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The evaluation of post-exposure prophylaxis models for use in the event of an aerosolized anthrax attack

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THESIS

THE EVALUATION OF POST-EXPOSURE PROPHYLAXIS MODELS FOR USE IN THE EVENT OF AN AEROSOLIZED ANTHRAX ATTACK

by

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September 2014

Thesis Co-Advisors: Robert Josefek
Lynda Peters

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The Strategic National Stockpile (SNS) can deliver large quantities of medications and medical supplies to anywhere in the United States and its territories within 12 hours of the federal decision to deploy. As an additional preparedness measure, many states and regions have elected to purchase and maintain similar medical countermeasure stockpiles locally. Theses stockpiles are a means of rapid access to critical medications necessary for use as post-exposure prophylaxis (PEP) before the arrival of SNS assets.

To assist state and local communities in determining the most efficient and cost-effective PEP model for use in the event of an anthrax attack, this thesis analyzes four potential models. This analysis provides a framework by which state and local jurisdictions can evaluate the suitability of models for the provision of PEP in the event of a large-scale anthrax attack. Readers may employ these findings in evaluating the efficacy of their own local programs, and in determining the most appropriate PEP model based upon local priorities given variations in perceived needs and resource availability among communities.

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THE EVALUATION OF POST-EXPOSURE PROPHYLAXIS MODELS FOR USE IN THE EVENT OF AN AEROSOLIZED ANTHRAX ATTACK

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TABLE OF CONTENTS

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LIST OF FIGURES

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LIST OF TABLES

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LIST OF ACRONYMS AND ABBREVIATIONS

ACLU	American Civil Liberties Union
ASPR	Assistant Secretary for Preparedness and Response
AVA	Anthrax Vaccine Adsorbed
BTRA	Biological Threat Risk Assessment
CDC	Centers for Disease Control and Prevention
CHDS	Center of Homeland Defense and Security
CRI	Cities Readiness Initiative
DHS	U.S. Department of Homeland Security
DMI	distributor-managed inventory
DOD	Department of Defense
DSNS	Department of the Strategic National Stockpile
DVA	Department of Veterans Affairs
EMS	emergency medical services
EUA	emergency use authorization
FDA	Food and Drug Administration
FEMA	Federal Emergency Management Agency
GAO	Government Accountability Office
HHS	U.S. Department of Health and Human Services
HLS	homeland security
HSDL	Homeland Security Digital Library
HSPD	Homeland Security Presidential Directive
IOM	Institute of Medicine
MCM	medical countermeasure
MIEMSS	Maryland Institute for Emergency Medical Services Systems
MMRS	Metropolitan Medical Response System
MSA	metropolitan statistical area
NAC	National Acquisition Center
NACCHO	National Association of County and City Health Officials
NGO	non-government organization
NIH	National Institutes of Health
NPS	National Pharmaceutical Stockpile

PEP	post-exposure prophylaxis
PHEMCE	Public Health Emergency Medical Countermeasures Enterprise
PHEP	Public Health Emergency Preparedness
POD	point of dispensing
RSS	receipt, staging and storage
SLEP	Shelf Life Extension Program
SNS	Strategic National Stockpile
UASI	Urban Area Security Initiative
UMI	user-managed inventory
USDA	United States Department of Agriculture
VA	Veterans Administration
VMI	vendor managed inventory
WMD	weapons of mass destruction

EXECUTIVE SUMMARY

A. INTRODUCTION

This thesis explores four models that are currently available for the provision of post-exposure prophylaxis (PEP) at the state or local level, in an effort to address the primary research questions:

- What model is best suited to provide the most efficient and cost effective PEP in the event of an anthrax attack?
- How can decision makers evaluate competing models given variation in perceived needs and resources available to meet those needs?

B. METHODOLOGY

This research is a policy options analysis that evaluates four potential policy options for use in the management of PEP in the event of an anthrax attack. The final result of the analysis is intended to provide the reader with a framework by which state or local planners can evaluate the appropriateness of a policy option relevant to their own jurisdiction-specific priorities.

1. Policy Options

The four policy options selected for analysis were the following.

- Policy Option 1—a locally managed antibiotic medication stockpile, purchased, stored, sustained and deployed at the state, regional or local level.
- Policy Option 2—a locally managed antibiotic medication stockpile, purchased and stored at the state, regional or local level, with its inventory sustained using a managed supply rotation model, through partnerships with public and/or private entities.
- Policy Option 3—the provision of PEP to first responders/first receivers via medications prescribed and pre-dispensed to individual responders and stored in their homes.
- Policy Option 4—reliance on the Strategic National Stockpile (SNS) as a sole source of PEP, beyond medications currently on hand in local commercial and hospital pharmacy inventories.

2. Evaluation Criteria and Outcome Values

Each of above-mentioned policy options were individually assessed using the following five criteria.

- Timeliness
  - A = PEP is immediately available for dispensing.
  - B = The availability of PEP for dispensing is likely to be <12 hours but not likely to be immediately accessible
  - C = The availability of PEP for dispensing is likely to be ≥12 hours
- Cost
  - A = It is likely that full funding for a model can be absorbed in the typical operating budget.
  - B = The model requires some supplementation from outside funding source(s).
  - C = The model is likely to require majority or full funding from outside sources.
- Logistics
  - A = It is likely that all logistical resources required for a model are readily available in most metropolitan areas.
  - B = Some outside or mutual aide assistance is likely to be required to meet the logistical demands of a model.
  - C = The model is likely to exceed the logistical capabilities of most metropolitan areas, thus requiring significant logistical support from outside resources.
- Stakeholder Acceptance
  - A = The model is likely to be viewed as favorable by the majority of relevant stakeholder groups.
  - B = It is likely that there will be divided support among relevant stakeholder groups.
  - C = It is likely that fewer than half of the relevant stakeholder groups are likely to consider the model as favorable.
- Comprehensiveness
  - A = The model is likely to provide sufficient quantities of PEP medications that are equally accessible to all population sectors.
  - B = The quantity of PEP medication available for dispensing is likely to be sufficient for only select portions of a population.

C = The model provides little or no availability to PEP medications.

C. FINDINGS

The following matrix provides a summary of the outcome values assigned to each of the evaluative criteria, specific to the four PEP models reviewed in this research. The results of this analysis are based on the general characteristics of each model as discussed throughout this research.

Policy Option	Timeliness	Cost	Logistics	Stakeholder Acceptance	Comprehensiveness
Local Stockpiles	**B**	**B**	**A**	**A**	**B**
Third Party Inventory Mgmt	**B**	**B**	**C**	**B**	**B**
Pre-Dispensed to Homes	**A**	**C**	**A**	**B**	**B**
SNS Only	**C**	**A**	**A**	**A**	**A**

D. RECOMMENDATIONS AND CONCLUSION

During the development of biological incident preparedness and response plans, the above matrix analysis will provide state and local planners with the framework to evaluate a PEP model based on the priorities of an individual jurisdiction. Some jurisdictions, especially those that are more rural, may find that limited financial and logistical resources might suggest that reliance on the SNS may be the most suitable model. In contrast, regions with less limited financial resources and sufficient administrative (logistical) capabilities may choose an alternative option, such as pre-dispensing antibiotics to first responders for storage in their homes. Policy options should be carefully considered using criteria that are likely to have the most significant impact on the suitability of a given policy option.

Consideration of factors beyond the scope of this thesis is crucial in determining the suitability of a PEP provision model. As an example, all PEP provision models that use points of dispensing (POD) as a means of distributing medications are heavily reliant upon the efficiency of POD activation and throughput processes for effective PEP distribution. The rapid availability of PEP for dispensing is likely to benefit only those jurisdictions with a demonstrated proficiency in POD activation and throughput procedures. Therefore, even an unlimited supply of PEP is likely to be of benefit to a jurisdiction with little or no POD throughput capability.

Despite the low probability, the catastrophic consequences of a bioterrorist attack are sufficient cause for concern. The size of an attack required to overwhelm the response system, and instill widespread fear remains unclear. Since financial resources are finite, policy makers at the federal, state and local levels must make difficult choices that require investments in people, technology, and materials, as well as strong partnerships between federal, state, and local governments. Strong partnerships between the public and private sectors are also paramount. Although terrorists have yet to carry out large-scale attacks with biological weapons, the events of September 11 have clearly demonstrated a willingness to inflict mass casualties. This thesis serves as a vital resource for decision makers tasked with balancing the needs of stakeholders and the resources available to meet those needs.

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I. INTRODUCTION

A. BACKGROUND

Since the dawn of civilization, man has used biological warfare against its enemies, both individual and in mass. In the year 1155, Emperor Barbarossa poisoned water wells with human bodies in Tortona, Italy. In 1763, the British distributed blankets from smallpox patients to native Americans in the New World.[1] In the 1930s, Japanese scientists developed modernized biological weapons. During World War II, both the United States and Britain developed biological weapons, including botulinum toxin, encephalitis virus, staph enterotoxin, anthrax, and other deadly agents.[2] More than ever, the 21st century threat of biological warfare persists.

> Bioterrorism is a real threat to our country. It's a threat to every nation that loves freedom. Terrorist groups seek biological weapons; we know some rogue states already have them....It's important that we confront these real threats to our country and prepare for future emergencies.[3]

The signing of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, which established the Department of Homeland Security (DHS), fueled the emergence of the public health discipline into the homeland security (HLS) arena. The act called for the department's collaboration with the Secretary of Health and Human Services (HHS) and the Attorney General, in determining threats posed to our nation's welfare by biological agents.[4] This emphasis on the threat of biological terrorism was largely motivated by the October 2001 anthrax attacks that lingered fresh in the minds of an anxious and frightened nation, still psychologically bruised and battered by the attacks of September 11, 2001.

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[1] Friedrich Frischknecht, "The History of Biological Warfare," *EMBO Reports* 4, no. 6S (2003): S47–S52.

[2] Ibid., S48.

[3] George W. Bush, as quoted in "Biodefense for the 21st Century," The White House, 2004, http://www.whitehouse.gov/homeland/20040430.html.

[4] *Homeland Security Act of 2002*, Pub. L. No. 107–296, (2002): H.R. 5005.

In the immediate years to follow, the perception of the threat of biological terrorism persisted. In February, 2004, President George W. Bush warned the nation that: "armed with a single vial of a biological agent, small groups of fanatics, or failing states, could gain the power to threaten great nations, threaten the world peace. America, and the entire civilized world, will face this threat for decades to come. We must confront the danger with open eyes, and unbending purpose."[5] At the direction of Homeland Security Presidential Directive (HSPD) 10, the first Biological Threat Risk Assessment (BTRA) was conducted in 2006, and was intended to serve as a focal point for the establishment of a national biodefense strategy.[6] Although the computer based probabilistic risk assessment tool used is not without controversy, the 2006 BTRA assessed the risk associated with the intentional release of 28 biological agents previously identified by the Centers for Disease Control and Prevention (CDC).[7] Based on its stability and lethality, *Bacillus anthracis,* the bacteria that causes anthrax, has emerged as a favorite among scientists as a potential biological weapons agent.[8] Although pandemic illness of new and historic origin continues to plague the world, it is the threat of the deliberate release of a biological agent that drives our nation's preparedness efforts.[9]

The establishment of the Strategic National Stockpile (SNS) has been a key federal health and medical preparedness initiative. This federal asset resulted from an expansion of the former National Pharmaceutical Stockpile (NPS), and was created by the CDC as directed by Congress in 1999. In accordance with the Homeland Security Act of 2002, the stockpile was renamed as the SNS, and responsibility for overall stockpile

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[5] Committee on Methodological Improvements to the Department of Homeland Security's Biological Agent Risk Analysis, *Department of Homeland Security Bioterrorism Risk Assessment: A Call for Change* (Washington, DC: National Academies Press, 2008), 172.

[6] Larry D. Brandt, *Homeland Security R&D Roadmapping—Risk-Based Methodological Options* (Livermore, CA: Sandia National Laboratories, 2008).

[7] Committee on Methodological Improvements to the Department of Homeland Security's Biological Agent Risk Analysis, *Department of Homeland Security Bioterrorism Risk Assessment: A Call for Change,* 172.

[8] David R. Franz, "Preparedness for an Anthrax Attack," *Molecular Aspects of Medicine* 30, no. 6 (2009): 503–510.

[9] Ibid., 506.

management was transferred to HHS, and then to DHS in May 2003.[10] The mission of the Department of the Strategic National Stockpile (DSNS) program is to provide a re-supply of large quantities of essential medical materiel to states and communities during an emergency.[11] Today, the SNS can deliver large quantities of medications and medical supplies to anywhere in the United States and its territories within 12 hours of the federal decision to deploy. As an additional preparedness measure, many states and regions have elected to purchase and maintain similar medical countermeasure (MCM) stockpiles locally. Theses stockpiles, consisting primarily of antivirals and antibiotics, are a means of rapid access to critical medications necessary for use as post-exposure prophylaxis (PEP) before the arrival of SNS assets.[12]

B. PROBLEM STATEMENT

The Region III Health and Medical Task Force, the primary advisory body for public health and medical preparedness efforts in the Baltimore Metropolitan region, utilized 2008 Urban Area Security Initiative (UASI) funding to establish a stockpile of antibiotic medications. These medications were intended to be used prophylactically to treat first responders/first receivers and their families in the event of an anthrax attack. The impetus behind this initiative was to maintain a viable and resilient workforce within the public health arena, so that providers remained available to respond as needed within their respective communities, particularly during declared states of emergency when call volumes are significantly increased. Similarly, many state and local jurisdictions throughout the nation have elected to stockpile medications in an effort to reduce the morbidity and mortality by making PEP immediately available.[13]

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[10] Stephen D. Prior, *Who You Gonna Call? Responding to a Medical Emergency with the Strategic National Stockpile* (Washington, DC: National Defense University Washington, DC Center for Technology and National Security Policy, 2004).

[11] "Strategic National Stockpile (SNS)," Centers for Disease Control and Prevention Office of Public Health Preparedness and Response, last updated July 10, 2014, http://www.cdc.gov/phpr/stockpile/stockpile.htm.

[12] Brooke Courtney et al., "Maximizing State and Local Medical Countermeasure Stockpile Investments through the Shelf-Life Extension Program," *Biosecurity and Bioterrorism* 7, no. 1 (2009): 101–107.

[13] Victor W. Sidel, Hillel W. Cohen, and Robert M. Gould, "Good Intentions and the Road to Bioterrorism Preparedness," *American Journal of Public Health* 91, no. 5 (2001): 716.

Unfortunately, the practice of procuring and maintaining local stockpiles does not come without sacrifices. Some have questioned the efficiency of this practice in light of the rapid availability of resources from the SNS, and the daunting logistical and administrative demands of maintaining local stockpiles. No best practice has been established, as there appears to be little consensus or federal guidance regarding the appropriate levels of inventories that should be maintained.[14] Obtaining stakeholder buy-in and funding for the initial purchase of prophylactic medications can be a difficult task, as HLS funding streams continue to diminish. Strict environmentally controlled and secure storage facilities must be established to properly maintain medications within the cache. From an administrative standpoint, localities maintaining these stockpiles must develop sound activation, delivejry, and distribution protocols. Lastly, there is no universal model for the rotation of these medications prior to their expiration, or alternatively, for their inclusion in expiry extension programs aimed at maximizing shelf life.[15]

An act of bioterrorism has significant potential to result in severe illness and death to masses. Without sufficient PEP, the public health infrastructure could be crippled through the drastic reduction of the first responder and healthcare workforce. High rates of workforce absenteeism could result in decreased surge capacity capabilities. The stress to the healthcare system would only be exacerbated by an increased influx of ill and worried well, resulting from a lack of adequate PEP for the civilian population. State and local jurisdictions must carefully consider the costs and benefits of the various models available for the provision of PEP, based on locally prioritized criteria.

C. RESEARCH QUESTIONS

In an effort to assist state and local level planners in assessing the adequacy of their bioterrorism preparedness plans, the following research questions were considered.

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[14] Richard Danzig, *Catastrophic Bioterrorism: What Is to Be Done?* (Washington, DC: Center for Technology and National Security Policy, National Defense University, 2003).

[15] Courtney et al., *Maximizing State and Local Medical Countermeasure Stockpile Investments through the Shelf-Life Extension Program*, 101–107.

- What model is best suited to provide the most efficient and cost effective PEP in the event of an anthrax attack?
- How can decision makers evaluate competing models given variation in perceived needs and resources available to meet those needs?

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II. LITERATURE REVIEW

A. INTRODUCTION

Since the October 2001 anthrax attacks, substantial funding and emergency planning resources have been allocated the expansion of pre-positioned MCMs, specifically antibiotic stockpiles, at the federal, state and local levels. This expansion is largely attributed to the Public Health Security and Bioterrorism Preparedness and Response Act, signed by President George W. Bush in June 2002.[16] This act not only authorized increased funding for public health preparedness, but also called for an improved ability to treat diseases associated with bioterrorism, and an acceleration of the process to develop MCMs. Unfortunately, a lack of specific federal guidance has resulted in a fragmented approach throughout the nation that has yet to identify the most appropriate means of providing a timely, sustainable, and cost-effective model for the provision of PEP.[17] As a result, portions of our nation are left reliant solely upon the availability of the SNS for the provision of PEP. Creating effective policy to mitigate the consequences of an anthrax attack requires data. A comparative analysis of current literature will assist in determining the appropriateness of a PEP model for a given jurisdiction.

B. IDENTIFYING RELEVANT LITERATURE

This review contains peer reviewed journal articles and government reports from 2001 through the present. Articles were obtained using various electronic databases including EBSCO, Wiley, Francis and Taylor, Medline Plus and PubMed. The Homeland Security Digital Library (HSDL) was also searched for previously published theses. Additional grey literature journal articles were found via Google Scholar searches using the terms: medical countermeasures, bioterrorism planning, first responder prophylaxis,

[16] Elin A. Gursky and Gregory Bice, "Assessing a Decade of Public Health Preparedness: Progress on the Precipice?" *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 10, no. 1 (2012): 55–65.

[17] Danzig, *Catastrophic Bioterrorism: What Is to Be Done?*

anthrax, post-exposure prophylaxis, public health preparedness, public health policy implementation, political acceptance, and Strategic National Stockpile. Literature was selected for inclusion if it contained information regarding the provision of prophylactic treatment for either first responders or the general public in the event of an act of bioterrorism, or if it contained recommendations based on specific PEP models. Literature was also collected if there was relevance to stockpile sustainment, cost effectiveness and the psycho-social implications of public health policy implementation. The following sections review literature on public health disaster planning and preparedness specific to the use of *B. anthracis* as a weapon of bioterrorism. Recommendations for PEP treatment, an analysis of proposed and currently employed PEP acquisition models, and psychological and sociological factors effecting political and social acceptance of public health policy are discussed.

C. CLINICAL RECOMMENDATIONS FOR PEP TREATMENT

1. Medication and Dosage

In attempting to determine the appropriate quantities required for the provision of PEP to a given geographical region, it is first necessary to understand the recommended clinical management of exposure to anthrax. Currently, the CDC recommends prophylaxis for all asymptomatic adult patients, ≥18 years of age, with suspected exposure to *B. anthracis* spores, with 60 days of oral doxycycline or ciprofloxican.[18] Additionally, a 3-dose series of Anthrax Vaccine Adsorbed (AVA) is recommended for long-term protection after exposure to anthrax.[19] Whether or not vaccination occurs, oral prophylaxis should be sustained for the full 60 days, by the administration of either ciprofloxican 500 mg every 12 hours, or doxycycline 100 mg every 12 hours.[20] This recommendation is supported by multiple studies, including an animal study in which a

[18] Katherine A. Hendricks et al., "Centers for Disease Control and Prevention Expert Panel Meetings on Prevention and Treatment of Anthrax in Adults," *Emerging Infectious Diseases* 20, no. 2 (February 2014), doi: 10.3201/eid2002.130687.

[19] Jennifer Gordon Wright et al., "Use of Anthrax Vaccine in the United States," *Morbid Mortal Wkly Rep* 59, no. rr06 (2010): 1–30.

[20] Hendricks et al., *Centers for Disease Control and Prevention Expert Panel Meetings*.

monkey developed anthrax 58 days post-exposure, demonstrating that anthrax spores can persist for prolonged periods in a host. That same study, also demonstrated that as many as 90% of the test cases survived if ciprofloxican or doxycycline were administered for a period that exceeds the length of time in which the level of persistent spores remaining the in the body falls to less than an infectious dose.[21] Once the medications to be used for PEP are identified and the recommended dosages are calculated, other factors, such as exposure area and distribution capabilities must be considered in determining the quantities needed for PEP.

2. Exposure Area—Determining Who Gets Treated

Very little literature currently exists on determining the exposure area in the event of an aerosolized anthrax spore disbursement. In a 2007 article, "Modeling Responses to Anthrax and Smallpox Attacks," it is suggested that due to the variability of factors, such as wind speed/direction and humidity, mode of disbursement, and the historical inaccuracy of plume modeling, that it is often more efficient to provide PEP to an entire population rather than to take the time to determine who has and who has not been exposed.[22] Plume modeling is conducted using computer models that simulate the downwind expansion of a pollution plume using information about the wind and atmospheric stability. In the case of aerosolized anthrax, the accuracy of a plume model is highly dependent upon variables, such as the amount of anthrax released, characteristics of the spores, and the exact location and mode of dispersal.[23] In the event of an anthrax attack, many of these variables are unknown. This same article, however, also provides a graphical interpretation of the results of delaying the distribution of antibiotics as a result of identifying a plume area.

Consideration of this data highlights the impact that the use of plume modeling can have on the determination of the quantities of medications necessary for PEP. Based

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[21] Arthur M. Friedlander et al., "Postexposure Prophylaxis Against Experimental Inhalation Anthrax," *The Journal of Infectious Diseases* 167, no. 5 (May 1993): 1239–1243.

[22] Diane C. Jamrog, Michael P. Shatz, and Cassandra Smith, "Modeling Responses to Anthrax and Smallpox Attacks," *Lincoln Laboratory Journal* 17, no. 1 (2007): 115–129.

[23] Dean A. Wilkening, "Sverdlovsk Revisited: Modeling Human Inhalation Anthrax," *Proceedings of the National Academy of Sciences of the United States of America* 103, no. 20 (May 16, 2006): 7589–7594.

on the model in Figure 1, plume modeling would change the distribution population from 2.1 million people to 120,000 people, thus substantially reducing the required number of antibiotics necessary for distribution.[24] Based on findings from the study of the accidental 1979 Sverdlovsk anthrax release in Russia, researchers have predicted that a 1-kg release of an anthrax preparation could contain more than 10^{12} spores.[25] However, others, such as UCLA Professor Dr. Ronald Brookmeyer, pointed out that dispersal factors, such as the type of spore preparation, method of release, and building insulation, are all critical factors to be considered in determining exposurearea.[26] Such variability has led many locals to the conclusion that it is simply more time and resource efficient to provide PEP to an entire population, rather that attempt to determine an exact exposure area.

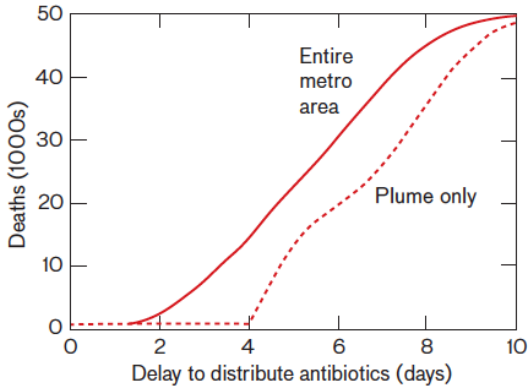

Figure 1. Fatalities are expressed as a function of delay to distribute antibiotics, assuming distribution to all 2.1 million people in a metropolitan area (solid line) and to only the 120,000 people estimated to be in the anthrax plume (dashed line) at a rate of 700,000 people per day.

[24] Jamrog, Shatz, and Smith, *Modeling Responses to Anthrax and Smallpox Attacks*, 115–129.

[25] Wilkening, "Sverdlovsk Revisited: Modeling Human Inhalation Anthrax," 7589–7594.

[26] Ron Brookmeyer, Elizabeth Johnson, and Robert Bollinger, "Public Health Vaccination Policies for Containing an Anthrax Outbreak," *Nature* 432, no. 7019 (2004): 901–904.

3. Distribution/Dispensing—How Soon Should PEP Be Administered?

As the majority of the literature agrees, time is of the essence when distributing PEP in the event of aerosolized anthrax exposure. Factors affecting the time to distribution include detection, medication accessibility (the focus of this review) and dispensing capabilities. Dr. Brockmeyer addressed this issue by supporting the findings of Wein et al. in stating that minimizing the delay until initiation of antibiotic prophylaxis is key to containing an anthrax outbreak.[27] To reinforce this statement, a 2006 study identified local dispensing capacity as the critical determinant of mortality following anthrax bioterrorism, however it is important to note that this statement was based upon the reported rapid availability of regional inventories.[28] It is worth noting that unlimited accessibility is of no benefit if dispensing capabilities are not adequate. Because data on human exposure to aerosolized *B. anthracis* is limited, uncertainty remains regarding the incubation period. In *Prepositioning Antibiotics for Anthrax*, Claire Stroud et al. discuss the impact that defining the minimum incubation period (time from exposure until the initial presentation of symptoms) has on decision-making about prepositioning antibiotics.[29] The average incubation period reported by this study and numerous others is four days for inhalational anthrax.[30] Despite these findings however, a scenario-based exercise conducted in the Chicago metropolitan area revealed that the initiation of PEP on Day 5 after an attack, as opposed to on Day 2, resulted in an increase in mortality from 28,612 to 69,136.[31]

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[27] Lawrence M. Wein, David L. Craft, and Edward H. Kaplan, "Emergency Response to an Anthrax Attack," *Proceedings of the National Academy of Sciences of the United States of America* 100, no. 7 (April 1, 2003): 4346–4351.

[28] Dena M. Bravata et al., "Reducing Mortality from Anthrax Bioterrorism: Strategies for Stockpiling and Dispensing Medical and Pharmaceutical Supplies," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 4, no. 3 (2006): 244–262.

[29] Clare Stroud et al., ed., *Prepositioning Antibiotics for Anthrax* (Washington, DC: National Academies Press, 2012).

[30] Daniel A. Sweeney et al., "Anthrax Infection," *American Journal of Respiratory and Critical Care Medicine* 184, no. 12 (2011): 1333–1341.

[31] Demetrios N. Kyriacou et al., "Cost-Effectiveness Comparison of Response Strategies to a Large-Scale Anthrax Attack on the Chicago Metropolitan Area: Impact of Timing and Surge Capacity," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 10, no. 3 (2012): 264–279.

D. MEDICAL COUNTERMEASURE ACQUISITION MODELS

In the United States, supplies for response to bioterrorism are held at the local, state and national level.[32] Anthrax exposure requires prophylaxis by oral antibiotics promptly after exposure, optimally within 48 hours, and before symptoms arise.[33] Figure 2 illustrates the basic MCM distribution and dispensing strategies currently in place in the United States. Although there are many components of systems for bioterrorism response, few have been evaluated for their ability to meet this goal.[34] A review of the literature relevant to each of the four proposed models follows.

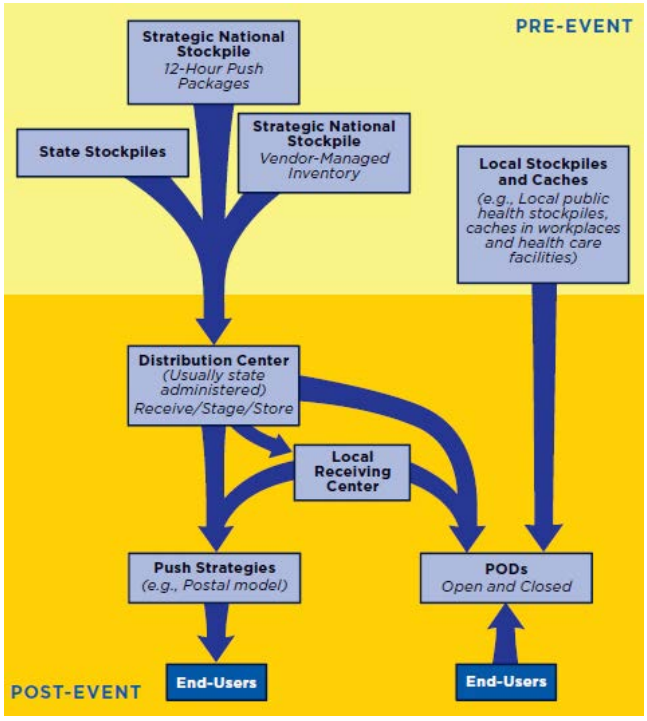

Figure 2. Basic MCM Distribution and Dispensing Strategies[35]

[32] Gregory S. Zaric et al., "Modeling the Logistics of Response to Anthrax Bioterrorism," *Medical Decision Making* 28, no. 3 (2008): 332–350.

[33] Bruce M. Altevogt, Miriam Davis, and Marnina S. Kammersell, *Dispensing Medical Countermeasures for Public Health Emergencies: Workshop Summary* (Washington, DC: National Academies Press, 2008).

[34] Dena M. Bravata et al., "Regionalization of Bioterrorism Preparedness and Response," *Evidence Report/Technology Assessment (Summary)* (96), no. 96 (April 2004): 1–7.

[35] Stroud et al., ed., *Prepositioning Antibiotics for Anthrax*, 70.

1. Local Stockpiling

In a 2008 article, "Modeling the Logistics of Response to Anthrax Bioterrorism," the authors developed a compartmental model to evaluate costs and benefits of various strategies for pre-attack stockpiling. The model was implemented in an Excel spreadsheet with an interface to facilitate data entry. Information was entered about local population size and local inventory stockpiles. Assumptions about the attack size, the chance of attack, the rate of detection, and assumptions about dispensing capacity were also input. Based on scenarios using these models to increase locally held inventories of PEP by 10-fold and twenty-fold, the study concluded that stockpiling large local inventories of pharmaceutical supplies is not likely to effectively reduce mortality.[36] A weapons of mass destruction (WMD) tabletop exercise conducted in Spokane, Washington, in May 2000, recommended that if financially feasible, communities like Spokane may need to establish and maintain enough pharmaceutical stockpiles to remain self-sufficient for at least 24 hours.[37] In the abovementioned 2008 study, however, this was not seen as practical, because locals are limited by their own dispensing capabilities, and are therefore better served by regional or national inventories.[38] While some communities throughout the United States have established large local stockpiles, others hold no antibiotic inventory for response to bioterrorism and plan to rely solely on the SNS.[39]

The City Readiness Initiative (CRI) is a public health preparedness program funded by HHS.[40] In their 2004 Alternative Dispensing Guide, the CRI identified the limited viability of medications as a prohibitive factor in maintaining local pharmaceutical stockpiles.[41] This problem of expired medications is also referenced in

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[36] Zaric et al., "Modeling the Logistics of Response to Anthrax Bioterrorism," 332–350.

[37] Colleen M. Terriff and Amy M. Tee, "Citywide Pharmaceutical Preparation for Bioterrorism," *American Journal of Health-System Pharmacy* 58, no. 3 (2001): 233–237.

[38] Zaric et al., *Modeling the Logistics of Response to Anthrax Bioterrorism*, 332–350.

[39] Ibid., 333.

[40] Henry H. Willis et al., *Initial Evaluation of the Cities Readiness Initiative* (Santa Monica, CA: RAND Corporation, Health, 2009), 52.

[41] Patrick J. Lindner, "CRI Alternative Dispensing Guide: A Collection of Model Practices and Pilot Projects," *National Association of City and County Health Officials* (2006): 10, http://www.Naccho.Org/ Topics/Emergency/Documents/AlternativeDispensin gGuide_Final_000.Pdf.

literature examining the application of the Shelf Life Extension Program (SLEP) to state and local MCM stockpiles in an attempt to optimize the value of medications.'[42]

2. Partnership Storage/Rotation Agreements

One possible solution offered for the problem of expired medications is presented in the option of partnering with private-sector entities for the rotation of state and local stockpile materials.[43] The 2011 Institute of Medicine (IOM) study conducted by Claire Stroud et al., suggested that national guidance be provided to address the range of roles that private-sector partners could play in MCM distribution and dispensing.[44] While the practice of rotating medications has been posed as a potential solution, one 2009 feasibility study found that the number of doses used annually in a local hospital pharmacy amounted to only 2–3% of the total antibiotic cache quantities needed to provide coverage to hospital employees and their families.[45] A similar experience had been noted in 2007 when a Baltimore UASI working group issued an Invitation for Bid, inviting vendors to submit a proposal for the rotation of antibiotics contained in a local prophylactic cache. None of the responding vendors was able to provide the service based on the quantities of medications to be rotated.[46] A 2003 article published in the *Journal of Toxicology* identified the use of a local pharmaceutical distribution company as a fiscally responsible means of providing PEP based upon a collaborative project with a Pennsylvania Metropolitain Medical Response System (MMRS) working group.[47] The article cites 24-hour availability via emergency pager, as well as credentialed drivers who are familiar with the contents and equipment as advantages of working with a

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[42] Courtney et al., *Maximizing State and Local Medical Countermeasure Stockpile Investments*, 101–107; Robbe C. Lyon et al., "Stability Profiles of Drug Products Extended Beyond Labeled Expiration Dates," *Journal of Pharmaceutical Sciences* 95, no. 7 (2006): 1549–1560.

[43] Lindner, *CRI Alternative Dispensing Guide*, 20.

[44] Stroud et al., ed., Prepositioning *Antibiotics for Anthrax*, 9.

[45] J. J. Lee, S. J. Johnson and M. J. Sohmer, "Guide for Mass Prophylaxis of Hospital Employees in Preparation for a Bioterrorist Attack," *American Journal of Health-System Pharmacy: AJHP: Official Journal of the American Society of Health-System Pharmacists* 66, no. 6 (March 15, 2009): 570–575.

[46] Courtney et al., *Maximizing State and Local Medical Countermeasure Stockpile Investments through the Shelf-Life Extension Program*, 106.

[47] Rita Mrvos et al., "Regional Pharmaceutical Preparation for Biological and Chemical Terrorism," *Clinical Toxicology* 41, no. 1 (2003): 17–21.

manufacturer. This article discouraged the option of a user-managed inventory (UMI) model where dual-use medications would be stored and distributed in hospital pharmacies, due to the burdens associated with maintaining accurate stock availabilities within the facilities, and the overwhelming stress inherently placed on a hospital during a public health emergency.[48] The UMI model is described more recently in a 2012 article as a developing concept that can "enhance MCM distribution and dispensing by supporting the activity of the SNS and increasing the capacity of state and local responses."[49] The article suggests the use of Department of Veteran Affairs (DVA) facilities, as opposed to local community hospitals, to create a supply line of MCMs. This article goes on to state however that to be a viable solution, the shelf life of the medication must be long enough to allow the amount of material in the supply line to be consumed by the community through normal business operations. Some jurisdictions have found this to be a limiting factor as antibiotics are now prescribed more restrictively due to the emergence of antibiotic resistant strains of bacteria, attributed to the over-use of antibiotics, such as ciprofloxacin and doxycycline.[50]

3. Pre-Event Distribution of PEP to First Responders

Recent publications, such as a 2011 Institute for Systems Research technical report, demonstrate that there is still no clear guidance on the rapid distribution of antibiotics in response to an anthrax attack. As a result, multiple models have been proposed for the acquisition and subsequent distribution of antibiotics for PEP.[51] Recognizing the predicted overwhelming burden on points of dispensing (POD), some literature advocates for the pre-event distribution of pharmaceuticals to individual

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[48] Mrvos et al., "Regional Pharmaceutical Preparation for Biological and Chemical Terrorism," 19.

[49] C. Norman Coleman et al., "User-Managed Inventory: An Approach to Forward-Deployment of Urgently Needed Medical Countermeasures for Mass-Casualty and Terrorism Incidents," *Disaster Medicine and Public Health Preparedness* 6, no. 04 (2012): 408–414.

[50] Robert Austin et al., "Hidden Complexity in Bacterial Evolution," *Bulletin of the American Physical Society* (2014).

[51] Michelle Houck and Jeffrey Herrmann, *Predicting the Impact of Placing Pre-Event Pharmaceuticals for Anthrax* (College Park, MD: Institute for Systems Research, University of Maryland, 2011).

households for use as directed by local health authorities.[52] This concept was examined in a 2006 partnership study conducted by the CDC and the Missouri Department of Health and Senior Services examining, among other things, the ability of households to maintain MedKits in the home as directed, and to reserve medications for emergency use.[53] The study contracted with a local physician to provide medical screening for the study, comprised of participants evenly distributed among community health clinic, corporate, and first responder cohorts. Once medically cleared, a MedKit was sent via FedEx to 13,289 persons in 4,259 households. Study participants were instructed not to use the medications unless directed to do so, and were asked to return the medications months later.[54] Follow-up interviews were conducted at randomly assigned two-, four- and eight-month intervals to assess social factors, such as awareness and willingness to purchase MedKits. Public health officials initially expressed strong opposition to the project due to the potential for adverse events attributed to self-medication and the development of antibiotic resistance.[55] Despite these concerns, the study revealed that individually issued MedKits were returned unopened in 97% of the cases, and that only four of the study participants had ingested the pills for another reason. Over 75% of the respondents reported an increase in awareness for the need to be prepared between baseline and follow-up interviews. Additionally, 85% reported a willingness to purchase a Medkit for their household at an average purchase price of $23. In 2011, the Office of the Assistant Secretary of Preparedness (ASPR) conducted a public engagement initiative in Seattle and King County, Washington to develop a better understanding of the goals,

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[52] Houck and Herrmann, *Predicting the Impact of Placing Pre-Event Pharmaceuticals for Anthrax*, 2.

[53] "CDC's Division of Strategic National Stockpile Emergency MedKit Evaluation Study Summary," U.S. Department of Health and Human Services, November 15, 2007, http://www.bt.cdc.gov/cri/pdf/medkit-evaluation-summary-2007updated.pdf.

[54] Houck and Herrmann, *Predicting the Impact of Placing Pre-Event Pharmaceuticals*, 2.

[55] George W. Korch Jr., "Doxycycline MedKits for Public Health Preparedness for an Anthrax Attack," U.S. Department of Health & Human Services Office of the Assistant Secretary for Preparedness and Response, April 2, 2012, http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Anti-InfectiveDrugsAdvisoryCommittee/UCM299211.pdf.

needs and behaviors of the public in response to a biological incident.[56] The findings of this initiative clearly demonstrated the utility of public engagement in the development of medical countermeasure systems, and also supported the 2006 Missouri study in that the public felt confident in their abilities to maintain individually issued medications for use only under the direction of a public health official.[57]

4. The Strategic National Stockpile for the Provision of PEP

According to the CDC, the SNS was developed with the intension of providing "medicine and medical supplies to protect the American public if there is a public health emergency (terrorist attack, flu outbreak, earthquake) severe enough to cause local supplies to run out."[58] Similarly, the other literature reviewed reinforced this notion that the SNS is not intended as a first response tool.[59] However, in 2012, the *Anticipated Responsibilities of the Strategic National Stockpile (SNS) in the Year 2020* report stated that in a survey of 300 state and local organizations, it was found that > 90% are dependent upon the SNS for MCM.[60] Factors contributing to state and local reliance on the SNS may include a lack of available funding to purchase regional or local stockpiles, or a lack of the logistics and infrastructure necessary to maintain, activate and distribute the stockpile. Additionally, the SNS has demonstrated efficiency during deployments to events, such as those of September 11, 2001, when the program's 12-hour Push Packages reached the New York City area within seven hours of request, despite travel restrictions.[61]

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[56] U.S. Department of Health and Human Services Office of the Assistant Secretary for Preparedness and Response, *Public Input on Medical Countermeasures Seattle and King County, Washington*, Executive Summary ed. (Washington, DC: U.S. Department of Health and Human Services Office of the Assistant Secretary for Preparedness and Response, 2012).

[57] Ibid.

[58] "Strategic National Stockpile (SNS)."

[59] Stroud et al., ed., Prepositioning *Antibiotics for Anthrax,* 71; Prior, *Who You Gonna Call?*, 3.

[60] National Biodefense Science Board and the Office of Public Health Preparedness and Response Board of Scientific Counselors, *Anticipated Responsibilities of the Strategic National Stockpile (SNS) in the Year 2020: An Examination with Recommendations* (Washington, DC: U.S. Department of Health and Human Services, 2012).

[61] Nicki Pesik, Sue Gorman, and Wayne D. Williams, "The National Pharmaceutical Stockpile Program: An Overview and Perspective for the Pacific Islands," *Pacific Health Dialog* 9, no. 1 (2002): 109–114.

E. MODEL EVALUATION CRITERIA

1. Timeliness of Response

In reviewing the literature, there were several factors to be considered in assessing the time to delivery of PEP in the event of an anthrax attack. Even states, regions or local jurisdictions that have sufficient quantities of PEP stockpiled must consider the logistics involved in getting the medications from their storage location to the POD. Those locations that do not have local stockpiles must consider the time associated with operations at receipt, staging and storage (RSS) sites when receiving materials from the SNS, in addition to transport time to PODs. A 2012 study on the location-allocation of stockpiles cited three noticeable delays in receiving and distributing assets from the SNS: the delay by the state in requesting federal assets, the delay in the federal process that releases assets only upon the declaration of a disaster, and the time it takes to rapidly move supplies from the SNS stockpile to where they are needed.[62] Figure 3 provides an illustration of the existing framework for the distribution of SNS assets.

[62] Jomon Aliyas Paul and Govind Hariharan, "Location-Allocation Planning of Stockpiles for Effective Disaster Mitigation," *Annals of Operations Research* 196, no. 1 (2012): 469–490.

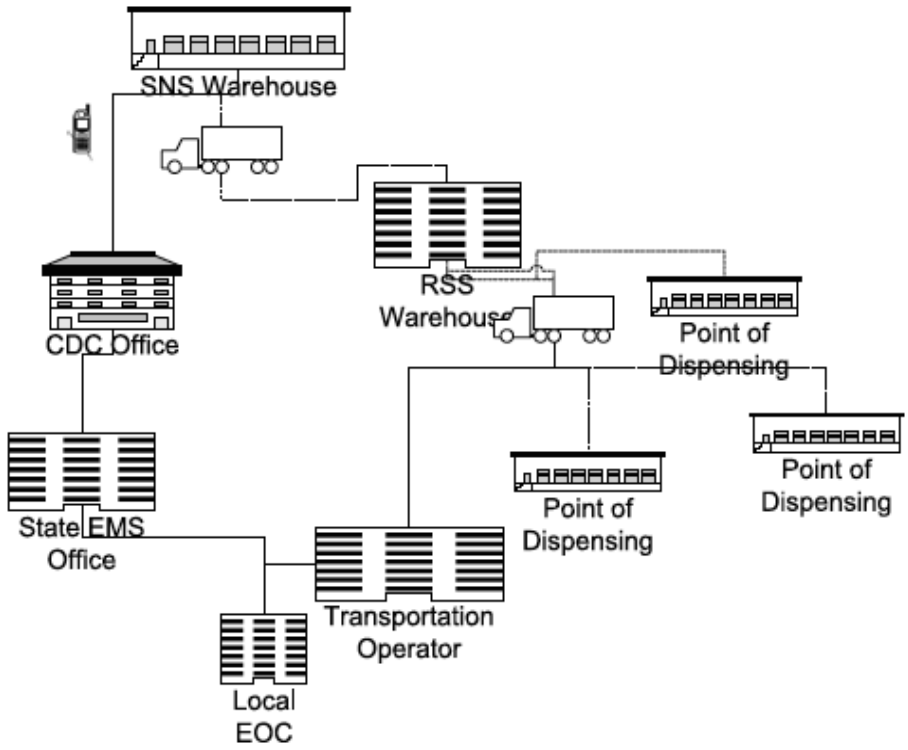

Figure 3. Illustration of existing framework for the distribution of SNS assets

While the efficiency of POD operations is beyond the scope of this thesis, it is important to acknowledge that although medications for PEP may reach a designated POD, they are not available for distribution until the POD is sufficiently staffed to perform the distribution; the availability of staffing must therefore be considered when assessing time to delivery.[63]

2. Cost

The literature reviewed cited numerous factors to be considered in determining the cost effectiveness of local stockpiling. In a study published in 2008, Zaric et al. listed factors beyond the initial purchase price to consider such as the annual maintenance costs, which include replacement, rotation and storage fees.[64] This same study found it more cost effective to increase local dispensing capacity then to increase local antibiotic

[63] Sinan Khan and Anke Richter, "Dispensing Mass Prophylaxis-the Search for the Perfect Solution," *Homeland Security Affairs* 8, art. 3 (February 2012).

[64] Zaric et al., *Modeling the Logistics of Response to Anthrax Bioterrorism*, 332–350.

inventories, as the ability to dispense medications rapidly is most frequently the limiting factor in the provision of PEP. This conclusion is consistent with the findings of a 2006 study published in *Biosecurity and Bioterrorism*, that further quantified the statement by suggesting that in the event of a large attack, local stockpiling should be considered cost effective only if the annual probability of an attack is greater than 0.0004.[65]

Still another factor to consider in determining cost effectiveness is the recommended course of post-exposure prophylactic treatment. In addition to oral post-exposure antimicrobial prophylaxis, the more recent literature reviewed recommends the administration of the 3-dose anthrax vaccine, AVA, as the most cost-effective response strategy.[66] While the CDC continues to recommend a 60-day course of antimicrobial treatment in combination with the vaccine regimen, a 2006 panel study done by the National Institutes of Health claimed that animal studies have shown that post-exposure antimicrobial administration for just 14 days provided complete protection against inhalational anthrax when combined with 3-dose vaccination therapy.[67] Similar findings were also noted in a 2005 comparison study conducted by Dr. Robert Fowler on the cost effectiveness of defending against bioterrorism.[68] A 2011 study, *Cost-Effectiveness Comparison of Response Strategies to a Large-Scale Anthrax Attack on the Chicago Metropolitan Area*, also concluded that the optimal cost effective response strategy is to provide antibiotic prophylaxis and vaccination for all exposed people within 48 hours of the recognition of a large-scale attack.[69]

A relatively limited amount of literature was located on the extension of pharmaceutical shelf life for containing MCM sustainment costs. The most recent and

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[65] Bravata et al., "Reducing Mortality from Anthrax Bioterrorism: Strategies for Stockpiling and Dispensing Medical and Pharmaceutical Supplies," 244–262.

[66] Kyriacou et al., *Cost-Effectiveness Comparison of Response Strategies*, 264–279.

[67] Nicholas J. Vietri et al., "Short-Course Postexposure Antibiotic Prophylaxis Combined with Vaccination Protects Against Experimental Inhalational Anthrax," *Proceedings of the National Academy of Sciences* 103, no. 20 (2006): 7813–7816.

[68] Robert A. Fowler et al., "Cost-Effectiveness of Defending Against Bioterrorism: A Comparison of Vaccination and Antibiotic Prophylaxis Against Anthrax," *Annals of Internal Medicine* 142, no. 8 (2005): 601–610.

[69] Kyriacou et al., *Cost-Effectiveness Comparison of Response Strategies*, 264–279.

relevant article found was published in 2009 and titled *Maximizing State and Local Medical Countermeasure Stockpile Investments through the Shelf-Life Extension Program.*[70] The article references prior data on drug stability profiles and concludes that efficient and cost effective management of state and local medical countermeasure stockpiles is dependent upon their inclusion in the federally administered SLEP, or a similarly managed program. The SLEP is a Department of Defense (DOD)/Food and Drug Administration (FDA) administered fee-for-service program, and is intended for large federal stockpiles of military significance or contingency use products.[71] The DOD and DSNS both maintain large stockpiles of medications and vaccines to ensure that both military and civilian populations have access to antidotes and treatments in the event of a medical emergency.[72] The FDA and DOD developed this program to save federal dollars by extending the shelf life of pharmaceuticals beyond the manufacturer's expiration date. All testing for extensions is done at FDA test facilities.[73] The claim that the cost-effective management of stockpiles is dependent upon inclusion in such a program is supported by research revealing that stability testing can extend the life of pharmaceutical products far beyond their manufacturer expiration dates.[74] Ciprofloxacin, a primary pharmaceutical component of the SNS, is provided as an example of a medication included in a national SLEP implemented in Israel that resulted in a substantial savings in MCM stockpiling.[75]

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[70] Courtney et al., *Maximizing State and Local Medical Countermeasure Stockpile Investments*, 101–107.

[71] Moran Bodas et al., "Shelf-Life Extension Program (SLEP) As a Significant Contributor to Strategic National Stockpile Maintenance: The Israeli Experience with Ciprofloxacin," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 10, no. 2 (2012): 182–187.

[72] Leissa B. Food and Drug Administration. "Shelf Life Extension Program," presentation at Federal, State, and Local Public Health Preparedness Meeting, Baltimore, MD, December 14–15, 2010, www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm247676.htm.

[73] United States Department of Health and Human Services, *Implementation Plan for the National Health Security Strategy of the United States of America* (Washington, DC: United States Department of Health and Human Services, 2012).

[74] Lyon et al., "Stability Profiles of Drug Products Extended Beyond Labeled Expiration Dates," 1549–1560.

[75] Bodas et al., "Shelf-Life Extension Program (SLEP) As a Significant Contributor to Strategic National Stockpile Maintenance: The Israeli Experience with Ciprofloxacin," 182–187.

3. Logistics

Some of the challenges associated with MCM stockpiling were highlighted during 2011 Government Accountability Office (GAO) testimony before the Subcommittee on Emergency Preparedness, Response, and Communications Committee on Homeland Security. Although substantial funding has been allocated to the development and acquisition of MCM, the testimony cited a high failure rate in research and development, and difficulties meeting regulatory requirements as ongoing obstacles to the development of new MCMs.[76] These and other challenges, such as a lack of local surge capacity, are detailed in a 2002 article published in the European Society of *Clinical Microbiology and Infectious Diseases*.[77] These articles describe difficulties in obtaining central storage, the burden of cache maintenance, and the cost of replenishment of expired medications as other matters to be considered in determining the feasibility of sustaining local stockpiles.[78] A 2006 *Biosecurity and Bioterrorism* study examined logistical factors, such as dispensing capacity, the number of individuals requiring PEP, local inventories and delays in detection.[79] The results of the study suggested that state and local jurisdictions focus efforts on maximizing local dispensing capacity, strategies that encourage adherence to PEP regimens, and technologies to identify those at risk for exposure. In 2008, Zaric et al. used a compartmental model to evaluate the logistics of a bioterrorism response supply chain.[80] Logistical factors incorporated included antibiotic inventories, as well as prophylaxis-dispensing strategies and capacities. Similar to the 2006 study, this article cited local dispensing capacity and the number of unexposed

[76] Cynthia Bascetta, *Public Health Preparedness: Developing and Acquiring Medical Countermeasures Against Chemical, Biological, Radiological, and Nuclear Agents* (GAO-11-567T) (Washington, DC: Government Accountability Office, 2011).

[77] R. Havlak, S.E. Gorman, and S. A. Adams, "Challenges Associated with Creating a Pharmaceutical Stockpile to Respond to a Terrorist Event," *Clinical Microbiology and Infection* 8, no. 8 (2002): 529–533.

[78] Dan Hanfling, "Equipment, Supplies, and Pharmaceuticals: How Much might it Cost to Achieve Basic Surge Capacity?" *Academic Emergency Medicine* 13, no. 11 (2006): 1232–1237.

[79] Bravata et al., *Reducing Mortality from Anthrax Bioterrorism*, 244–262.

[80] Zaric et al., *Modeling the Logistics of Response to Anthrax Bioterrorism*, 332–350.

individuals requesting PEP as the most significant factors influencing morbidity and mortality in the event of an anthrax attack.[81]

Previous efforts to establish an activation and deployment plan for a locally held PEP cache in the Baltimore metropolitan region revealed the logistical challenges resulting from a lack of properly trained and credentialed personnel to transport medications in the event of a large-scale biological event. Personnel from first responder organizations that housed the stockpile were not available to serve as transporters in already over-burdened jurisdictions. Furthermore, personnel from outside the jurisdiction were not insured to operate the housing jurisdiction's vehicles, and lastly, local law enforcement agencies were not able to commit resources to providing escorts during medication transport.[82]

4. Stakeholder Acceptance

Transforming evidence-based public health research into public health policy is not an easy task, as highlighted by Petticrew et al. in a 2004 study stating, "while researchers would like their research to influence policy, in practice this often does not happen because they take little account of the needs of policymakers and of the reality of the policy process."[83] Principles of Emergency Management, published by the Federal Emergency Management Agency (FEMA) in 2006, define stakeholders as "people who have, or think they have, a personal interest in the outcome of a policy."[84] Stakeholders can be social groups, political groups, or economic groups, and can vary substantially in the power and resources that they bring to the table. The mobilization of the appropriate stakeholder groups is a crucial step in ensuring the adoption of policy.[85] Policymakers engage stakeholder groups to influence relevant levels of government by presenting a

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[81] Zaric et al., *Modeling the Logistics of Response to Anthrax Bioterrorism*, 334.

[82] This information is based on the personal observations of this researcher during participation in the Region III Health and Medical Task Force Post-exposure Prophylaxis Subcommittee.

[83] Mark Petticrew et al., "Evidence for Public Health Policy on Inequalities: 1: The Reality According to Policymakers," *Journal of Epidemiology and Community Health* 58, no. 10 (October 2004): 811–816.

[84] Michael K. Lindell, Carla S. Prater, and Ronald W. Perry, "Emergency Management Stakeholders," in *Fundamentals of Emergency Management* (Washington, DC: FEMA, 2006), 33.

[85] Ibid.

policy in a manner that highlights the policy's benefit to the stakeholder and justifies investment in the policy. To achieve this mission comprehensively, the National Association of County and City Health Officials (NACCHO) suggested developing key relationships with the private sector, public sector, beneficiaries, volunteer sector, practitioners and resource partners as stakeholders.[86] A 2006 *BMC Public Health* research article showcased an example of public health and business collaboration by examining the case of a partnership formed between public health officials, and a business executive group in the Metropolitan Atlanta Region.[87] Beyond the realization that combining government and business resources increases the opportunity for successful emergency preparation and response, the article cites shared objectives and mutual trust as key factors in the sustainment of these partnerships.

5. Comprehensiveness

The week-long TOPOFF-2 exercise conducted in 2003 demonstrated the challenge of determining a prophylaxis distribution policy for first responders and citizenry across local jurisdictions.[88] Planners and policy makers must continuously assess the enormous logistical challenges associated with the distribution of PEP in a large metropolitan area, as well as the potential for limited quantities of the amount of PEP immediately available, to ensure equitable access for all citizens. Significant research was found on the allocation of scare medical interventions and resources. Persad et al. review the advantages and disadvantages of the most commonly used principles for the allocation of scarce resources, which include a lottery, prioritarianism approaches, utilitarianism approaches, and approaches that promote and reward social usefulness.[89] The writers cite the utilitarianism approach as that which has historically been used in

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[86] "Engaging Partners, Stakeholders and Community Members," National Association of County and City Health Officials, accessed May 23, 2014, www.naccho.org/topics/infrastructure/CHAIP/partner-engegement.cfm.

[87] James W. Buehler, Ellen A. Whitney, and Ruth L. Berkelman, "Business and Public Health Collaboration for Emergency Preparedness in Georgia: A Case Study," *BMC Public Health* 6, no. 1 (2006): 1–13.

[88] Prior, *Who You Gonna Call?*, 12.

[89] Govind Persad, Alan Wertheimer, and Ezekiel J. Emanuel, "Principles for Allocation of Scarce Medical Interventions," *The Lancet* 373, no. 9661 (2009): 423–431.

bioterrorism policy, providing the most good to the most people. In promoting equity of access through the utilitarian principle, establishing and sustaining public trust and effective communication is critical. During a public health emergency, diverse populations may require individualized approaches to ensure that messages are delivered appropriately.[90] Within the context of bioterrorism, distrust of government has emerged as an issue in numerous studies. During the 2001 anthrax attack, many African American postal workers saw racial discrimination as the underlying explanation for the different treatment they received as compared to the U.S. Senate staff in the Hart Senate Office Building.[91] In a report titled "Pandemic Preparedness: The Need for a Public Health, Not Law Enforcement/National Security, Approach," the American Civil Liberties Union (ACLU) argues for government actions based on principles of justice and transparency.[92] In defining justice, the article states that preparation for a potential pandemic should ensure a fair distribution of precautions and responses, and "equal respect for the dignity and autonomy of each individual." Transparency, with regard to pandemic or disaster preparedness, requires transparent communication of accurate information.

F. SUMMARY

The literature that was reviewed reinforced the notion that no national standard exists for the local acquisition and stockpiling of medical countermeasures. Controversy also exists as to whether or not this practice is even warranted, given the challenges faced in storing, maintaining, and activating the asset, as well as the rapid availability of the SNS and relatively low probability of an attack. The literature does however support that there is strong consensus, based on guidelines provided by the CDC, regarding the course of post-exposure prophylaxis treatment for those exposed to *B. anthracis.* Based on these

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[90] Janice C. Blanchard et al., "In Their Own Words: Lessons Learned from Those Exposed to Anthrax," *American Journal of Public Health* 95, no. 3 (2005): 489–495.

[91] Sandra Crouse Quinn, Tammy Thomas, and Carol McAllister, "Postal Workers' Perspectives on Communication during the Anthrax Attack," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 3, no. 3 (2005): 207–215; Bradley D. Stein et al., "A Bitter Pill to Swallow: Nonadherence with Prophylactic Antibiotics during the Anthrax Attacks and the Role of Private Physicians," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 2, no. 3 (2004): 175–185.

[92] George J. Annas, "Bioterrorism, Public Health, and Civil Liberties," *New England Journal of Medicine* 346, no. 17 (2002): 1337–1342.

guidelines, the federally administered SNS program, its mission, program objectives, and capabilities, are clearly defined as a means of reducing morbidity and mortality in the event of a public health emergency. Further research needs to be conducted regarding several aspects of bioterrorism preparedness in the form of PEP during an anthrax attack. From the literature that was reviewed, it is not clear what parameters are used in determining what the most appropriate model for providing PEP is for a given population. Further research is needed to determine if a model that is deemed to be appropriate and effective is universally applicable, or if there are location specific variables effecting the decision. These and other questions remain to be answered. While it is conceivable that there is no one-size-fits-all solution, more specific guidance on cost-effective preparedness solutions would undoubtedly result in more informed, and consequently better-prepared communities.

III. METHODOLOGY

A. POLICY ANALYSIS

This research evaluated the efficiency of four potential policy options for the management of PEP in the event of a *B. anthracis* anthrax attack. The policy options examined were the following.

- Policy Option 1—a locally managed antibiotic medication stockpile, purchased, stored, sustained and deployed at the state, regional or local level.
- Policy Option 2—a locally managed antibiotic medication stockpile, purchased and stored at the state, regional or local level, with its inventory sustained using a supply rotation model, managed through partnerships with public and/or private entities.
- Policy Option 3—the provision of PEP to first responders/first receivers via medications prescribed and pre-dispensed to individual responders and stored in their homes.
- Policy Option 4—reliance on the SNS as a sole source of PEP, beyond medications currently on hand in local commercial and hospital pharmacy inventories.

B. SELECTING POLICY OPTIONS

The policy options described below were chosen based upon their relevance as either current or proposed models for the provision of PEP in various jurisdictions throughout the nation.

Policy Option 1: The use of a locally managed antibiotic stockpile is used by numerous state and local jurisdictions throughout the United States, including the Baltimore metropolitan region. This region was chosen for analysis based upon the personal observations and first-hand experiences of this researcher with regard to local stockpile planning, procurement and sustainment efforts.

Policy Option 2: The second policy option evaluated was selected based on the fact that numerous jurisdictions throughout the nation have previously employed such a

model through rotation agreements with local hospital pharmacies or pharmaceutical distributors.

Policy option 3: The third policy option is based upon a model that was recently proposed by the ASPR. This model proposes the pre-placement of prophylactic medications in the homes of emergency services personnel. The FDA, under an annually renewed emergency use authorization (EUA), has approved the use of this model, which is currently being considered by many state and local jurisdictions.

Policy Option 4: The fourth and final policy option examined the reliance of the CDC's SNS as a sole source for the provision of PEP, and was chosen for comparison as the federally coordinated model for the distribution of prophylaxis in the event of an anthrax incident.

C. DATA SOURCES

Data sources for this research included peer-reviewed literature, current government and non-government organization (NGO) program reports, exercise after-action reports, jurisdiction specific policies detailing the management of PEP for a given population, and SNS program policies and data.

D. TYPE AND MODE OF ANALYSIS

This research is a policy options analysis. The steps involved included the analysis of the four aforementioned policy options to determine the feasibility of the application of each of the models in a state or local jurisdiction. The following metrics were used in the analysis and subsequent assessment of each of the options:

- Timeliness of response—refers to the amount of time that lapses from the detection of anthrax until the availability of PEP. For the purposes of this study, availability was defined as directly accessible to those who have been exposed or potentially exposed. Factors effecting this time to delivery may include geographical distance, the availability of manpower and transportation resources, medication shortages and/or time delays associated with legal and regulatory procedures.[93]

[93] Lawrence O. Gostin, "Medical Countermeasures for Pandemic Influenza: Ethics and the Law," *Jama* 295, no. 5 (2006): 554–556.

- Cost—the determination of cost considered the rate by which the investment in any particular model reduced the probability of a successful attack. Factors, such as procurement, storage, maintenance, sustainment and administrative costs, were all considered.
- Logistics—the logistical requirements that accompany the provision of PEP can be extensive. Models were evaluated based on the demands placed on the human and non-human resources of federal, state, and local government organizations, as well as private industry stakeholders.
- Stakeholder Acceptance—There are numerous organizations that comprise the list of stakeholders in the event of a public health emergency. Stakeholders can include, but are not limited to, first responders, public health personnel, local private industry executives, and elected officials. The evaluation of a PEP model based on stakeholder acceptance entailed the identification and subsequent assessment of all parties affected by the employment of a given model. Factors, such as cost, convenience, perception of risk, and trust in government, can all influence stakeholder acceptance.[94]
- Comprehensiveness—refers to the overall ability of a model to provide the most timely PEP coverage to the greatest number of people. This criterion is evaluated based upon the quantity of medication available from a model, the mode of distribution, and the equality of access. Healthcare access and health outcomes are highly variable within communities, and are frequently unevenly distributed based on levels of income, education, insurance status, and ethnicity.[95] A model was considered as providing equitable access if it provided equivalent benefits to the various groups within a population, and did not subject any particular group to a disproportionate burden that might reduce the likelihood of obtaining PEP.[96]

A policy options matrix was used to evaluate the options based on the stated criteria, with relative outcome values assigned and designated as "A," "B," or "C."

E. OUTPUT

The finished product of this analysis provides a framework by which state and local jurisdictions can evaluate the suitability of models for the provision of PEP in the

[94] Petticrew et al., *Evidence for Public Health Policy on Inequalities*, 811–816.

[95] David P. Eisenman et al., "Will Public Health's Response to Terrorism be Fair? Racial/Ethnic Variations in Perceived Fairness during a Bioterrorist Event," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 2, no. 3 (2004): 146–156.

[96] Stroud et al., ed., *Prepositioning Antibiotics for Anthrax*, 165–170.

event of a large-scale anthrax attack. Readers may employ these findings in evaluating the efficacy of their own local programs, and in determining the most appropriate PEP model based upon local priorities.

Policy Option	Timeliness	Cost	Logistics	Stakeholder Acceptance	Comprehensiveness
1					
2					
3					
4					

IV. POLICY OPTION 1: LOCAL STOCKPILES

A. INTRODUCTION

The 2001 anthrax attacks thrust public health into the media spotlight, simultaneously highlighting the strengths and weaknesses of the nation's public health infrastructure. Congressional testimony and other writings revealed warnings from within the public health community and beyond, of the problems likely to result from a struggling public health system operating under a national bioterror plan, marked by confused lines of authority and overlapping responsibilities.[97] Although these warnings were issued prior to 2001, it was not until the events of September 11, and the anthrax attacks that followed shortly thereafter, that the warnings captured the attention of state and local planners. With the threat of bioterrorism looming, many state and local jurisdictions throughout the United States sought protection in the form of the establishment of local PEP stockpiles.

No national consensus exists regarding the appropriate levels of local pharmaceutical supply inventories.[98] A 2000 WMD tabletop exercise after-action report recommended that local communities be self-sufficient for at least 24 hours.[99] In contrast, a 2002 U.S. Medicine Institute for Health Studies report suggested that there was no recommendation for individual communities to stockpile pharmaceuticals.[100] Such conflicting guidance has resulted in inconsistency in local planning efforts throughout the nation.

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[97] Thomas B. Cole, "When a Bioweapon Strikes, Who Will Be in Charge?" *JAMA: The Journal of the American Medical Association* 284, no. 8 (August 23–30, 2000): 944, 947–8.

[98] Bravata et al., *Reducing Mortality from Anthrax Bioterrorism*, 244–262.

[99] Terriff and Tee, *Citywide Pharmaceutical Preparation for Bioterrorism*, 233–237.

[100] U.S. Medicine Institute for Health Studies, *Surge Capacity: Is It Time to Move Beyond 'Just-in-Time'?* (Washington, DC: U.S. Medicine Institute for Health Studies, 2002).

B. PROGRAM STRUCTURE

The experiences of planners from the Baltimore metropolitan region are provided as an example of a local stockpiling model.[101] The Health and Medical Task Force of the Baltimore metropolitan area took a regional approach to securing antibiotics to be used for post-exposure prophylaxis in the event of an aerosolized anthrax attack. This region consists of Baltimore City, and the six surrounding emergency services jurisdictions (counties or municipalities). With funding provided by the UASI, the group purchased a three-day course of medications, consisting of 85% doxycycline and 15% ciprofloxacin. The determination of this quantity was based upon an estimation of the number of "first responders" in the region, as defined by HSPD–8 as "those individuals who in the early stages of an incident are responsible for the protection and preservation of life, property, evidence, and the environment, including emergency response providers as defined in section 2 of the Homeland Security Act of 2002 (6 U.S.C. 101), as well as emergency management, public health, clinical care, public works, and other skilled support personnel (such as equipment operators) that provide immediate support services during prevention, response, and recovery operations."[102] These numbers, provided by the respective discipline Task Force representatives, included personnel from law enforcement, fire, emergency medical services (EMS), emergency management, public health, essential hospital personnel, public works, shelter personnel, and key agency leadership. The estimated number of persons was then multiplied by three to account for the first responders' families, based on an average household size of three persons, resulting in an initial order of medication for 354,000 individuals.

A secure and environmentally controlled storage facility was constructed, also with UASI funding, to house the medications for the entire region. Medications were ordered and upon receipt, were repackaged and relabeled in accordance with Maryland Board of Pharmacy laws for individual distribution in three-day courses. Activation and

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[101] Information regarding this model is provided from the first-hand experiences of this researcher as an active member of the Region III Health and Medical Task Force, operating in Baltimore, Maryland.

[102] The White House, *Homeland Security Presidential Directive 8: National Preparedness* (Washington, DC: The White House, December 2003).

deployment plans were crafted with the assistance of the University of Maryland Center for Health and Homeland Security.

Although unsuccessful, significant effort was made to have state and local pharmaceutical caches included in the federally administered SLEP prior to the cache's expiration. Upon expiration, the medications must be properly destroyed and repurchased at the current market price.

C. ANALYSIS

1. Timeliness of Response

It would seem reasonable to assume that the pre-positioning of PEP at the local level would result in a relatively short amount of time required to access the medications. However, when assessing the timeliness of this model, it is important to consider the time required to access and distribute the stockpile utilizing local resources. Based on the activation policy in the Baltimore case for instance, it was incumbent upon the jurisdiction requesting the medications to initiate the activation of the stockpile utilizing pre-defined emergency management resource request procedures. Once approved, the requesting jurisdiction was responsible for providing the personnel and equipment necessary to retrieve the medications from the storage site and to provide secure, police escorted transport to the requested location. Estimations of timeliness for this model should consider the coordination of resources, and must also account for confounding factors, such as traffic delays, personnel shortages and civil unrest, which commonly present during a state of emergency.

2. Cost

The establishment, maintenance and sustainment costs associated with local stockpiling can vary depending upon multiple factors. The cost of medications is variable based upon the current market price, which is driven by primary healthcare

consumption.[103] Additionally, larger jurisdictions are typically afforded greater discounts through bulk purchasing. The annual maintenance costs of stockpiled antibiotics consist of rotation and storage costs.[104] For instance, in the previously discussed Baltimore example, the initial purchase price of the medications was $226,227.00. Annual maintenance costs were budgeted at $56,556.00 based upon an estimated 0.25 per daily dose. The designation of a secure and climate controlled storage facility, and administrative costs, such as those associated with medication re-packaging and labeling, are other costs that must be considered. The ability to sustain local stockpiles is dependent upon the anticipated availability of funding streams. Medications contained in many state and local stockpiles have relatively short expiration dates, as many state pharmacy laws mandate that expiration dates not exceed one year.[105] Sustaining these stockpiles requires the replacement of medications, which results in associated costs to include disposal fees and the cost of repurchase. Given that Federal funding for HLS grant programs has decreased by more than 75% since the program's inception in 2003, the availability of future funding seems unpredictable at best.[106]

An additional cost that would be incurred with this model is the cost associated with the transport of the stockpile materials to the various points of distribution. This task could be accomplished by a private contractor, a designated state or local government agency, or could be shared among the jurisdictions receiving the medications. In the previously discussed Baltimore case, the requesting jurisdiction was responsible for providing secure transportation for the medications, and would incur the associated manpower and logistical costs.

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[103] Ulrich S. Jensen et al., "Effect of Generics on Price and Consumption of Ciprofloxacin in Primary Healthcare: The Relationship to Increasing Resistance," *The Journal of Antimicrobial Chemotherapy* 65, no. 6 (June 2010): 1286–1291.

[104] Zaric et al., *Modeling the Logistics of Response to Anthrax Bioterrorism*, 332–350.

[105] Stroud et al., ed., Prepositioning *Antibiotics for Anthrax*, 88–89.

[106] *Are We Prepared? Measuring the Impact of Preparedness Grants since 9/11*, Senate Subcommittee on Emergency Management, Intergovernmental Relations, 1st. sess., 2014.

3. Logistics

Stockpile storage sites must prevent unauthorized access, must be environmentally controlled so that medications are not exposed to extreme temperatures, and must be protected from elements, such as water damage and rodent infestation.[107] Additionally, storage sites must be easily accessible, and located in a place that provides for timely distribution to the coverage area. This sight may be constructed solely for this purpose, as was the case in the Baltimore example, or may be a leased facility. Additional logistical requirements to be considered are those for medication repackaging and labeling in accordance with state and federal laws. Because the purchase of drugs in unit-of-dose packaging is typically cost prohibitive, it is likely that purchasers will have to repackage and re-label medications upon receipt.[108]

4. Stakeholder Acceptance

Political agendas can be of systemic, governmental or institutional nature.[109] As the events of 2001 become a distant memory, policy issues, such as bioterrorism preparedness, are not receiving daily media attention, and are far less likely than in 2002 to become a systemic issue among stakeholders. The current government agenda at the state and local level is heavily concentrated on such stressed issues as the economy, crime, immigration, and education, leaving bioterrorism as a back-burner issue for some stakeholders.[110]

From the clinical perspective, healthcare experts suggest that the most effective strategy for mitigating the effects of a large-scale anthrax attack is believed to be the pre-event vaccination of a large portion of the general population.[111] The findings of a study comparing response strategies to a large-scale anthrax attack in Chicago however

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[107] Havlak, Gorman, and Adams, "Challenges Associated with Creating a Pharmaceutical Stockpile to Respond to a Terrorist Event," 529–533.

[108] Stroud et al., ed., Prepositioning *Antibiotics for Anthrax*, 196.

[109] Lindell et al., *Emergency Management Stakeholders*, 33.

[110] Liz Farmer et al., "The Top 10 Legislative Issues to Watch in 2014," Governing, January 2014, http://www.governing.com/topics/politics/gov-2014-legislative-issues-to-watch.html.

[111] Kyriacou et al., *Cost-Effectiveness Comparison of Response Strategies to a Large-Scale Anthrax Attack on the Chicago Metropolitan Area: Impact of Timing and Surge Capacity*, 264–279.

revealed that pre-event vaccination would be cost effective only if a large-scale attack was a credible risk, and if there was substantial delay in public health intervention.[112] Given the current state of the economy, it seems unlikely that local and state government stakeholders would support such costly initiatives as pre-event vaccination, and would instead endorse programs, such as local stockpiling.

At the local level, the agencies most involved with public health emergencies are the fire and police departments, which are first to respond to most health related emergencies. Some communities have a separate EMS agency, but this function is frequently provided by the fire department in conjunction with local hospitals and private ambulance companies. The possibility exists that the intentional release of a large quantity of a biological agent could span multiple jurisdictions and even states. For instance, given the ideal atmospheric conditions, an aerosolized anthrax release in the Washington, DC area could result in significant impact to not only Washington, DC, but also to portions of Maryland and Virginia. Given this possibility, one must consider the consequences of the availability of PEP to first responder stakeholders in one jurisdiction, and not in another.

State and local level public works, transportation, and community development departments are important stakeholders in the mitigation process as well, as they also have responsibilities during the response and recovery phases.[113] At the state level, stakeholders include the state emergency management agencies and state health, and human services departments also have important emergency management functions, and many members of these agencies belong to professional associations that lobby for disaster-relevant legislation.[114] These agencies provide the major direction for their subordinate local organizations, and interact with state legislatures to provide the legal framework within which they function, and serve to link local governments with federal resources.

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[112] Kyriacou et al., *Cost-Effectiveness Comparison of Response Strategies to a Large-Scale Anthrax Attack on the Chicago Metropolitan Area: Impact of Timing and Surge Capacity*, 264–279.

[113] Lindell et al., *Emergency Management Stakeholders*, 39.

[114] Ibid., 33.

Private stakeholders, such as community business leaders, have come to understand the importance of the connection of the health of the community to the health of their businesses. These politically influential stakeholders are therefore likely to be supportive of emergency management goals that diminish business interruption by providing the timely distribution of PEP.[115]

5. Comprehensiveness

The comprehensiveness of this model is primarily dependent upon the quantities of medications stockpiled. As this model utilizes PODs as a distribution mechanism, equality of access must also be considered. Local stockpiles are typically limited in quantity due to the cost of purchase and the space required for storage. These limited quantities frequently result in the pre-designation of stockpiles for use by local first responders, hospital, and emergency management personnel and their families, to ensure that they are ready to report to work as soon as possible.[116] With public health as the priority, it is essential to protect individuals who provide treatment and protect the public's health, as these are critical missions necessary to save lives and provide care for those in need.[117] While many agree with the concept of priority distribution for first responders, concerns regarding the equality of access may arise among those who are not a member of these groups, and who are not advocates of the concept of triage by social worth.[118]

The local stockpile model's heavy reliance upon PODs for the distribution of medications requires that planners consider an alternate means of distribution to those populations for which PODs may not be easily accessible. This may include the physically and mentally disabled, as well as elderly and indigent populations. Likewise, it

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[115] Yang Zhang, Michael K. Lindell, and Carla S. Prater, "Vulnerability of Community Businesses to Environmental Disasters," *Disasters* 33, no. 1 (2009): 38–57.

[116] Nathaniel Hupert et al., *Community-Based Mass Prophylaxis: A Planning Guide for Public Health Preparedness* (Weill Medical College of Cornell University: U.S. Department of Health and Human Services, Agency for Healthcare Research and Quality, 2004.

[117] Gostin, *Medical Countermeasures for Pandemic Influenza: Ethics and the Law*, 554–556.

[118] Persad, Wertheimer, and Emanuel, *Principles for Allocation of Scarce Medical Interventions*, 423–431.

is crucial that this model be accompanied by a strong messaging component to ensure equality in the clarity of messaging to all, including non-English speaking populations.[119]

[119] Anne Rinchiuso-Hasselmann et al., "Public Compliance with Mass Prophylaxis Guidance," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 8, no. 3 (2010): 255–263.

V. POLICY OPTION 2—JURISDICTIONAL CACHE ACQUISITION WITH THIRD PARTY INVENTORY MANAGEMENT

A. INTRODUCTION

The effective medical response to a bioterrorism attack requires planning for substantial resources, supplies and storage space. Stockpiling in a central repository can be problematic for drugs with short shelf lives, as frequent replacement is costly and administratively burdensome. A managed inventory model allows local, regional, or state jurisdictions to procure a pharmaceutical stockpile with the intent of providing PEP to a designated population. This model aims to manage pharmaceutical stockpiles more efficiently by avoiding costs due to the expiration, disposal and repurchase of expired medications.[120] Inventory management techniques, such as UMI and distributor-managed inventory (DMI), can decrease costs through the rotation of MCM medications into routine use.

B. PROGRAM STRUCTURE

1. User-Managed Inventory

The UMI concept is characterized by four key features: (1) the use of dual-utility MCMs; (2) storage of MCMs at multiple local or regional pharmacies, who would maintain a sufficient inventory, or ‘‘bubble,’’ to help meet immediate surge MCM needs; (3) MCMs would be managed to ensure that inventory would not expire before use, using first-in, first-out protocols; and (4) the UMI ‘‘bubble’’ inventory would be used locally to treat casualties in an emergency, including evacuees from other localities.[121] Similar to central stockpiling and vendor-managed inventory (VMI), the ‘‘bubble’’ inventory could also be allocated locally to areas of greatest immediate need. The UMI model differs

[120] C. Norman Coleman et al., “User-Managed Inventory: An Approach to Forward-Deployment of Urgently Needed Medical Countermeasures for Mass-Casualty and Terrorism Incidents,” 408–414.

[121] C. Norman Coleman et al., “Medical Planning and Response for a Nuclear Detonation: A Practical Guide,” *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 10, no. 4 (2012): 346–71.

from VMI in that it does not rely on a product vendor to resupply goods when an inventory gets low. Instead, regular users (e.g., pharmacies) of inventory assets rotate the goods through daily use with the intention of avoiding expiration.[122] A 2012 Disaster Medicine and Public Health Preparedness article provides the extensive network of facilities that are included within the DVA as an example of a user-managed inventory model.[123] These facilities include Veterans Administration (VA) hospitals, community and hospital-based outpatient clinics, community pharmacies, and veteran centers. In the absence of a mass-casualty incident, dual-utility MCMs (useful for both mass casualty emergencies and routine medical care) are cycled through pharmacy inventories so that they are used prior to expiration. The daily medical use of these medications offers the added benefit of familiarity by those who use them for routine medical purposes.[124]

2. Distributor-Managed Inventory

The DMI model utilizes a single local distribution company for the management of PEP stockpile inventory, as opposed to the multiple facilities employed in the UMI model. An example of this model is provided in the case of a regional MMRS working group from Pennsylvania who developed a DMI system to maintain a regional pharmaceutical stockpile in the Pittsburgh area.[125] With the assistance of a regional poison center, the group partnered with a pharmaceutical distributor, located within a two-hour driving radius, to store, and deliver the MCM materials. Stockpiles are also rotated through normal distribution channels to retailers. This system was intended to provide PEP to treat an at-risk population for a 24-hour period following a chemical or biological incident. The model employs the use of well-established distribution routes to guarantee that PEP medications are available at all times. Company employees provide

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[122] Davis, Miriam, Megan Reeve, and Bruce Altevogt, "Reorienting and Augmenting Professional Approaches." In *Nationwide Response Issues After an Improvised Nuclear Device Attack*, 71 (Washington, DC: National Academies Press, 2013).

[123] Coleman et al., *User-Managed Inventory*, 408–414.

[124] Leigh Sawyer, "Where are the Countermeasures? Protecting America's Health from CBRN Threats: A Report of the National Biodefense Science Board," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 8, no. 2 (June 2010): 203–207.

[125] Mrvos et al., "Regional Pharmaceutical Preparation for Biological and Chemical Terrorism," 17–21.

24-hr/day, 7 day/week availability, and are familiar with warehouse contents and equipment operations. The limited number of potential transporters allows for the creation of emergency transport identities for each, to allow drivers to enter restricted areas.[126]

C. ANALYSIS

1. Timeliness of Response

UMI and DMI models do not eliminate the need for a SNS response, but instead provide more immediate access to MCM resources. Both models are activated locally, and can therefore be activated more quickly than the SNS, as there are fewer layers of bureaucracy to be traversed.

A second factor affecting the timeliness of these models is the fact that medications that are stored by pharmacies or distributors must be rapidly repackaged prior to distribution as PEP. Pharmacies typically store bulk bottles of 100 or 500 tablets for daily use dispensing.[127] These medications must be converted to unit-of-use packaging to facilitate rapid dispensing to individuals as PEP; doing so requires time and manpower.

a. Factors Influencing UMI Timeliness

Although UMI resources may be stored closer than SNS assets, the time, manpower, and transportation resources required to distribute the medications to PODs can be extensive due to the high number of storage locations. Retrieval of PEP from numerous facilities for redistribution to PODs is likely to be time consuming, especially if traffic delays occur. Some proponents of UMI have touted the model as being available for distribution from the location at which they are stored, thereby eliminating the time

[126] Mrvos et al., "Regional Pharmaceutical Preparation for Biological and Chemical Terrorism," 17–21.

[127] Havlak, Gorman, and Adams, "Challenges Associated with Creating a Pharmaceutical Stockpile to Respond to a Terrorist Event," 529–533.

associated with delivery.[128] Others however, have discouraged the placement of PEP assets at hospitals because of the increased demand for services already placed on the facility in the event of a public health emergency.[129]

b. Factors Influencing DMI Timeliness

The timeliness of DMI assets is highly dependent upon the location of the distributor storage facility, relative to PODs. As mentioned earlier, a significant advantage of the DMI model is that transportation resources, including vehicles and drivers, are pre-designated and credentialed.[130] Furthermore, assets are stored at a single location, eliminating the need for multiple pick-ups. Factors, such as traffic congestion, although unpredictable, should always be considered.

2. Cost

In general, prepositioning MCMs closer to intended users increases costs, as it requires management of a larger number of stockpiles to provide equivalent coverage.[131] Inventory models, such as UMI and DMI, however, reduce costs through the elimination of the need for local jurisdictions to construct secure and climate controlled storage facilities.

a. Factors Influencing UMI Cost

Beyond the initial medication purchase, the costs associated with a UMI model involve the storage of additional drugs at medical facilities, and the administrative management of MCM rotation.[132] In this model, the cost of storage is shared among multiple facilities. These facilities rotate the stockpiled assets in an effort to forgo the periodic disposal and repurchase of expired medications, thereby reducing the costs

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[128] Coleman et al., *User-Managed Inventory: An Approach to Forward-Deployment of Urgently Needed Medical Countermeasures for Mass-Casualty and Terrorism Incidents*, 408–414.

[129] Mrvos et al., "Regional Pharmaceutical Preparation for Biological and Chemical Terrorism," 17–21.

[130] Ibid.

[131] Stroud et al., ed., *Prepositioning Antibiotics for Anthrax*, 16.

[132] Coleman et al., *User-Managed Inventory: An Approach to Forward-Deployment of Urgently Needed Medical Countermeasures for Mass-Casualty and Terrorism Incidents*, 408–414.

associated with local stockpiling.[133] Countering these cost savings however, are the extensive transportation resources (vehicles and manpower) necessary for the delivery of UMI assets to numerous storage facilities.[134]

b. Factors Influencing DMI Cost

Considering the decreased use of antibiotics in everyday medical use, the wide distribution networks of the regional pharmaceutical warehouses may afford more efficient rotation operations. While many business executives have come to realize that their engagement in disaster response is essential to community resilience, some distributors may still assess fees for inventory management services.[135]

3. Logistics

For UMI and DMI models to be viable options for the provision of PEP, the shelf life of MCMs must be long enough to allow the amount of material in the supply bubble to be consumed by the daily medical use of a healthcare system. The recent emergence of drug-resistant bacteria from the suspected over-use of antibiotics has resulted in a significant decline in the number of antibiotics prescribed in the day-to-day healthcare setting.[136] Consequently, the typical market demand for medications, such as ciprofloxacin and doxycycline, has diminished to a volume that has made it impractical for many healthcare entities, and even some distributors, to enter into medication rotation agreements.[137]

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[133] Mrvos et al., "Regional Pharmaceutical Preparation for Biological and Chemical Terrorism," 17–21.

[134] Stroud et al., ed., Prepositioning *Antibiotics for Anthrax*, 171.

[135] Mrvos et al., "Regional Pharmaceutical Preparation for Biological and Chemical Terrorism," 17–21.

[136] Qiucen Zhang and Robert Austin, "The Goldilocks Principle and Rapid Evolution of Antibiotic Resistance in Bacteria," APS March Meeting 2011, Dallas, TX, March 21–25, 2011, *Bulletin of the American Physical Society*, 56, no. 1 (2011).

[137] Coleman et al., *User-Managed Inventory: An Approach to Forward-Deployment of Urgently Needed Medical Countermeasures for Mass-Casualty and Terrorism Incidents*, 408–414.

a. UMI Logistical Considerations

The UMI model will require a moderate to high level of logistical planning due to the increased number of storage sites. If MCMs are to be retrieved from multiple local storage facilities and delivered to PODs, robust communications plans are essential to ensure that PEP supplies are distributed appropriately. The use of transportation and security resources from multiple organizations, to deliver supplies to multiple PODs, will require a clearly defined chain of command, and a pre-determined and reliable communications infrastructure.

Some have discouraged the use of hospital pharmacies for PEP storage and distribution. Hospital pharmaceutical storage space is a precious resource, and is frequently restricted by the ever-increasing demand for patient care space.[138] Furthermore, it is anticipated that maintaining accurate real-time inventories from multiple facilities may prove difficult.[139]

Furthermore, it is expected that during a public health emergency, the demands on local hospitals will already be extensive, and that the emergency need for medications from within the facility will overwhelm hospital pharmacies.[140]

An advantage of the widespread storage of MCMs in the UMI model is the reduction of the risk of mass MCM destruction at a single storage facility. Another ancillary benefit of UMI is that the on-site supply bubble can help buffer against temporary medication shortages due to unusual fluctuations in routine demand.

b. DMI Logistical Considerations

In the DMI model, all assets are typically stored in a single distribution warehouse. Although a centralized storage location increases the risk of mass MCM inventory destruction, the DMI model requires fewer resources for activation and

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[138] James Little and Brian Coughlan, "Optimal Inventory Policy within Hospital Space Constraints," *Health Care Management Science* 11, no. 2 (2008), 177–183.

[139] Mrvos et al., "Regional Pharmaceutical Preparation for Biological and Chemical Terrorism," 17–21.

[140] Ibid.

delivery to PODs.[141] As discussed previously, this model takes advantage of the full-time availability of trained and pre-credentialed delivery personnel.[142]

The number of personnel that are appropriately trained and available to perform unit-of-dose repackaging must also be considered. The traditional role of a pharmaceutical distributor is to provide medications to end-users in standard bulk packaging. Additional personnel and packaging resources may be necessary to rapidly prepare mass quantities of MCM for distribution.[143]

4. Stakeholder Acceptance

By nature, both UMI and DMI models require partnership agreements. As with other models, first responders, healthcare workers, and state and local planners all have vested interests in ensuring the availability of PEP. Due to the decentralized nature of the model however, the number of stakeholders in a functional UMI system is typically far greater than is DMI.

a. UMI Stakeholder Acceptance

The employment of a UMI model for the provision of PEP requires the engagement and careful collaboration among health care system and emergency services partners. This model requires comprehensive partnership agreements between state or local planners, and the hospitals, specialty care networks, or pharmacies that are providing the storage and rotation of MCM assets.[144] These partnerships require participants to acknowledge and address multiple challenges, including differences in organizational cultures. Operational constraints, such as concerns about liability, the confidentiality of healthcare information, and the limits of volunteerism must also be overcome.

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[141] Coleman et al., *User-Managed Inventory*, 408–414.

[142] Mrvos et al., *Regional Pharmaceutical Preparation*, 17–21.

[143] Havlak, Gorman and Adams, "Challenges Associated with Creating a Pharmaceutical Stockpile to Respond to a Terrorist Event," 529–533.

[144] Coleman et al., *User-Managed Inventory*, 408–414.

b. DMI Stakeholder Acceptance

Beyond the shared values of public health and community service, many private entities view their involvement in local disaster planning as an extension of business continuity planning.[145] Business owners are keenly aware that the survival of businesses following a disaster is dependent upon the survival of the community. For emergency services and healthcare stakeholders, the advantages to partnering with private industry are clear. Public health and government officials are acutely aware of their organizational limitations, and welcome the logistical expertise, potential for volunteers, and operational infrastructure.[146] While partnerships with community business organizations can prove mutually beneficial, these relationships require substantial time commitments to maintain. Activation plans should be routinely exercised to maintain solid working relationships and overcome challenges to collaboration.[147]

5. Comprehensiveness

Multiple factors affect the comprehensiveness of a user or distributor managed inventory model for the provision of PEP. Regardless of model, the total quantity of PEP on hand must be adequate to provide coverage until the arrival of outside assets, such as the SNS. In calculating the quantities of antibiotics needed for PODs, many use a simplistic calculation that factors the population, the target time for complete delivery of PEP, the hourly throughput of PODs, and the number of PODs available to provide PEP.[148] Unfortunately, the assumptions that accompany this calculation rarely hold true. For instance, the exact number of a population is not known, and an equal number of people do not report to each POD. Similarly, throughput rates among PODs have been

[145] Buehler, Whitney, and Berkelman, "Business and Public Health Collaboration for Emergency Preparedness in Georgia: A Case Study," 1–13.

[146] Ibid.

[147] Ibid.

[148] Young M. Lee, "Analyzing Dispensing Plan for Emergency Medical Supplies in the Event of Bioterrorism," Proceedings of the 2008 Winter Simulation Conference, Global Gateway to Discovery, WSC 2008, InterContinental Hotel, Miami, FL, December 7–10, 2008 in Winter Simulation Conference, 2008.

found to vary widely from 162 to 1,700 people per hours per site.[149] These variations are based on influences, such as the number of available staff, the demographics of those receiving PEP, and the availability of supplies, which are dependent upon transportation resources.[150]

Although user and distributor managed inventory models differ in the centralization of medication storage, no notable differences exist in the comprehensiveness of the two models.

[149] Zaric et al., *Modeling the Logistics of Response*, 332–350.

[150] Lee, *Analyzing Dispensing Plans for Emergency Medical Supplies*, 2600–2608.

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VI. POLICY OPTION 3—PRE-EVENT DISTRIBUTION TO FIRST RESPONDERS

A. INTRODUCTION

The advanced placement of medications in the individual households of first responders is a suggested strategy for the distribution of antibiotics in the event of an anthrax attack. These pre-distributed medications would allow exposed or potentially exposed first responders to begin immediate treatment at the direction of public health authorities.[151]

B. PROGRAM STRUCTURE

In 2006, the Missouri Department of Health and Senior Services partnered with the CDC to conduct a MedKit evaluation study. The MedKit prototype, designed by the CDC in collaboration with the FDA, consisted of a five-day supply of medication, packaged in a four-fold cardboard blister pack. The blister pack was then packaged inside of a sealed transparent bag, with instructions for use contained in an outside open pouch.[152] The prototype was evaluated as an investigational new drug and the study was approved to meet all federal and state regulatory requirements. The predominant goals of the study were to evaluate a strategy to distribute antibiotics to the general public in a timely manner in the event of an anthrax attack, and to assess the ability of households to adequately maintain MedKits in the home.[153] Social factors, such as attitude and perception, which might influence participant behavior were also examined, in an effort to gather data regarding the acceptability of the concept. The study listed five proposed modalities to bolster the nation's response capacity, naming the Medkit model as one that could be used either alone, or in combination with other strategies, based upon a community's need. At the conclusion of the study, 97% of the MedKits were returned in

[151] Michelle L. Houck and Jeffrey W. Herrmann, "Preparing for an Anthrax Attack: The Impact of Distributing MedKits," Proceedings of the 2011 Industrial Engineering Research Conference, T. Doolen and E. Van Aken, ed., Reno, Nevada, May 21–25, 2011.

[152] "CDC's Division of Strategic National Stockpile Emergency MedKit Evaluation Study Summary."

[153] Ibid.

accordance with the instructions provided, and of those, 99% were intact. The remaining 3% were either lost, or participants simply refused to return them. During follow-up interviews, study participants reported that having the MedKits in their homes increased their awareness of the need to prepare for a bioterror attack, with 94% stating that they would like to have a MedKit in their home based on the study experience.[154]

In 2009, President Barrack Obama issued an executive order: *Establishing Federal Capability for the Timely Provision of Medical Countermeasures Following a Biological Attack.*[155] The order states: "The Federal Government must establish mechanisms for the provision of medical countermeasures to personnel performing mission-essential functions to ensure that mission-essential functions of Federal agencies continue to be performed following a biological attack."[156] Consequently, the FDA authorized an EUA for the mass dispensing of doxycycline as PEP for inhalational anthrax.

In a 2012 joint meeting of the Anti-Infective Drugs and the Non-Prescription Drugs Advisory Committees, Dr. George Korch Jr., Senior Science Advisor from ASPR, sought guidance on the feasibility of the development pathway for MedKits for the first responder community. Dr. Korch affirmed ASPR's desire to provide protection to first responders and their household members as soon as possible after an incident, "so the first responders have peace of mind to be available to assist the rest of the community."[157] The contents of the MedKits, as presented during this meeting were as follows:

- Ten-day course (20 tablets) of doxycycline hyclate per household member
- Directions for crushing and dosing for children and individuals who cannot swallow tablets
- 10mL syringe
- Directions for safe disposal of unused, expired kits

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[154] "CDC's Division of Strategic National Stockpile Emergency MedKit Evaluation Study Summary."

[155] Ibid.

[156] Exec. Order No. 13527 of December 30, 2009, Establishing Federal Capability for the Timely Provision of Medical Countermeasures Following a Biological Attack, 3 C.F. R. (2010).

[157] Korch Jr., "Doxycycline MedKits for Public Health Preparedness for an Anthrax Attack," 2.

- Warning that the kit should only be used as directed by public health officials during an anthrax emergency.

The proposed concept of operations required that MedKits would only be available from a licensed physician and dispensed through a pharmacy, with the remaining 50-day supply of medications to be obtained from PODs.[158] To date, concerns about safety and the inappropriate use of pre-dispensed antibiotics have slowed the development of this program, and participation has not been expanded beyond those in the first responder community.[159]

On December 2, 2013, senior officials from ASPR and DHS issued a memo addressed to "Occupational Health Directors or equivalent professional," detailing the nature of the program.[160] The letter encouraged those who are licensed to prescribe medications in their state of practice to consider, in the spirit of preparedness, providing a 10-day antibacterial drug supply for first responders to keep in their homes. The letter listed three oral antibacterial drugs (ciprofloxacin, doxycycline, and levofloxacin) that are indicated and FDA approved for PEP, and emphasized the criticality of providing appropriate storage and usage instructions. It is important to note that as approved, this program differs from the MedKit program in that it does not recommend issuing medications to family members of first responders, stating that they will received their PEP with the general public.[161]

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[158] "Doxycycline Medkits for Public Health Preparedness for an Anthrax Attack," U.S. Department of Health and Human Services, Assistant Secretary for Preparedness and Response, Biomedical Advanced Research and Development Authority, Anti-Infective Drugs Advisory Committee of the Federal Drug Administration, April 2, 2012, http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeeting Materials/Drugs/Anti-InfectiveDrugsAdvisoryCommittee/UCM297762.pdf.

[159] Houck and Herrmann, "Preparing for an Anthrax Attack: The Impact of Distributing MedKits."

[160] Nicole Lurie and Kathryn Brinsfield, "Letter to Occupational Health Directors or Equivalent Professional," December 2, 2013, http://www.dhs.gov/sites/default/files/publications/Letter%20to%20 Occupational%20Health%20Directors%20for%20First%20Responder%20Doxycycline%20from%20HHS %20and%20DHS%20Dec%202013.pdf.

[161] Ibid.

C. ANALYSIS

1. Timeliness of Response

Upon receiving direction from public health authorities, first responders with current pre-distributed antibiotics would have immediate access to PEP. Medications could be kept at home, at work, or on a person for rapid access, and would eliminate the need for first responders to seek access to PEP from other sources. A study conducted in 2011 using a compartmental model to predict the deaths from an anthrax attack consistently found that the number of deaths decreased as more pre-dispensed antibiotics (MedKits) were distributed.[162] This finding is illustrated in Figure 4, which is based upon a scenario in which the rate of prophylaxis adherence is 90%, and the SNS push-pack delay is 24 hours.[163]

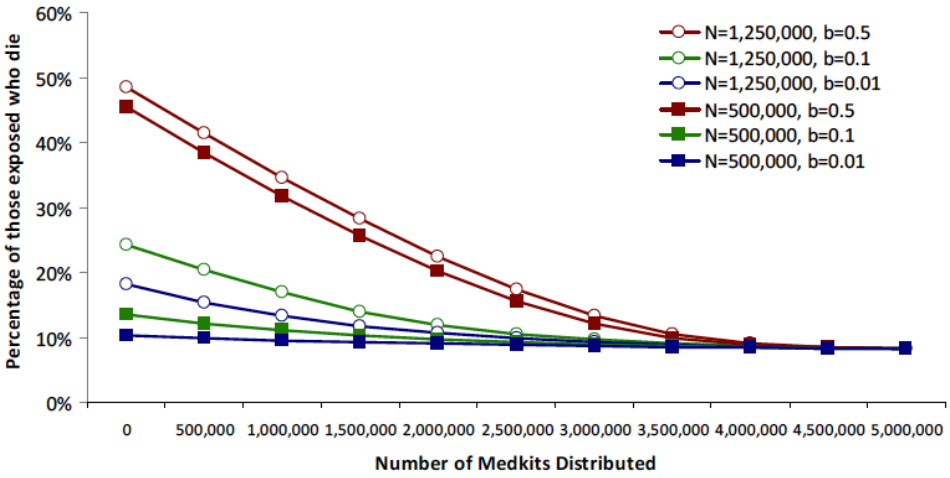

Figure 4. The mortality rate decreases when more MedKits are distributed before an attack. N = number exposed. b = percentage of non-exposed persons seeking prophylaxis (potential exposures).

Although this program is only available for first responders, the elimination of these individuals from those to which PEP must be distributed post-attack would reduce the burden on PODs. Based on workforce estimates, making antibiotics available to the first

[162] Lurie and Brinsfield, "Letter to Occupational Health Directors or Equivalent Professional."

[163] Houck and Herrmann, *Predicting the Impact of Placing Pre-Event Pharmaceuticals*, 17.

responder community could result in a nationwide reduction of approximately of 3.2 million people from POD throughput.[164] Furthermore, the availability of first responders to assist in the distribution of PEP to the general public can increase POD throughput, thereby increasing the likelihood of providing PEP to an entire population within the recommended 48-hour window.[165]

2. Cost

There is no comparable program history from which to gauge the cost of pre-dispensing antibiotics to first responders. As stated in the 2013 DHS memo to healthcare practitioners however, it is anticipated that any costs associated with this model will be deferred to the individual first responder.[166] This would include the cost of a pre-screening doctor's visit, as well as the cost of the actual prescription, which would vary significantly dependent upon individual prescription medication coverage. This transference of cost may be the result of a 2011 report commissioned by the IOM, estimating MedKits to be 215% more costly than the use of the SNS for PEP, and 127% more than the U.S. Postal Service delivery model.[167] It should be noted that an extreme case was used for illustrative purposes, assuming no use of PODs for distributing the initial 10-day prophylactic course of antibiotics. The high cost of this model can be attributed to the costs associated with packaging ($5.12/person/10-day supply), and delivery ($5.45 million) of medications.[168] Although the currently approved pre-dispensing model has eliminated the prohibitive costs associated with packaging and shipping, the less expensive telephone pre-screening method used for home MedKits has been replaced by the added financial burden of a physician office visit.[169]

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[164] "Doxycycline Medkits for Public Health Preparedness for an Anthrax Attack."

[165] Charles DiMaggio et al., "The Willingness of U.S. Emergency Medical Technicians to Respond to Terrorist Incidents," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 3, no. 4 (2005): 331–337.

[166] Lurie and Brinsfield, "Letter to Occupational Health Directors or Equivalent Professional."

[167] Clare Stroud et al., "Commissioned Paper: A Cost and Speed Analysis of Strategies," National Center for Biotechnology Information, 2011, http://www.ncbi.nlm.nih.gov/books/NBK190050/?report=printable.

[168] Ibid.

[169] "Doxycycline Medkits for Public Health Preparedness for an Anthrax Attack."

This model carries the highest sustainment cost as well, as current FDA EUA regulations would require the annual replacement of medications.[170] This cost includes not only medication replacement, but also the annual medical screening required for re-issue. Although the option exists for first responder organizations to absorb the cost of this program, consistently diminishing federal HLS grant dollars would challenge the ability to sustain this alternative source of funding.

3. Logistics

Pre-dispensing antibiotics to first responders may relieve some logistical burdens, however other models of distribution must still be available for the general public. This model requires that individuals classified as first responders obtain a prescription directly from their occupational health or personal physicians, and in turn obtain the medications from a pharmacy. While it is not expected that removing this population from the POD distribution model will significantly diminish the logistical requirements of any one POD, the requirement for storage space would be eliminated if this model were employed as an alternative to local stockpiling for first responders.[171]

Administratively, first responder organizations attempting to track employee participation in this voluntary program would need to develop a means to differentiate those who have obtained the medications from those who have not. This data would be necessary to estimate accurately those who would still need PEP from an alternate source in the event of an incident. Without accurate documentation, the anticipated number of first responders left to rely on PODs may be grossly over-estimated, resulting in the need to redistribute medications among public PODs.

4. Stakeholder Acceptance

First responders are critical stakeholders in the issue of PEP, as they are expected to respond to calls for assistance during an emergency. Immediate access to PEP would provide incentive for responders to report to duty, and would reduce the burden on those

[170] Stroud et al., ed., Prepositioning *Antibiotics for Anthrax*, 257–259.

[171] Stroud et al., "Commissioned Paper: A Cost and Speed Analysis of Strategies."

tasked with post-incident dispensing to the first responder community.[172] Unlike the proposed MedKit model however, this program does not offer pre-event distribution to the family members of first responders. Studies examining the ability and willingness of responders to report in a variety of disaster situations revealed a willingness to respond as low as 50% for biological events.[173] However, when PEP is made available for first responders and their families in advance of an emergency event, these same studies revealed an increased responder willingness to report for duty. The Emergency Services Coalition for Medical Preparedness, comprised of national associations representing emergency services organizations and personnel, further supports these findings.[174] The Coalition represents millions of career and volunteer personnel in the law enforcement, fire and emergency services, EMS, emergency management, and public works disciplines.[175] Citing the statistics in the above study, the Coalition and its member organizations advocated for increasing national resilience via the provision of MedKits for emergency services personnel and their families.[176] Based on this information, first responders may be less apt to report for duty if their families are not provided with adequate PEP.

Federal stakeholders, such as DHS, ASPR, CDC and the FDA, have all endorsed this model, although it is not mandated. Likewise, the determination of which populations are considered first responders is left to the discretion of individual jurisdictions.[177] Based upon the already existing variability of policies and standard operating procedures among jurisdictions, it is reasonable to expect that leaving this determination up to state and local officials will result in inconsistent and inequitable policies.

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[172] Michael Chervenic, "Wide Area Recovery and Resiliency Program (WARRP) Biological Attack Response and Recovery: End to End Medical Countermeasure Distribution and Dispensing Processes," *National Technical Information Services* (April 2012): 1–118.

[173] DiMaggio et al., *The Willingness of U.S. Emergency Medical Technicians to Respond to Terrorist Incidents,* 331–337.

[174] "About the Coalition," Emergency Services Coalition for Medical Preparedness, June 13, 2014, http://www.emergencyservicescoalition.org/aboutus.htm.

[175] Ibid.

[176] "Doxycycline Medkits for Public Health Preparedness for an Anthrax Attack."

[177] Ibid.

Psychosocial factors should also be considered when assessing this model. Because this model involves the individual distribution of medications, the responsibility lies with the first responder to obtain the requisite medical screening and prescription necessary for the medications to be issued.[178] Likewise, the annual renewal process also requires the initiative of the individual first responder. Although the instances of anthrax exposure in the United States are few, studies on the willingness to accept prophylaxis after the 2001 anthrax attacks revealed an overall adherence rate of only 44% among postal workers who were provided the recommended 60-day post-exposure course of medication.[179] This finding suggests that a large portion of those with potential for exposure may not value the availability of PEP, and would therefore be less likely to maintain personal supplies. Conversely, inconsistent policies between neighboring jurisdictions resulting in the employer absorbed costs of PEP in one organization and not in another, invites the notion that some first responders may be unwilling to respond if they are not provided the same coverage as their peers.

Lastly, this model requires the willingness of physicians to prescribe medications prior to the occurrence of an incident. There has been considerable concern of late regarding antimicrobial resistance due to the frequent misuse of antibiotics.[180] These and concerns over the inappropriate use for other illnesses have prevailed over the findings of the MedKit study, which demonstrated a 97% return rate.[181] Healthcare practitioners may elect not to prescribe PEP medications if their perceived risk of antimicrobial resistance is greater than their perceived risk of an anthrax attack.

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[178] "Frequently Asked Questions: For the HHS/DHS Letter to Occupational Health Directors regarding Doxycycline Prescriptions for First Responders," U.S. Department of Health and Human Services, last reviewed March 18, 2014, http://www.phe.gov/Preparedness/responders/Pages/faq-responder-doxycycline.aspx.

[179] Colin W. Shepard et al., "Antimicrobial Postexposure Prophylaxis for Anthrax: Adverse Events and Adherence," *Emerging Infectious Diseases* 8, no. 10 (2002): 1124–1132.

[180] Zhang and Austin, *The Goldilocks Principle and Rapid Evolution of Antibiotic Resistance in Bacteria*.

[181] Korch Jr., "Doxycycline MedKits for Public Health Preparedness for an Anthrax Attack," 22.

5. Comprehensiveness

The pre-dispensing model provides PEP coverage to those first responders that have elected to participate in the program, but requires that the remainder of the population, including the families of first responders, obtain PEP elsewhere. While some may view this model as giving priority to first responders, it is important to recognize that rapid PEP access for these individuals may result in more timely distribution to others. Although cost prohibitive, the pre-event distribution to an entire population would provide the most equitable distribution of all proposed models.[182] Nevertheless, this would still exclude those that are unable to afford the cost of the medications, or those without a physician willing to prescribe the kit.

Because medications are not to be taken unless directed by public health officials, methods of communication must also be comprehensive and well thought out when considering this model.[183] Delivering this information to all citizens equitably requires ensuring that messaging is transmitted in multiple languages and via multiple mediums. The enlistment of civic organizations, the anticipation of the needs of special-needs populations, and the delivery of messages that reflect the values and priorities of affected populations are all valuable communication tactics to enhance the equitable dissemination of information.[184]

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[182] Stroud et al., "Commissioned Paper: A Cost and Speed Analysis of Strategies."

[183] Houck and Herrmann, *Predicting the Impact of Placing Pre-Event Pharmaceuticals*, 2.

[184] Thomas A. Glass and Monica Schoch-Spana, "Bioterrorism and the People: How to Vaccinate a City Against Panic," *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America* 34, no. 2 (January 15, 2002): 217–223.

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VII. POLICY OPTION 4—SOLE RELIANCE ON THE SNS FOR PEP

A. INTRODUCTION

The SNS is a national repository of antibiotics, chemical antidotes, antitoxins, life-support medications, IV administration, airway maintenance supplies, and medical/surgical items and is managed by the CDC. Although exact quantities are not published, the SNS contains enough medications to provide coverage to 10 million exposed individuals in several large cities in the event of multiple simultaneous attacks.[185] Designed to supplement and re-supply state and local public health agencies in the event of a national emergency, the SNS can be delivered anywhere and at any time within the U.S. or its territories within 12-hours of the federal decision to deploy. This rapid delivery process is assured through the strategic placement of twelve Push Packages, located in undisclosed locations around the United States.[186] The Push Package model was built primarily for the purposes of chemical and biological terrorism response.[187] Each of these 50-ton packages consists of approximately 100 specialized cargo containers, and includes antimicrobial medications and chemical antidotes, as well as various other medical supplies. Once the exact nature of an incident is known, additional supplies are available from the SNS via the VMI portion of the program, which can be specifically tailored to the emergency needs of an incident.[188] On September 11, 2001, the State of New York requested a 12-hour Push Pack. Despite the suspension of all air and ground transportation in an around New York City, the Push Pack arrived, with a police escort, within seven hours of the official request.[189]

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[185] Maged M. Dessouky and Fernando Ordonez, *Supply Chain Management of the Strategic National Stockpiles* (Los Angeles, CA: University of Southern California, Research Project Summaries, 2009).

[186] Raphael M. Barishansky, "The Strategic National Stockpile (and What It Can Do for You)," EMS World, February 24, 2010, http://www.emsworld.com/article/10319802/the-strategic-national-stockpile.

[187] Havlak, Gorman, and Adams, "Challenges Associated with Creating a Pharmaceutical Stockpile to Respond to a Terrorist Event," 529–533.

[188] Ibid.

[189] Ibid.

B. PROGRAM STRUCTURE

The HHS and the CDC established the NPS in 1999. This action was ordered by the United States Congress, with the intent of establishing the capability to re-supply large quantities of essential medical materiel to states and communities, within 12 hours of the federal decision to deploy.[190] Effective March 2003, the NPS became the SNS, managed jointly by DHS and HHS. The Homeland Security Act of 2002 tasked the DHS with defining the goals and performance requirements of the SNS Program, as well as with managing the actual deployment of assets. This task, formally assigned to HHS in 2003, has been subsequently delegated to ASPR, who leads the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE). The PHEMCE includes three primary HHS internal agency partners: the CDC, the FDA, and the National Institutes of Health (NIH), as well as several interagency partners: the DOD, the VA, the DHS, and the U.S. Department of Agriculture (USDA).[191] The Enterprise works with governmental and non-governmental partners to upgrade the nation's public health capacity to respond to a national emergency. HHS lists "develop logistics and operational plans for optimized use of medical countermeasures at all levels of response" as one of their primary goals in their December 2012 PHEMCE Implementation Plan.[192] To achieve this goal, the document proposes the promotion of innovative approaches to inventory management, to enable a sustainable preparedness infrastructure through the optimization of the SNS formulary and the cost-effective management of all SNS assets.

Critical to the success of this initiative is ensuring that capacity is developed at federal, state, and local levels to receive, stage, and dispense SNS assets.[193] Once SNS assets are received in a requesting jurisdiction's RSS site, authority for the SNS materials is transferred to the state and local authorities. State and local authorities are responsible

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190 "Strategic National Stockpile (SNS)."

191 "PHEMCE Governance—PHE," U.S. Department of Health and Human Services, last reviewed June 20, 2012, http://www.phe.gov/Preparedness/mcm/phemce/Pages/governance.aspx.

192 U.S. Department of Health and Human Services, *Public Health Emergency Medical Countermeasures Enterprise Strategy and Implementation Plan* (Washington, DC: U.S. Department of Health and Human Services, Office of the Assistant Secretary for Preparedness and Response, 2012), 73.

193 "Strategic National Stockpile (SNS)."

for the breakdown of the Push Packs for distribution. Members of the SNS technical assistance team will remain on site to assist and advise state and local officials in putting the SNS assets to prompt and effective use. To assist metropolitan regions in preparing to receive materials from the SNS, the CRI, established in 2004, focuses on enhancing preparedness in the nation's largest cities and metropolitan statistical areas (MSA), which account for more than 50% of the U.S. population.[194] Through the CRI program, state and local public health officials have developed pre-designated RSS sites and plans to respond to bioterrorism events by dispensing antibiotics to the entire population of an identified MSA within 48 hours of event detection.[195]

C. ANALYSIS

1. Timeliness of Response

SNS response objectives were developed after consultation with panels of experts on the subjects of biological and chemical terrorism, and based on published treatment recommendations for the threat agents deemed to have the highest degree of lethality.[196] The SNS is designed around two tiers of response: the 12-hour Push Package, and VMI.[197] Through partnership transportation agreements with public, federal and private airfreight carriers to ensure timeliness, a SNS Push Package can be deployed anywhere in the United States and its territories within 12 hours.[198]

While it may take longer to receive VMI (24–36 hours), the smaller size and more specialized content require less time to sort and prepare the assets once delivered.[199] During the October 2001 anthrax attacks, the CDC responded with VMI to provide antimicrobials for PEP for exposed mail handlers, employees of Congressional office

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[194] C. D. Nelson et al., "Federal Initiative Increases Community Preparedness for Public Health Emergencies," *Health Affairs (Project Hope)* 29, no. 12 (December 2010): 2286–2293.

[195] "Strategic National Stockpile (SNS)."

[196] Havlak, Gorman, and Adams, *Challenges Associated with Creating a Pharmaceutical Stockpile*, 529–533.

[197] "Strategic National Stockpile (SNS)."

[198] Steven D. Bice, *The U.S. National Pharmaceutical Stockpile Program* (Atlanta, GA: Centers for Disease Control and Prevention, 2001), 451.

[199] "Strategic National Stockpile (SNS)."

buildings and personnel from affected media organizations. During fall 2001, the SNS filled at least 80 VMI requests across the United States, with an average delivery time of five hours from the receipt of the request.[200] A state or jurisdiction's capacity to receive, sort and redistribute these assets must be considered when calculating the time until PEP is available for dispensing.

Although specific practices regarding POD operations are beyond the scope of this research, it is important to note that achieving maximum POD throughput is essential to the viability of this model.[201] A 2012 RAND study evaluating the effectiveness of the CRI reported that although jurisdictions conducted and reported data on 2,768 drills from 2008–2010, few had tested their capabilities at a large scale. For example, many jurisdictions have tested staff call-down procedures, but nearly 90% of these tests involved 100 or fewer people, thus limiting efforts to estimate the capability to contact all essential staff during a large-scale event.[202] Similarly, in 2009 and 2010, only 32% of drills that tested dispensing at PODs involved 500 clients or more. POD drills with higher numbers of clients reported higher throughputs, suggesting that greater countermeasure dispensing capability might be revealed in more high-stress PODs.[203]

2. Cost

Significant costs are associated with the disposal and repurchase of expired medications in quantities as sizeable as those held by the SNS.[204] Unlike state and local stockpiles, the SNS is afforded the benefit of inclusion in the SLEP. This fee-for-service program is intended for certain large federal stockpiles of military significance or contingency use products, and is administered by the DOD.[205] The DOD and SNS both

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[200] Havlak, Gorman, and Adams, *Challenges Associated with Creating a Pharmaceutical Stockpile*, 529–533.

[201] Onora Lien et al., "Getting Medicine to Millions: New Strategies for Mass Distribution," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 4, no. 2 (2006): 176–182.

[202] Nelson et al., *Analysis of the Cities Readiness Initiative* (Santa Monica, CA: RAND Corporation, 2012), 13, http://lbr.rand.org/content/dam/rand/pubs/technical_reports/2012/RAND_TR1200.pdf.

[203] Ibid.

[204] Stroud et al., ed., Prepositioning *Antibiotics for Anthrax*, 133–136.

[205] Bodas et al., "Shelf-Life Extension Program (SLEP) As a Significant Contributor to Strategic National Stockpile Maintenance: The Israeli Experience with Ciprofloxacin," 182–187.

maintain large stockpiles of medications and vaccines to ensure that both military and civilian populations have access to antidotes and treatments in the event of a medical emergency. The FDA and DOD developed this system to save federal dollars by extending the shelf life of pharmaceuticals beyond the manufacturer's expiration date. All testing for extensions is done at FDA test facilities.[206]

While the cost-savings advantage afforded by the SLEP program is significant, another factor to consider when evaluating cost effectiveness is the purchasing power afforded to the SNS through a partnership agreement with the VA's National Acquisition Center (NAC). This innovative purchasing agreement allows the CDC to take advantage of the VA's existing contract pricing arrangements with pharmaceutical vendors, which provides for a purchase price far lower than those extended to other buyers.[207] While the NAC is provided a fee for their procurement services, the savings attributed to this agreement more than offset the cost of doing business.[208]

The federal government passed new legislation and approved vast increases in federal biodefense programs as a result of post-9/11 biological weapons concerns.[209] Beginning in 2005, however, federal preparedness dollars have steadily decreased.[210] More recent trends in funding have demonstrated a reorganization of funds that has resulted in a decrease in the SNS budget. For example, the FY2013 HHS budget for civilian biodefense was $3.96 billion.[211] Although this number appears to be a 1% increase over FY2012 funding, the reality is that several biodefense programs have been combined with other line items, such as chemical and all-hazards preparedness programs. The end result is actually a $54 million decrease in the Public Health Emergency

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206 "Implementation Plan for the National Health Security Strategy of the United States of America," U.S. Department of Health and Human Services, May 2012, http://www. phe.gov/Preparedness/planning/ authority/nhss/ip/Documents/nhss-ip.pdf.

207 Bice, *The U.S. National Pharmaceutical Stockpile Program*, 52.

208 Ibid.

209 Kathleen Vogel, "Bioweapons Proliferation Where Science Studies and Public Policy Collide," *Social Studies of Science* 36, no. 5 (2006): 659–690.

210 Gursky and Bice, *Assessing a Decade of Public Health Preparedness*, 55–65.

211 Crystal Franco and Tara Kirk Sell, "Federal Agency Biodefense Funding, FY2012–FY2013," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 10, no. 2 (2012): 162–181.

Preparedness (PHEP) and SNS programs.[212] The future of bioterrorism funding is uncertain, and many predict that funding streams will continue to diminish. In moving forward, the HHS will need to be innovative in maintaining the current SNS response capabilities, with a diminishing budget. An increase in state and local dependency on the SNS requiring larger inventories and more robust transportation capabilities only proliferates these challenges. A projected increase in needs for sustainment is not compatible with consistently decreasing funding levels.

3. Logistics

The logistical requirements for this model include manpower, physical space and transportation resources from federal, state, and local governments, as well as private industry. The CDC consulted extensively with major worldwide transportation carriers and the DOD in selecting push-pack storage sites. Consideration was given to factors, such as air traffic hub locations, traffic volume, air courier staff availability, regional weather characteristics and the proximity of DOD assets.[213] Although the exact locations are undisclosed for security reasons, the 12 storage sites were carefully chosen to ensure timeliness in response to any location within the United States and its territories.[214]

The CDC requires that state and local public health agencies be prepared to receive, manage, and dispense the SNS under a cooperative agreement that provides funding to states and select cities for public health emergency preparedness.[215] Once assets are delivered to a requesting state's RSS site, PEP distribution is the responsibility of the receiving jurisdiction. The SNS 12-hour Push Pack consists of 50 tons of pharmaceuticals and medical material that will arrive in 12 hours or less by air or ground transport. The push pack fills a wide-body aircraft, occupies 130 cargo containers, and requires 12,000 cubic feet of ground/floor space for proper receiving, staging and

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[212] Franco and Sell, "Federal Agency Biodefense Funding, FY2012–FY2013," 162–181.

[213] Bice, *The U.S. National Pharmaceutical Stockpile Program*, 26–27.

[214] Havlak, Gorman and Adams, *Challenges Associated with Creating a Pharmaceutical Stockpile*, 529–533.

[215] Lien et al., "Getting Medicine to Millions," 176–182.

sorting.[216] Upon receipt, the assets must be unpacked, sorted and distributed. Through the CRI, all states and Washington, DC, have established plans to receive and distribute supplies from the SNS.[217] State and local public health agencies are charged with overall RSS site management and provide the personnel necessary to sort incoming assets.

Due to the massive quantities maintained by the SNS, unit-dose packaging of all medications is cost prohibitive and limits stock rotation capabilities.[218] Although each 12-hour push package does contain a limited quantity of individually wrapped tablets (blister packs), the majority of the SNS is supplied in bulk packaging. Appropriately trained personnel must be available to repackage medications for individual dosing upon receipt.

4. Stakeholder Acceptance

The identity and motivations of stakeholders must be analyzed when determining the feasibility of using the SNS for nationwide PEP. While bioterrorism preparedness may be deemed a top priority by politicians and lawmakers in Washington, DC, this may not be the case for those in less populated regions that are considered to have a lessor likelihood of attack. To complicate matters further, the role of federal, versus state and local authorities after a biological attack has yet to be clarified.[219] Despite the fact that many states currently rely upon the SNS as their primary source of PEP in the event of an anthrax attack, the CDC continues to maintain that the SNS is not intended as a primary response mechanism.[220] Formal acceptance of the charge to provide first-line coverage will require expansion of the current SNS capabilities to facilitate larger inventories, and more robust rotation and deployment capabilities. Furthermore, to provide clarity of

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[216] Bice, *The U.S. National Pharmaceutical Stockpile Program.*

[217] Jeffrey Levi et al., *Ready Or Not?: Protecting the Public's Health from Diseases, Disasters, and Bioterrorism* (Washington, DC: Trust for America's Health, 2012).

[218] Bice, *The U.S. National Pharmaceutical Stockpile Program.*

[219] Richard Danzig, "A Decade of Countering Bioterrorism: Incremental Progress, Fundamental Failings," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 10, no. 1 (2012), 49–54.

[220] Amesh A. Adalja et al., "The Globalization of U.S. Medical Countermeasure Production and its Implications for National Security," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 10, no. 3 (2012): 255–257.

command authority, assigning the provision of PEP as a primary responsibility of the federal government would require a reconfiguration of power relationships among major bureaucracies. The United States Congress is organized into a series of committees and subcommittees, often with overlapping jurisdictions, through which legislation must pass before it comes to the House and Senate for vote. This structure results in an institutional bias in U.S. politics favoring the status quo, and makes reform a process that must clear multiple legislative hurdles.[221] Assuring that federal government leaders and elected officials do not sacrifice the progress made since 2001 to new priorities and shifting political interests is paramount. In the 2012 report *Anticipated Responsibilities of the Strategic National Stockpile in the Year 2020: An Examination with Recommendations*, the National Biodefense Science Board and the Office of Public Health Preparedness and Response Board of Scientific Counselors urge the continued use of emerging computational modeling and simulation technologies to improve the decision-making capabilities of the DSNS.[222] The report goes on to suggest that scientific and consistent cost-benefit analysis can reduce the logistical burdens associated with the program through the more efficient management of SNS inventories.

In the United States, the existing bioterrorism response framework is built on the principle of local response and control.[223] The 2001 anthrax attacks in the United States forced the insertion of public health into the emergency management/emergency response arena.[224] Cooperative planning and response among local law enforcement, fire and emergency management officials led to a mutual understanding of roles, responsibilities and capabilities. Although PEP for first responders would likely be dispensed through closed (intended only for first responders) PODs or workplace distribution mechanisms,

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[221] Jonathan Oberlander, "The Politics of Health Reform: Why Do Bad Things Happen to Good Plans?" *Health Affairs* (2003): W3–391.

[222] National Biodefense Science Board and the Office of Public Health Preparedness and Response Board of Scientific Counselors, *Anticipated Responsibilities of the Strategic National Stockpile (SNS) in the Year 2020: An Examination with Recommendations.*

[223] Justin W. Timbie et al., "Allocation of Scarce Resources during Mass Casualty Events," *Agency for Healthcare Research and Quality (US) Evidence Reports/Technology Assessments*, no. 207 (June 2012): 1–6, http://www.ncbi.nlm.nih.gov/books/NBK98854/.

[224] David Rosner and Gerald Markowitz, *Are We Ready? Public Health since 9/11* (Berkeley, CA: University of California Press, 2006), 211.

the sole use of this model would force first responders to delay PEP until supplies are received from the SNS.

5. Comprehensiveness

Researchers have used several criteria to determine the priority of distribution of resources: the individual's role in society (occupation), equity, survivability (the number of anticipated years of survival if treated), vulnerability, risk of exposure and the likelihood of recovery.[225] Of these criteria, the concerns regarding equity play the most significant role in the public health arena as all participants, in all studies, unanimously agreed that decisions based on race, gender, culture, legal status, nationality, language, or income were unacceptable.[226]

The strategic placement of SNS push-packs ensures delivery to any U.S. state or territory within 12 hours of the federal decision to deploy. For the sake of security, the exact locations of the storage sites are undisclosed, however based on the probability of attack in a major metropolitan area, it would seem reasonable to assume that the anticipated delivery time to more high-risk regions, such as Washington, DC, New York City, and Los Angeles, would perhaps be shorter than the less populous regions throughout the country. Although the POD distribution model has proven an efficient means of timely distribution of medications, it leaves portions of the population that are unable to access a POD unprotected. Such at-risk groups might include the elderly, those that are mentally or physically disabled, vagrant populations, or those that simply may not have transportation to a POD.

[225] Timbie et al., "Allocation of Scarce Resources during Mass Casualty Events."

[226] Ibid.

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VIII. DISCUSSION AND RECOMMENDATIONS

> If there is a one percent chance of terrorists getting a weapon of mass destruction…the United States must now act as if it were a certainty.
>
> –Ron Suskind in *The One Percent Doctrine*

A. RESEARCH FINDINGS

In the 21st century, it is rarely the case that emergency planners are faced with a threat of such magnitude, for which they have such limited experience. Despite the plethora of scientific data and modeling to support the exceptionally destructive potential of an aerosolized *B. anthracis* attack, the fact remains that there are no universally accepted guidelines for the provision of PEP at the regional, state or local levels. Consequently, many jurisdictions have experienced failed initiatives in planning to provide adequate PEP in the event of an anthrax attack. Furthermore, planning inconsistencies among neighboring jurisdictions have resulted in incongruent response plans that only exacerbate already chaotic incidents. There is no perfect, one-size-fits-all solution, as jurisdictional capabilities and limitations vary significantly across the country. When fused with the current literature on preparation and response to an anthrax attack, the model analysis presented in this thesis offers guidance to assist planners at the state, local, or regional levels in establishing an appropriate anthrax post-exposure prophylaxis plan. The careful evaluation of the characteristics of the individual models presented here can assist in determining the most efficient means of providing PEP to populations of all sizes.

This research used timeliness, cost, logistics, stakeholder acceptance and comprehensiveness as the evaluative criteria for each PEP model. This chapter defines these criteria and describes the assigned outcome values for each. The chapter concludes with recommendations for the analysis of policy options and a brief discussion of opportunities for future research.

B. EVALUATION CRITERIA AND OUTCOME VALUES

Outcome values were applied in the evaluation of research and available data based on the following criteria.

- Timeliness: The evaluation of timeliness is based upon the time from the recognition of the need for PEP, until the availability for dispensing.
    - A = PEP is immediately available for dispensing.
    - B = The availability of PEP for dispensing is likely to be <12 hours but not likely to be immediately accessible
    - C = The availability of PEP for dispensing is likely to be ≥12 hours
- Cost: The determination of cost considers the funding required for procurement, maintenance, activation and sustainment of a PEP model. Variables include fees associated with storage space, administration, rotation, delivery and packaging.
    - A = It is likely that full funding for a model can be absorbed in the typical operating budget.
    - B = The model requires some supplementation from outside funding source(s).
    - C = The model is likely to require majority or full funding from outside sources.
- Logistics: The logistical requirements of a model are measured based on requirements for storage space, manpower, transportation resources, and administrative coordination.
    - A = It is likely that all logistical resources required for a model are readily available in most metropolitan areas.
    - B = Some outside or mutual aide assistance is likely to be required to meet the logistical demands of a model.
    - C = The model is likely to exceed the logistical capabilities of most metropolitan areas, thus requiring significant logistical support from outside resources.
- Stakeholder Acceptance: The evaluation of stakeholder acceptance is based upon the likelihood that primary stakeholder groups will regard a model as appropriate for their jurisdiction. Stakeholders can include, but are not limited to, first responders, lawmakers and politicians, business community executives, and citizens.
    - A = The model is likely to be viewed as favorable by the majority of relevant stakeholder groups.

- B = It is likely that there will be divided support among relevant stakeholder groups.
- C = It is likely that fewer than half of the relevant stakeholder groups are likely to consider the model as favorable.

- Comprehensiveness: The comprehensiveness of a PEP model is evaluated based upon its ability to provide equal access to PEP for as many people as necessary, within the recommended 48-hour dispensing window.
  - A = The model is likely to provide sufficient quantities of PEP medications that are equally accessible to all population sectors.
  - B = The quantity of PEP medication available for dispensing is likely to be sufficient for only select portions of a population.
  - C = The model provides little or no availability to PEP medications.

C. DISCUSSION

The following provides a brief discussion of the outcome values assigned to each of the evaluative criteria, specific to the four PEP models reviewed in this research. The results of this analysis are based on the general characteristics of each model as discussed throughout this research, and are summarized in an outcomes matrix at the conclusion of this section in Table 1.

1. Local Stockpiles

- Timeliness (B): Locally stored PEP stockpiles must be activated and delivered to dispensing points. The timeliness of this model is therefore dependent upon a jurisdiction's activation approval process and on the resources available to deliver the assets. While these processes do not offer immediate availability, it is expected that PEP would be available for dispensing in less than 12 hours.
- Cost (B): The costs associated with this model include the initial purchase of PEP medications, local storage, manpower for sorting and delivery, and the costs associated with the use of transportation resources. It is reasonable to suggest that some of these costs, such as those associated with storage and/or delivery, may be absorbed by individual stakeholder organizations. The initial purchase and replacement costs however often exceed the financial resources of a jurisdiction and require grant funding to procure. As an example, the Baltimore metropolitan region's efforts to establish and sustain a PEP stockpile required the use of UASI monies to fund the initial purchase of medications and packaging supplies. UASI

dollars were also used to construct a secure and environmentally controlled storage facility that was monitored and maintained by a local jurisdiction at the site of their fire headquarters. Upon activation, costs for manpower and transportation resources are assumed by the jurisdiction requesting assets. To sustain the stockpile, replacement of the medications is currently dependent upon the availability of additional grant funding.

- Logistics (A): It is likely that the combined logistical resources of stakeholders within most metropolitan jurisdictions will prove adequate for this model. Throughout the course of daily business, area public health, fire/EMS, law enforcement, and emergency management organizations operate under pre-existing mutual aide or resource sharing agreements. Although the demand for personnel, transportation and security resources is increased during times of crisis, meticulous pre-planning, and resource pooling can typically be employed to overcome logistical barriers.
- Stakeholder Acceptance (A): The practice of stockpiling medications for an entire population has traditionally been deemed as cost prohibitive. Consequently, most local PEP stockpiles are established with the intent of providing PEP to first responders and their families. These groups may be comprised of individuals from law enforcement, fire/EMS, public health, emergency management and often public works. These individuals are likely to view this model as highly favorable, as they would be among the first recipients of PEP, thereby decreasing the likelihood of infection during response to an incident. It is anticipated that stakeholder groups, such as politicians and government officials, will also favor this model as it results in increased local preparedness levels, and a decreased reliance on federal government resources from the SNS.
- Comprehensiveness (B): The local stockpile model, which provides limited quantities of medication, is only moderately comprehensive in its ability to provide PEP to an entire population. From a societal perspective, although this model provides early protection to first responders, it leaves the majority of a population dependent upon response from the SNS.

2. Jurisdictional Cache Acquisition with Third Party Inventory Management

- Timeliness (B): Much like the local stockpiling policy option, this model is likely to make PEP available for dispensing in less than 12 hours. The potential for multiple storage/rotation sites however suggests that availability will not be immediate and will likely be longer than those models that offer a single point of storage.
- Cost (B): The rotation of PEP medications into the daily use market prior to expiration reduces replacement costs. This model may still result in some expired medications due to the diminished market demand for antibiotics. It is anticipated however, that any cost-savings incurred

through medication rotation will be offset by fees for rotation and storage services.

- Logistics (C): This model has substantial logistical requirements. Due to the potential for multiple storage locations, demand for transportation resources will be high if medications are to be delivered in a timely and equitable manner. Additionally, constant administrative monitoring is required to ensure that accurate inventory levels are maintained for each storage location, and that the medications are rotated prior to expiration. Jurisdictions electing to employ a DMI model transfer these logistical burdens to the distributor.

- Stakeholder Acceptance (B): Relative to the other models presented in this study, this model incorporates more individual stakeholder organizations. UMI models typically use healthcare network partners, such as hospital or clinics, to provide storage and rotation services. Although these organizations acknowledge the importance of public health preparedness, they are unlikely to favor this policy option based on the increased logistical burdens assumed by each facility. On the other hand, first responder organizations are likely to prefer this model as it provides more timely access to PEP than does the SNS, and they are relieved of many of the model's logistical responsibilities.

- Comprehensiveness (B): Jurisdictions that have implemented this model are afforded the opportunity to purchase larger quantities of PEP due to the cost savings realized through the rotation of medications prior to expiration. While more medication provides the potential for distribution to a greater portion of the population, the logistical burdens of this model make it unlikely that PEP resources will reach PODs equitably.

3. Pre-Event Distribution to First Responders

- Timeliness (A): Pre-dispensing PEP provides immediate availability to first responders.

- Cost (C): As previously discussed, this is the most costly model of those studied due to the costs associated with packaging and pre-screening doctor's visits. This model also has the potential to be the most costly for the individual first responder, as some jurisdictions may not reimburse for the cost of pre-screening doctor's visits or medications.

- Logistics (A): This model delegates the majority of the logistical requirements to the individual first responder. Prior to an incident, first responders must obtain a prescription via a pre-screening doctor's exam, and must obtain the medications from a pharmacy. The burden then falls to the individual to store the medications in an environmentally controlled and easily accessible area in their home or workplace. Furthermore, the individual first responder must also ensure that the medications are

replaced prior to expiration, which would require a follow-up doctor's visit and subsequent re-purchase of medications.

- Stakeholder Acceptance (B): It is likely that individual first responders will be divided in their support of this model. Many, particularly those that are uninsured or without prescription drug coverage, will not assume the financial responsibilities associated with the model. Others however, will be willing to incur the associated costs to have immediate access and personal responsibility for the administration of PEP. From the perspective of public safety organizational leadership, transferring the responsibility to the individual first responder may relieve the organization of dispensing medications through closed PODs. If an organization does not mandate participation in the pre-dispensed PEP program however, it is apparent that the administrative requirements would be substantial in accurately tracking who do and do not have current medications.
- Comprehensiveness (B): Because this model is only available for use in first responder organizations, it does not appear to be a comprehensive model for an entire population. Furthermore, the fact that this model does not allow for pre-event dispensing to the families of first responders, may significantly impact the willingness of first responders to report for duty, thus challenging the intent of providing early PEP for first responders.

4. Sole Reliance on the SNS for PEP

- Timeliness (C): The mission of the DSNS is to deliver PEP push packages to any location in the United States and its territories, within 12 hours of the approval to deploy. In reality, the response time for these assets may be less than 12 hours, dependent upon incident location. Yet while it seems reasonable to expect that SNS assets are stored in relative close proximity to high-risk areas, such as Washington, DC, and New York City, additional logistical operations may extend the time required to dispense PEP beyond this 12-hour delivery benchmark. Factors to be considered when estimating time until dispensing include the time required to obtain approval to deploy, as well as the time required to receive, sort and deliver the assets from RSS sites.
- Cost (A): Jurisdictions electing to rely solely on the SNS bear little direct cost for the provision of PEP. Costs associated with procurement, rotation, storage and replacement are the burden of the DSNS. Although these direct costs are deferred to federal agencies, communities should assess the possible economic impacts associated with the delay of PEP medication. A decreased workforce due to fear or illness, as well as increased hospital admissions resulting from the delay in availability of PEP, may have long-term financial impacts at the local and state level.
- Logistics (A): RSS and POD site operations are the obligation of local jurisdictions once SNS assets are delivered, and are typically the

responsibility of state and local public health agencies. Law enforcement resources are also needed to provide security for RSS sites, during delivery, and at PODs. As required by the CRI, state and local jurisdictions regularly exercise RSS and POD operations.

- Stakeholder Acceptance (A): Sole reliance on the SNS is likely to result in disparity in the level of acceptance among various stakeholder groups. Local government officials with tight budgets will likely favor this model, as there is minimal direct financial impact. First responders on the other hand, may be reluctant to report for duty if they and their families are not provided with timely and adequate PEP protection. Similarly, it is probable that business community members with the knowledge that community down-time means business down-time, will favor a more timely means of PEP for the entire population. Lastly, it is expected that healthcare professionals from private practice and hospital settings are likely to experience an increased number of patient encounters, many motivated by fear, associated with any delay in the availability of PEP. To alleviate any unnecessary burden on the health care system, it is likely that healthcare professionals will favor a model that allows for earlier access to PEP.
- Comprehensiveness (A): The mass quantities of medications maintained by the SNS are sufficient to provide ample coverage for the entire population of any metropolitan region in the U.S. or its territories. Once states receive assets from the SNS, they must strive to ensure equitable distribution among all populations. From a societal perspective, this is perhaps the most equitable of the models, as no preference is given to first responders or other select portions of the population. To maintain this equality however, jurisdictions must consider a dispensing mechanism beyond PODs, as they may not be accessible to elderly, special needs, or indigent populations. It is important to consider nevertheless, that failure to provide early access to PEP for first responders and healthcare providers may actually slow the overall dispensing process due to a lack of personnel resources.

Policy Option	Timeliness	Cost	Logistics	Stakeholder Acceptance	Comprehensiveness
Local Stockpiles	**B**	**B**	**A**	**A**	**B**
Third Party Inventory Mgmt	**B**	**B**	**C**	**B**	**B**
Pre-Dispensed to Homes	**A**	**C**	**A**	**B**	**B**
SNS Only	**C**	**A**	**A**	**A**	**A**

Table 1. Outcomes matrix

D. RECOMMENDATIONS

The above discussion and matrix analysis provides a framework by which state and local stakeholders can evaluate a PEP model based on the priorities of an individual jurisdiction. Some jurisdictions, especially those that are more rural, may find that limited financial and logistical resources might suggest that reliance on the SNS may be the most suitable model. In contrast, regions with less limited financial resources and sufficient administrative (logistical) capabilities may choose an alternative option, such as pre-dispensing antibiotics to first responders for storage in their homes.

Under ideal circumstances, the collective goal of all jurisdictions is to provide complete and immediate PEP coverage in the event of an aerosolized anthrax attack, although this practice typically is cost prohibitive. The evaluation of factors, such as transportation resource availability, may lead neighboring states or jurisdictions to the conclusion that a different PEP model is most suitable for each. Furthermore, the rapid availability of PEP for dispensing is likely to benefit only those jurisdictions with a demonstrated proficiency in POD activation and throughput procedures. A jurisdiction with little or no POD throughput capability is unlikely to benefit from an unlimited supply of PEP. In this case, allocating funding to stockpile more medications than can be distributed prior to SNS arrival is not practical.

E. FUTURE RESEARCH OPPORTUNITIES

This study evaluates the characteristics of four models that are currently available for the provision of PEP. The data collected and analyzed was unclassified, open source data. PEP models that are employed outside of the United States were not analyzed as part of this study. Beyond the scope of this study, there are numerous opportunities for future research, some of which include the following.

- The consideration of the availability of pediatric dosing for PEP, as each of the models discussed in this research provides only adult dosing.
- An evaluation of the vulnerabilities presented in the event that an attack is executed utilizing a strain of anthrax that is resistant to pre-dispensed or stockpiled antibiotics.

- The exploration of clinical research specific to the status of the development of future alternative medical countermeasures for biological incidents.

F. CONCLUSION

Much like the public fear of bioterrorism, funding has waned in the years since the 2001 Amerithrax attacks. The threat of bioterrorism is not going away. State and local planners must remain vigilant in their preparedness efforts to provide effective post-exposure prophylaxis distribution while optimizing resources. Doing so requires the comprehensive engagement of stakeholders from multiple disciplines. Evaluative tools, such as the decision matrix presented in this thesis, should be employed to continuously assess whether or not communities have employed the most effective mass prophylaxis strategy for use in the event of an aerosolized anthrax attack. Although it is impossible to predict if and when an anthrax attack will occur, history, as well as the words of French microbiologist Louis Pasteur remind us that "chance favors the prepared mind."[227]

[227] *Wikipedia*, s.v. "Louis Pasteur," last modified June 20, 2014, http://en.wikiquote.org/wiki/Louis_Pasteur.

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