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CROSSCUTTING AREAS

OR Forum—Public Health Preparedness: Answering (Largely Unanswerable) Questions with Operations Research—The 2016–2017 Philip McCord Morse Lecture

Margaret L. Brandeau[a]

[a] Department of Management Science and Engineering, Huang Engineering Center, Stanford University, Stanford, California 94305
Contact: brandeau@stanford.edu, http://orcid.org/0000-0001-9331-8920 (MLB)

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Abstract. Public health security—achieved by effectively preventing, detecting, and responding to events that affect public health such as bioterrorism, disasters, and naturally occurring disease outbreaks—is a key aspect of national security. However, effective public health preparedness depends on answering largely unanswerable questions. For example: What is the chance of a bioterror attack in the United States in the next five years? What is the chance of an anthrax attack? What might be the location and magnitude of such an attack? This paper describes how OR-based analyses can provide insight into complex public health preparedness planning problems—and thus support good decisions. Three examples from the author's research are presented: logistics of response to an anthrax attack, prepositioning of medical countermeasures for anthrax, and stockpiling decisions for the United States' Strategic National Stockpile.

Keywords: professional addresses • government planning • ORMS philosophy

1. Introduction

This paper discusses public health preparedness and, in particular, how we can use operations research to help obtain answers to questions that are in many ways unanswerable.

Public health security—achieved by effectively preventing, detecting, and responding to events that affect public health such as bioterrorism, disasters, and naturally occurring disease outbreaks—is a key aspect of national security. However, effective public health preparedness depends on answering questions that are largely unanswerable. For example: What is the chance of a bioterror attack in the United States in the next five years? What is the chance of an anthrax attack? What might be the location and magnitude of such an attack? The fact that these questions are in many ways unanswerable, however, does not mean that we should not try to address them.

I will describe how OR-based analyses can provide insight into complex public health preparedness planning problems—and thus support good decisions. I will begin by discussing public health preparedness (what does that mean, exactly?), and will then describe three different preparedness problems that I have worked on where OR models led to actionable insights. These problems are: logistics of response to an anthrax attack, prepositioning of medical countermeasures for anthrax, and stockpiling decisions for the United States' Strategic National Stockpile. The first two problems relate to planning for a potential bioterror attack. The third problem, the stockpiling problem, deals more broadly with planning for any type of public health emergency. We analyzed these problems using a variety of techniques ranging from one simple equation (for analysis of the prepositioning problem) to a relatively detailed model of disease progression and the supply chain for response (for analysis of the logistics of response to an anthrax attack).

I will conclude with some thoughts about how we can use OR models to influence policy.

2. Public Health Preparedness

2.1. Public Health Threats

In 2001, the United States experienced unprecedented terror attacks. The events of September 11, 2001, including the attacks on the World Trade Center, led to nearly 3,000 deaths and $10 billion in damage. The anthrax letters of 2001, the so-called Amerithrax attacks, made 20 people sick and caused 10 deaths.

In response to these events, the U.S. government created the Department of Homeland Security (DHS) in November 2002. The DHS strategic plan states that, "The Department of Homeland Security's overriding and urgent mission is to lead the unified national effort to secure the country and preserve our freedoms. While the Department was created to secure our country against those who seek to disrupt the American way of life, our charter also includes preparation for and response to all hazards and disasters" (U.S. Department of Homeland Security 2011). The DHS began with a $20 billion budget in 2002. Its 2016 budget was $41 billion, more than double that amount.

One aspect of national security is public health security; that is, preparing for and responding to large-scale public health events that may affect our national security. As part of our nation's efforts to strengthen national security, significant preparedness efforts were initiated at the Centers for Disease Control and Prevention (CDC) when DHS was created. The CDC's Office of Public Health Preparedness and Response is "committed to strengthening the nation's health security by saving lives and protecting against public health threats, whether at home or abroad, natural or manmade. . . . Health security depends on the ability of our nation to prevent, protect against, mitigate, respond to, and recover from public health threats" (Centers for Disease Control and Prevention Office of Public Health Preparedness and Response 2016).

Public health threats can be grouped into four categories: terrorist attacks, manmade disasters, natural disasters, and disease outbreaks. Terrorist attacks include chemical, biological, radiological, nuclear, and explosive attacks (so-called CBRNE threats). Manmade disasters include events such as chemical spills, radiation leaks, and accidental release of environmental toxins. Natural disasters include floods, earthquakes, hurricanes, tornadoes, and the like. Disease outbreaks include outbreaks of illness due to known pathogens such as food-borne illnesses and seasonal influenza, as well as outbreaks due to emerging pathogens such as the Ebola, Zika, and chikungunya viruses.

2.2. Preparing for Public Health Threats

What should we do to prepare for such possible events? The CDC engages in a number of preparedness activities. For instance, they work with state and local health departments "to save lives and safeguard communities from public health threats." The CDC has initiated preparedness planning efforts for many types of public health emergencies. For example, a planning poster for tornadoes instructs the public to watch the sky when a tornado occurs, get into a stable shelter, and never try to outrun the tornado. The CDC has even developed preparedness plans for a possible zombie apocalypse (Centers for Disease Control and Prevention Office of Public Health Preparedness and Response 2015). The thinking is that if you are prepared to deal with a zombie apocalypse, you will also be prepared for a hurricane, pandemic, earthquake, or terrorist attack!

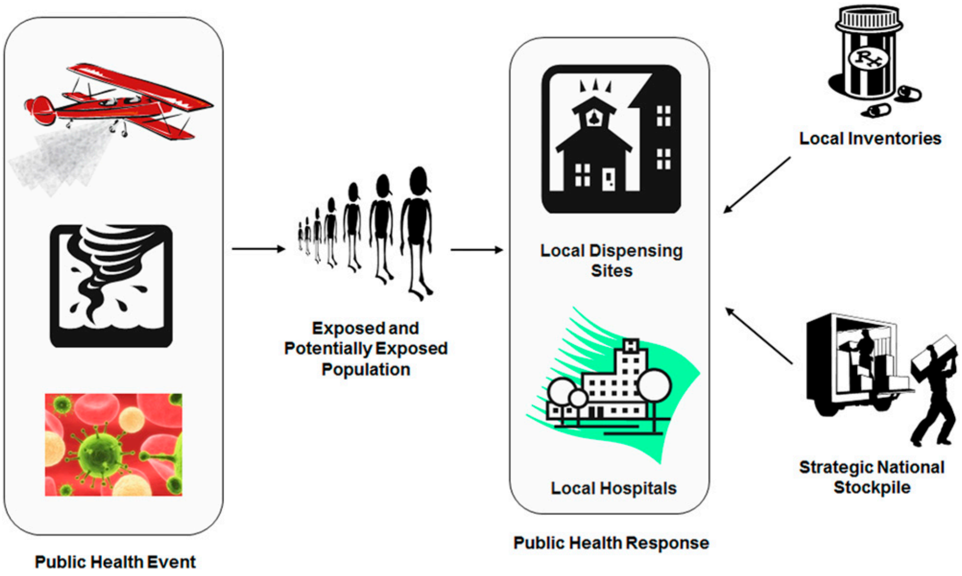
In terms of investment, the most significant preparedness effort of the Office of Public Health Preparedness and Response is the Strategic National Stockpile (SNS). The stockpile (originally named the National Pharmaceutical Stockpile) was created in 1999 with a budget of $50 million. The goal was to be able to provide large quantities of essential medical material to states and communities in the event of an emergency (105th Congress of the United States 1998). In 2002, after the events of 9/11, the mission of the stockpile was expanded "to provide for the emergency health security of the United States" (107th Congress of the United States 2001). This includes not only delivering critical medical assets to the site of a national emergency, but also working to mitigate morbidity, mortality, and social consequences.

The original mission of the stockpile (to respond to CBRNE events) has gradually expanded to that of "all hazards preparedness." The budget for the SNS was $50 million in 2002; in 2015 it was $500 million. The stockpile has gradually grown to include significant amounts of inventory, both for priority threats and for new and emerging threats (Sun 2018).

Currently, the stockpile holds approximately $7.5 billion in inventory (National Academies of Sciences Engineering and Medicine 2016). The stockpile contains close to 1,000 different inventory items that are reported to include, for example, tens of millions of doses of anthrax vaccine, 300 million doses of smallpox vaccine, two million doses of smallpox antiviral medication, 80 million doses of Tamiflu, and millions of doses of antibiotics (McNeil 2013). This inventory is held in a variety of locations around the country. To give an idea of the total size of the stockpile, this inventory would fill seven Walmart Supercenters from floor to ceiling. Each year approximately $500 million in new supplies is added to the stockpile, much of this to replenish expiring inventory. The largest inventory expense is for anthrax vaccine.

Figure 1 shows the role of the stockpile in public health response. First, an event occurs. This could be any of the types of events previously described (for example, a bioterror attack, a natural disaster, or an outbreak of disease). Members of the population may be exposed to the event (e.g., sick) or potentially exposed (e.g., near a chemical spill and unsure whether their health has been harmed). Depending on the event and their health status, they may receive care either at local dispensing sites (for example, to receive vaccinations) or in a hospital. Some inventories for response may be held locally (e.g., in pharmacies or in state or local stockpiles). The remaining inventories come from the SNS, which has three components. Push Packs are fully loaded jumbo jets that contain antibiotics, antidotes, and other medical supplies necessary to treat a wide range of biological and chemical agents. Push Packs can arrive at a city within six hours. Other SNS inventories are also available, as

Figure 1. (Color online) Schematic of Public Health Event and Response



well as some inventories that come directly from the manufacturers (so-called vendor-managed inventories).

2.3. Preparedness Planning Questions

Two of the analyses I will describe deal with questions of bioterror preparedness and response. Although no large-scale bioterror attacks have ever occurred in the United States, bioterror is still considered a significant public health threat because of its casualty-producing capabilities. For example, a virulent outbreak of smallpox or a large-scale attack with aerosolized anthrax could kill thousands, maybe even millions, of people. Although such events are far less likely to occur than other public health events such as pandemic influenza (a large-scale bioterror attack is likely very difficult to carry out), such an event could cause significant harm, not only in terms of illness and deaths, but also in social and economic disruption.

So, the threat of bioterror is significant, and we should do something to prepare. To begin analyzing the problem, we would like to know the following: What is the chance of a terror attack in the United States in the next five years? What is the chance of a bioterror attack? What is the chance of a large-scale, deadly disease outbreak? What is the chance of such an event occurring in the San Francisco Bay Area, or Washington, DC, or the town where you live? What should we do now to prepare? Although these questions are in many ways unanswerable, we must still make preparedness plans now.

We have carried out analyses to address some of these difficult questions. Three of these analyses are described below. The first analysis dealt with the logistics of response to an anthrax attack. The subtext here is: “Should local communities rely completely on the federal government if an anthrax attack occurs?” The second analysis considers prepositioning of medical countermeasures. The subtext of this analysis is: “Should we all store antibiotics for anthrax in our homes?” The third analysis considers stockpiling decisions for the Strategic National Stockpile. The subtext here is: “Do we really need tens of millions of doses of anthrax vaccine in the Strategic National Stockpile?”

3. Logistics of Response to an Anthrax Attack

3.1. Background

In 2002, our research group at Stanford was asked by the Agency for Healthcare Research and Quality to prepare a report summarizing evidence regarding where inventories for bioterror response should be stored—whether inventories should be held at the federal, state, or local level (Bravata et al. 2003). We found that there was no agreement about the required level of local preparedness: different communities had very different plans for responding to potential bioterror attacks. We identified two critical questions for which no clear consensus exists: What amount of medical and pharmaceutical supply inventory should be held locally versus regionally? What is the necessary capacity for rapidly dispensing these supplies to an exposed population?

Because no “evidence” exists regarding the effects of different levels of local preparedness (specifically, inventories and dispensing capacity), we decided to investigate this problem using an OR model (Bravata et al. 2006, Zaric et al. 2008). To make the problem manageable, we focused on the case of an anthrax attack. The goal of the model was to evaluate the costs and benefits of various strategies for stockpiling and dispensing medical and pharmaceutical supplies, and to evaluate the benefits of improved surveillance.

Anthrax is viewed as a major bioterror threat. According to one preparedness poster, anthrax has "no cloud, no color, no smell, no boom or bang—just death." If untreated, anthrax is almost always fatal. The disease has an initial asymptomatic period (median 11 days), followed by prodromal, flu-like illness (median 4–5 days), followed by fulminant infection (severe respiratory distress, median 1–2 days), and then death (Holty et al. 2006). The good news is that anthrax can be treated with either of two common antibiotics (ciprofloxacin and doxycycline). The bad news is that unless treatment is provided while the patient is still asymptomatic, these antibiotics are significantly less effective.

3.2. Anthrax Response Model

We assumed the following sequence of events during and after an aerosolized anthrax attack. When an attack occurs, some individuals in the population inhale enough spores to become ill. As time progresses, they pass through the various stages of infection. At some point, it is known that an anthrax attack has occurred. This may happen if the terrorists announce the attack, or through other means such as hospital surveillance systems or testing of individual patients. Once asymptomatic individuals became aware of their potential exposure to anthrax, they enter a queue at local dispensing sites for prophylactic antibiotics consisting of a single antibiotic, either ciprofloxacin or doxycycline. Individuals who develop symptoms enter a queue for treatment consisting of triple antibiotics administered intravenously in an intensive care setting. Local dispensing sites can obtain antibiotics from two sources: local inventories (such as those held in retail and hospital pharmacies) and the SNS, consisting of the Push Packs and other inventories.

To model this process, we developed a dynamic compartmental model of anthrax disease progression in a population combined with a model of the anthrax response supply chain and a model of dispensing, as illustrated in Figure 2. The rate at which individuals receive prophylaxis and treatment depends on many factors including the number of people who need treatment, available dispensing capacity, and the available supply of antibiotics. As time progresses, exposed individuals either recover or die. The model calculates outcomes associated with alternative policies for inventorying, distributing, and dispensing antibiotics.

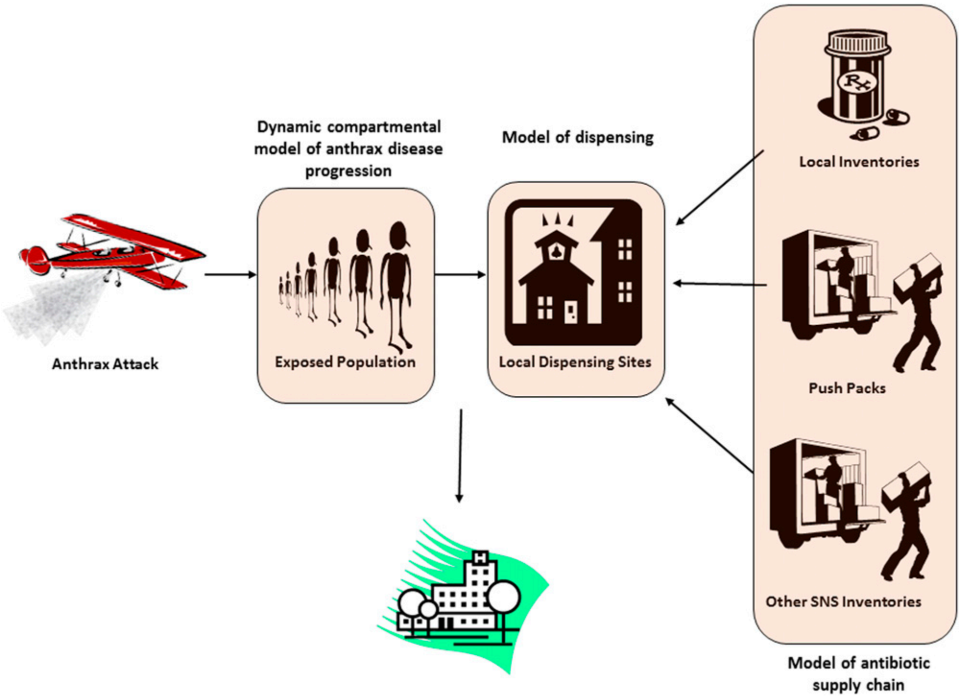
We implemented the model in an Excel spreadsheet. The model consists of difference equations, simulated in one-hour time increments over 100 days. We used data for a "typical city." Key inputs include the chance that an attack occurs and the size of the attack, the rate at which people become aware of their potential exposure, dispensing capacity and hospital capacity, availability of local inventories and inventories from the SNS, and costs. The model calculates useful outcomes such as costs, deaths, queue lengths, and life years gained.

As highlighted, there is an enormous amount of uncertainty regarding a potential anthrax attack. The model can be used to explore many possible occurrences. In the simplest implementation, one could consider the effects of a given preparedness plan (e.g., no local antibiotic stockpile) for a particular assumed event (e.g., an attack that exposes 50,000 people and is detected after 24 hours). One could compare different preparedness plans (e.g., different levels of local inventory) for the same assumed event and then calculate the incremental costs and effectiveness of different plans. One could also evaluate the effect of a given policy under many different scenarios, a technique commonly used by military systems planners who also must make plans now for uncertain future events. If desired, one can assign probabilities to different scenarios and then determine a probabilistic range of outcomes (e.g., in 95% of cases, deaths will be less than 20,000), as well as the expected value or expected utility of the outcomes.

3.3. Analysis and Insights

We performed numerous analyses with the model, exploring a broad range of attack scenarios and preparedness plans. Several important, actionable insights emerged from these analyses (Bravata et al. 2006, Zaric et al. 2008). First, in the event of a large-scale anthrax attack, the limiting factor in response is not likely to be the availability of antibiotics, but rather the local community's dispensing capacity. Thus, it is better for most communities to rely on regional and national inventories for anthrax response, rather than on local inventories. So the answer to the question posed earlier is, "Yes, most communities should rely on the federal government for anthrax response inventories." Second, local antibiotic stockpiling only makes sense if there is thought to be a high probability of attack. This may be true in major metropolitan areas. Third, improved surveillance might significantly reduce mortality from such an attack, but only if the local community has adequate dispensing capacity. These results were remarkably consistent over a wide range of analyses. Thus, although the problem is highly complex and stochastic, use of the relatively simple planning model led to insights that can be acted on now when developing preparedness plans.

Figure 2. (Color online) Schematic of Anthrax Response Model



4. Prepositioning of Medical Countermeasures

4.1. Background

In 2009, the Institute of Medicine (an independent, nongovernmental organization) was asked by the Office of the Assistant Secretary for Preparedness and Response (a division of the U.S. Department of Health and Human Services) to undertake a study to inform the use of prepositioned medical countermeasures. The Institute of Medicine formed a committee, which I was a member of, to undertake the study. The committee was asked to address the following questions, among others: To what extent should local communities build up stocks of medical countermeasures for use in response to a terrorist attack? Should such countermeasures be held in local stockpiles? Should countermeasures be held in workplace caches? Should they be held in people's homes?

These questions are extremely broad. Many types of terrorist attacks could occur, and many types of medical countermeasures for response to such attacks could be stockpiled. To create a manageable task, the committee decided to focus on the case of an anthrax attack, as anthrax is thought to be a major bioterror threat.

In the current distribution strategy, stockpiles of medical countermeasures are held in the Strategic National Stockpile, at manufacturers (in the form of vendor-managed inventory), and in some state stockpiles. Local communities often also have inventories: these include, for example, supplies of antibiotics in hospital and retail pharmacies. When an event occurs, countermeasures are sent to state distribution centers, then to local receiving centers, and finally to the points of dispensing. The preponderance of inventory under the current distribution system comes from the SNS.

The idea behind prepositioning is that, when medical countermeasures are stored closer to the end user, they can be given to patients sooner if an attack occurs. The committee examined three levels of prepositioning: forward deployed, in which medical countermeasures are held in local stockpiles; workplace caches, where countermeasures are held in workplaces (e.g., hospitals or companies) to be distributed to employees; and predispensed, in which countermeasures are held in people's homes. If the latter strategy were implemented, prepackaged antibiotic kits would be developed by the U.S. government and provided to individual households (Hansen and Borio 2008).

4.2. Prepositioning Model

We evaluated the three prepositioning strategies by considering their relative costs and benefits. To assess costs, we performed sample calculations for the Minneapolis–St. Paul Metropolitan Statistical Area. These included estimates of initial inventory purchase costs as well as annual costs associated with inventory replacement (antibiotics expire and must be replaced), inventory management, and training dispensing personnel (annual training is needed to ensure readiness). As shown in Table 1, the cost of predispensed antibiotics is at least an order of magnitude higher than the cost of the other strategies. Of the three prepositioning strategies, stockpiling in local pharmacies/hospitals has the lowest cost because antibiotics that are set to expire can be rotated back into inventory at essentially no cost.

Cost calculations of this type are relatively straightforward. The difficult question is how much benefit will be obtained from prepositioning. To estimate the likely benefit of each prepositioning strategy, we estimated the time to receive prophylaxis for each strategy, and then translated the time to receive prophylaxis into the chance of survival, *assuming that an attack occurs*. This simple yet powerful analysis relies on one simple equation, described next.

Consider the timeline of events when an anthrax attack occurs. At some point the attack is detected through surveillance or other means. After laboratory confirmation, an order is given to dispense antibiotics. Inventory is deployed and dispensing begins. Dispensing continues until all patients have received antibiotics. Prepositioning can reduce the time required for inventory deployment as well as the time required to dispense antibiotics (particularly if antibiotics are held in people's homes). How much will this help?

To answer this question, we need to know how patient survival changes as a function of the time when the patient begins taking antibiotics. Based on cases associated with the accidental release of spores from a Soviet bioweapons facility in Sverdlovsk, Russia (Meselson et al. 1994), we can estimate the chance that a patient is still asymptomatic at time t (i.e., in the incubation period and thus curable with antibiotics) using the following function (Brookmeyer et al. 2001, Brookmeyer et al. 2005, Wilkening 2006, Wilkening 2008): $f(t) = e^{-(.004t)^2}$. This curve is a good approximation for t up to 200 hours. This function can in turn be approximated (for t up to 150 hours) by $f(t) \approx 1 - (.004t)^2$. We created this latter approximation so that our calculations could be readily implemented in a spreadsheet.

Let us assume that dispensing begins some time δ after the attack occurs, and that dispensing occurs uniformly during some time interval $g > 0$ (thus, at rate $1/g$). With the function $f(t)$ and the parameters δ and g, we can calculate the fraction of exposed individuals who survive as

$$S = \int_{\delta}^{\delta+g} f(t)\left(\frac{1}{g}\right)dt = 1 - \frac{[(.004)^2((\delta+g)^3 - (\delta)^3)]}{3g}.$$

4.3. Analysis and Insights

Example benefits calculations are shown in Table 2. For the case of no prepositioning, it is assumed that prophylaxis is completed within 48 hours of the decision to dispense ($g = 48$ hours); this is the current goal. For the case of hospital or workplace caches, it is assumed that prophylaxis is completed within 12 hours of the decision to dispense ($g = 12$). For the case of predispensed antibiotics, it is assumed that prophylaxis occurs immediately when the decision to dispense is made ($g = 0$; in this case, $S = f(\delta)$).

In this example, we assume that the attack is detected in 24 hours, an additional 24 hours are required until the first positive anthrax diagnosis is made, and an additional 12 hours are required for confirmation. We considered four scenarios: (1) prophylaxis begins as soon as the attack is detected ($\delta = 24$ hours); (2) prophylaxis begins as soon as the first anthrax diagnosis is made ($\delta = 48$); (3) prophylaxis begins as soon as the first positive diagnosis is confirmed through laboratory testing ($\delta = 60$); and (4) prophylaxis begins after delayed detection and diagnosis ($\delta = 120$). For each scenario, the simple model above was used to calculate the expected fraction of exposed individuals who will survive (the quantity S) for each of the three prepositioning strategies.

Table 1. Estimated Costs of Alternative Anthrax Antibiotic Prepositioning Strategies for the Minneapolis–St. Paul Metropolitan Statistical Area

	Annual costs			
Strategy	Initial inventory purchase/stockpiling cost	Inventory replacement cost	Inventory management cost for prepositioned antibiotics	Costs of training dispensing personnel
No prepositioning	—	—	—	$895,000
Prepositioning in hospital/pharmacy caches that would serve 20% of the population	$718,000	0	$6,000	$895,000
Prepositioning in workplace caches that would serve 20% of the population	$723,000	$726,000	$6,000	$4,578,000
Prepositioning in all homes	$16,542,000	$14,154,000	0	0

In the first scenario, 96% of individuals will survive if prophylaxis is completed within 48 hours (no local stockpiling). If local stockpiles enable completion of prophylaxis within 12 hours, or if prophylaxis is completed immediately, the expected fraction of lives saved increases to 99%. If prophylaxis dispensing begins 48 hours after the attack, 91% of exposed individuals will survive if there are no local stockpiles, 95% of those who can receive stockpiles from local caches will survive, and 96% of individuals with predispensed antibiotics will survive. If the delay in dispensing is 120 hours, these percentages decrease to 65%, 75%, and 77%, respectively. These results suggest that prepositioning provides greater benefits when the time from the attack until dispensing begins is relatively long.

Finally, to evaluate the relative costs and benefits of the strategies, it is useful to create a figure showing costs and benefits incremental to the base case of no prepositioning, similar to cost-effectiveness graphs used in health and medicine (Gold et al. 1996). From such a figure, one can determine the cost–benefit frontier: these are strategies for which no other strategy or linear combination of strategies achieves greater benefits for less cost. It is important to present both costs and benefits for each prepositioning strategy and attack scenario so that decision makers can make their own value judgments about how to trade off these opposing attributes.

Although highly stylized, this model generated several useful insights (Stroud et al. 2011). First, and most important, prepositioning does not make sense in most locales. Thus, to answer the question posed earlier: "No, we should not all stockpile anthrax antibiotics in our homes." Second, not all locales are the same; that is, one size does not fit all. The appropriate prepositioning strategy for any community depends on factors such as the probability of an attack, local surveillance capability, and local dispensing capacity. Third, although prepositioning is likely too expensive compared with its benefits, forward deployment and local caches may make sense in some locales. This analysis led to an important, actionable insight: the U.S. government should not pursue a strategy of developing home antibiotic kits for bioterror response preparedness.

5. Stockpiling Decisions for the Strategic National Stockpile

5.1. Background

As previously mentioned, the Strategic National Stockpile currently contains approximately $7.5 billion in inventory, and each year some $500 million is spent to replace expiring inventories. Since its inception in 1998, the stockpile has grown in an essentially unconstrained manner. However, several recent changes have created a need for fresh scrutiny of the stockpile contents.

First, the mission of the stockpile has expanded. Originally intended as a stockpile for response to bioterror, the mission has expanded over time to include preparedness for all public health threats. As an example, the Office of Public Health Preparedness and Response is currently using SNS assets to carry out mosquito spraying to control Zika virus in affected areas of the United States and its territories. Second, it is believed that the threat landscape is changing: although there is always the threat of a large-scale bioterror or other attack, terror threats are increasingly likely to come from homegrown violent extremists and lone offenders. Terrorists may also be increasingly likely to attack the United States using conventional methods (e.g., bombings, shootings) or chemicals. Additionally, the potential for new infectious diseases is likely increasing because of climate change, and it is thought that there may be increasing threats to agriculture and the food sector. Third, and most important, budgets are increasingly becoming constrained. Federal appropriations for the CDC's preparedness efforts have remained relatively flat in recent years and are not likely to increase appreciably in the near future, despite the expansion of its mission.

So, what should be in the SNS, and how can we develop appropriate models to support these stockpiling decisions?

5.2. Stockpiling Model, Analysis, and Insights

The prepositioning analysis described above calculated benefits under the assumption that an attack occurs. However, the type and magnitude of events that will occur cannot be known in advance, so

Table 2. Estimated Benefits of Alternative Anthrax Antibiotic Prepositioning Strategies, Assuming an Attack Occurs

		Fraction of exposed individuals saved			
Strategy	Time needed to dispense all prophylaxis in hours (g)	Scenario 1: δ = 24 hours	Scenario 2: δ = 48 hours	Scenario 3: δ = 60 hours	Scenario 4: δ = 120 hours
No prepositioning	48	0.96	0.91	0.88	0.67
Prepositioned caches serving everyone	12	0.99	0.95	0.93	0.75
Predispensed antibiotics in every home	0	0.99	0.96	0.94	0.77

stockpiling decisions must be made with incomplete information. This is a classic case of decision making under (a great deal of) uncertainty.

Let us first consider the case of a single item. If we knew the probability density function of demand for that item we might wish to determine a stockpile level for the item using a newsvendor analysis (Hillier and Lieberman 2014). However, such a function is usually not available. As an alternative, one can consider a set of event scenarios. Planning scenarios have been developed for a variety of public health events that could occur including, for example, an improvised nuclear device, an attack with aerosolized anthrax, an outbreak of pandemic influenza, food contamination, and a major earthquake or hurricane (Scenario Working Group 2006).

To see how such an analysis could work (Brandeau 2018), consider the example in Table 3. We consider a hypothetical case of anthrax vaccine stockpiling. We consider the case of 100,000, 500,000, 1 million, 5 million, 30 million, and 60 million vaccine doses held. We assume that the vaccine costs $20 per dose, has a four-year shelf life, and has a 3% annual inventory management fee. Vaccination of an individual requires five doses. We consider costs and benefits over 10 years.

We evaluate these alternative inventory levels for two possible scenarios (second column of Table 3), which are specified by the probability that all of the vaccine doses are needed. These scenarios are meant to be illustrative of the modeling approach. Scenario estimates that would be used in practice for planning purposes (attack size and associated probability) are classified information. The scenario generation process used in practice "evaluates the intelligence and threat information and develops and models a highly plausible consequence scenario taking into account acquisition, production, dissemination efficacy, source strength and meteorological conditions" (U.S. Department of Health and Human Services 2018). For example, a consequence scenario for anthrax attack exposure that was generated by Sandia National Laboratories for the CDC used a Gaussian plume dispersion model of 1 kg of dry anthrax spores spreading over a major metropolitan area, taking into account factors such as weather, the number of people indoors versus outdoors, the dose that individuals might receive, and the consequent probability of individuals becoming sick (Baccam and Boechler 2007).

In our stylized example, Scenario 2 assumes a higher chance of an anthrax attack than Scenario 1 (we also assume that at most one attack occurs over the time horizon). It is straightforward to calculate inventory costs for each stockpile level (third column of Table 3). For each scenario and inventory level, we can calculate the number of lives saved as well as the number of lives lost. For example, if an event occurs where five million doses are needed (thus, one million people needing vaccination), but only one million are stockpiled, then 200,000 lives will be saved and 800,000 lives will be lost. Table 3 shows the expected number of lives saved over 10 years for each inventory level and scenario, as well as the expected number of lives lost.

One way to evaluate the alternative stockpiling levels is to calculate the cost per expected life saved, as is commonly done for interventions that affect health (Gold et al. 1996). We compare incremental levels of investment with incremental levels of benefit. This is shown in the rightmost column of Table 3. As can be seen, for the hypothetical risk scenarios we assumed, even for the higher risk scenario, the incremental cost of lives saved increases dramatically to tens of millions of dollars for stockpile levels for anthrax

Table 3. Estimated Costs and Benefits of Alternative Anthrax Vaccine Stockpiling Strategies, for Two Hypothetical Risk Scenarios

No. anthrax vaccine doses held, *n*	10-year probability of an event requiring *n* doses	Net present 10-year cost	Expected lives saved over 10 years	Expected lives lost over 10 years	Incremental cost/life saved, compared with next lower stockpiling level
Scenario 1					
100,000	1%	$6.07 million	222	120	$0.03 million
500,000	0.1%	$30.35 million	311	31	$0.27 million
1 million	0.01%	$82.50 million	322	20	$2.72 million
5 million	0.001%	$303.5 million	331	11	$26.39 million
30 million	0.0001%	$1,821 million	339	3	$202.33 million
60 million	0.00005%	$3,642 million	342	0	$606.98 million
Scenario 2					
100,000	1%	$6.07 million	311	629	$0.02 million
500,000	0.5%	$30.35 million	756	184	$0.05 million
1 million	0.05%	$82.50 million	812	128	$0.54 million
5 million	0.005%	$303.5 million	860	80	$5.06 million
30 million	0.0005%	$1,821 million	910	30	$30.35 million
60 million	0.00005%	$3,642 million	940	0	$60.70 million

vaccine doses in the 30–60 million range. Analysts have reported a number of $7–$9 million as the value of a statistical life in U.S. analyses (Viscusi 2005, Trottenburg and Rivkin 2013): this is the risk–money trade-off for low risk of death. For our example, this would indicate that stockpiling of 30–60 million doses of anthrax vaccine is quite expensive compared with its likely benefit.

Thus far we have only considered a single inventory item—but the stockpile contains nearly 1,000 different inventory items. One way to approach the broader problem is to focus only on high-dollar-value items in the stockpile (defined as dollar value per item multiplied by the quantity stockpiled), as we have done for anthrax, and attempt to rationalize investment in these high-value items. However, stockpiling is constrained by a budget.

Thus, another approach (not carried out by my research group) considers different fixed-budget stockpiles in the face of alternative risk scenarios (National Academies of Sciences Engineering and Medicine 2016). The federal government considers thousands of such (classified) scenarios for various forms of national security planning. In the simulation approach, a set of different fixed-budget stockpiles are evaluated for a random subset of high-risk scenarios. This analysis allows planners to assess the robustness of different stockpiles: for example, to determine whether it is better to plan for a single, high-consequence event (e.g., a large-scale anthrax attack) or numerous, low-consequence events. A simulation approach of this type can provide useful insights into appropriate stockpile composition.

However, the simple single-item analysis can also provide useful insights, and is particularly useful for items for which significant investment has been (or might be) made. Although a definitive answer to the question posed earlier about whether it is reasonable to stockpile tens of millions of doses of anthrax vaccine must rely on classified information, simple analyses of the type described here suggest that the answer is “Maybe not.”

6. Conclusion

I have described how OR-based analyses can yield insight into complex public health preparedness planning problems. Of course, many other factors are relevant to decision making. For instance, in the example of the bioterrorism response supply chain, behavior of the public during such an event can significantly influence response outcomes (Brandeau et al. 2008). In the analysis of medical countermeasure prepositioning, factors such as equity of access are relevant (Stroud et al. 2011). In the analysis of public health stockpiling, factors such as deterrence (terrorists may be less likely to attack if they know the United States is prepared) and political views of U.S. government leaders are important.

Despite the complexities of many public health preparedness decisions, OR models can play an important role in such decision making. Models of the type described here tend to be relatively easy and quick to develop, with relatively modest data requirements. Such models are particularly useful for identifying when a decision is justified without further analysis and when further analysis is needed. Most importantly, analyses based on simple models, if properly communicated, can be readily understood by decision makers, thus increasing the chance that the analysis will have impact. Although many planning problems involve questions that are seemingly unanswerable, simple OR models can often yield powerful insights and thus help inform good decisions.

As shown in the examples in this paper, one way to address such seemingly unanswerable questions (e.g., what should we do to prevent, detect, and respond to public health events caused by terrorist attacks, manmade disasters, natural disasters, and disease outbreaks) is to answer different questions that address parts of the problem (e.g., to what extent should we preposition antibiotic countermeasures for anthrax), thereby developing actionable insights for decision making. The three models we describe address different aspects of the highly complex problem of public health preparedness planning and, in particular, the problem of preparing for response to public health events. Our model of the logistics of response to an anthrax attack yields the insight that for response to large-scale events where mass distribution of countermeasures will take place, local dispensing capacity and not countermeasure inventories is likely to be the bottleneck for achieving a rapid response. Our model of anthrax antibiotic prepositioning yields the insight that forward positioning in the supply chain of some types of medical countermeasures (e.g., countermeasures for a disease that does not need instant response) does not make sense in most locales. Our model of SNS stockpiling decisions yields the insight that significant investment in millions of doses of certain expensive medical countermeasures may not make sense if the chance that the countermeasure is needed in great quantities is very low.

The models presented in this paper are quite simple and represent useful, relatively quick analyses with relatively low data requirements that are aimed at generating insight for current decision making. More sophisticated models could be employed to address many of the complex, stochastic aspects of public health preparedness planning. For example, I have suggested the use of scenario analysis (Wilson and Ralston 2006) as a means of considering different events that could occur. One could more formally incorporate stochastic elements using a decision analytic framework (e.g., with the use of a utility function to value outcomes across scenarios) (Howard and Abbas 2015) or a robust optimization framework (Ben-Tal et al. 2009). Analyses of this type would likely require more data and more time to implement than the analyses presented in this paper, but could perhaps generate more refined insights into key public health security planning problems.

The models presented in this paper address only a few aspects of public health preparedness. Many other models have been developed to address various aspects of public health preparedness and bioterror preparedness. For example, a number of authors have developed models addressing questions of preparedness for anthrax and smallpox (e.g., Kaplan et al. 2002, Kaplan et al. 2003, Wein et al. 2003, Brookmeyer et al. 2004, Craft et al. 2005, Wein and Craft 2005, Braithwaite et al. 2006, Miller et al. 2006, Whitworth 2006, Baccam and Boechler 2007, Longini et al. 2007, Kyriacou et al. 2012, Abbas et al. 2017). Much more work remains to be done.

Philip McCord Morse was a pioneer in developing the field of operations research. He stated that "operations research is a scientific method of providing executive departments with a quantitative basis for decisions regarding the operations under their control" (Morse and Kimball 1951). Since the early days of operations research the set of problems under study has expanded, as has the set of problems where operations research could be usefully applied. We now face challenges in a broad range of areas such as transportation, defense, education, energy and the environment, healthcare, and justice and democracy. Thus, I am issuing what I am calling "The Morse Challenge" to everyone in our profession: let us work to identify important, practical, high-impact problems and work to solve them using the tools of operations research.

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Margaret Brandeau is the Coleman F. Fung Professor in the School of Engineering and professor (by courtesy) of medicine at Stanford University. She is a Fellow of INFORMS and a member of the Omega Rho Honor Society for Operations Research and Management Science. From INFORMS, she has received the President's Award, the Award for the Advancement of Women in Operations Research and the Management Sciences, the Pierskalla Prize, and the Philip McCord Morse Lectureship Award. Her recent work has examined HIV and drug abuse prevention and treatment programs, programs to control the opioid epidemic, and preparedness plans for public health emergencies.