Ideally, surveillance data should be collected from the majority of exposed or ill persons (or representative samples of these) in a geographical region.[586] Current bioterrorism surveillance systems collect a variety of non-traditional data including emergency room,[74, 588, 604] health clinics,[585, 590] calls to poison control,[591] and calls to 911,[69] school absenteeism,[67, 592] and pharmacy sales[593] surveillance data sources. Thus, the geographical areas and patient populations under surveillance will differ dramatically depending on the surveillance data collected. For example, the Electronic Surveillance System for the Early Notification of Community-Based Epidemics (ESSENCE system) developed by the Department of Defense-Global Emerging Infections Systems collects International Classification of Diseases, 9th Revision (ICD-9) data from military installations worldwide.[594] This system has been modified to collect data from civilian facilities in the geographic region around Washington, DC to increase the population under surveillance.[67] The geographic area under surveillance also depends upon which health systems, hospitals, and clinics participate in a given surveillance effort. For example, a surveillance system in the Boston area that utilizes ambulatory data from the Harvard Vanguard Medical Associates is limited to the 5-10% of the population of Eastern Massachusetts covered by this medical group.[590] In contrast, the Syndromic Surveillance Information Collection system,[73] a collaborative project between the University of Washington and the public health department of Seattle/King County, includes four health care systems in King County, and collects data from three emergency departments/urgent cares and nine primary care clinics in the area. While these sites were chosen initially out of "convenience," they were later noted by the system's designers to represent good geographic dispersion with wide patient catchment areas and diverse populations.[73]

Data Analysis. The objective of analyzing surveillance data is to determine whether the observed number of cases exceeds the expected number for a given region or time period. Regionalized analysis of surveillance data can occur in three ways. First, the manner in which data are pooled for analysis can serve to change the geographic region under surveillance. Data collection occurs locally, but data analysis typically integrates data from several local sources (e.g., clinicians, hospitals, and county health departments) to assess the likelihood of an outbreak within a larger geographic region. Second, data analysis can attempt to integrate a variety of data sources in a given geographic region (e.g., West Nile virus in sentinel flocks, clinician reports of flu-like illness, and work absenteeism data). Third, regionalized data analyses collapse data into various time periods (e.g., weekly analyses of the incidence of influenza-like syndrome may be a more sensitive marker of influenza than analyses using daily incidence).[74]

All bioterrorism surveillance systems centralize analysis functions to some degree, and many have automated analysis processes. For example, ESSENCE creates 2,700 syndrome- and location-specific graphs each day; these are automatically analyzed for patterns that require additional investigation.[595] A regionalized approach to data analysis offers four potential benefits. First, it may increase the ability to detect an outbreak over a larger geographic region.

Second, it may improve the ability to identify aberrant trends if data received from one region can be compared to other regions. Third, it may increase cost efficiencies related both to scale (i.e., reduction of redundant analytic activities) and standardization (i.e., single system rather than multiple systems). Fourth, many local health departments do not have personnel with sufficient statistical and epidemiological training to perform the necessary data analysis.[65] Reliance on state or other regional resources may be the only feasible means for performing adequate data analysis. These arguments might suggest that a completely centralized approach to data analysis (i.e., a single, national analysis center) would be the most effective and efficient. However, as Mostashari and Hartman describe, such an approach has several important limitations.[435] Centralized data analysis from hundreds of localities could lead to many alarms triggered by chance alone.[435] Furthermore, centralized data analysis still requires substantial infrastructure investments at the local level to respond successfully to outbreaks.[435] Finally, analysis at a single rather than multiple levels creates the possibility of a single point of catastrophic system failure.[435]

Decision-Making and Response. A key principle of public health surveillance is the use of surveillance data to take appropriate action to minimize resulting morbidity and mortality.[586] Traditionally, this decision-making process occurs primarily at the local level. Ideally, astute clinicians report unusual disease patterns to their local public health departments, which then have jurisdiction to investigate the potential outbreak and disseminate information to public health officials at the state and national levels as appropriate. Clinicians, who typically receive little, if any, training in public health reporting, are not always familiar with standard reporting procedures. They may bypass their local public health department and report directly to the state health department or to CDC. As automated syndromic surveillance systems are implemented at regional and national levels, this issue of where data reporting and decision-making occurs will become increasingly important. While a number of surveillance systems, such as the ones operating in Santa Clara County[74] and Seattle/King County[73] perform decision-making processes primarily at the local level, others, such as the systems operating in New Mexico[76] and Connecticut[64] perform these processes at the state level. Other larger regional systems allow for decision-making at multiple levels. For example, the National Bioterrorism Syndromic Surveillance Demonstration Project, a collaborative project between CDC, American Association of Health Plans, Harvard Medical School, and five health plans based in Massachusetts, Minnesota, Colorado, and Texas, will cover more than 20 million individuals from all 50 states.[68] Data will be analyzed at a centralized data center and decisions on new cluster identification will be performed centrally, but identification of an abnormal cluster of events will generate an alarm that will be automatically sent to the local health department in the affected area for further decision making and response.[68]

Given the lack of experience interpreting syndromic surveillance data, response protocols have yet to be fully defined. In general, the public health officials responsible for analysis of surveillance data are also responsible for the initial outbreak investigation. However, questions remain as to who owns these surveillance systems. With ownership comes responsibility and accountability for decisions made based on surveillance data and their analyses. As some authors have previously noted, many organizations are key stakeholders of surveillance systems, including local, state and national public health departments; academic centers; and commercial entities.[435] While local public health officials often have the legal mandate for decision making and response, expertise and resources are often concentrated at the state and national public

health level or in the academic and commercial sectors.[435] Successful surveillance will likely require a collaborative effort between key stakeholders, but ultimate ownership still remains to be determined.

Application of Evaluation Criteria to the Surveillance Literature

This section discusses the results of applying the relevant evaluation criteria to the surveillance literature: network design, coordination of surveillance and management of incentives, management of information, volume-outcome associations, and incident command. None of the included articles presented information relevant to inventory management or postponement and modularization.

Network Design. The concept of network design as applied to surveillance systems describes how the structure of a surveillance system affects its detection characteristics. An ideal surveillance network will not only detect aberrant disease patterns but will do so in an efficient and timely manner. Our review highlighted four key network design issues affecting implementation and evaluation of regionalized surveillance systems.

First, the geographic range of a surveillance system should be sufficiently far-reaching to enable detection of an outbreak that may be spread over a large geographic area. For example, detection of a bioterrorism event occurring in the New York City subway system requires a surveillance system with detection capability not only in Manhattan and other boroughs of New York City, but also in the outlying suburban regions of New York State, New Jersey, and Connecticut. Currently, many surveillance systems are designed along county or state lines. As the recent outbreaks of SARS and monkey pox have shown, disease is not limited to these politically-oriented geographic divisions. Accordingly, it is likely that current artificial geographic boundaries will have to be overcome if surveillance systems are to be maximally effective.

Second, a key objective in analyzing surveillance data is to maximize detection of the signal to noise ratio. Research is currently ongoing to assess how best to divide a surveillance region into subregions so as to maximize the ability to detect abnormal events. For example, ESSENCE uses SaTScan—free software developed with federal funds to detect geographic trends in cancer incidence—to facilitate detection of abnormal clusters within surveillance regions.[592] Other systems perform similar analyses.[596, 597] Determining the optimum size and location of data collection regions is critical for effective surveillance. A region that is too small may result in missed cases and unacceptable data variability due to the small sample size. A region that is too large may result in reduced ability to detect small variations due to increased scale.[592] It is often not possible to perfectly subdivide geographic regions given pre-existing constraints on supplied data. This can be particularly problematic when combining surveillance data from civilian hospitals within a given geographic region with data from local military or VA facilities, which tend to have patients from significantly broader geographic areas. Interpretation of these surveillance data may be enhanced by temporospatial analyses.

Third, the literature provides no consensus about how much data must be collected to have a representative sample of the population under surveillance. Evidence suggests that a surveillance system need not cover the entire population to be able to detect an outbreak, and that coverage as low as 5-10% of the population surveyed may be clinically useful.[590] Additionally, a

system that collects surveillance data from only a representative segment of the population may be more cost-effective than collecting data on the entire population in a geographic region, as has been proposed.[435] It is unknown what the ideal distribution of surveillance collections sites is for a cost-effective bioterrorism surveillance system.

Fourth, an ideal surveillance network incorporates redundancy so as to avoid system failure at any process step. Redundancy in surveillance systems can occur in a number of ways; two are highlighted here. First, while an effective surveillance system will have centralized analysis functions, some (limited) analysis could also be performed by other entities within the system, or even by entities outside of the surveillance system. Such overlap will help prevent detection failure due to incorrect analytic methodology or data types, as may have occurred during the drop-in surveillance in Japan during the 2000 G8 meeting when the system missed an outbreak of *Vibrio parahemolyticus* among policemen who ate prepared lunches.[598] Second, an effective system will likely include a large number of potentially redundant data sources to increase detection capability. An evaluation of ESSENCE performance during a simulated bioterrorist outbreak using four data sets (ER visits, office visits, over-the-counter influenza medication sales, and school absenteeism) showed improved detection capability when all four data types were used for analysis rather than just ER visits or school absenteeism alone.[67]

Coordination of Surveillance System and Management of Incentives. A clear understanding and alignment of incentives of key stakeholders involved in each of the surveillance processes may facilitate bioterrorism surveillance. Key stakeholders involved in surveillance systems include: data collectors, data analysts, and decisionmakers.

***Data Collectors*.** Data collectors for surveillance systems include: those providing traditional clinical surveillance data such as outpatient clinicians, emergency department personnel, and clinical laboratories, as well as non-traditional data providers such as schools (providing absenteeism data), animal control personnel, and retail pharmacies. Providing incentives to data collectors is critical and difficult for three reasons. First, a surveillance system is only as good as its data. Second, many data collectors have few available resources to devote to surveillance, as they are already overburdened by their routine workloads. In an implementation of the Real-time Outbreak Detection System (RODS) system in the Pittsburgh area, local health departments requested that the RODS laboratory monitor output of the surveillance system because they did not have sufficient resources.[65] Third, data collectors may have the least to gain from implementing surveillance systems. Some may be fulfilling legally mandated requirements, while others satisfy a sense of civic responsibility, but data collectors may not perceive any other benefits. Indeed, many institutions may have disincentives to providing data. A hospital that provides data that sets off an alarm may be closed until further investigation; a pharmacy that provides over-the-counter sales data that becomes public might be at a competitive disadvantage; and a school that reports increased absenteeism may lose funding due to high absenteeism rates.

Chavin and Valleron studied the motivation of 560 French general practitioners for participating in a public health surveillance network.[599] These clinicians reported an interest in contributing to the public health (39.5%), a scientific interest in epidemiology (24.8%) or in receiving epidemiologic feedback (17%), and receiving gratification for their supplementary role (10.5%) as their primary motivations for contributing to the surveillance network.[599] Efforts to motivate data collectors, provide them with timely feedback, and emphasize “dual use” characteristics of the data or their analyses may lead to improved collection of surveillance data.

In general, designers of surveillance systems have recognized the need to reduce the burden on data collectors. One goal of the National Bioterrorism Syndromic Surveillance Demonstration Project will be to utilize data that is already routinely collected as part of daily operations, so as to generate minimal incremental costs and resources.[68] Economic benefits, ranging from resources to help implement such surveillance systems, to tax benefits for those who participate, may provide additional incentives to data collectors.

Public Health Data Analysts and Decisionmakers. The incentives for public health officials to implement and maintain bioterrorism surveillance systems include: their legal mandate and responsibility for the protection of public health, resources made available for these activities, and the potential costs of inaction. However, given the lack of evidence demonstrating effectiveness of surveillance systems, some public health departments have chosen to allocate bioterrorism preparedness resources away from surveillance programs and toward clinician education, the purchase of decontamination equipment, and other preparedness programs. Thus, a priority in incentivizing public health decisionmakers to deploy and maintain surveillance systems is to demonstrate that surveillance systems can fulfill their stated purpose. While this may be difficult, particularly in the absence of a large-scale bioterrorism event, effectiveness in simulated scenarios and capability to detect other naturally occurring outbreaks may lend credence to such systems. In addition, while legal authority to investigate outbreaks is often given at the state and local level, funding for surveillance systems is increasingly provided at the federal level. Should a national surveillance system be implemented, a disincentive might arise, particularly at the local level, if such a system bypasses the traditional reporting and decision-making hierarchy and leaves local health officials effectively out of the loop. Because local public health officials often have limited resources and personnel to devote to surveillance, they might prefer that analysis be performed by other entities.[65] Therefore, a careful balance must be achieved between not over-burdening local health officials with surveillance activities while keeping them intimately involved in the surveillance process. Finally, to the extent that public health decisionmakers are motivated by the cost of inaction, it may be useful to convey the potentially high cost of inaction during a bioterrorist attack. Conservative estimates of the cost of a bioterrorist attack range from $478 million per 100,000 persons exposed to brucellosis to $26.2 billion per 100,000 persons exposed to anthrax.[600]

Volume-Outcome Associations. An increased volume of data collection and analysis should improve surveillance to the extent that it results in systems with more rigorous data sets, smaller confidence intervals, and analysts with improved capacity for recognizing abnormal disease clusters. This reasoning has contributed to the expansion and centralization of surveillance networks. For example, increasing data volume has allowed ESSENCE investigators to refine their surveillance algorithms and improve detection capability.[67] However, increased volume does not always ensure improved outcomes. Increased volume will necessitate increased resources for data collection and analysis. If routinely collected data are used, the incremental costs may be small, but substantial investments still must be made in computing infrastructure and personnel training as a system increases in size and complexity. Such investments may be barriers to implementing a high-volume system. In addition, high volume does not necessarily ensure good outcomes if there is not a concomitant emphasis on quality. Without quality controls in surveillance processes, an increase in volume will only

result in propagation of errors. Therefore, evaluation of a surveillance system's volume and outcomes must also include an assessment of incremental costs and overall quality.

Incident Command. Effective surveillance systems will almost certainly facilitate incident command during bioterrorism responses. Identifying which entity has ultimate decision-making capability and responsibility is often complicated by the many stakeholders involved in the surveillance process. Ideally, the structure of public health response should be determined before an outbreak and should depend upon the severity of outbreak. Drop-in surveillance efforts provide good examples of how incident command and response protocols can be established before an event occurs. For example, the surveillance program developed for the 2000 Olympic Games in Sydney, Australia established a Health Olympic Coordinating Centre which received input from the regional Department of Health, metropolitan Sydney public health units, area sentinel hospitals, and other health-related facilities.[601] This center assessed health surveillance information and coordinated data analysis.[601] Participation in this surveillance effort resulted in strong ties between the regional health department, local public health units, local governments, and other area health facilities and providers.[602] Perhaps more importantly, this program led to an improved understanding of "respective roles and functions" in surveillance preparedness, a key benefit that will help in responding to potential future outbreaks.[602]

Management of Information. Surveillance systems must transfer and manage information between participants within and outside of the system. As surveillance networks expand to include participants with different computing infrastructures, management of information will likely become increasingly complex. This may involve integrating different computing systems and data streams, while allowing information and analysis to flow upwards and downwards within the system to appropriate end-users. Several barriers impede efficient management of information, including lack of national reporting standards, lack of conversion and translation systems for communication between systems, and legal requirements regarding patient confidentiality. CDC has initiated the National Electronic Disease Surveillance System partly to address the lack of standardization among surveillance systems.[587] This program focuses on developing national standards for computing infrastructure and reporting for surveillance systems. Other initiatives, like the Frontlines of Medicine Project, aim to develop non-proprietary, "open" standards for communication between emergency rooms.[587] The development of multiple industry standards may be avoided by increased collaboration among major systems developers, as has occurred in the National Bioterrorism Syndromic Surveillance Demonstration Program.[68] Integration of new participants into surveillance programs is often hampered by differing computing platforms. In the Syndromic Surveillance Information Collection System[73] in Seattle, many of the information technology groups involved in the network developed their own reporting and transfer strategies.[65] In response, investigators had to develop central conversion capabilities. Such translation capabilities will become increasingly important as surveillance systems expand to include data collectors who may have legacy computing platforms. Finally, new privacy regulations from the Health Insurance Portability and Accountability Act (HIPAA) require additional measures to be undertaken to ensure patient confidentiality.[603] Existing systems that lack standardized confidentiality and security procedures may violate HIPAA standards. One of the National Electronic Disease Surveillance System's goals is to establish standardized security and confidentiality protocols.[603] Surveillance

systems have evolved as well. Several state-of-the-art systems strip away individual-level information, utilizing these data only when an abnormal disease pattern has been identified.[68]

Lessons Learned From Regionalization of Surveillance Systems

Regionalization of surveillance systems has important implications for key processes related to data collection, analysis, and decision making and response.

1. *There is a need for evaluations of regionalization of surveillance data collection and analysis.* Although numerous syndromic surveillance efforts in local areas are promising, there has not been an evaluation of the tradeoffs in terms of costs and benefits of regionalizing some components of bioterrorism surveillance (e.g., costs of data collection, analysis and reporting, false positive and false negative rates). Given this lack of evaluative data, we developed a simulation model to evaluate some of these costs and benefits. This model is presented in the next section.

2. *Local data collectors may not be incentivized to collect surveillance data, particularly if they are analyzed regionally.* If a regionalized surveillance system is based on a model of local data collection with regional analysis, considerations of means to reduce costs of data collection and to share relevant analyses with local data collectors may enhance local participation.

3. *Decision-making and chain of command must be clear to all stakeholders.* Decision-making and response could occur at the local, state, regional, or national level, and would depend on outbreak characteristics and the level of response needed.

4. *A common technology platform may facilitate the collection and analysis of surveillance data.* This common platform may be composed of new technologic infrastructure or translation tools that enable existing legacy systems to communicate with one another.

5. *Privacy issues are a key concern as increasingly detailed surveillance data is collected and disseminated.* Collection and analysis of surveillance data must be able to protect individual privacy while being sufficiently detailed to detect new outbreaks.

Table 13. Syndromic Surveillance Systems

System	Geographic Area Under Surveillance	Participants	Data Sources/Types
Connecticut Hospital Admissions Syndromic Surveillance[64]	Connecticut	Connecticut Dept of Health, 31 acute care hospitals	Non-scheduled hospital admission data

System	Geographic Area Under Surveillance	Participants	Data Sources/Types
Denver Center for Public Health Preparedness[65]	Denver, Colorado area	Denver Public Health Dept, one hospital, one ED*, EMS, ~24 community- and school-based clinics, poison/drug center	Chief complaint data (nurse advice line, ED, EMS), ICD-9 data (ED, hospital, clinics)
Electronic Surveillance System for the Early Notification of Community-based Epidemics I (ESSENCE I)[66]	All military installations worldwide	104 DoD primary care and emergency clinics, 121 Army, 100 Navy, 80 Air Force, and two Coast Guard installations	ICD-9 data
Electronic Surveillance System for the Early Notification of Community-based Epidemics II (ESSENCE II)[67]	Northern Capital Area (Washington, D.C. area)	Military and civilian data from area emergency rooms and clinics, local pharmacies, nurse hotline, school system local veterinaries, area laboratories	ICD-9 data (clinics), chief complaint data (ED), over the counter drug sales, nurse hotline calls, school absenteeism reports, veterinary reports, laboratory reports
Indianapolis Network for Patient Care[65]	Indianapolis, Indiana area	Five health systems, Indiana University School of Medicine, Regenstrief Institute, 11 hospitals, county health dept, MD practices	Chief complaint data, coded diagnoses and procedures, immunizations, medications, allergies, electrocardiogram tracings, echocardiogram data, radiographic images, vital signs, demographic data
National Bioterrorism Syndromic Surveillance Demonstration Program[68]	National, although data from five health plans based in four states	CDC, American Assoc of Health Plans, Harvard University, five health plans based in Massachusetts, Minnesota, Colorado, and Texas	Ambulatory care data – focus on aggregated data rather than encounter level data
New Hampshire ED Syndromic Surveillance System[68]	New Hampshire	16 sentinel EDs	Data manually collected on four syndromic categories
New York City System[69]	New York City metropolitan area	EMS data	EMS data, pharmacy sales data
Real-Time Outbreak Detection System[65, 70, 71]	Pittsburgh, Pennsylvania area	17 hospitals, University of Pittsburgh	ICD-9 data, chief complaint data
Syndromic Surveillance for Bioterrorism[72]	Minneapolis/St Paul Minnesota area	HealthPartners Medical Group, Minnesota Dept of Health	Pt encounter data, ICD-9 data
Syndromic Surveillance Information Collection System[73]	Seattle, Washington area	Four health care systems, University of Wash, three EDs, 10 clinics, EMS, school system	ICD-9 data, demographics, chief complaint data, school absenteeism reports, EMS dispatch data

System	Geographic Area Under Surveillance	Participants	Data Sources/Types
Syndromic Surveillance Tally Sheet[74]	Santa Clara County, California	12 EDs, one telephone care center	Data manually collected on six syndromic categories
Syndromic Surveillance Using Automated Medical Records[75]	Boston, Massachusetts area	All clinics associated with Harvard Vanguard Medical Associates	Automated medical records of large group practice including ICD-9 data, vital signs, full text notes, telephone call data
The Biosurveillance Analysis, Feedback, Evaluation and Response System[76]	New Mexico	Six EDs, University of New Mexico, New Mexico Department of Health, EMS, regional poison center, state medical examiner's office	Clinical data elements from ED/EMS, hospital data (admission, discharge, transfer, utilization, chief complaints, demographics), calls to poison center, laboratory tests results, medical examiner office's reports
West Nile Virus Passive Surveillance System[77]	New York City	Dead bird sightings by residents	Dead bird data compared with virologic testing

*ED = emergency department

Simulation Model Results: Regionalization of Surveillance

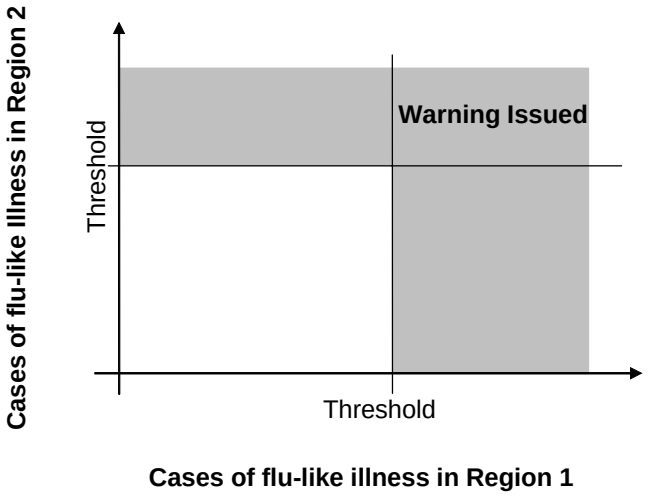
We found no evaluative evidence regarding regionalized analysis of surveillance data for the detection of a bioterrorism event. Therefore, we developed a simulation model to explore the tradeoffs associated with strategies for regionalizing the analysis of surveillance data. In this section we present a summary of the methods and assumptions used to develop our simulation model and our preliminary results from it. We direct readers interested in the details of our simulation elsewhere.[78]

Changing Thresholds When Pooling Surveillance Data

To illustrate the general tradeoffs that occur when analysis of surveillance data is regionalized, we simulated a syndromic surveillance system that collects daily reports of a syndrome of interest from two regions (i.e., cases of flu-like illness). Analysis of these surveillance data could be unpooled (in which case reports from the two regions are analyzed separately) or pooled (in which case data from the two regions are combined before analysis). We assumed that if the number of cases of flu-like illness exceeds a threshold, then a warning will be issued. Since the number of patients with these symptoms varies from day to day, there is a chance that normal variation will cause the observed number of cases to exceed the warning threshold even when there is no outbreak resulting from bioterrorism. We refer to such a situation as a false positive (i.e., a false alarm). We assume that the thresholds are set so that the probability of a false positive does not exceed a level that represents a decisionmaker's preferences for false positives.

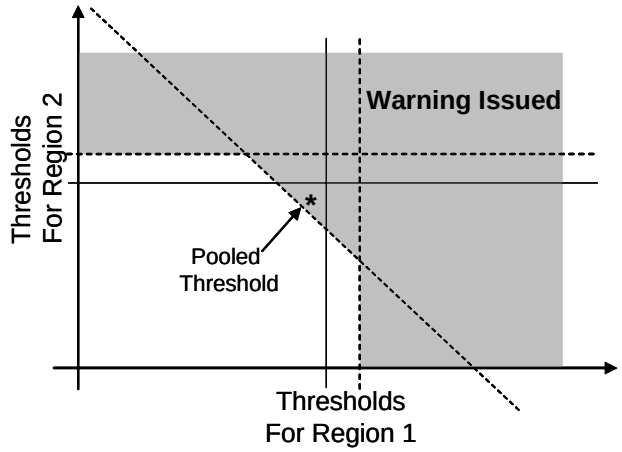
Figure 8 illustrates the detection thresholds for two regions. The number of cases of flu-like illness for Region 1 is plotted on the *x*-axis and the number of cases for Region 2 is plotted on the *y*-axis. For each of the two regions we illustrate the threshold above which a warning will be issued indicating an unexpected peak in cases of flu-like illness. The entire shaded area in Figure 8 represents the numbers of case reports from the regions that would cause a warning to be issued.

Figure 8. Thresholds for Detection of Outbreaks in Two Regions



When data from two regions are pooled, the warning thresholds may need to be modified to prevent an increase in the probability of false positives. This situation is illustrated in Figure 9. A simple way to pool data is to calculate the sum of cases in both regions. Figure 9 shows a diagonal line that represents a threshold for the pooled data. The space between the diagonal line and the individual thresholds (indicated by an asterisk) represents case reports in the two regions for which a warning would not be issued if data from the two regions were analyzed individually (unpooled) but a warning would be issued it the data were pooled (using the sum). If the thresholds for the two regions are not adjusted, then the use of pooled data will increase not only the probability of detecting an outbreak associated with bioterrorism but also the probability of a false positive. The overall probability of a false positive can be held constant by increasing the values of the individual thresholds. In Figure 9, the thresholds for Regions 1 and 2 have been increased so that the probability of exceeding either threshold decreases by an amount that offsets the increase in probability associated with using pooled data.

Figure 9: Illustration of Pooled and Individual Thresholds for Detection of Outbreaks in Two Regions



Unpooled thresholds are denoted by the solid lines.
Pooled thresholds are denoted by the broken lines.

*The area indicated with an asterisk indicates cases for which a warning would be issued with the pooled thresholds but not the unpooled thresholds.

The Effect of Inter-Regional Correlation on Pooled Surveillance Data

To investigate tradeoffs that occur when pooling surveillance data, we simulated data representing a bioterrorism attack in two regions that collect syndromic surveillance data. We simulated the daily number of cases for a syndrome of interest (i.e., fever and rash) representing both naturally occurring cases and an increase in the number of cases associated with bioterrorism. The baseline number of cases for each region was normally distributed with a mean of 100 cases per day and standard deviation of 100 cases per day. We varied the attack size so that between 0 and 350 additional patients with fever and rash presented per region per day. We set the threshold for detecting an outbreak as the total number of cases more than two standard deviations above the daily average.

We simulated correlations that may exist in surveillance data collected from two sources eligible for pooling. The correlation between two regions describes the extent to which the number of cases in each region is similar on a day-to-day basis. The correlation varies between 1 and -1. A correlation of 1 indicates a perfect positive relationship between the number of cases in each region and a correlation of -1 indicates a perfect negative relationship between the number of cases in each region. If the inter-regional correlation was 1, an increase of one case in Region 1 would always correspond with an increase of one case in Region 2. A correlation of zero would indicate that there is no relationship between the numbers of cases in the two regions. The correlation between two sources of surveillance data may vary according to the geographic proximity of the two regions, the types of surveillance data collected (e.g., one region may report cases of patients presenting to triage nurses with fever and rash as opposed to cases of fever and

rash collected from ICD-9 codes from outpatient clinics), and the patient populations under surveillance (e.g., pediatric as opposed to nursing home patients). We varied the correlation between the two regions between 0 and 0.5.

We compared the probability of detecting an outbreak of cases of fever and rash when using pooled data as opposed to using individual data. We found that pooling surveillance data may yield modest benefits in the probability of detecting an outbreak, particularly when there is no correlation between the regions. The benefits of pooling are smallest when attack sizes are very large or very small. We found that the rate of false alarms increases as the correlation between the pooled data sources increases. We evaluated a number of different strategies for pooling data and determining thresholds. For all strategies that we considered, all large attacks were readily detected. However, pooling did yield some benefit for smaller attacks.

Lessons Learned for Regionalization of Analysis of Surveillance Data

Our simulations demonstrate two primary effects of pooling surveillance data.

1. *Large outbreaks are relatively easy to detect when using either pooled or unpooled data. However, smaller outbreaks can be difficult to detect under both strategies.* In part, it is difficult to detect small outbreaks because the standard deviation about the mean is relatively large compared to small increases in numbers of cases. When the pooled threshold is increased to avoid increasing the false positive rate, small outbreaks can be missed.

2. *Pooling strategies may improve detection capabilities but are highly situation-specific.* Pooling of surveillance data enhanced detection capabilities when the correlation between the individual regions was very low. We plan addition analyses to determine the effects of pooling over time and extending our analyses to pool more than two regions.

Simulation Model Results: Inventory Management

In this section, we present a summary of the methods and assumptions used to develop our simulation model and preliminary results from it. We direct readers interested in the details of our simulation elsewhere.[79]

Summary of Inventory Management Simulation Model

We simulated a bioterrorism attack with *Bacillus anthracis* on a metropolitan area with a population of 5 million. Selection of parameter values was informed by our review of the U.S. experience with inhalational anthrax.[152] We assumed that exposed individuals enter the incubation phase of the disease and may then progress to first stage anthrax, second stage anthrax, or death.[152, 605, 606] We defined first stage anthrax as symptomatic disease with a

nonspecific flu-like syndrome consisting of low-grade fevers, nonproductive cough, myalgias, and malaise (sometimes referred to as the "latent" phase of the disease).[152, 605, 606] We defined second stage anthrax is severe symptomatic disease characterized by abrupt respiratory distress, shock, and death within 24 hours (sometimes called the "acute" phase of the disease).[152, 605, 606] We assumed no anthrax-related deaths would occur except among individuals in the second stage of infection.

We assumed that all exposed individuals were initially unaware of the attack and that exposed individuals might become aware of the attack either through development of symptoms or through the media or public health alerts. After becoming aware of the attack, individuals who are aware of their potential exposure may seek post-exposure prophylaxis and enter a queue for prophylactic antibiotics.[607] For exposed individuals, we assumed that the rate of disease progression (from incubation to first stage) is reduced by prophylactic antibiotics and that prophylactic antibiotics are distributed on a first-come, first-served basis.[607, 608] We assumed that the rate at which individuals receive prophylactic antibiotics is limited by the availability of prophylactic antibiotics and the distribution capacity for these antibiotics. We based estimates of adherence to prophylactic antibiotic regimens on the 2001 experience.[152, 206, 605]

Individuals who develop symptoms associated with first or second stage anthrax may enter a queue for treatment. Treatment consists of a triple antibiotic regimen (ciprofloxacin or doxycycline with rifampin and clindamycin) administered intravenously in an intensive care setting and may also include supportive care (e.g., pleural fluid drainage, respiratory or cardiac support, etc.).[*607, 611] We assumed that treatment would be restricted to symptomatic individuals. We assumed that the ability to treat patients is limited by the inventory of intravenous antibiotics, the number of available intensive care unit beds, the number of available ventilators, and the number of available respiratory technicians. We assumed that when patients begin treatment a small supply of antibiotics is reserved for them so that there is little chance that they will need to leave treatment due to a lack of antibiotics.

We considered scenarios that differ in the number of people exposed to anthrax. In the low-exposure scenario (such as an aerosol release over a sports stadium), we assumed that 50,000 people were exposed.[605, 612] In the high-exposure scenario (such as an aerosol release from an airplane over the downtown area of the city), we assumed that 250,000 people were exposed.[605, 612] We also considered scenarios that differ in the number of people likely to require prophylactic antibiotics. If an attack occurs in such a way that responders can determine whether or not a person was likely to have been exposed, the number of people requiring prophylaxis will be lower than if an attack occurs such that responders cannot make this determination. In the latter scenario, we assumed that only exposed people would request prophylaxis; whereas, in the former, we assumed that both exposed and non-exposed people would request prophylaxis, resulting in inefficiently allocated resources, and slowed queues.

We assumed that responders would first use the local inventories of antibiotics (if available), then Push Packs from the Strategic National Stockpile, then regional Vendor Managed Inventories or additional Push Packs.[613, 614] We based our estimates of the antibiotic inventories of local communities on a survey of ten hospitals in New Jersey[13] and other reports.[†201, 616-619]

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[*] All drug costs were derived from the Department of Veterans Affairs' product pricing and fee schedules (VA 340B program) except for the price of oral ciprofloxacin, which was based on agreements between Bayer A.G. and the Department of Health and Human Resources.[609, 610]

[†] We assumed that the annual cost to maintain a local inventory of antibiotics includes annual rotation costs plus storage fees.[615] We assumed that all local stocks must be replaced if an attack occurs, and that the annual maintenance costs are incurred in perpetuity.

We based our estimates of the types and numbers of individuals needed to operate and staff a mass prophylaxis distribution center from the Weill-Cornell Mass Prophylaxis/Vaccination model.[620]

Summary of Preliminary Results of an Inventory Management Simulation Model

We found that mortality associated with anthrax bioterrorism in our simulation is very sensitive to the number of people seeking prophylactic antibiotics. For both the low and high exposure attacks, we found that approximately 30% of the exposed population died given a low demand for prophylaxis (i.e., the situation in which exposure can be readily determined) compared to approximately 45% of the exposed population given high demand for prophylaxis (i.e., the situation in which exposure cannot be readily determined so many unexposed persons seek prophylaxis). This difference represents an increase in mortality of approximately 8000 exposed individuals for the low exposure attack and 35,000 exposed individuals for the high exposure attack attributed to high demand for prophylactic antibiotics.

We compared the mortality that resulted if only a single Push Pack was delivered to the site of attack (and then the local responders had to wait until the regional Vendor Managed Inventory arrived) compared with an alternative strategy in which a Push Pack was delivered every six hours following the arrival of the first Push Pack, until either all 12 Push Packs have been delivered or the regional Vendor Managed Inventory becomes available. We refer to these as Single Push Pack and Multiple Push Pack strategies. We found that the Multiple Push Pack strategy has little benefit for a low exposure attack but can have a significant benefit for the high exposure attack (i.e., 1-2% reduction in mortality compared with the Single Push Pack strategy).

We evaluated whether increasing or decreasing the number of Push Packs would change the delay in delivery of a Push Pack to an attack site. There are currently 12 Push Packs in the United States that are reportedly able to arrive at the site of an attack within 12 hours of a request.[621] The locations of these Push Packs are not publicly available. If we assume that the Push Packs are geographically distributed across the United States, then every location in the United States could be reached with a maximum of approximately one hour of flight time. We found that our model was much less sensitive to increasing or decreasing the number of Push Packs than it was to increasing or decreasing the time it takes to dispense the contents of the Push Pack. However, for a high exposure attack, an additional Push Pack may have some benefit when the Multiple Push Pack strategy is used. The risk of a bioterrorism event may be proportional to population density. Thus, we plan to evaluate the effects of changing the number of Push Packs, if the Push Packs are initially distributed according to population density.

We evaluated the cost effectiveness of changing the size of the local inventory of antibiotics. Increasing the local stockpile would require a one-time cost to purchase the supplies, plus annual costs associated with maintaining the inventory. Because the net present value of all costs and health benefits is a function of the probability of an attack, we estimated the cost effectiveness of increasing the size of the local inventory if the annual probability of an attack ranges between 0.01% to 1%. We found that the cost effectiveness of increasing the size of the local stockpile is highly dependent on the annual probability of an attack. However, the total costs are not very sensitive to the probability of an attack. This is because the annual maintenance costs of the additional stock accounts for 80-85% of the total costs, and these costs are completely insensitive

to the probability of an attack, as they must be incurred every year regardless of whether an attack takes place.

Lessons Learned from the Inventory Management Simulation Model

We draw four lessons from the preliminary results of our inventory management simulation model.

1. *The mortality associated with anthrax bioterrorism may be highly sensitive to the number of people seeking prophylactic antibiotics.* Whereas responders and the public may be able to estimate the probability of exposure for an attack in a localized area (e.g., an attack in a particular building), establishing whether an individual has been exposed to a biothreat agent may be difficult for many types of bioterrorism events (e.g., an aerosolized attack over a metropolitan area).

2. *For a large-scale bioterrorism event, delivering multiple Push Packs until delivery of the regional Vendor Managed Inventory may reduce mortality.* In our preliminary analyses, we explored two strategies for delivering Push Packs to an affected area and found that a strategy of deploying a second Push Pack before the first one is depleted may save lives during a large-scale bioterrorism event. In our subsequent analyses, we plan to evaluate other strategies for dispensing antibiotics on the basis of the on-hand inventory (e.g., dispensing only short courses of prophylactic antibiotics if the on-hand inventory is low or if the demand for antibiotics is high).

3. *Assuming uniform geographic distribution of the Push Packs, we found no significant change in the time required to deliver a Push Pack to an attack site with changes in total Push Pack numbers.* However, the risk of a bioterrorism event may be higher in areas of the greatest population density. In future analysis, we plan to evaluate the impact of changes in the number of Push Packs if they are geographically distributed according to population density.

4. *Increasing the size of the local inventories of antibiotics may be cost effective if the annual probability of an attack is high.* The cost effectiveness of increasing the size of local inventories of antibiotics was sensitive to both the probability of an attack and the costs of the inventory.

Summary Synthesis of Evidence about Regionalization for Bioterrorism Preparedness and Response

This section summarizes the evidence from each of the preceding results sections and provides our responses to each of the Key Questions.

Key Question 1. What are the key tasks of local responders during a bioterrorism event?

Key Question 2. What resources do local responders require to perform the tasks identified in Key Question 1?

The preceding sections in this chapter have discussed the regionalization of supply chains; existing infrastructure for regional response to bioterrorism; actual regional responses to the 2001 anthrax attacks, naturally occurring outbreaks, and natural disasters; regionalization of emergency trauma care; and regionalized surveillance systems. From the literature described in each section, we abstracted information about the tasks of local responders during a bioterrorism response (Key Question 1) and information about the resources required to perform those tasks (Key Question 2). In this section we synthesize all of the information about the tasks of local responders during bioterrorism-relevant events. We present our response to Key Questions 1 and 2 in Table 14.

The included articles describe nine main task categories: preparedness planning, field assessment and triage, diagnosis, management of the acutely ill, prevention of the spread of disease, surveillance, outbreak investigation, communication, and emergency management. For each of these main tasks, we considered the subtasks responders are required to perform. For example, subtasks of surveillance include collection, analysis, and reporting of surveillance data.

Broadly, the resources required for these tasks and subtasks are described by three main categories: personnel, material, and information. Additionally, for each task, financial resources are required to train and employ the relevant personnel and to procure and maintain the relevant materials and information.

We conclude that a bioterrorism response requires numerous, heterogeneous tasks requiring a complex array of trained personnel, material, and information. We define these three categories broadly. For example, material resources include any of the physical resources required for a bioterrorism response ranging from vaccines and pharmaceutical supplies to hospital beds and isolation rooms. The performance of these tasks and the delivery of these resources are potential targets for regionalization.

Table 14. Examples of Tasks, Subtasks, and Resources Required for a Bioterrorism Response

Main Task	Example Subtasks	Example Resources
Preparedness planning	• Planning for distribution and dispensing of prophylactic antibiotics • Relationship development (partnering) among responder groups • Pre-event vaccinations of first responders and health care workers • Planning, execution, and evaluation of preparedness drills	<u>Personnel</u> • Decisionmakers from hospitals, emergency management, and public health (e.g., CDC) • Representatives of relevant government agencies (e.g., FEMA and HRSA) • Representatives of relevant non-government bodies (e.g., Joint Commission on Accreditation of Healthcare Organizations, American Hospital Association) • Logisticians <u>Material</u> • Necessary vaccines and supplies for pre-attack vaccination • Guidelines for preparedness planning

Main Task	Example Subtasks	Example Resources
	• Determination of local capacity (e.g., hospital and laboratory capacity) and planning for surge capacity	Information • Understanding of relevant organizations and their scope of responsibility at each regional response level • Understanding of the regional and national resources in place to assist a local community in the event of a bioterrorism event • Familiarity with preparedness plans through drills and other training exercises • Understanding of changes needed to guidelines based on real-time feedback from bioterrorism affected areas (e.g., revisions to treatment protocol based on what is working in field during an attack)
Field assessment and triage	• Transportation of victims • Use of portable diagnostic and detection equipment • First responder protection • Determination of probability of exposure to biothreat agent • Environmental testing for biothreat agents	Personnel • Local first responders and those obtained through mutual aid agreements • Logisticians Material • Transportation equipment • Decontamination equipment • First responder protective gear • Portable diagnostic detection equipment Information • Sensitivity and specificity data for portable detection equipment • Updated information about emerging outbreaks and necessary personal protective equipment
Diagnosis	• Ordering of appropriate diagnostic tests • Interpretation of diagnostic test results	Personnel • Clinicians • First responders Material • Decision support systems to facilitate diagnostic decision making • Sufficient laboratory surge capacity for large increases in test requests Information • Test result data • Updated information about emerging outbreak updates to inform assessments of pretest probability of disease • Information about the natural history of bioterrorism-related diseases, their clinical presentation, and relevant diagnostic tests
Management of acutely ill	• Provision of definitive medical care • Fatality management • Distribution of supplies, equipment, and pharmaceuticals	Personnel • Clinicians • Security personnel to maintain security of hospitals • Mental health professionals • Pharmacists • Logisticians Material • Inventories of pharmaceuticals • Negative pressure isolation facilities • Critical care equipment: ventilators, chest tubes, oxygen delivery systems • Morgue facilities • Hospital surge capacity Information • Management guidelines from public health officials for clinicians • Information systems to manage the flow of patients through the hospital • Radiographic, laboratory, and clinical data

Main Task	Example Subtasks	Example Resources
Prevention of the spread of disease	• Prophylaxis of the exposed • Mass immunization • Isolation of infectious patients • Evacuation • Quarantine • Crowd and traffic control • Vector control	Personnel • Clinicians • Public health officials • Other public employees to serve as non-medical staff at dispensing sites • Members of the media to inform the public about prophylaxis and quarantine policies • Logisticians • Pharmacists to sort, re-package, and dispense medications • Security personnel to enforce quarantine and evacuation, maintain social order, manage traffic near hospitals and distribution sites • Vector control professionals Material • Pharmaceuticals and supplies for prophylaxis (e.g., vaccines, antibiotics, needles, and dressings) • Negative pressure isolation facilities • Sites for mass vaccination (e.g., schools and military facilities) • Parking • Supplies for mass care in the event of a large-scale evacuation (e.g., tents, food, portable toilets, etc.) Information • Prevention guidelines from public health officials for clinicians • Statutes and regulations relevant to quarantine decisions • Contraindications for prophylactic treatment • Home-care instructions for patients receiving prophylaxis and home treatment • Information regarding characteristics of infectious agent for decision making about quarantine, isolation, and evacuation
Surveillance	• Collection of surveillance data • Analysis of surveillance data • Reporting of surveillance analyses to relevant decisionmakers	Personnel • Clinicians, laboratory personnel, vector control professionals, animal control professionals, pharmacists and others for collection of bioterrorism surveillance data • Public health officials to collect, analyze and interpret surveillance data Material • Environmental detectors • Collection equipment for taking environmental samples in the field Information • Baseline data for bioterrorism-related syndromes • Sensitivity and specificity data for portable detection equipment
Outbreak investigation	• Contact tracing • Verification that the cases identified from the surveillance data represent an outbreak	Personnel • Epidemiologists and other public health officials • EIS officers Material • Laboratory capacity to verify suspected cases Information • Information about the characteristics of the exposure • Information about the person-to-person transmissibility of the biothreat agent used
Communication	• Communication system development • Clinicians' reporting of information about suspicious cases to public health authorities	Personnel • Public health officers • Clinicians and first responders • Members of the media • Trained personnel to staff information hotlines • Public health officials at all response levels

Main Task	Example Subtasks	Example Resources
	• Public health officials communicating news of outbreak to clinicians • Distribution of protocols for hospital preparedness planning; for field detection, triage, and management by first responders and clinicians • Communication with the public and prevention of mass panic	Material • Secure Web site to allow the rapid and safe electronic transmission of data and guidelines • Hotlines • Secure Web site to allow the rapid and safe electronic transmission of data and guidelines Information • Information regarding the nature of the biothreat agent, its potential for harm to first responders and clinicians, and its natural history • Guidelines for personal protection • Guidelines for the management of the acutely ill, the exposed, and family members of both • Guidelines for the public to protect themselves, or to seek care when appropriate
Emergency management	• Declaration of emergency • Command/Control • Crowd and traffic control • Shelter and feeding of evacuated/displaced persons • Process for continuous evaluation of needs and resources • Mental health services for responders, victims, caregivers, and their families • Volunteer management	Personnel • Emergency management professionals • Elected officials to declare emergency • Security personnel (e.g., police and military) • Mass care professionals (e.g., American Red Cross) • Mental health professionals • Logisticians Material • Command/control center • Supplies for mass care in the event of a large-scale evacuation (e.g., tents, food, portable toilets, etc.) Information • Information about capacity and need for services • Understanding of command control protocols, such as Incident Management System and the Hospital Emergency Incident Management System

Key Question 3. Which existing regional systems of delivery of goods and services could be relevant to supplying the resources identified in Key Question 2?

We found numerous systems and organizations with regionalized infrastructures engaged in the timely delivery of bioterrorism-relevant material, personnel, and information. These systems and organizations can be broadly categorized in two ways: by the level at which they primarily operate (local as opposed to regional) and by the type of response task they perform.

For this Evidence Report, we define a local response to bioterrorism as occurring under the jurisdiction of the local health officer. However, many relevant local responders and response organizations (such as clinicians, first responders, hospitals, and emergency management professionals) may not organize themselves in relationship to the local public health jurisdiction in which they work. Thus, if an article used a different definition of local, we deferred to their definition.

Regional responses fall into three broad categories: sub-state, multi-state, and federal. Most states utilize sub-state regions (often drawn according to county lines) for disaster planning. For example, in California (where regions encompass up to ten counties) these regions are an integral organizational element of the state's mutual aid agreements. Multi-state regions are typically defined by one or more federal agencies. For example, there are ten FEMA regions, each made up of between four and eight states. These same regional designations are also used by other federal agencies, such as HRSA and HHS. The Department of Homeland Security, which has

responsibility for many of the existing systems that would contribute to regionalized response to bioterrorism, is currently undergoing a reorganization of its U.S. regions and regional infrastructure.

In general, most of the existing systems and organizations are organized according the response task they perform. We found systems for each of the response tasks described in our answer to Key Question 1: those responsible for preparedness planning (e.g., the Joint Commission on Accreditation of Healthcare Organizations and the American Hospital Association), field assessment and triage (e.g., U.S. trauma care system), diagnosis (e.g., Laboratory Response Network), management of the acutely ill (e.g. Modular Emergency Medical System, Medicins Sans Frontieres), prevention of the spread of disease (e.g., Strategic National Stockpile), surveillance (e.g., Electronic Surveillance System for the Early Notification of Community-Based Epidemics), outbreak investigation (e.g., Epidemic Intelligence Service), communication (e.g., ProMed, Health Alert Network, and FirstWatch), and emergency management (e.g., Emergency Management Assistance Compacts).

Some of the existing regional organizations were designed specifically to enhance U.S. preparedness for bioterrorism, whereas others were designed to provide ongoing services to promote the public health and respond to natural disasters (e.g., U.S. public health system, the National Disaster Medical System, Disaster Medical Assistance Teams, and the Metropolitan Medical Response System). The Laboratory Response Network was designed specifically to enhance regional capacity for bioterrorism responses but has the dual use of expanding laboratory capacity for naturally occurring outbreaks. Our review of the 2001 anthrax attacks suggests that the Laboratory Response Network significantly enhanced regional laboratory surge capacity. Whether the surge capacity provided by the Laboratory Response Network will be adequate for a bioterrorism event of larger magnitude remains untested.

In addition to the specific programs described in the preceding paragraphs, the included articles demonstrate that mutual aid agreements (such as the Master Mutual Aid agreement in California and the Emergency Management Assistance Compact in the rest of the United States) are key to providing surge capacity for regional responses to disasters. These agreements ensure that every locale does not have to be staffed and prepared for a maximal intensity event. They enable risk to be spread among several locales and disaster preparedness costs to be shared. The literature suggests that mutual aid agreements for bioterrorism are likely to benefit from careful pre-event consideration of liability issues, remuneration, and licensing.

We conclude that there are numerous existing systems and organizations that could contribute to a regionalized bioterrorism response. Many of these systems have long histories of successful participation in bioterrorism-related events such as infectious disease outbreaks and natural disasters. However, most of these systems were designed independently, typically to facilitate particular response tasks. Efforts to coordinate them are ongoing and have not been evaluated.

Key Question 4. Can regionalization of bioterrorism preparedness planning facilitate supplying needed resources to local responders during a bioterrorism event?

To answer Key Question 4, we searched four sources—medical, emergency management, and supply chain literatures and government documents—for descriptions and evaluations of regional systems designed to facilitate the delivery of resources during a regionalized response to bioterrorism. We found very few evaluations of regional systems from any of the literatures. Specifically, we found no evaluations (only descriptions) of the responses to the 2001 anthrax

attack, SARS and other naturally occurring outbreaks, responses to natural disasters, or bioterrorism surveillance efforts. Only our review of the trauma care literature included evaluations of the process of regionalization of the U.S. and Canadian trauma care delivery systems.

From each of our literature sources, we sought relevant methods of evaluating the included articles as to whether regionalization may benefit a bioterrorism response. For example, evaluations of medical interventions (e.g., treatments for bioterrorism-related illness) may be designed to determine whether the intervention is effective, cost-effective, or safe. Thus, from each included article we abstracted information about any evaluative outcomes of interest including clinical, financial, and process outcomes such as morbidity, mortality, cost of the intervention, adherence to clinical protocols, and timeliness of administration of definitive medical care. Similarly, we sought descriptions and evaluations of innovations in supply chain management to determine criteria for evaluating the bioterrorism response supply chain. We found supply chain management concepts are directly relevant to those elements of a bioterrorism response that require the purchase, inventorying, distribution, and rapid dispensing of medical supplies (e.g., antibiotics, vaccines, and equipment) to remotely located users (e.g., hospitals, pharmacies, local dispensing sites). Thus, from evaluations of supply chain, we found five concepts relevant to the bioterrorism response supply chain: network design, inventory management, postponement and modularization, supply chain coordination and management of incentives, and management of information.

Despite the lack of evaluative evidence, the application of our evaluation criteria to the included articles suggests that regionalization of some aspects of a bioterrorism response may result in a more effective, less costly, timely delivery of key response personnel, material, and information. The next sections summarize the evidence about regionalization of these response resources.

Personnel. Our review of regionalized responses to disasters and outbreaks suggests that local personnel are typically the first responders to any event. Thus, even in a regionalized system of response personnel, well-trained local responders are essential. Training of local first responders facilitates their personal protection; their mental health; and their ability to perform key initial response tasks such as triage, diagnosis, management of the acutely ill and worried well, and prevention of the spread of disease. Regionalization of personnel serves to increase the expertise of responders (i.e., teams of trained responders serving a region can increase their experience by responding to numerous events over a region) at reduced cost to any given community. The included articles present numerous examples of teams of regionalized personnel enhancing local capacity for nearly every type of response personnel (e.g., clinicians, logisticians, public health officials, emergency management professions, pharmacists, etc.). Often, these personnel can be obtained through mutual aid agreements or specific requests to the relevant organizations.

The included articles emphasize three considerations relevant to regionalization of response personnel. First, they highlight the importance of accurate accounting of regional personnel to avoid the problems associated with double-counting of individuals who serve more than one response unit (e.g., a single person may be a member of the Army National Guard, a Disaster Medical Assistance Team, and a key part of the local response). A single database or coordinated information system to record all response personnel and resources could address this issue.

Second, for a large-scale response that includes numerous personnel, often from a variety of sponsoring organizations, incident command must be well defined and familiar to all responders. Thus, the chain of command during a bioterrorism event may benefit from pre-event planning, and establishment and acceptance by relevant response agencies of protocols that delineate the chain of command for an event commanded at the local level. Pre-event planning should include codified protocols as to how the chain of command changes when regional and federal response agencies become involved.

Finally, particularly during a response to an outbreak resulting from an emerging or communicable biothreat agent, it is essential to carefully consider and address responder incentives. During a bioterrorism event, strategies to protect responders and their families may be an essential component of maintaining the necessary work force.

Material. Our synthesis of the included articles emphasizes two considerations for regionalization of the materials required for a bioterrorism response. First, the principal program for regionalization of material for a bioterrorism response is the Strategic National Stockpile, designed to deliver a wide variety of pharmaceutical and medical supplies anywhere in the United States within 12 hours. This program has been deployed successfully during recent years and its leaders are working with states to develop plans for rapid dispensing of materials once they are delivered locally. However, we found no evaluations of the capacity of local jurisdictions to distribute and dispense these materials—although these plans are actively being tested in simulations and exercises. Regionalization of bioterrorism response material in the Strategic National Stockpile has the benefit of being able to reduce the total inventory that must be stored at the national level, while still being available to local regions in a timely manner as long as sufficient distribution capacity is available locally. Some bioterrorism response supplies have limited shelf lives, so minimizing inventory may be important from economic and logistics perspectives.

Second, we found several descriptions of programs of local stockpiling of antibiotics and other bioterrorism response materials. In most cases, these local inventories are intended to provide immediate material support to local responders before the arrival of supplies from the Strategic National Stockpile. However, the costs and benefits of acquiring, storing, and maintaining local inventories of medical supplies have not been established. Thus, we developed a simulation model to evaluate the tradeoffs involved in purchasing, storing, and maintaining local inventories. We found that increasing local inventories becomes more cost effective as the annual probability of an attack increases. We conclude that strategies of developing and maintaining local inventories may be highly costly, particularly in areas where the probability of an attack is low.

Information. Our evidence review highlights three considerations relevant to regionalization of information management. First, information management, using common technology platforms, is essential for assessing the needs of the local community and the resources available to it, and for coordinating responses from regional agencies. The disaster literature and supply chain cases studies emphasize the need for updated information so that response resources can be supplied to those in need in a timely and efficient manner. Bioterrorism responses may benefit from a common technology platform used by multiple response organizations. These may be as simple as a common radio frequency or as complicated

as multiple computer networks from different regions communicating with each other to exchange information about resource demands and availability.

Second, our review of the SARS and other recent outbreaks demonstrated that communication and cooperation between health authorities of neighboring regions is needed. Infectious diseases can spread quickly and communication and cooperation among neighboring communities can facilitate a response. Often this communication can be difficult to achieve rapidly through interim agreements. Thus, cooperation during a large-scale bioterrorism response may benefit from pre-event development and routine use of communication systems and specific protocols for information flow.

Third, we found no evidence specifically addressing regionalization or pooling of surveillance information. Thus, we developed a simulation model to evaluate the effects of pooling surveillance data from several regions. We found that some methods for setting thresholds for determining when an outbreak has occurred may increase the false positive (i.e., false alarm) rate. We also found that pooling strategies may improve detection capabilities but are highly situation-specific. In our simulation, pooling of surveillance data enhanced detection capabilities when the correlation in cases presenting with syndromes of interest between the individual regions was very low. Given the importance of surveillance for early detection of bioterrorism, these preliminary analyses warrant further investigation to more accurately characterize the effects of pooling on the sensitivity, specificity, and timeliness of surveillance analyses.

Key Question 5. How do geographic variations in the affected population (e.g., urban as opposed to rural), special populations (e.g., children, elderly, or disabled), and the interplay of private and public sector players affect regionalization systems?

At any given time in the United States, there are approximately 58 million children (younger than 14 years), 13 million elderly (older than 75 years), 50 million disabled people, and 3 million pregnant women.[622-625] These special populations may require bioterrorism preparedness planners to consider alternative treatment strategies (e.g., pediatric dosing), plans for home delivery of resources and services, and alternative methods of transporting patients to triage and treatment sites. Similarly, rural planners typically have to consider the increased distances that patients and response personnel have to travel to obtain prophylaxis and treatment.

The only included articles that evaluated variations in regionalized responses on the basis of geography were those describing the regionalization of trauma care. Specifically, several articles reported that when care in rural areas was regionalized, survival rates improved and costs decreased.[35-37, 521, 525] However, none of the included articles described the effects of regionalization on the care of vulnerable populations or the interplay of private and public sector players. Given the proportion of the U.S. population that may have special needs, such as limited English-language skills, poor mobility or vision, or impaired ability to metabolize standard doses of medications for prophylaxis or treatment; tailored response protocols are likely to benefit from regional bioterrorism response plans.

Chapter 4. Discussion

We must first succeed alone, that we may enjoy our success together.
—Henry David Thoreau[626]

Given the complexity and cost of training, staffing, equipping, and mobilizing an adequate bioterrorism response infrastructure, no single community can be expected to develop and maintain the necessary capacity for a large-scale bioterrorism response. Instead, regionalization may benefit some bioterrorism preparedness and response capabilities. Our extensive search of four literatures relevant to bioterrorism responses (medical, emergency management, supply chain and government documents) found that the response infrastructure for a bioterrorism event includes numerous agencies with regionalized organizational structures. However, most of these structures have been developed independently and efforts to coordinate them are underway but not yet widespread. Specifically, the Department of Homeland Security, which has oversight and coordination responsibilities for many of the agencies that would contribute to a regionalized bioterrorism response is currently reorganizing its regional structure.

Our literature review provides six key results about regionalization of services for bioterrorism preparedness and response. First, there have been very few evaluations of whether regionalization has benefited a particular response organization or task. Evaluations of regionalization were essentially limited to those of trauma care systems, which demonstrated significant improvements in both clinical and process outcomes after regionalization. These improvements were largely attributed to concentrating specialized trauma services in pre-designated hospitals. Efforts to develop a regionalized infrastructure for bioterrorism responses will likely benefit from careful evaluations of the numerous tasks involved in a bioterrorism response and the alternative strategies for providing the necessary resources to perform these tasks.

Second, regionalization has benefited disaster responses. Our review of the responses to natural disasters such as hurricanes, earthquakes, and wildfires and manmade disasters such as the destruction of the Alfred P. Murrah Federal Building in Oklahoma City and the terrorist attacks of September 11, 2001 emphasize that during large-scale disasters, local response capacity can be quickly overwhelmed. The key method of organizing regionalized disaster responses is mutual aid agreements. These agreements provide the necessary surge capacity when health services, firefighting, law enforcement and other essential services are overwhelmed in local jurisdictions. The Emergency Management Assistance Compact has been adopted by all states and U.S. territories except for Hawaii and California (which has longstanding mutual aid agreements in place). The elements of successful mutual aid agreements include pre-event ratification of legislation by all signatories to resolve issues of compensation, liability, and insurance and uniform information systems to track needs and resources. Efforts are ongoing to expand existing mutual aid agreements for bioterrorism responses. Specifically, bioterrorism responses are likely to benefit from mutual aid agreements that are uniform across the United States, that include agreements with neighboring regions of Mexico and Canada, and that provide surge capacity for public health services.

Third, regionalization efforts have successfully expanded surge capacity for laboratory services. Our review of the literature describing the response to SARS and the 2001 anthrax

attacks highlighted the ability of the regionalized networks of public health and research laboratories to rapidly expand surge capacity for pathogen identification and testing of clinical and environmental samples. During the anthrax attacks, the Laboratory Response Network successfully provided laboratory surge capacity. Whether this Network would be able to respond as well to a larger bioterrorism event remains untested.

Fourth, information technologies facilitate accurate determination of response needs and available resources, effective application of the chain of command, communication among responders and with the public, and surveillance. Our review of evaluations of supply chains emphasized the importance of accurate information for coordination of all elements of the supply chain. Additionally, they demonstrated that investments in information technologies often resulted in net cost savings for the supply chain while improving customer service. Conversely, the disaster response literature provided examples of how inadequate information infrastructures led to delays in responses. Regionalization of bioterrorism preparedness and response efforts will likely benefit from careful consideration of the information technologies that can facilitate sharing of information by different response organizations and by responders at local and regional levels.

Fifth, local personnel are the first to respond and typically comprise a considerable proportion of the work force during an emergency response. The disaster literature emphasizes that local responders are often at great risk of personal injury during a response. Our literature review emphasizes three considerations for preparedness planning efforts to enhance the capacity of local responders. First, because local responders will always be the first on a scene during an emergency, bioterrorism responses may benefit from first responder training that emphasizes personal safety, triage, diagnosis, and outbreak management tasks. Second, because local responders with training in bioterrorism preparedness may participate in more than one response organization, careful accounting of response personnel may avoid the problems associated with double counting of responders. Third, particularly during responses to emerging infectious diseases or communicable bioterrorism events, strategies to protect first responders and their families may be essential to maintaining an adequate work force.

Finally, few included articles specifically articulated lessons learned from their bioterrorism-related preparedness or response experiences. Our review of government documents, particularly responses of military personnel, found that organizational commitment is a key factor in implementing a ‘lessons learned’ approach to ensuring that knowledge gained from both good and bad experiences is maintained in institutional memory. Plans to regionalize services for a response to a large-scale bioterrorism event could benefit from the experiences of responses to small bioterrorism events and relevant naturally occurring outbreaks if the lessons learned from these experiences were documented and used to improve planning efforts. Given the complexity of a bioterrorism response, the iterative application of lessons learned from one experience to the next requires commitment from all relevant response organizations to institutionalize a ‘lessons learned’ approach.

Our review of the supply chain literature yielded two results. First, recognizing that several key components of a response to large-scale bioterrorism are essentially supply chain management issues (e.g., purchasing, inventorying, and distributing relevant supplies), we used six criteria commonly applied to evaluations of traditional supply chains to evaluate the literature about the bioterrorism response supply chain. These evaluations include network design, inventory management, postponement and modularization, supply chain coordination and management of incentives, and management of information. They supplement the evaluation

criteria derived from other relevant literatures and serve as a framework that can be applied to future evaluations of bioterrorism preparedness and response systems. Second, there is scant evidence about the incentives of bioterrorism response personnel and organizations. The complexity of a large-scale bioterrorism event suggests that coordination of such a response may benefit from a careful pre-event evaluation and from attempts to align the incentives of relevant response organizations.

We found no evidence about regionalization of two essential components of bioterrorism preparedness and response: surveillance and the timely delivery of medical supplies for prophylaxis and treatment. To address these significant gaps in the literature, we created two simulation models. The preliminary results of our surveillance model suggest that whereas large outbreaks can be relatively easy to detect using either unpooled or pooled (i.e., regionalized) data analysis methods; small outbreaks can be difficult to detect by both methods. Additionally, we found that pooling strategies may improve detection capabilities but the circumstances under which pooling strategies are consistently more effective or cost effective than using unpooled data, remain poorly characterized.

Our inventory management simulation model yielded three interesting results. First, we found that the mortality associated with anthrax bioterrorism may be highly sensitive to the demand for prophylactic antibiotics. This is a critical finding given that for many types of bioterrorism responses, it will be difficult to determine whether an individual has been exposed to the biothreat agent. Second, for a large-scale bioterrorism event, strategies that deliver multiple Push Packs until the regional Vendor Managed Inventory has been delivered may reduce mortality. We plan future analyses to evaluate other inventory-dependent strategies for delivering and dispensing antibiotics (e.g., dispensing short courses of antibiotics if the on-hand inventory is low or the demand is high). Finally, whereas our literature search found several references to local organizations purchasing and maintaining local inventories of pharmaceuticals and supplies for a bioterrorism response, our simulation model found that increasing the availability of local inventories may be cost effective only if the annual probability of attack is high.

Our conclusions are limited by quality of available evidence in two ways. First, very few of the included articles were evaluations of regionalization of bioterrorism-related services; rather, most were descriptions of responses to outbreaks or disasters. The design and implementation of rigorous evaluations of regionalization of bioterrorism-related services may be technically difficult. However, bioterrorism preparedness planning efforts would likely benefit from detailed evaluations of various strategies to regionalize each of the heterogeneous tasks required of a bioterrorism response. Second, we found little evidence regarding regionalization of bioterrorism preparedness for special populations such as children, pregnant women, the elderly, and the disabled. Recent Census data indicates that nearly 130 million people in the United States can be considered a member of one or more “special populations.” Without information about bioterrorism response services for them, policy makers are limited in their ability to specifically plan for the needs of these vulnerable populations during a bioterrorism response.

We conclude that regionalization is likely to benefit elements of a bioterrorism response including the provision of surge capacity in essential response services such as triage, the provision of medical care, distribution and dispensing of prophylactic therapies, outbreak investigation, security management, and emergency management. Additionally, regionalization is likely to be a cost effective strategy for developing teams of trained response personnel and maintaining inventories of response equipment. There are numerous response organizations with

regionalized infrastructures that will serve key functions during a large-scale bioterrorism response. Coordination of these organizations may benefit from implementation of information management strategies and pre-event agreements that specify response roles, remuneration, and chain of command.

Future Research

As we noted, despite the large number of studies and articles we reviewed, we found very few evaluations of systems relevant to bioterrorism preparedness, and even fewer evaluations of the regionalization of a system relevant to bioterrorism preparedness. Future research is needed to fill this gap in the literature. Specifically, evaluations are needed for a better understanding of the costs and benefits of regionalization of surveillance, inventory management and distribution systems, and information management.

Because of the challenges of performing comprehensive evaluations of bioterrorism-relevant responses, modeling may be an effective means of supplementing this evaluative evidence. Specifically, future modeling efforts might investigate the costs and benefits of various strategies for regionalizing or pooling surveillance data (e.g., determining how pooling of surveillance data changes the surveillance system's sensitivity, specificity, and timeliness). Additionally, simulation models may evaluate the costs and benefits of strategies of inventory management and distribution for a communicable bioterrorism outbreak such as smallpox. Such a model would likely require the evaluation of dispensing strategies like door-to-door, postal-type distribution to avoid contact between the exposed and infectious populations at dispensing sites.

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Appendix A: Expert Advisors and Peer Reviewers

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Appendix B: Data Abstraction Form

Reference #_____ **Abstractor Name**
☐Dena Bravata
☐Emilee Wilhelm
☐Other:

References Cited
☐None circled
☐Numbers circled:

Included? ☐Yes ☐No **If no, reason for rejection:**

How many systems relevant to bioterrorism does this article describe? _____

System name: _____

Purpose of the system:_____

_____

At what regional level(s) does the system principally operate? ☐Local ☐Regional ☐Integrated

Which of the following are addressed by the system?

Tasks
☐Planning/preparedness
☐Field assessment and triage
☐Diagnosis
☐Detection
☐Management
☐Prevention
☐Surveillance
☐Outbreak investigation
☐Communication
☐Emergency management
☐Incident command
☐Other:

Resources
☐Material
☐Hospital capacity
☐Laboratory capacity
☐Surveillance information
☐Other information
☐Personnel
☐Other:
☐Special populations:

Bioterrorism-Relevant Events
☐Bioterrorism event (incl. hoaxes)
☐Disaster/WMD drill
☐Natural outbreak
☐Natural disaster
☐Man-made disaster
☐Terrorism event
☐Supply chain case study
☐Other:

Does this article discuss the regionalization of this system? ☐Yes ☐No If yes, please describe:
_____

_____

Which of the following evaluative criteria are relevant to a discussion of the system?

☐Network Design ☐Inventory Management ☐Postponement	☐Management of Incentives ☐Volume-Outcome Associations	☐Incident Command ☐Management of Information ☐Other:

Has the system been evaluated? ☐Yes ☐No If yes, please describe the evaluation and its outcomes: _____

_____

_____

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