

# Analyzing Bioterror Response Logistics: The Case of Anthrax

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To aid in understanding how best to respond to a bioterror anthrax attack, we analyze a system of differential equations that includes an atmospheric release model, a spatial array of biosensors, a dose-response model, a disease progression model, and a set of spatially distributed tandem queues for distributing antibiotics and providing hospital care. We derive approximate closed-form expressions for the number of deaths as a function of key parameters and management levers, including the size of the attack, the time at which the attack is detected via symptomatic patients, the number of days to distribute antibiotics, the efficacy (both for treatment and prevention) of antibiotics, the prophylactic antibiotic distribution strategy, the prioritization of the antibiotics queue, and the detection limit, deployment density, and delay time of biosensors.

*Key words:* bioterrorism; queueing

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## 1. Introduction

The two most feared biological agents in a terrorist attack are smallpox and anthrax (Henderson 1999). Of the two, anthrax appears to be more readily available, as evidenced by its fatal delivery in the U.S. postal system in the fall of 2001 (Thompson 2003). Absent intervention, anthrax is nearly always fatal (Inglesby et al. 2002). It is also highly durable, having survived in a viable form in soil for 35 years (Manchee et al. 1981). When properly weaponized into spores several microns in size, an aerosol release of anthrax can be dispersed over wide areas, which has led to dire warnings that an airborne attack could kill millions of people (World Health Organization 1970; Office of Technology Assessment, U.S. Congress 1993; Alibek 2000). In a companion to this paper, Wein et al. (2003) estimate that under assumptions attempting to capture current response capabilities, over 100,000 people would die as a result of a 1 kg release over a major metropolitan area. Anthrax's combination of deadliness and hardiness makes its threat to the nation's human and physical assets surpassed only by a nuclear weapon.

Because deterrence is not a reliable strategy against terrorists, and because it is difficult to get biological agents out of the hands of terrorists before they attack, our security against a biological attack rests largely on

consequence management, i.e., what can be done after the attack to minimize the number of deaths. The U.S. government has no detailed response plan in place for anthrax, and this paper is part of a four-paper series whose goal is to provide a broad outline of the main elements of an effective response plan. The first paper in this series (Wein et al. 2003) contains a mathematical model of the aftermath of an airborne anthrax attack and a computational study that compares various response strategies. The crux of this model is a set of spatially distributed two-stage queueing networks for distributing antibiotics and providing care to symptomatic patients. The model also incorporates an atmospheric release model to determine the dose inhaled at each location, an array of biosensors that attempts to detect the attack, a dose-response model to compute the fraction of people infected at each location, and a model for disease progression, which can be truncated by medical intervention if service at each of the two queues is provided quickly enough.

The computational study in Wein et al. (2003) also includes a proposed response plan. The second paper in this series (Wein and Kaplan 2003) provides a succinct summary of this response plan and contains five main points: (1) antibiotics need to be distributed very rapidly after an attack is detected, ideally within 12 hours by police-escorted postal workers; (2) a tenfold

increase in surge medical care capacity is needed and requires flying pulmonary experts from around the country into the afflicted region on a voluntary basis; (3) the U.S. population needs to be educated about the importance of adherence to the 60-day antibiotic regimen; (4) biosensors are an unreliable substitute for rapid antibiotic distribution; and (5) serious consideration should be given to voluntary, preattack mass vaccination.

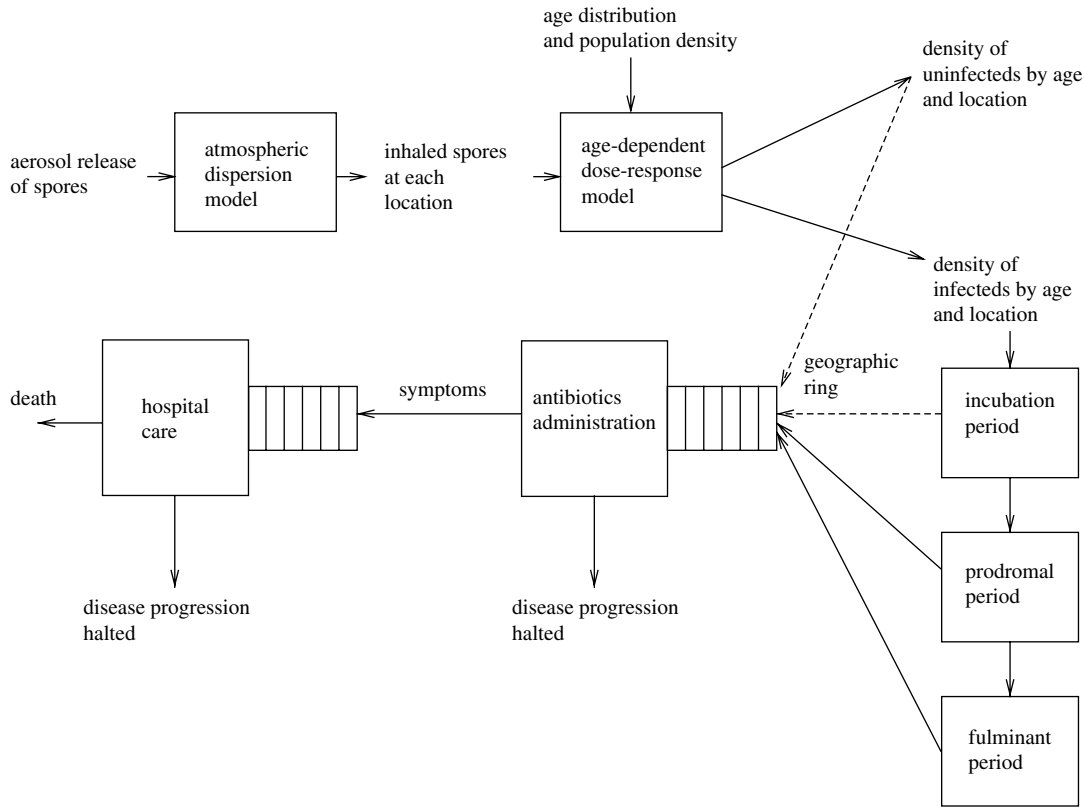
These first two papers had mixed success in influencing policymakers' thinking. The U.S. Postal Service (2004) has announced that it will use postal workers to aid in the distribution of antibiotics in the event of a large-scale anthrax attack in Washington D.C., and a national roll-out of this plan is under consideration. We believe this adoption of point (1) occurred for a variety of reasons: our ability to convince policymakers about point (4) and the large number (approximately 10,000) of people who could die for each day of delay in distributing antibiotics, postal distribution can be completed in one day with existing infrastructure, preattack antibiotic distribution is undesirable due to misuse and subsequent antibiotic resistance, there are fewer legal issues (regarding who can distribute antibiotics) to address than with other alternatives, there will be less panic and fleeing of the population, and, given that the federal government has pushed most of bioterrorism planning and response to the states and cities, the U.S. Postal Service represents one of the few ways to provide improvement in a centralized manner while maintaining a hands-off policy. However, we know of no substantial progress on points (2) and (3). Policymakers deemed the implementation of point (2) as too expensive and logistically difficult (due to credentialing issues at the afflicted sites—there were problems with people passing themselves off as doctors in New York City on September 11, 2001) and we made no specific proposals about how to achieve point (3). Finally, the Secretary's Council on Public Health Preparedness (SCPHP) within the Health and Human Services Department funded us and two researchers from Innovative Emergency Management, Sid Baccam and Michael Boechler, to perform further analysis aimed at assessing point (5); a member of this council reports directly to the U.S. president on this issue.

The last two papers in this four-part series are the present paper and a paper for the SCPHP (Wein and Craft 2004). The present paper provides a mathematical analysis—culminating in closed-form approximate expressions for the fraction of infected people who die—of a slightly simplified version of the model in Wein et al. (2003). Just as Kaplan et al. (2003) (see also Kaplan and Wein 2003) refined our understanding of the smallpox response problem but did not cause us to qualitatively change any of our

smallpox policy recommendations in Kaplan et al. (2002), so too does the present paper improve our understanding of the anthrax problem without causing us to update the policy recommendations in Wein et al. (2003) and Wein and Kaplan (2003). Although the initial aim of the present study was primarily academic, the analytical results reported here—more specifically, Equation (66) and the log-normal version of Equation (67), together with analytical results of Brookmeyer and Johnson's (2004) competing risks model for the fate of inhaled anthrax spores—were used to assess various preattack and postattack vaccination policies requested of us by the SCPHP (Wein and Craft 2004). Wein and Craft (2004) assess the value of pre-event vaccination and whether postattack vaccination can compensate for drug noncompliance and/or allow less antibiotic use, which could reduce cost and adverse events and increase antibiotic supply. Wein and Craft (2004) make an argument for offering the next-generation anthrax vaccine (which is currently undergoing clinical testing) to the public on a voluntary basis, but we are not yet in a position to assess whether our SCPHP paper will influence the decision makers. The results in Wein and Craft (2004) were virtually indistinguishable from the results from Baccam and Boechler's (2004) much more detailed stochastic simulation model (see Figure 1 of Baccam and Boechler 2004). The SCPHP's confidence in the modeling efforts were high for two reasons: the agreement between the two models (Wein and Craft 2004, Baccam and Boechler 2004) was reassuring, and the greater transparency and simplicity of our model and our results (due to the analysis presented in the present paper) allowed the policymakers to both understand the assumptions underlying our recommendations and better internalize the results (e.g., to understand Equation (63) instead of only Figure 5b). In our view, the government favors funding huge, expensive, agent-based models in lieu of simpler, more transparent models, and we hope that SCPHP's experience helps to reverse this bias. Hence, although we initially chose to employ this paper's analytical results rather than numerically solve the Wein et al. (2003) model to perform the SCPHP analysis because we thought it would be less tedious, we believe that this approach was ultimately more persuasive.

The model is presented in §2, and a biosensor analysis, which determines when intervention is initiated, is presented in §3. A single service zone is analyzed in §4 and several generalizations are considered in §5 and the online appendix (available at <http://mansci.pubs.informs.org/ecompanion.html>). The deaths are spatially aggregated across service zones in §6. As an illustration of the types of policy tradeoffs that can be performed with this analysis, we present a

Figure 1 Graphical Depiction of the Model



Note. Asymptomatics enter the antibiotics queue according to a geographic ring strategy (---). Intervention is initiated 24 hours after the attack is detected, via either early symptomatics or biosensors. Source: Wein et al. (2003). Copyright 2003 by The National Academy of Sciences of the United States of America, all rights reserved.

comparison of biosensors and antibiotic distribution in the online appendix. Concluding remarks, including other uses of our results and avenues for future research, are offered in §7.

## 2. The Model

The model is depicted in Figure 1, and consists of an atmospheric release model, a biosensor model, a dose-response model, a disease progression model, and a queueing network model. A comparison of this model and the one in Wein et al. (2003) is given at the end of this section.

We use the Gaussian plume model, which is the workhorse of atmospheric models (Hanna et al. 1982), to track the dispersal of  $Q$  anthrax spores that are released at a height of  $h$  meters when the wind speed is  $u$ . If we let  $b$  denote the breathing rate, then the number of spores inhaled by a person  $x$  meters directly downstream of the release point, and  $y$  meters crosswind is

$$s(x, y) = \frac{bQ}{\pi u \sigma_y \sigma_z} \exp\left(-\frac{y^2}{2\sigma_y^2} - \frac{h^2}{2\sigma_z^2}\right), \quad (1)$$

where  $\sigma_y = a_1 x^d$ ,  $\sigma_z = a_2 x^d$ , with the Brookhaven(C) parameters (i.e.,  $a_1 = 0.32$ ,  $a_2 = 0.22$ ,  $d = 0.78$ ), which

are empirically estimated parameters found in Hanna et al. (1982, Table 4.4). Table 1 contains a list of parameter values used in our computational studies; unless otherwise noted, these values are taken from Wein et al. (2003).

As in Wein et al. (2003), we superimpose on this spatial model a set of biosensors, which are laid out in a square array. The biosensors are characterized by three parameters: the time delay to obtain results ( $\tau_b$ ), the detection limit ( $l_b$ ), which is the minimum number of spores that generates an alarm, and the distance (in meters) between adjacent biosensors ( $w_b$ ), so that the geographical density of biosensors is  $w_b^{-2}$ . We ignore the possibility of false-positive test results.

Let  $\tau$  be the intervention delay, i.e., the time from the onset of the attack until antibiotic distribution begins. We assume there is a time lag of  $\tau_l = 24$  hours between detection and the initiation of intervention, which is needed to get the antibiotics and the distributors in place. The attack can be detected either by biosensors or via early symptomatic patients. The detection delay via early symptomatics, denoted by  $\tau_s$ , is assumed to occur when the  $k$ th person develops symptoms. Let the total number of infected people be  $I_T$ , which is computed in §6, and let  $X_i$ ,  $i = 1, \dots, I_T$  be the associated incubation times (i.e., the time from the onset

**Table 1** Parameter Values for the Model in the Base Case

Parameter	Description	Value
$Q$	Amount released	$10^{15}$ spores
$u$	Wind speed	5 m/s
$h$	Release height	100 m
$b$	Breathing rate	$5 \times 10^{-4}$ m <sup>3</sup> /s
$N$	Zone population	90,000
$l$	Number of infected people in zone (in §§4 and 5)	45,000
$r_1^{-1}$	Mean incubation	12.5 days
$e_1$	Prophylactic efficacy during incubation	0.9
$r_2^{-1}$	Mean of prodromal phase	1 day
$r_3^{-1}$	Mean of fulminant phase	1.5 days
$e_2$	Probability of infinite postantibiotic prodromal	0.4
$\tau_l$	Time lag between detection and intervention	24 hours
$\tau$	Intervention delay	48 hours
$n_A$	Number of antibiotic servers per zone	109.4
$\mu_A$	Service rate for antibiotics	(7 min) <sup>-1</sup>
$n_H$	Number of hospital servers per zone	12.69
$\mu_H$	Service rate in hospital	(6 hours) <sup>-1</sup>
$\rho$	Ring parameter	0
$\tau_b$	Biosensor time delay	6 hours
$l_b$	Biosensor detection limit	$10^4$ spores
$w_b$	Distance between adjacent biosensors	3 km
$k$	Number of symptomatics before detection	20

of attack until symptoms develop), which are specified in more detail later in this section. If we define the order statistics  $X_{1:I_T} \leq X_{2:I_T} \leq \dots \leq X_{k:I_T}$ , then the detection delay via early symptomatics is  $\tau_s = X_{k:I_T}$ . Taken together, we have

$$\tau = \begin{cases} \tau_l + \min\{\tau_b, \tau_s\} & \text{if the maximum spore count at a biosensor} > l_b; \\ \tau_l + \tau_s & \text{otherwise.} \end{cases} \quad (2)$$

We will not be in a position to use (2) until §5 of the online appendix because  $I_T$  is not computed until §6; consequently, the analyses in §§4–5 derives the fraction of infected who die in terms of the generic parameter  $\tau$ .

We use an age-dependent linear dose-response model,

$$P(s, a) = \min\left(1, \frac{s}{c_1 - c_2 a}\right), \quad (3)$$

where  $c_1 = 38,000$ ,  $c_2 = 450$ , and maximum age  $A = 80$ . Here,  $P(s, a)$  is the probability that someone of age  $a$  would become infected from inhaling  $s$  spores. This functional form coincides with the data in Table 3 of Webb and Blaser (2002). The age distribution is  $U[0, A]$  with pdf  $f(a) = A^{-1}$ .

Absent intervention, all infected people progress through three exponential stages with means  $r_j^{-1}$ , for  $j = 1, 2, 3$ ; because the exponential assumption may be of some consequence, we consider nonexponential

disease progression in §5.1. The  $r_j$  values in Table 1 are taken from studies of the only two significant outbreaks to date: the accidental release in Sverdlovsk (Brookmeyer et al. 2001) and the 2001 postal attack (Jernigan et al. 2001). These three stages represent incubation, prodromal, and fulminant. Symptoms are observed at the end of the incubation period. We adopt the approach of Jernigan et al. (2001), who describe the clinical evolution of the first 10 inhalation anthrax patients from 2001, and assume there are two phases of symptomatic disease: patients are feverish in the prodromal stage, and the toxin released by the anthrax takes over the body in the fulminant (or exploding) stage.

With New York City in mind, we assume in §§2–5 that two-dimensional  $(x, y)$  space is broken into 9 km<sup>2</sup> service zones, each populated by  $N = 90,000$  people. For simplicity, we let the dose in each service zone be fixed at the value of the Gaussian plume model evaluated in the center of each square zone. Let  $I_j(x, y, a, t)$  be the number of people of age  $a$  at location  $(x, y)$  and in disease stage  $j$  at time  $t$ , where stage 0 corresponds to uninfected people, and stage 4 is death. The above assumptions imply that, just after the attack,

$$I_1(x, y, a, 0) = Nf(a)P(s(x, y), a) \quad (4)$$

$$= \frac{N}{A} \min\left(1, \frac{k_1 x^{-2d} \exp(-k_2 y^2 x^{-2d} - k_3 x^{-2d})}{c_1 - c_2 a}\right), \quad (5)$$

where

$$k_1 = \frac{bQ}{\pi u a_1 a_2}, \quad k_2 = \frac{1}{2a_1^2}, \quad k_3 = \frac{h^2}{2a_2^2}. \quad (6)$$

We now aggregate over age, and after Equation (7) suppress the spatial dependence until §6, where we aggregate the deaths over service zones. For a generic service zone, let us denote the number of infected people by

$$I = \int_0^A I_1(x, y, a, 0) da. \quad (7)$$

For  $t \in [0, \tau]$  and  $j = 1, \dots, 4$ , the system state is given by

$$I_j(t) = C_j(t)I, \quad (8)$$

where

$$C_1(t) = e^{-r_1 t}, \quad (9)$$

$$C_2(t) = \frac{r_1(e^{-r_1 t} - e^{-r_2 t})}{r_2 - r_1}, \quad (10)$$

$$C_3(t) = e^{-(r_1+2r_2+r_3)t} r_1 r_2 ((r_1 - r_2)e^{(r_1+2r_2)t} + (r_2 - r_3)e^{(2r_2+r_3)t} + (r_3 - r_1)e^{(r_1+r_2+r_3)t}) / ((r_1 - r_2)(r_1 - r_3)(r_2 - r_3)), \quad (11)$$

$$C_4(t) = 1 - C_1(t) - C_2(t) - C_3(t). \quad (12)$$

For notational simplicity, for  $j = 1, \dots, 4$ , we define  $C_j$  as  $C_j(t)$  evaluated at  $t = \tau$ , so that  $C_j$  represents the fraction of infected people who are in disease stage  $j$  at time  $\tau$ .

Intervention begins at time  $\tau$  and consists of people in each service zone arriving to the zone’s two-stage multiserver queueing system, which distributes oral antibiotics and provides medical care. In our model, each zone has its own set of servers and people do not switch zones. In reality, there will also be a set of mobile servers representing national resources (e.g., Red Cross, National Guard), although these mobile resources are likely to be used in supportive but vital roles (e.g., body disposal, peacekeeping). Some people may either flee the afflicted region or change service zones if they perceive that service is quicker elsewhere, but this is not captured in our model. Our modeling assumptions imply that each zone behaves independently, and a generic service zone is analyzed in isolation in §§4–5. The total number of deaths in the entire afflicted area is computed in §6 by summing the deaths over all the service zones.

While antibiotic distribution can be performed by relatively low-skilled medical personnel, medical care needs to be provided by highly skilled physicians and nurses. The service rate and number of servers at the antibiotics queue are set so that antibiotics can be distributed to the entire population in four days, which is representative of current goals. The number of medical care providers is estimated from the number of emergency care providers per capita nationwide (Wein et al. 2003) and the mean service time at the hospital queue is a result of conversations with physicians who treated the patients from the 2001 attack. As mentioned in §1, there is a policy shift underway from distributing antibiotics via Points of Distribution (PODs) (people traveling to the server center, e.g., the local high school, to receive antibiotics) to using the postal system (servers traveling to customers to deliver antibiotics). Each city or state has responsibility for how to deliver antibiotics, and there is likely to be a mix of both types of strategies. Although our model was developed with PODs in mind, as will be seen in Equation (29) and §4.1, the antibiotics queue is modeled very crudely: this queue has no planned idle time and, consequently, is also applicable to the postal delivery setting. We assume that there is an adequate supply of antibiotics; surge manufacturing capacity for antibiotics production appears to be available, which might be needed if there is a campaign of attacks. Finally, while the service capacity at the antibiotics and hospital queues may vary over time due to ramp up, fatigue (although most of the deaths occur within the first 10 days), and workers falling ill, fleeing or attending to their families, we

do not incorporate these details into our model. Similarly, we assume the service rate of antibiotic distribution is constant over time, whereas a small fraction of the population will not show up to PODs and/or do not have a residential address; it is best to think of these people as noncompliers in the discussion of the antibiotic efficacy  $e_1$  below.

There are three types of transitions in Equations (13)–(22) below: arrivals to the antibiotics queue (denoted by  $A_j(t)$  for people in disease stage  $j$ ), service completions of people in disease stage  $j$  at queue  $i$  (denoted by  $S_j^i(t)$  where  $i = \{A, H\}$  are mnemonic for Antibiotics and Hospital), and disease progression (at rate  $r_j$ ), which continues while people reside in the queueing network. People entering the antibiotics queue leave the  $I_j$  compartments in (8) and enter the  $Q_j^A$  compartments in (14), (16), (18), and (19) below; the state variables are described on the left sides of (13)–(22) and are also listed in Table 2. Antibiotics have prophylactic and treatment effects: they prevent a fraction  $e_1 = 0.9$  of people in the incubation period from progressing to symptoms. The 10% ineffectiveness is due to noncompliance to the drug regimen (as opposed to ineffectiveness of the antibiotics), and these people enter compartment  $U_1$  in (17) and eventually move to the hospital queue when they progress to the prodromal stage. As soon as these people enter the hospital queue, they are given (and adhere to) antibiotics. These antibiotics cause headaches and nausea in some people (Inglesby et al. 2002), and a 60-day regimen is difficult to maintain. In Wein and Craft (2004), we combine the results in this paper with Brookmeyer and Johnson’s (2004) results, thereby allowing some people to discontinue antibiotics early. This generalization permitted us to assess whether postattack

**Table 2 Description of the State Variables**

State variable	Description
$I_0$	Uninfected people who have not entered the antibiotics queue
$Q_0^A$	Uninfected people in the antibiotics queue
$I_1$	People in the incubation stage who have not entered the antibiotics queue
$Q_1^A$	People in the incubation stage who are in the antibiotics queue
$U_1$	People in the incubation stage who departed the antibiotics queue but do not comply with the antibiotic regimen
$Q_2^A$	People in the prodromal stage who are in the antibiotics queue
$Q_3^A$	People in the fulminant stage who are in the antibiotics queue
$Q_2^H$	People in the prodromal stage and in the hospital queue who have received antibiotics, but may progress to the fulminant stage
$Q_2^H$	People in the prodromal stage and in the hospital queue who have received antibiotics, and will not progress to the fulminant stage
$Q_3^H$	People in the fulminant stage in the hospital queue

vaccination would offset premature antibiotic discontinuation, but it turned out that this effect was not significant.

Antibiotics also prevent a fraction  $e_2 = 0.4$  of people in the prodromal phase from ever progressing to the fulminant stage; these people enter compartment  $Q_2^H$  in (21) upon receiving antibiotics. The remaining 60% of prodromals receiving antibiotics have their prodromal clock restarted (they join compartment  $Q_2^H$  in (20)) and need to complete their hospital care while still in the prodromal stage in order to survive. Patients entering the fulminant stage (either while in the antibiotics queue  $Q_3^A$  or in the hospital  $Q_3^H$ ) eventually die, regardless of antibiotics or hospital care.

When intervention is initiated, all symptomatic people immediately enter the antibiotics queue. Hence, the state of the system at time  $\tau$  is  $Q_2^A(\tau) = I_2(\tau)$ ,  $Q_3^A(\tau) = I_3(\tau)$ , and  $Q_0^A(\tau) = Q_1^A(\tau) = Q_2^H(\tau) = Q_3^H(\tau) = 0$ . In addition,  $I_2(t) = I_3(t) = 0$  for  $t > \tau$  because symptomatic people enter the hospital during this time period. The dynamics for  $t \geq \tau$  are given by (the rates  $A_j(t)$  and  $S_j^i(t)$  are defined after these equations)

$$\underbrace{\frac{dI_0(t)}{dt}}_{\text{uninfected}} = - \underbrace{A_0(t)}_{\text{ring policy}}, \quad (13)$$

$$\underbrace{\frac{dQ_0^A(t)}{dt}}_{\text{uninfected, antibiotics queue}} = \underbrace{A_0(t)}_{\text{ring arrivals}} - \underbrace{S_0^A(t)Q_0^A(t)}_{\text{receive antibiotics}}, \quad (14)$$

$$\underbrace{\frac{dI_1(t)}{dt}}_{\text{incubating}} = - \underbrace{A_1(t)}_{\text{ring policy}} - \underbrace{r_1 I_1(t)}_{\text{develop symptoms}}, \quad (15)$$

$$\underbrace{\frac{dQ_1^A(t)}{dt}}_{\text{incubating, antibiotics queue}} = \underbrace{A_1(t)}_{\text{ring policy}} - \underbrace{r_1 Q_1^A(t)}_{\text{develop symptoms}} - \underbrace{S_1^A(t)Q_1^A(t)}_{\text{receive antibiotics}}, \quad (16)$$

$$\underbrace{\frac{dU_1(t)}{dt}}_{\text{noncompliers}} = \underbrace{(1 - e_1)S_1^A(t)Q_1^A(t)}_{\text{noncompliance}} - \underbrace{r_1 U_1(t)}_{\text{develop symptoms}}, \quad (17)$$

$$\underbrace{\frac{dQ_2^A(t)}{dt}}_{\text{prodromals, antibiotics queue}} = \underbrace{r_1 I_1(t) + r_1 Q_1^A(t)}_{\text{develop symptoms}} - \underbrace{r_2 Q_2^A(t)}_{\text{disease progression}} - \underbrace{S_2^A(t)Q_2^A(t)}_{\text{receive antibiotics}}, \quad (18)$$

$$\underbrace{\frac{dQ_3^A(t)}{dt}}_{\text{fulminant, antibiotics queue}} = \underbrace{r_2 Q_2^A(t)}_{\text{disease progression}} - \underbrace{r_3 Q_3^A(t)}_{\text{death}} - \underbrace{S_3^A(t)Q_3^A(t)}_{\text{receive antibiotics}}, \quad (19)$$

$$\underbrace{\frac{dQ_2^H(t)}{dt}}_{\text{prodromal, not saved}} = \underbrace{(1 - e_2)r_1 U_1(t)}_{\text{develop symptoms}} + \underbrace{(1 - e_2)S_2^A(t)Q_2^A(t)}_{\text{receive antibiotics}} - \underbrace{r_2 Q_2^H(t)}_{\text{disease progression}} - \underbrace{S_2^H(t)Q_2^H(t)}_{\text{medical care}}, \quad (20)$$

$$\underbrace{\frac{dQ_2^H(t)}{dt}}_{\text{prodromal, saved}} = \underbrace{e_2 r_1 U_1(t)}_{\text{develop symptoms}} + \underbrace{e_2 S_2^A(t)Q_2^A(t)}_{\text{receive antibiotics}} - \underbrace{S_2^H(t)Q_2^H(t)}_{\text{medical care}}, \quad (21)$$

$$\underbrace{\frac{dQ_3^H(t)}{dt}}_{\text{fulminant, hospital}} = \underbrace{r_2 Q_2^H(t)}_{\text{disease progression}} + \underbrace{S_3^A(t)Q_3^A(t)}_{\text{receive antibiotics}} - \underbrace{r_3 Q_3^H(t)}_{\text{death}} - \underbrace{S_3^H(t)Q_3^H(t)}_{\text{medical care}}. \quad (22)$$

Those who die progress from states  $Q_2^A$  and  $Q_2^H$ , and so the total dead is

$$D = \int_0^\infty (r_2 Q_2^A(t) + r_2 Q_2^H(t)) dt. \quad (23)$$

We complete this section by defining the rates  $A_j(t)$  and  $S_j^i(t)$  appearing in the above equations, which represent the prophylactic antibiotic strategy and the service discipline, respectively. The prophylactic strategy is a ring-based strategy (this ring is unrelated to the ring strategy used to trace and vaccinate people after a smallpox attack), which tracks the fraction of symptomatic anthrax cases at each location by time  $t$ , assuming that this location has not entered the ring by time  $t$ . This quantity, which we call the observed anthrax burden, is  $I_1(0)(1 - e^{-r_1 t})/N$ . The ring at time  $t$  consists of all locations that have burdens at least as large as the threshold  $p$ ; although  $p = 0$  in our base case, we allow  $p$  to vary between 0 and 1 in §3 of the online appendix. Hence, a given location enters the ring at time

$$t_p = -\frac{1}{r_1} \ln\left(1 - \frac{pN}{I_1(0)}\right) \text{ if } I_1(0) > pN, \quad (24)$$

and  $t_p = \infty$  otherwise. Because intervention does not begin until time  $\tau$ , if we let  $I_{\{x\}}$  denote the Dirac delta function of the event  $x$ , then

$$A_0(\tau) = I_0(0)I_{\{\tau \geq t_p\}}, \quad (25)$$

$$A_1(\tau) = I_1(0)e^{-r_1 \tau} I_{\{\tau \geq t_p\}}, \quad (26)$$

and, for  $t > \tau$ ,

$$A_0(t) = I_0(0)I_{\{t=t_p\}}, \quad (27)$$

$$A_1(t) = I_1(0)e^{-r_1 t_p} I_{\{t=t_p\}}. \quad (28)$$

Turning to the service terms  $S_j^i(t)$ , define  $Q_2^H(t) = \sum_{j=\tilde{2}, \hat{2}} Q_j^H(t)$  to be the total number of prodromals at the hospital queue at time  $t$ , and  $Q^i(t) = \sum_{j=0}^3 Q_j^i(t)$  to be the total number of people in queue  $i$  at time  $t$ . The mass service policy is defined by

$$S_j^i(t) = \mu_i \min\left(1, \frac{n_i}{Q^i(t)}\right) \quad (29)$$

for  $i = A, j = 0, \dots, 3$  and for  $i = H, j = \tilde{2}, \hat{2}, 3$ . Hence, the queue departure rates from each disease stage is proportional to the relative numbers in queue. Note that we are not modeling the queue according to a typical first-come–first-served discipline, which would not likely be adhered to in the chaotic, post-attack environment.

In §2 of the online appendix, we also consider the symptomatic priority policy, where asymptomatic people in the antibiotics queue are only served if the number of servers exceeds the number of symptomatics in queue. This policy is defined by (29) for  $i = H, j = \tilde{2}, \hat{2}, 3$ , and by

$$S_j^A(t) = \mu_A \min\left(1, \frac{[n_A - Q_2^A(t) - Q_3^A(t)]^+}{Q_0^A(t) + Q_1^A(t)}\right) \quad \text{for } j=0,1, \quad (30)$$

$$S_j^A(t) = \mu_A \min\left(1, \frac{n_A}{Q_2^A(t) + Q_3^A(t)}\right) \quad \text{for } j=2,3. \quad (31)$$

The model presented in this section simplifies the model in Wein et al. (2003) in nine ways: (i) the Brookhaven version of the functions  $\sigma_y$  and  $\sigma_z$  in the Gaussian plume model are used in place of the Briggs version (Hanna et al. 1982); (ii) the total area of study is unbounded and has a constant population density, whereas the region in Wein et al. (2003) is bounded and divided into a rural and urban area; (iii) the dose is fixed for each 9 km<sup>2</sup> service zone, but the dose varies over each square km region in Wein et al. (2003); (iv) a uniform age density is used; (v) the dose-response model is an age-dependent linear model rather than an age-dependent probit model; (vi) disease stages are exponential rather than log-normal random variables; (vii) the progression rate from disease stage  $\tilde{2}$  is taken to be the same as disease stage 2; (viii) Wein et al. (2003) also consider an antibiotic priority policy based on age (people over 55 get priority) and a hospital priority policy that depends on disease stage (prodromals get priority over fulminants); and (ix) Wein et al. (2003) also consider a set of mobile hospital servers (representing federal and military resources) that can dynamically move among zones to treat overflow patients. Among the first six simplifications, only simplification (vi) significantly alters the qualitative nature of our model outputs; consequently, this simplification is

relaxed in §5.1. The last two simplifications force us to ignore other aspects of the problem that are difficult to address analytically. Finally, this paper generalizes the Wein et al. (2003) model in one way: they assume that the symptomatic detection time  $\tau_s$  is independent of the attack size, whereas we assume it occurs when the  $k$ th infected person develops symptoms.

### 3. Biosensor Analysis

Our goal in this section is to derive analytical expressions for the efficacy of biosensors in terms of their detection limit  $l_b$  (in terms of inhaled spores) and their spatial density (assuming they are placed on a lattice with a width of  $w$  meters). These results are used in §5 of the online appendix.

#### 3.1. The Dense Limit

First, we consider the case where  $w \rightarrow 0$ , i.e., there are biosensors everywhere. We can find the maximum spore count by setting  $y = 0$  and differentiating (1) with respect to  $x$ . This yields

$$x^* = \left(\frac{2a_2^2}{h^2}\right)^{-1/(2d)} \quad (32)$$

and

$$s(x^*, 0) = \frac{2bQa_2}{\pi u h^2 e a_1}. \quad (33)$$

For the parameter values in Table 1,  $x^* = 1637$  meters, or 1.6 km. By (33), if the detection limit of a biosensor is  $l_b$ , then we could detect an attack of size

$$Q^* = \frac{\pi u h^2 e a_1 l_b}{2b a_2} = 6.2 \times 10^8 l_b. \quad (34)$$

Equation (34) provides a lower bound on the size of an attack that could be detected by any spatial deployment.

#### 3.2. General Deployment

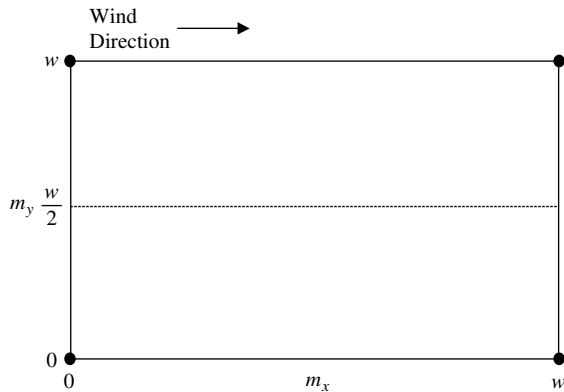
We assume that the terrorists release the anthrax in a random location that is independent of the locations of the biosensors. A natural performance measure is the likelihood of detecting an attack of a given size. Because

$$\begin{aligned} & \Pr(\text{release of size } Q \text{ detected} \mid l_b = s) \\ &= \Pr(\text{max dose at sensors} \geq s \mid \text{release} = Q), \end{aligned} \quad (35)$$

we could try to derive the probability distribution of the maximum dose received at any sensor. However, to more easily incorporate the biosensor analysis with the rest of the analysis, as we do in §5 of the online appendix, we focus instead on estimating the expected maximum dose received at any sensor, which in turn provides an estimate of  $Q^*$ , which is the expected minimum attack size that can be detected.

By the unimodal nature of the Gaussian plume model, we only need to consider the four biosensors

**Figure 2** Random Location  $(m_x, m_y)$  of Maximum Dose, Relative to Its Four Surrounding Biosensors, Which Are Located at  $(x, y) = (0, 0), (w, 0), (0, w),$  and  $(w, w)$



surrounding the location of the maximum dose. Let us fix these four sensors at  $(0, 0), (w, 0), (0, w),$  and  $(w, w),$  and assume that the maximum dose occurs at location  $(m_x, m_y)$  that is uniformly distributed in this square; this state of affairs is depicted in Figure 2. We need to figure out which of these four biosensors receives the maximum dose, as a function of  $(m_x, m_y).$  By the crosswind symmetry of the Gaussian plume model, it is clear that the maximum biosensor is one of the two “southern” sensors (where the wind is blowing east, in the positive  $x$  direction) if  $m_y < w/2,$  and is one of the two northern sensors if  $m_y > w/2.$  Hence, we can restrict ourselves to a  $w \times w/2$  rectangle, i.e., assume  $(m_x, m_y)$  is uniformly distributed in  $[0, w] \times [0, w/2]$  and consider only the southern sensors, so that  $m_y = 0$  means that the southern biosensors are located precisely downwind of the point of release. Moreover, if  $m_x > x^*,$  then the upwind (or “western”) sensor (which is located  $x^* - m_x$  meters downwind and  $m_y$  meters crosswind of the point of release) is upwind of the point of release, and so the downwind sensor (which is located  $x^* - m_x + w$  meters downwind and  $m_y$  meters crosswind of the point of release) receives the maximum dose. This occurs with probability  $(w - x^*)/w,$  which goes to 1 as  $w \rightarrow \infty.$  If  $m_x < x^*$  then the maximum dose of a biosensor is

$$c_1 \max\{(x^* - m_x)^{-2d} e^{-c_2(m_y)(x^* - m_x)^{-2d}}, (x^* - m_x + w)^{-2d} e^{-c_2(m_y)(x^* - m_x + w)^{-2d}}\}, \quad (36)$$

where

$$c_1 = \frac{bQ}{\pi u a_1 a_2}, \quad c_2(m_y) = \frac{m_y^2}{2a_1^2} + \frac{h^2}{2a_2^2}. \quad (37)$$

Hence, if we define

$$g(m_x, m_y) = \max\{(x^* - m_x)^{-2d} e^{-c_2(m_y)(x^* - m_x)^{-2d}}, (x^* - m_x + w)^{-2d} e^{-c_2(m_y)(x^* - m_x + w)^{-2d}}\} \quad (38)$$

and

$$f(m_x, m_y) = \begin{cases} (x^* - m_x + w)^{-2d} e^{-c_2(m_y)(x^* - m_x + w)^{-2d}} & \text{if } m_x > x^*; \\ g(m_x, m_y) & \text{if } m_x < x^*, \end{cases} \quad (39)$$

then the expected maximum dose received by any sensor given a release of size  $Q$  is

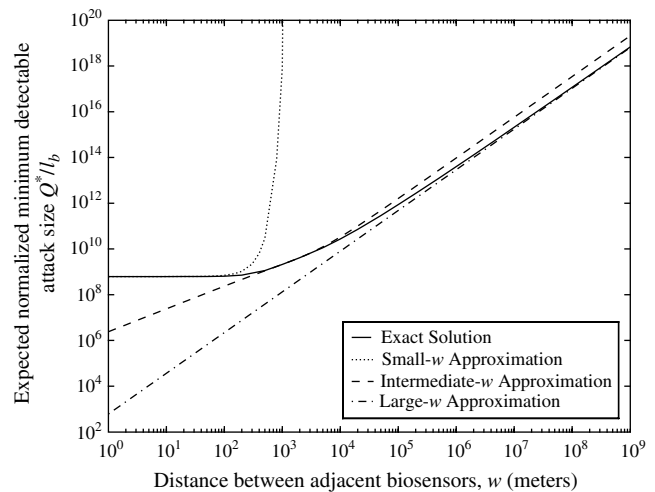
$$\frac{2c_1}{w^2} \int_0^w \int_0^{w/2} f(m_x, m_y) dm_y dm_x. \quad (40)$$

The value of  $w$  could vary from tens of meters in the case of an asset critical to national security, to hundreds of kilometers in a rural region. In §1 of the online appendix, we perform three different approximate analyses to derive the expected minimum detectable attack size  $Q^*,$  which are relevant for small  $w,$  intermediate  $w,$  and large  $w,$  respectively.

**3.3. Accuracy of Estimates**

Figure 3 compares our three estimates of  $Q^*$  (normalized by the detection limit  $l_b$ ) to the exact value from (40). As predicted, our small- $w$  approximation is valid for  $w < 200$  m, but rapidly explodes after that point. Our intermediate- $w$  approximation becomes reasonably accurate at approximately  $w = 400$  m and remains so until  $w = 20$  km. It remains useful as an upper bound for some time after but displays extreme swings in value after  $w = 10^5$  km. Finally, our large- $w$  approximation starts to be fairly accurate at 400 km, and captures the asymptotic behavior of the function. We should note, however, that the Gaussian plume model is typically not applicable in this last regime (Hanna et al. 1982).

**Figure 3** Exact vs. Approximate Values of the Expected Minimum Detectable Release Size Divided by the Detection Limit,  $Q^*/l_b,$  vs. the Biosensor Grid Width  $w$



### 4. Analysis of Base Case

In this section, we estimate  $D/I$ , which is the fraction of infected people who die in a service zone. Note that all deaths are avoidable (i.e.,  $D/I = 0$ ) if detection is instantaneous, the antibiotic service rate is infinite, and antibiotic prophylactic efficacy is 100%, i.e., if biosensors immediately detect the attack, everyone stockpiles antibiotics prior to the attack and start taking them upon detection. Our base case uses the ring parameter  $p = 0$ , so that  $A_0(t) = A_1(t)$  for  $t > \tau$ . The antibiotics queue is analyzed in §4.1, which allows us to characterize the arrivals to the hospital queue. Subsections 4.2 and 4.3 consider the scenarios in which the hospital is overcongested and uncongested, respectively, and §4.4 computationally assesses the accuracy of these approximations.

In the simulation study in Wein et al. (2003), the medical care facility becomes completely overwhelmed. This prediction was confirmed by a classified exercise run by the federal government in the fall of 2003 (Flynn 2004). This suggests that our overcongested approximation in §4.2 should be reasonably accurate and that a comparison of the overcongested and uncongested approximations allows us to assess the potential value of providing ample medical care capacity.

#### 4.1. Antibiotics Queue

Summing Equations (14), (16), (18), and (19) gives a differential equation for the total number of people in the antibiotics queue,

$$\frac{dQ^A(t)}{dt} = -\mu_A \min(Q_A(t), n_A) - r_3 Q_3^A(t). \quad (41)$$

Because every survivor enters the antibiotics queue at time  $\tau$  when the ring parameter  $p = 0$  (see (24)–(25)) and because the zone population size  $N$  is about 1,000 times larger than  $n_A$ , we assume  $\min(Q_A(t), n_A) = n_A$  in (41). Neglecting the second term and assuming no one has exited the system by time  $\tau$ , we solve (41) and get

$$Q^A(t) = N - n_A \mu_A (t - \tau) \quad \text{for } t \in [\tau, \tau + N/(n_A \mu_A)], \quad (42)$$

$$= N \left( \frac{t_e - t}{t_e - \tau} \right) \quad \text{for } t \in [\tau, t_e], \quad (43)$$

where

$$t_e = \tau + \frac{N}{n_A \mu_A} \quad (44)$$

is the emptying time of the antibiotics queue. Note that this crude analysis does not capture server idle time caused by variable interarrival and service times as in a typical queue that has a traffic intensity less than one: these servers are swamped from time  $\tau$  and work until everyone has been given antibiotics.

This simple expression for  $Q^A(t)$  allows us to solve for  $Q_1^A(t)$  and  $Q_2^A(t)$ , which are needed later in this section. Equation (16) is of the form  $\dot{Q}_1^A(t) = -h_1(t)Q_1^A(t)$  where  $h_1(t) = n_A \mu_A / Q^A(t) + r_1$ . The solution is

$$\begin{aligned} Q_1^A(t) &= Q_1^A(\tau) e^{-\int_{\tau}^t h_1(t) dt} \\ &= Q_1^A(\tau) e^{-r_1(t-\tau)} \left( 1 - \frac{n_A \mu_A (t - \tau)}{P} \right) \\ &= I e^{-r_1 t} \left( \frac{t_e - t}{t_e - \tau} \right). \end{aligned} \quad (45)$$

The solution for  $Q_2^A$  is

$$\begin{aligned} Q_2^A(t) &= \frac{I(t_e - t)}{(t_e - \tau)(r_2 - r_1)} (r_1 C_1 (e^{-r_1(t-\tau)} - e^{-r_2(t-\tau)}) \\ &\quad + (r_2 - r_1) C_2 e^{-r_2(t-\tau)}), \end{aligned} \quad (46)$$

where  $C_1$  and  $C_2$  are given by (9)–(10), evaluated at  $t = \tau$ . It turns out that  $(r_1 C_1 (e^{-r_1(t-\tau)} - e^{-r_2(t-\tau)}) + (r_2 - r_1) C_2 e^{-r_2(t-\tau)}) \approx (r_2 - r_1) C_2$  for  $t \in [\tau, t_e]$ , at least for the base-case parameter values. We therefore employ the following simplification:

$$Q_2^A(t) = I C_2 \left( \frac{t_e - t}{t_e - \tau} \right). \quad (47)$$

#### 4.2. Overcongested Hospital Queue

If we assume that the hospital is so congested that anyone who enters  $Q_2^H$  dies, then the number of deaths can be calculated without solving the hospital queue equations. Unfortunately, this is a good approximation in many practical instances (Wein et al. 2003), and allows us to understand all parameters in the model except the hospital service parameters. Using this idea, we can categorize the people who die as follows: those who leave  $Q_2^A$  via progression,  $(1 - e_2)$  of those who leave  $Q_2^A$  via service, and  $(1 - e_1)(1 - e_2)$  of those who leave  $Q_1^A$  via service. Add to this the people who are in stages 3 and 4 by time  $\tau$  and we have, by (18), (29), (43), and (44),

$$\begin{aligned} D &= I(C_3 + C_4) + \int_{\tau}^{t_e} \left[ r_2 Q_2^A(t) + (1 - e_2) \frac{1}{t_e - t} Q_2^A(t) \right. \\ &\quad \left. + (1 - e_1)(1 - e_2) \frac{1}{t_e - t} Q_1^A(t) \right] dt. \end{aligned} \quad (48)$$

Substituting Equations (12), (45), and (47) into (48) and integrating yields

$$\begin{aligned} \frac{D}{I} &= 1 - C_1 + \frac{r_2}{2} C_2 (t_e - \tau) - e_2 C_2 \\ &\quad + (1 - e_1)(1 - e_2) \frac{C_1}{r_1 (t_e - \tau)} (1 - e^{-r_1(t_e - \tau)}). \end{aligned} \quad (49)$$

**4.3. Uncongested Hospital Queue**

Next is an expression for the number of deaths assuming that the hospital queue is uncongested, i.e., the total number of people in the hospital queue,  $Q^H(t)$ , satisfies  $Q^H(t) < n_H$  for all  $t$ . We follow the same logic as the derivation of Equation (48), except that now the  $(1 - e_2)$  people do not die with certainty, but with probability  $r_2/(r_2 + \mu_H)$  due to the competing exponentials. This gives

$$\frac{D}{I} = 1 - C_1 + \left[ \frac{r_2(t_e - \tau)}{2} - 1 + \frac{r_2(1 - e_2)}{r_2 + \mu_H} \right] C_2 + \frac{r_2(1 - e_1)(1 - e_2)}{r_2 + \mu_H} \frac{C_1}{r_1(t_e - \tau)} (1 - e^{-r_1(t_e - \tau)}). \quad (50)$$

Equations (49)–(50) are the paper’s main analytical results, and are investigated further in the next subsection.

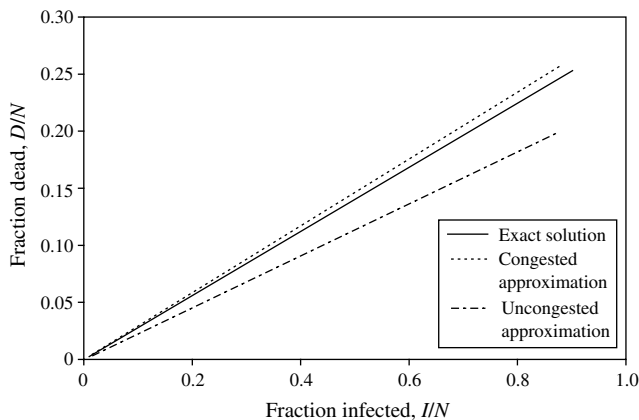
**4.4. Computational Study**

We complete this section with a computational study to determine the accuracy of our approximations in Equations (49)–(50), and to gain an understanding of how these quantities are influenced by various parameters. Figure 4 compares these approximations to the actual fraction of deaths,  $D/N$ , as a function of  $I/N$ , which is the fraction of people infected in the service zone. The overcongested approximation (49) is accurate over the entire range, and the difference between the overcongested and uncongested estimates is modest.

We now investigate three special cases where the response is rapid: preattack antibiotic distribution, instantaneous detection, and a combination of the two. For preattack antibiotic distribution, we have  $t_e = \tau$ . We use l’Hôpital’s rule in (49) and (50) to obtain

$$\frac{D}{I} = 1 - (e_1 + e_2 - e_1 e_2) C_1 - e_2 C_2 \quad \text{if overcongested,} \quad (51)$$

**Figure 4** Fraction Dead vs. Fraction Infected



$$\frac{D}{I} = 1 - \left( 1 - \frac{r_2(1 - e_1)(1 - e_2)}{r_2 + \mu_H} \right) C_1 - \left( 1 - \frac{r_2(1 - e_2)}{r_2 + \mu_H} \right) C_2 \quad \text{if uncongested.} \quad (52)$$

Setting  $\tau = 0$  in (49) and (50) for instantaneous detection, together with the second-order Taylor-series approximation  $e^{-x} \approx 1 - x + x^2/2$ , gives

$$\frac{D}{I} = \frac{(1 - e_1)(1 - e_2)(1 - e^{-r_1(t_e - \tau)})}{r_1(t_e - \tau)} \quad (53)$$

$$\approx (1 - e_1)(1 - e_2) \left( 1 - \frac{r_1(t_e - \tau)}{2} \right) \quad \text{if overcongested,} \quad (54)$$

$$\frac{D}{I} = \frac{r_2}{r_2 + \mu_H} \frac{(1 - e_1)(1 - e_2)(1 - e^{-r_1(t_e - \tau)})}{r_1(t_e - \tau)} \quad (55)$$

$$\approx \frac{r_2}{r_2 + \mu_H} (1 - e_1)(1 - e_2) \left( 1 - \frac{r_1(t_e - \tau)}{2} \right) \quad \text{if uncongested.} \quad (56)$$

The simultaneous use of instantaneous detection and preattack antibiotic distribution gives, via l’Hôpital’s rule,

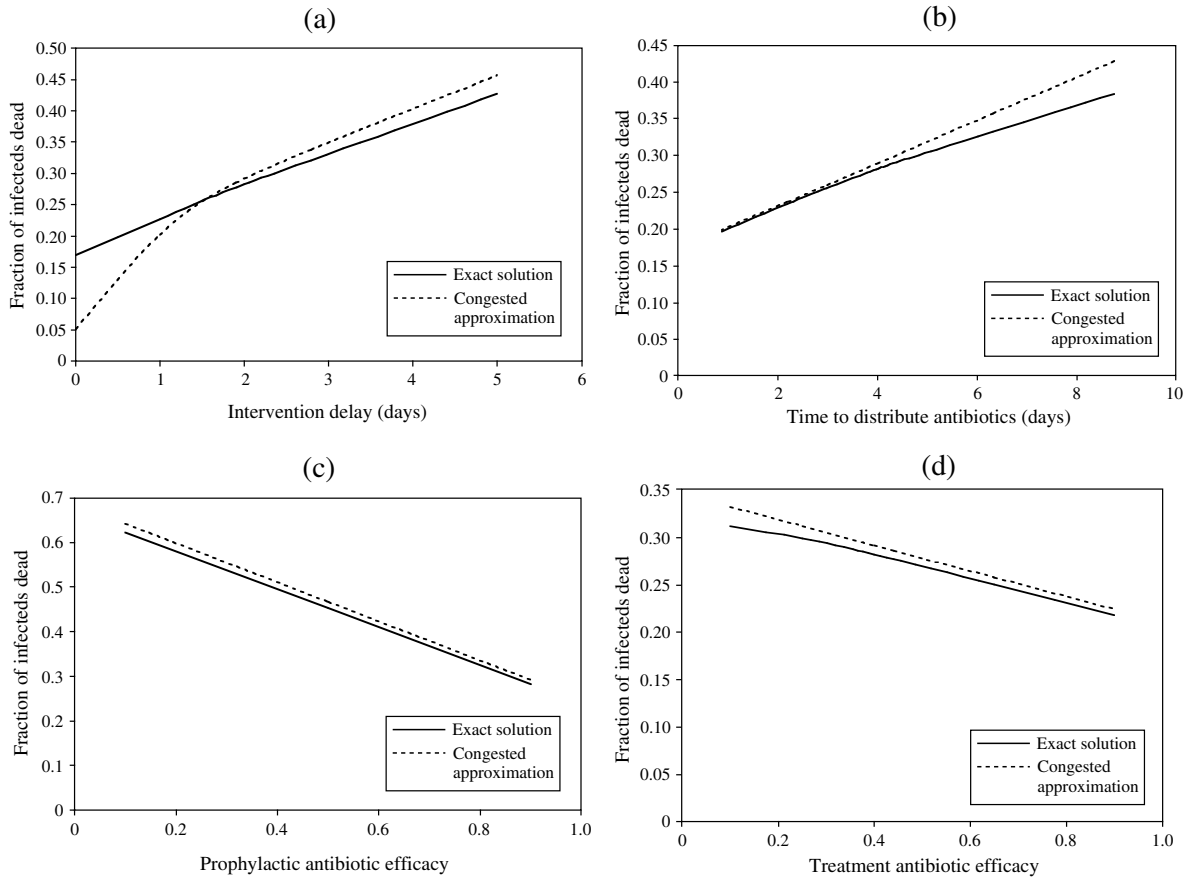
$$\frac{D}{I} = (1 - e_1)(1 - e_2) \quad \text{if overcongested,} \quad (57)$$

$$\frac{D}{I} = \frac{r_2}{r_2 + \mu_H} (1 - e_1)(1 - e_2) \quad \text{if uncongested.} \quad (58)$$

Equations (51)–(58) offer several useful observations. Equation (57), which optimistically employs instantaneous detection, preattack distribution and ample hospital service, provides a lower bound (over all conceivable logistical responses) on the fraction of infected who die, which is 0.012 with our parameter values; that is, almost 99% of the infected people survive. Also, the modest difference between the overcongested and uncongested estimates in Figure 4 depends on having an intervention delay of  $\tau = 2$  days. If  $\tau = 0$ , as in (54)–(58), then the uncongested case reduces the fraction dead by a factor of five.

We now turn our attention to how the key parameters influence the fraction dead in the overcongested case. For the fixed value of  $I/N = 0.5$  (Table 1), Figure 5 shows the actual and estimated (according to the overcongested approximation (49)) fraction of infecteds who die as a function of four key parameters: the intervention delay ( $\tau$ ), the time it takes to distribute antibiotics ( $t_e - \tau$ ), the prophylactic efficacy of antibiotics ( $e_1$ ), and the treatment efficacy of antibiotics ( $e_2$ ).

Figure 5 Fraction of Infected People Who Die vs. Four Key Intervention Parameters



Substituting the base-case parameter values aside from  $\tau$  (but keeping  $t_e - \tau$  fixed) into (49) gives

$$\frac{D}{I} = 1 - 0.81e^{-0.08\tau} - 0.139e^{-\tau}. \quad (59)$$

Differentiating (59) gives

$$\frac{d(D/I)}{d\tau} = 0.065e^{-0.08\tau} + 0.139e^{-\tau} \quad (60)$$

$$\approx 0.065e^{-0.08\tau}. \quad (61)$$

Equation (61) implies that at  $\tau = 2$  days, an additional  $0.065e^{-0.16} \times 100\% = 5.5\%$  of the people die if intervention is delayed an additional day, and the rate at which deaths increase for every day's delay decreases exponentially, but at the rather slow rate of 8% per day; for example, the increase in deaths from day 6 to day 7 is 4.0%, which is 16% less (8% times two days) than the 4.7% increase from day 4 to day 5. Figure 5(a) confirms the accuracy of these observations. Our approximation deteriorates for  $\tau < 1$  day (this is infeasible in light of our 24-hour lag between detection and intervention) because of (47); using (46) in place of (47) increases the accuracy in this parameter range. The deleterious impact of detection delay is

heightened as the antibiotics become more effective, and is lessened as the time to distribute antibiotics is shortened. Because of the simple relationship between the detection-to-intervention time lag  $\tau_l$  and  $\tau$  in (2), Equation (61) can also be used to understand the impact of changing  $\tau_l$ .

Substituting the base-case parameter values (aside from  $t_e - \tau$ ) into (49) gives, using the second-order Taylor-series approximation  $e^{-x} \approx 1 - x + x^2/2$ ,

$$\frac{D}{I} = 0.123 + 0.031(t_e - \tau) + \frac{0.639(1 - e^{-0.08(t_e - \tau)})}{t_e - \tau} \quad (62)$$

$$\approx 0.174 + 0.029(t_e - \tau). \quad (63)$$

Approximation (63) holds for antibiotic distribution times up to about one week, and suggests that an additional 2.9% of infected people perish for every day that it takes to deliver antibiotics. Figure 5(b) confirms the accuracy of this simple formula. As in (61), the effect in (63) is exacerbated as the antibiotics become more effective, and is mitigated as the intervention delay is decreased. Hence, rapid antibiotic distribution and biosensors are partial substitutes.

Figures 5(c) and 5(d) confirm Equation (49)'s assertion that the number of deaths is linearly decreasing in the prophylactic and treatment efficacies of the

antibiotics. Equation (49) shows that the slope in Figure 5(c) gets steeper (i.e., prophylactic efficacy has more of an impact) as the number infected increases, as the time to distribute antibiotics decreases and as the treatment efficacy of antibiotics decreases. Similarly, the slope in Figure 5(d) steepens (i.e., treatment efficacy has more impact) as the number infected increases, the prophylactic efficacy decreases and the time to distribute antibiotics decreases. Hence, the prophylactic and treatment efficacies are partial substitutes for each other. Substituting base-case parameter values into (49) shows that

$$\frac{D}{I} = 0.685 - 0.437e_1, \tag{64}$$

$$\frac{D}{I} = 0.346 - 0.135e_2. \tag{65}$$

Comparing the coefficients in (64)–(65), we see that the prophylactic efficacy, which is partially controllable via drug compliance, is about three times more influential on a percentage basis than the treatment efficacy, which is an exogenous and largely unknown parameter (www.anthrax.mil estimates its range between 0.2 and 0.55).

### 5. Generalizations

This section considers two generalizations of our model: nonexponential disease progression and voluntary preattack vaccination. Sections 2 and 3 of the online appendix consider two other generalizations: the symptomatic priority policy and the ring policy with  $p > 0$ .

#### 5.1. Nonexponential Disease Progression

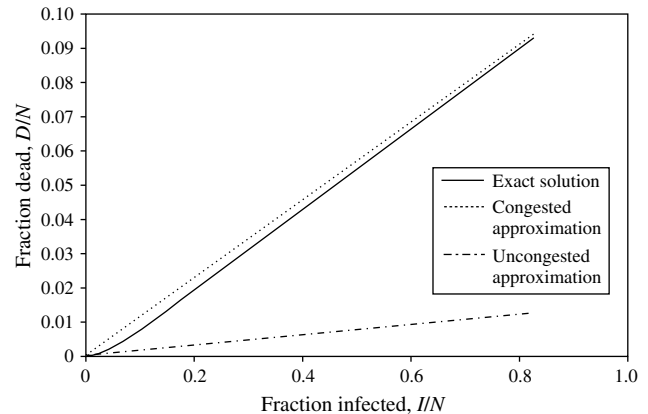
In this subsection, our base-case result (48) is generalized to allow for nonexponential disease-stage durations. For  $i = 1, 2, 3$ , let  $X_i$  denote the random time a person spends in disease stage  $i$  (in the absence of medical intervention), and denote by  $f_i$  and  $F_i$  the pdf and cdf. Also, let  $T_s$  denote the random time that a typical infected person receives antibiotics. By Equation (43),  $T_s \sim U[\tau, t_e]$  under the mass service discipline.

Under mass service, an infected person dies if he (i) reaches stage 3 before receiving antibiotics, (ii) is in stage 2 when receiving antibiotics and then progresses, or (iii) receives antibiotics in stage 1 but needs hospitalization anyways and then progresses in the hospital.

These three disjoint events give

$$\begin{aligned} \frac{D}{I} &= P(X_1 + X_2 < T_s) + (1 - e_2)P(X_1 < T_s < X_1 + X_2) \\ &\quad + (1 - e_1)(1 - e_2)P(X_1 > T_s) \\ &= \frac{1}{t_e - \tau} \left[ \int_{\tau}^{t_e} \int_0^s f_1(t)F_2(s - t) dt ds \right. \end{aligned}$$

**Figure 6** Fraction Dead vs. Fraction Infected with Log-Normal Disease Progression



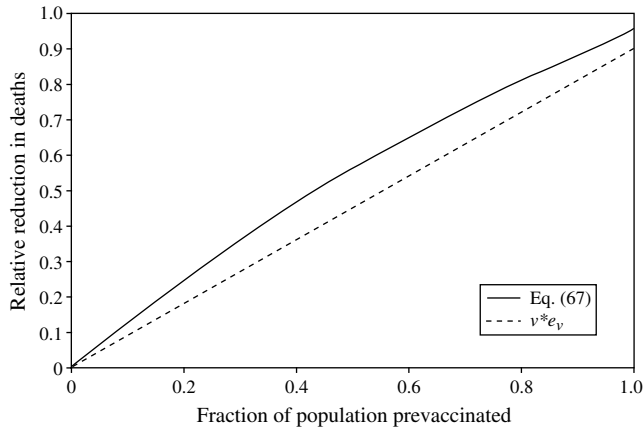
$$\begin{aligned} &+ (1 - e_2) \int_{\tau}^{t_e} \int_0^s f_1(t)(1 - F_2(s - t)) dt ds \\ &+ (1 - e_1)(1 - e_2) \int_{\tau}^{t_e} (1 - F_1(s)) ds \Big]. \tag{66} \end{aligned}$$

The nonexponential analog to the uncongested death estimate in Equation (50) is to replace  $(1 - e_2)$  in (66) with  $(1 - e_2) \int_0^{\infty} F_2(s)\mu_H e^{-\mu_H s} ds$ , because for the fraction  $1 - e_2$  for whom antibiotics provide ineffective treatment, these people progress if their prodromal time is less than their service time. Figure 6 shows the overcongested, uncongested, and exact numbers of deaths versus the fraction infected, in the case where the disease durations are log-normal random variables with parameters given in Table 2 of Wein et al. (2003). A comparison of Figures 4 and 6 leads to two observations. First, the exponential case leads to about 2.5 times as many anthrax infections than the log-normal case. Second, the number of hospital servers has a slightly bigger impact in the log-normal case, i.e., the difference in magnitude between the exact and uncongested slopes is approximately 0.1 in the log-normal case and 0.06 (which by (63) is equivalent to a two-day reduction in the time to distribute antibiotics) in the exponential case. The underlying reason for these differences is the fatter left tail of the exponential distribution.

#### 5.2. Voluntary Preattack Vaccination

Because of the nonnegligible probability of another anthrax attack, and because of the great cost and difficulty of mounting an effective postattack response, serious consideration should be given to a voluntary preattack anthrax vaccination program (Wein and Kaplan 2003). Although a safe and reliable anthrax vaccine exists, it requires a series of six shots over 18 months plus an annual booster, and hence is not viable for widespread civilian use (Inglesby et al. 2002). A more practical vaccine may become available within the next several years.

**Figure 7** The Synergistic Effect of Preattack Vaccination



Suppose a fraction  $v$  of the population opts to be vaccinated prior to an attack, and assume that the vaccine’s prophylactic efficacy is  $e_v$  (i.e., a fraction  $e_v$  of vaccinees will be protected from an attack). Further suppose that prevaccinated people do not receive antibiotics after an attack; if prevaccinated people were to receive antibiotics after all of the unvaccinated people, then more lives would be saved by the vaccine, but because  $e_v$  is likely to be high, we omit this for simplicity. Preattack vaccination changes our base-case result (49) in two ways: the number initially infected would shrink by the factor  $(1 - ve_v)$  and the time to distribute antibiotics,  $t_e - \tau$ , would decrease by the factor  $(1 - v)$ . Hence, if we define  $D_v$  to be the number dead in a service zone under preattack vaccination, then the relative reduction in deaths is (after substituting in base-case values from Table 1)

$$\frac{D - D_v}{D} = 1 - (1 - ve_v) \left( 0.847 - 0.425v + \frac{0.545(1 - e^{-0.32(1-v)})}{1 - v} \right). \quad (67)$$

If the only effect of preattack vaccination was to reduce the number of initially infected people, then we would expect that  $(D - D_v)/D = ve_v$ . However, as shown in Figure 7 with  $e_v$  set equal to 0.9, preattack vaccination has a secondary benefit by easing the logistics of antibiotic distribution: people that were not prevaccinated receive their postattack antibiotics more quickly, and additional lives are saved. For example, if 50% of the population is prevaccinated with a vaccine that is 90% effective, then the relative reduction in deaths is 56% rather than 45%.

## 6. Spatial Aggregation of Service Zones

Because the estimated fraction of infected people who die,  $D/I$ , is independent of  $I$ , and because the great majority of infections occur in overcongested zones

(see Figure 2b in Wein et al. 2003), we can estimate the total number of deaths over the entire region by replacing the  $I$  in Equation (48) with the total number infected over the whole region, a quantity we denote by  $I_T$ . For example, for a release of  $10^{15}$  spores (Table 1), which is about 1 kg, the exact  $D/I$  value in our model (found by spatially integrating out to 6,000 km downwind and 40 km crosswind—we intentionally integrate over a large area leading to many uncongested zones) is 0.253, compared to the approximated value of 0.29. This calculation assumes that intervention begins at the same time  $\tau$  in all service zones. In our base case where the ring parameter  $p = 0$ , this assumption implies that everyone gets in the antibiotics queue at time  $\tau$ . There may actually be a few extremely lightly affected service zones that do not have any symptomatics at time  $\tau$ , but delaying their entrance into the antibiotics queue would have a negligible impact on our results. Similarly, for  $p > 0$ ,  $\tau$  tends to vary only on the order of minutes across heavily affected zones.

By Equation (5), rewritten in terms of the population density  $\theta$  rather than population  $N$ , the total number of infected people is

$$I_T = \frac{\theta}{A} \int_0^A \int_0^\infty \int_{-\infty}^\infty \min(1, (k_1 x^{-2d} \exp(-k_2 y^2 x^{-2d} - k_3 x^{-2d})) / (c_1 - c_2 a)) dy dx da. \quad (68)$$

While we have not been able to integrate (68), for a release size less than about eight grams (roughly the amount in all the tainted envelopes in the 2001 postal attack), the first argument in the minimum function in (68) is not needed, and the total number of infected people is given by (see §4 of the online appendix for a derivation)

$$I_T = - \frac{\theta k_1 \sqrt{\pi} \Gamma((d-1)/2d) \log(c_1 / (c_1 - c_2 A))}{2A \sqrt{k_2} d c_2 k_3^{(d-1)/(2d)}}. \quad (69)$$

Hence, for an attack under eight grams in size, the total number of dead is linear in the release size, and is concave for larger releases.

As an illustration of how the biosensor analysis in §3, the analysis of a service zone in §§4–5, and the spatial aggregation across zones in §6 can be combined to assess policy tradeoffs, in §5 of the online appendix we compare the value of biosensors and rapid antibiotic distribution, under both exponential and log-normal disease progression.

## 7. Concluding Remarks

This paper is the first to our knowledge to attempt to derive mathematical expressions for the number of deaths resulting from an aerosol bioterror attack with a noncontagious agent. As in Kaplan et al. (2003), we combine the traditional solution approach to differential equations with a probabilistic interpretation and

subsequent analysis of these equations. This leads to relatively simple equations for the number of deaths (e.g., Equation (49)), and reveals how this performance measure is impacted by various key parameter values; indeed, this probabilistic approach even works in the nonexponential case (see §5.1), where the model is an unwieldy system of partial differential equations (Wein et al. 2003). As mentioned in §1, this analysis does not lead us to alter the policy recommendations in Wein et al. (2003) and Wein and Kaplan (2003), but it does sharpen our understanding of the problem. In particular, we find that the number of deaths in a service zone is nearly linear in the number of infected people in the service zone; i.e., the fraction of infected people that die is nearly a constant. In our dealings with the SCPHP, this result led the policymakers to decompose the threat assessment and consequence management aspects of the problem and to focus on how the management levers affect the fraction of people who die, rather than the number of deaths. Because of the huge uncertainty in the magnitude of an attack (e.g., it depends on terrorists' capabilities and the weather), this decomposition led to more focused (and less political) discussion, and is probably the most valuable contribution of the analysis in this paper.

The fraction of infected people who die is shown to be linear in the length of time it takes to distribute antibiotics and in the efficacy of the antibiotics, both as prophylactic and as treatment; moreover, prophylactic efficacy is approximately three times more effective (on a percentage basis) than treatment efficacy. This fraction is also increasing and concave in the intervention delay, i.e., the delay from the time of the attack until intervention begins. This delay itself depends on whether the attack is detected by biosensors or by early symptomatics (we assume the public health system detects the attack after a certain number of infected people develop symptoms): large attacks will be detected by biosensors and will have shorter symptomatic detection delays, whereas small attacks will evade the biosensors and have longer symptomatic detection delays. Our biosensor analysis shows that the minimal detectable attack size is linear in the biosensor detection limit and, in the sparse geographical density limit, varies with  $w^{2d}$ , where  $w$  is the grid width and  $d = 0.78$  for slightly unstable meteorological conditions and varies between 0.71 and 0.91 for other weather conditions (Hanna et al. 1982). In the online appendix, we also show how queue management policies, namely the geographical ring policy that places people in queue and the symptomatic priority policy that distributes antibiotics to symptomatic people first, impact the death toll. Finally, Figure 7 reveals the synergistic effect of voluntary preattack vaccination, which protects

the people who are prevaccinated and allows the unvaccinated to receive their postattack antibiotics more quickly, and Figure 1 in the online appendix shows how biosensors and antibiotic distribution are partial substitutes.

The biggest shortcoming of our analysis is our failure to estimate the number of deaths in the moderately congested case, which would have allowed us to explicitly quantify how the number of deaths is reduced by adding servers to the medical care queue. However, our analyses of the uncongested and overcongested cases permit us to estimate the difference in deaths between having no medical care providers (which is a good approximation for a large attack) and having an ample number of them.

Relative to the computational study in Wein et al. (2003), the present analysis allows us to investigate the impact of the incubation period distribution. Wein et al. (2003) assume a log-normal incubation period and find that biosensors have a modest impact that is less than that of rapid antibiotic distribution, the number of deaths is significantly affected by the number of medical care providers, and the symptomatic priority policy has only a modest impact. In contrast, with exponential incubation times, we find that biosensors have essentially no impact, medical care providers have a somewhat smaller impact on the number of deaths (at most, equivalent to a two-day reduction in the time to distribute antibiotics), and the symptomatic priority policy is reasonably effective. The single biggest difference is that the exponential case leads to approximately 2.5 times as many deaths as the log-normal case. The discrepancy in these results is due to the fatter left tail of the exponential distribution. However, Wein et al. (2003) assume that the time to detect early symptomatics is a constant (48 hours), independent of the size of the attack. If we had used this simplifying assumption, then biosensors would have a bigger impact than rapid antibiotic distribution in the exponential disease progression case. By assuming that the attack is detected with the  $k$ th ( $k = 20$ ) asymptomatic is revealed, a large attack is detected instantaneously and biosensors become superfluous.

Although the exponential vs. log-normal discrepancy does not significantly alter the nature of our bottom-line policy recommendations, the exponential case leads to much higher mortality rates and hence to more aggressive investments in intervention. Unfortunately, only limited knowledge exists about the incubation period distribution. Brookmeyer et al. (2001) fit intervention-censored data from the unintentional release of a former Soviet bioweapons factory (Guillemin 1999), which is the only relatively large human data set in existence, to a log-normal distribution that is independent of dose; Wein et al. (2003) could not identify any

dose dependence (or age dependence) in the incubation period from an earlier version of the same data set (Meselson et al. 1994), perhaps because of the somewhat small size of the attack. Brookmeyer et al. (2003) develop a simple competing-risks mathematical model of inhalation anthrax, where inhaled spores either are cleared or germinate (eventually causing disease), which suggests that the incubation period distribution approaches an exponential distribution at very low doses, and that the incubation period may depend inversely on dose. The incubation period in monkeys is inversely related to dose (e.g., Gleiser et al. 1963), and if a dose-dependent incubation distribution is integrated over dose in a large attack, the dose-aggregated incubation distribution may be similar to an exponential distribution. However, the paucity and questionable integrity (despite heroic efforts by researchers to uncover the truth; see Meselson et al. 1994, Guillemin 1999) of the underlying Sverdlovsk data (for over a decade, the Soviet government claimed that the cause of deaths was bad meat because the clandestine factory was in defiance of a bioweapons treaty it signed), coupled with the impracticality of performing human studies, suggest that the precise nature of the incubation period distribution will remain unknown, at least until a large bioterror attack occurs. In the meantime, it would be prudent to hedge our bets and assume that either a log-normal or an exponential distribution, with or without dose dependence, could transpire.

There are many possible extensions of this model, both modest and more open ended. An example of a modest extension is the optimal static allocation of antibiotic servers across service zones, which appears in §6 of the online appendix. An example of a more significant extension that would require developing new model components (and parameter estimates) is the joint optimization of antibiotics and antitoxins. While antibiotics kill the bacteria, they do not kill the toxin secreted by the bacteria, which is the eventual cause of death. An anthrax antitoxin is under development (e.g., Mourez et al. 2001) that would neutralize the toxin that has already been produced, thereby providing a potentially life-saving alternative for patients with advanced disease. Because antitoxin administration requires only a simple injection, the uncongested analysis in §4.3, perhaps generalized slightly to include an antitoxin efficacy, may provide an accurate estimate of the death reduction achievable by antitoxin treatment.

The modeling and analysis for this class of problems is still in its relative infancy and much remains to be done. In our view, the biggest shortcoming of the model—and the most difficult challenge to address—is its omission of people’s behavioral responses to various strategies. For example, what proportion of people will flee by car, shelter in place with plastic and

duct tape, or go to their nearest hospital or pharmacy and belligerently demand antibiotics, and how are these proportions affected by the antibiotic distribution approach (PODs vs. postal delivery)? Although we have argued that postal delivery will reduce these proportions (Wein and Kaplan 2003), we have not backed up this claim with any modeling or empirical support. Similarly, will any improvements achieved by prioritized queue disciplines be negated by the havoc wreaked by the low-priority customers? There appears to be considerable opportunity for operations researchers and management scientists to collaborate with behavioral scientists and risk communication specialists on these types of issues.

Another avenue of possible work is a cost-benefit analysis. Cost estimation is not straightforward for several reasons and is beyond the scope of this paper. Biosensors test for a relatively large number of biological and chemical agents, and so even if biosensors are not very valuable for anthrax, they may be of considerable utility for a longer-incubating agent such as smallpox. Hence, it is not clear how much, if any, of the fixed cost (which accounts for virtually all of the cost associated with the distance between adjacent biosensors,  $w_b$ , and much of the sampling cost associated with the time delay to obtain results,  $\tau_b$ ) should be attributed to detecting an anthrax attack. Similarly, the cost of antibiotic distribution also has a broad-spectrum component to it, in that costs associated with preattack training of distributors and supporting personnel (many of whom will be no-shows during an actual attack, opting to stay with their family instead), as well as costs for preattack preparation of points of distribution, can also be amortized across other types of biological attacks. Furthermore, because of the broad-spectrum benefits achieved by some of the interventions (e.g., biosensors, public health infrastructure), the relative risks of various types of bioterror attacks and the side benefits accrued during peacetime operations and from natural outbreaks (e.g., SARS) need to be taken into account. Finally, antibiotic distribution plans are being left to the individual municipalities, and hence costs may vary widely across regions. The SPCHP discouraged us from incorporating costs into our analysis (partly because they perceive this as a problem for the individual municipalities), and tended to think in terms of achievable levels for intervention delay and antibiotic distribution.

While our model is complex when considered in its entirety, the individual elements are rather simple. Although we believe this simplicity is appropriate for the purposes of developing a national strategy, more detailed submodels are needed for tactical and operational analyses. For example, atmospheric models that account for the urban terrain could be employed

when addressing the optimal density and sampling for biosensors in a particular city. Similarly, it would be helpful to determine the optimal topology of antibiotic distribution centers for a particular municipality, which incorporates transportation of people and stockpiles, and the interaction of these PODs with the hospitals; see Hupert (2003) for simulation modeling along these lines. Such models might incorporate multiresource services (e.g., beds, care providers, ventilators) that have time-varying capacities (e.g., due to medical evacuation of nonanthrax patients, ramp up, absenteeism, and fatigue). Our proposal of using police-escorted postal workers (Wein and Kaplan 2003) to help distribute antibiotics has been adopted in Washington D.C. (United States Postal Service 2004), and the logistical details of this proposal have yet to be worked out. Finally, anthrax is unique among biological agents in causing widespread contamination: the 2001 anthrax attack required several hundred million dollars and three years to decontaminate a handful of buildings, and an airborne attack of the type considered here could cause a portion of a major city to be uninhabitable for decades. Wein et al. (2005) propose and evaluate a plan based on vaccinating reoccupants and using HEPA air cleaners and vacuums, and compare this plan to the fumigation strategy used in the 2001 attack.

An online appendix to this paper is available at <http://mansci.pubs.informs.org/ecompaniion.html>.

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# Online Appendix for “Analyzing Bioterror Response Logistics: The Case of Anthrax”

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This appendix is an online companion to the main text. The biosensor analysis is carried out in §1, and the symptomatic priority policy and the ring policy are analyzed in §2 and §3, respectively. The spatial aggregation across service zones is performed in §4, a comparison of biosensors and antibiotics is presented in §5, and the optimal static allocation of antibiotic servers across service zones is derived in §6.

## 1 Three Approximate Analyses for Biosensors

Beginning with the small- $w$  regime, we try to find the curve that partitions  $[0, w] \times [0, w/2]$  into two regions, depending upon whether the maximum dose occurs at the upwind sensor or the downwind sensor. This curve is found by equating, for each given value of  $m_y \in [0, w/2]$ , the two terms in (36) in the main text and solving for  $m_x$ . The equation that equates the two terms in (36) in the main

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text can be expressed as

$$(x^* - m_x + w)^{-2d} = (x^* - m_x)^{-2d} + \frac{2d}{c_2(m_y)} \ln \left( \frac{x^* - m_x}{x^* - m_x + w} \right). \quad (1)$$

We use three approximations to estimate the expected minimum detectable attack size,  $Q^*$ . First, we substitute the Taylor series approximation  $(x^* - m_x + w)^{-2d} \sim (x^* - m_x)^{-2d} - 2dw(x^* - m_x)^{-2d-1}$  into the left side of (1) to get

$$(x^* - m_x)^{-2d-1} = -\frac{1}{wc_2(m_y)} \ln \left( \frac{x^* - m_x}{x^* - m_x + w} \right). \quad (2)$$

We then use a crude iterative method: let  $m_x = 0$  be an initial estimate, and substitute this value on the right side of (2) to get our estimate,  $m_x^S$ , for the  $x$  coordinate of the location separating the two regions:

$$(x^* - m_x^S)^{-2d-1} = -\frac{1}{wc_2(m_y)} \ln \left( \frac{x^*}{x^* + w} \right), \quad (3)$$

or

$$m_x^S = x^* - \left( -\frac{1}{wc_2(m_y)} \ln \left( \frac{x^*}{x^* + w} \right) \right)^{-\frac{1}{2d+1}}. \quad (4)$$

Therefore, the maximum dose of a biosensor is approximately

$$\begin{cases} c_1(x^* - m_x^S)^{-2d} e^{-c_2(m_y)(x^* - m_x^S)^{-2d}} & \text{if } m_x < m_x^S; \\ c_1(x^* - m_x^S + w)^{-2d} e^{-c_2(m_y)(x^* - m_x^S + w)^{-2d}} & \text{if } m_x > m_x^S. \end{cases} \quad (5)$$

Setting the quantities in (5) equal to  $l_b$  and solving for  $Q$ , we estimate the minimum detectable size of a release to be

$$Q^* = \begin{cases} \frac{\pi u a_1 a_2 l_b}{b} (x^* - m_x)^{-2d} e^{-c_2(m_y)(x^* - m_x)^{-2d}} & \text{if } m_x < m_x^S; \\ \frac{\pi u a_1 a_2 l_b}{b} (x^* - m_x + w)^{-2d} e^{-c_2(m_y)(x^* - m_x + w)^{-2d}} & \text{if } m_x > m_x^S. \end{cases} \quad (6)$$

As a last approximation, to get a deterministic estimate for  $Q^*$  we set  $m_x$  and  $m_y$  equal to the midpoint

of their range (i.e.,  $m_x = w/2$ ,  $m_y = w/4$ ) and get

$$Q^* = \begin{cases} \frac{\pi u a_1 a_2 l_b}{b} \left[ (x^* - \frac{w}{2})^{-2d} e^{-c_2(w/4)(x^* - w/2)^{-2d}} \right]^{-1} & \text{if } m_x^S > w/2; \\ \frac{\pi u a_1 a_2 l_b}{b} \left[ (x^* + \frac{w}{2})^{-2d} e^{-c_2(w/4)(x^* + w/2)^{-2d}} \right]^{-1} & \text{if } m_x^S < w/2, \end{cases} \quad (7)$$

which coincides with the dense-limit result (equation (34) in the main text) as  $w \rightarrow 0$ . The exponential term in (7) causes this approximation for  $Q^*$  to increase rapidly for sufficiently large values of  $w$ . To find the range of applicability of this approximation, we determine the value of  $w$  that generates a 10% increase over the dense limit, assuming that the other terms in (7) remain at their dense limit values (i.e., that  $x^* + w/2 \sim x^* - w/2 \sim x^*$ ). This occurs when

$$e^{c_2(w/4)(x^*)^{-2d}} = 1.1 e^{c_2(0)(x^*)^{-2d}}. \quad (8)$$

Using (37) in the main text and solving for  $w$ , we find that (7) breaks down at

$$w = 4a_1(x^*)^d \sqrt{2 \ln 1.1} = 180 \text{ meters}. \quad (9)$$

Our second line of attack, appropriate for intermediate values of  $w$ , also uses three approximations. First, we assume that the downwind biosensor is always the biosensor that receives the maximum dose. While this assumption causes us to overestimate the size of the smallest detectable attack, it is likely to be accurate if  $w$  is significantly larger than  $x^*$ . In this case, the expected maximum dose received at a sensor, given a release of size  $Q$ , is

$$\frac{2c_1}{w^2} \int_0^w \int_0^{w/2} (x^* - m_x + w)^{-2d} e^{-c_2(m_y)(x^* - m_x + w)^{-2d}} dm_y dm_x. \quad (10)$$

Because

$$\int_0^x e^{-cy^2} dy = \frac{\sqrt{\pi}}{2\sqrt{c}} \Phi(\sqrt{c}x) \rightarrow \frac{\sqrt{\pi}}{2\sqrt{c}} \text{ as } x \rightarrow \infty, \quad (11)$$

we approximate (10) by

$$\frac{\sqrt{2\pi}c_1a_1}{w^2} \int_0^w (x^* - m_x + w)^{-d} e^{-\frac{h^2}{2a_2^2}(x^* - m_x + w)^{-2d}} dm_x. \quad (12)$$

We can then substitute the Taylor series approximations

$$(x^* - m_x + w)^{-2d} \sim (x^* + w)^{-2d} + 2dm_x(x^* + w)^{-2d-1} \quad (13)$$

and

$$(x^* - m_x + w)^{-d} \sim (x^* + w)^{-d} + dm_x(x^* + w)^{-d-1} \quad (14)$$

into (12) and integrate to get

$$\begin{aligned} & \frac{\sqrt{2\pi}c_1a_1a_2^2}{dw^2h^2}(x^* + w)^{d+1}e^{-\frac{h^2}{2a_2^2}(x^*+w)^{-2d}} \left[ \left( 1 - e^{-\frac{dh^2}{a_2^2}(x^*+w)^{-2d-1}w} \right) + \right. \\ & \left. \frac{a_2^2}{h^2}(x^* + w)^{2d} \left( 1 - e^{-\frac{dh^2}{a_2^2}(x^*+w)^{-2d-1}w} \left( \frac{dh^2}{a_2^2}(x^* + w)^{-2d-1}w + 1 \right) \right) \right]. \end{aligned} \quad (15)$$

Solving for  $Q$  gives

$$\begin{aligned} Q^* = & \frac{\sqrt{2\pi}udw^2h^2}{2ba_2}(x^* + w)^{-d-1}e^{\frac{h^2}{2a_2^2}(x^*+w)^{-2d}} \left[ \left( 1 - e^{-\frac{dh^2}{a_2^2}(x^*+w)^{-2d-1}w} \right) + \right. \\ & \left. \frac{a_2^2}{h^2}(x^* + w)^{2d} \left( 1 - e^{-\frac{dh^2}{a_2^2}(x^*+w)^{-2d-1}w} \left( \frac{dh^2}{a_2^2}(x^* + w)^{-2d-1}w + 1 \right) \right) \right]^{-1}. \end{aligned} \quad (16)$$

If we define

$$c_3 = \frac{dh^2}{a_2^2}(x^* + w)^{-2d-1}w \quad (17)$$

and make the Taylor series approximation  $e^{-c_3} \sim 1 - c_3 + \frac{c_3^2}{2}$ , then (16) simplifies to

$$Q^* = \frac{3\sqrt{2\pi}uwa_2(x^* + w)^de^{\frac{h^2}{2a_2^2}(x^*+w)^{-2d}}}{b \left[ 6 - 3c_3 + \frac{dw}{(x^*+w)}(3 - 2c_3) \right]}. \quad (18)$$

Our last approach starts from (12) and makes two further large- $w$  approximations. The Taylor series approximation  $e^{-\frac{h^2}{2a_2^2}(x^*-m_x+w)^{-d}} \approx 1$  again allows the integral in (12) to be taken explicitly, giving

$$\frac{\sqrt{2\pi}c_1a_1}{w^2} \left( \frac{(x^*)^{1-d} - (x^* + w)^{1-d}}{d-1} \right). \quad (19)$$

The assumption  $x^* \ll w$  allows us to make the further approximations  $(x^* + w)^{1-d} \approx w^{1-d}$  and  $(x^*)^{1-d} - w^{1-d} \approx -w^{1-d}$ , yielding

$$\frac{\sqrt{2\pi}c_1a_1}{w^{1+d}(1-d)}. \quad (20)$$

Setting this result equal to  $l_b$  and solving for  $Q$  gives

$$Q^* = \frac{\sqrt{2\pi}ua_2(1-d)l_b}{2b}w^{1+d} \quad (21)$$

as an estimate for the limiting behavior of  $Q^*$  as  $w \rightarrow \infty$ .

## 2 Analysis of the Symptomatic Priority Policy

This section considers the symptomatic priority policy in (30)-(31) of the main text in the overcongested case, where asymptomatic people in the antibiotics queue are only served if the number of servers exceeds the number of symptomatics in queue. As in §4 of the main text, we begin our analysis by studying the antibiotics queue. We approximate the queue lengths by dividing the time interval  $[\tau, t_e]$  into two phases. From time  $\tau$  to time  $t_s$ , we assume that the  $Q_2^A(\tau) + Q_3^A(\tau)$  people who are symptomatic at time  $\tau$  are served. Hence, the first phase ends at time

$$t_s = \tau + \frac{Q_2^A(\tau) + Q_3^A(\tau)}{n_A\mu_A} = \tau + \frac{I(C_2 + C_3)}{n_A\mu_A}, \quad (22)$$

at which time we have  $Q_0^A(t_s) = Q_0^A(\tau)$  and  $Q_1^A(t_s) = Q_1^A(\tau)e^{-r_1(t_s-\tau)}$  because  $Q_0^A(t)$  is constant and  $Q_1^A(t)$  is exponentially decreasing during phase one. The asymptomatic people are served in the

second phase, and we make the simplifying assumption that all servers are always busy distributing antibiotics to the asymptomatic people (in reality, a small fraction of these servers will be processing the new symptomatics), giving for  $t \in [t_s, t_e]$ ,

$$\frac{dQ_0^A(t)}{dt} = -\frac{Q_0^A(t)}{Q_0^A(t) + Q_1^A(t)} n_A \mu_A, \quad (23)$$

$$\frac{dQ_1^A(t)}{dt} = -\frac{Q_1^A(t)}{Q_0^A(t) + Q_1^A(t)} n_A \mu_A - r_1 Q_1^A(t). \quad (24)$$

Letting  $g(t) = \frac{n_A \mu_A}{Q_0^A(t) + Q_1^A(t)}$ , we can solve (23)-(24) in terms of the unknown function  $g(t)$ ,

$$Q_0^A(t) = Q_0^A(t_s) e^{-\int_{t_s}^t g(u) du}, \quad (25)$$

$$Q_1^A(t) = Q_1^A(t_s) e^{-\int_{t_s}^t (r_1 + g(u)) du}. \quad (26)$$

Substituting these solutions into the definition of  $g(t)$  gives the following integral equation that  $g(t)$  must satisfy,

$$g(t) [Q_0^A(t_s) e^{-\int_{t_s}^t g(u) du} + Q_1^A(t_s) e^{-\int_{t_s}^t (r_1 + g(u)) du}] = n_A \mu_A. \quad (27)$$

The substitution  $z(t) = \int_{t_s}^t g(u) du$  turns (27) into the differential equation

$$\dot{z}(t) [Q_0^A(t_s) e^{-z(t)} + Q_1^A(t_s) e^{-r_1(t-t_s) - z(t)}] = n_A \mu_A, \quad (28)$$

which can be rewritten in the separable form

$$e^{-z} dz = \frac{n_A \mu_A dt}{Q_0^A(t_s) + Q_1^A(t_s) e^{-r_1(t-t_s)}}. \quad (29)$$

The solution, using the initial condition  $z(t_s) = 0$ , is

$$z(t) = -\ln \left( \frac{r_1(Q_0^A(t_s) - n_A \mu_A (t - t_s)) + n_A \mu_A \ln \left( \frac{Q_0^A(t_s) + Q_1^A(t_s)}{Q_0^A(t_s) + Q_1^A(t_s) e^{-r_1(t-t_s)}} \right)}{Q_0^A(t_s) r_1} \right). \quad (30)$$

Because  $\int g = z$ , equations (25)-(26) can be expressed as

$$Q_0^A(t) = Q_0^A(t_s) e^{-z(t)}, \quad (31)$$

$$Q_1^A(t) = Q_1^A(t_s) e^{-r_1(t-t_s) - z(t)}, \quad (32)$$

where  $z(t)$  is given in (30). Equations (31)-(32) hold until the antibiotics queue empties at time  $t_e$ , which is computed by solving for when  $z(t)$  goes to infinity in (30).

Now we mimic equation (48) in the main text to find the number of deaths in the overcongested regime. For simplicity, we assume that during the relatively short duration of the first phase, people in stage 2 are in a competing exponentials situation (i.e., service versus progression), whereas the queue congestion during the first phase implies that an exponential versus uniform competition would be more realistic. The result is

$$\begin{aligned} D &= I(C_3 + C_4) + \left( \frac{r_2}{r_2 + \mu_A} + \frac{\mu_A}{r_2 + \mu_A} (1 - e_2) \right) (IC_2 + \int_{\tau}^{t_e} r_1 Q_1^A(t) dt) \\ &\quad + (1 - e_1)(1 - e_2) \int_{t_s}^{t_e} g(t) Q_1^A(t) dt \\ &\approx I(C_3 + C_4) + (1 - e_2) (IC_2 + \int_{\tau}^{t_e} r_1 Q_1^A(t) dt) + \\ &\quad (1 - e_1)(1 - e_2) \int_{t_s}^{t_e} g(t) Q_1^A(t) dt, \end{aligned} \quad (33)$$

where (33) follows from the fact (see Table 1 in the main text) that  $\mu_A \gg r_2$ . To carry out the integrations in (33), we observe that  $r_1 Q_1^A(t) + g(t) Q_1^A(t)$  is exactly  $-\dot{Q}_1^A(t)$ . However, the constants in front of each integral in (33) are different. We only need to compute the easier of the two integrals

because for any constants  $a$  and  $b$  we have

$$a \int r_1 Q_1^A + b \int g Q_1^A = b \int (r_1 Q_1^A + g Q_1^A) - (b - a) \int r_1 Q_1^A = -b \int \dot{Q}_1^A - (b - a) \int r_1 Q_1^A. \quad (34)$$

Turning to the integral of  $Q_1^A(t)$ , we have by (30) and (32) that

$$\begin{aligned} & \int_{t_s}^{t_e} Q_1^A(t) dt \\ &= \int_{t_s}^{t_e} \frac{Q_1^A(t_s) e^{-r_1(t-t_s)}}{Q_0^A(t_s) r_1} \left( r_1(Q_0^A(\tau) - n_{A\mu_A}(t - t_s)) + n_{A\mu_A} \ln \left( \frac{Q_0^A(t_s) + Q_1^A(t_s)}{Q_0^A(t_s) + Q_1^A(t_s) e^{-r_1(t-t_s)}} \right) \right) dt. \end{aligned} \quad (35)$$

We could directly integrate this expression, but the result is simpler and quite accurate if we replace the logarithmic term with its first-order Taylor expansion, which gives

$$\begin{aligned} \int_{t_s}^{t_e} Q_1^A(t) dt &\approx \int_{t_s}^{t_e} \frac{Q_1^A(t_s) e^{-r_1(t-t_s)}}{Q_0^A(t_s) r_1} \\ &\quad \left( r_1(Q_0^A(\tau) - n_{A\mu_A}(t - t_s)) + \frac{n_{A\mu_A} r_1 Q_1^A(t_s)(t - t_s)}{Q_0^A(t_s) + Q_1^A(t_s)} \right) dt \\ &= \frac{Q_1^A(t_s)}{r_1^2} \left( r_1 - \alpha + e^{-r_1(t_e-t_s)} \left( -r_1 + \alpha(1 + r_1(t_e - t_s)) \right) \right), \end{aligned} \quad (36)$$

where  $\alpha = n_{A\mu_A}/(Q_0^A(t_s) + Q_1^A(t_s))$ .

Using (34), we rewrite equation (33) as

$$\begin{aligned} D &= I(C_3 + C_4) + (1 - e_2)IC_2 + (1 - e_2) \int_{\tau}^{t_s} r_1 Q_1^A(t) dt + (1 - e_1)(1 - e_2)Q_1^A(t_s) \\ &\quad + e_1(1 - e_2)r_1 \int_{t_s}^{t_e} Q_1^A(t) dt. \end{aligned} \quad (37)$$

Finally, substituting in the integrations, we find that the approximate number of deaths is

$$\begin{aligned}
D = & I(C_3 + C_4) + (1 - e_2)I[C_2 + C_1(1 - e^{-r_1(t_s - \tau)})] + (1 - e_1)(1 - e_2)IC_1e^{-r_1(t_s - \tau)} \\
& + e_1(1 - e_2)\frac{Q_1^A(t_s)}{r_1}\left(r_1 - \alpha + e^{-r_1(t_e - t_s)}(-r_1 + \alpha(1 + r_1(t_e - t_s)))\right), \tag{38}
\end{aligned}$$

where  $\alpha = n_A\mu_A/(Q_0^A(t_s) + Q_1^A(t_s))$

Computational results (not shown here) reveal that (38) is quite accurate (e.g., similar to Figures 4 and 5 in the main text), except when the time to distribute antibiotics exceeds about 8 days. While the expression in (38) is rather cumbersome, it still allows for some observations. As in the mass service case, the number of deaths is linear in the number infected, and the fraction of infected people who die is linearly decreasing in both the prophylactic and treatment antibiotic efficacies. Substituting base-case parameter values yields

$$\frac{D}{I} = 0.695 - 0.502e_1, \tag{39}$$

$$\frac{D}{I} = 0.308 - 0.162e_2. \tag{40}$$

Substituting the base-case parameter values of  $e_1$  and  $e_2$  into (39)-(40), we find that the fraction of infected people who die is reduced from 0.292 for the mass service policy to 0.243 for the symptomatic priority policy; this 0.049 difference is considerably larger than the 0.004 difference in the base case in Wein *et al.* (2003), which assumes log-normal disease progression. Numerical computations (not shown here) reveal that the difference in performance between these two policies goes down as  $t_e - \tau$  is reduced. Comparing the coefficients in (39)-(40) with those in (64)-(65) in the main text shows that the impact of prophylactic effectiveness is slightly greater under the symptomatic priority policy than the mass service policy. As in the mass service case, prophylactic efficacy is about three times more effective on a percentage basis than treatment efficacy.

### 3 Analysis of the Ring Policy

This section analyzes how the number of deaths depends on the ring parameter  $p$  in the overcongested scenario. Since for a given zone location,  $p$  maps to time  $t_p$  via (24) in the main text, we instead work with  $t_p$ . Symptomatics start receiving medical intervention at time  $\tau$ , and at time  $t_p$  mass service is initiated for everyone in the zone. In light of our analysis of the symptomatic priority policy, it is likely that the death-minimizing time to start serving asymptomatics is close to time  $t_s$  as defined in (22). That is, it is probably optimal to clear the queue of symptomatics, and then switch to mass service. Symptomatics may not be served fast enough if  $t_p < t_s$ , and capacity is wasted if  $t_p > t_s$ .

Hence, we assume that the ring time  $t_p = t_s + \Delta t$ , where  $\Delta t$  is the additional wait before switching to mass service. For practical (i.e., not too large) values of  $\Delta t$ , the antibiotics queue will be emptied at roughly time  $t_e + \Delta t$ , where  $t_e$  is given in (44) in the main text, because the antibiotic distributors are mostly idle during the interval  $[t_s, t_s + \Delta t]$ . To compute the number of deaths, we perform a separate analysis over three time intervals:  $[\tau, t_s]$ ,  $[t_s, t_s + \Delta t]$ , and  $[t_s + \Delta t, t_e + \Delta t]$ . Letting  $D_1, D_2$  and  $D_3$  denote the number of deaths in  $[\tau, t_s]$ ,  $[t_s, t_s + \Delta t]$ , and  $[t_s + \Delta t, t_e + \Delta t]$ , we have

$$D = I(C_3 + C_4) + D_1 + D_2 + D_3. \quad (41)$$

The quantity  $D_1$  was computed in §2, and consists of those who are in stage 2 at time  $\tau$  and all those who enter stage 2 during  $[\tau, t_s]$ ,

$$D_1 = (1 - e_2)(IC_2 + I(e^{-r_1\tau} - e^{-r_1t_s})). \quad (42)$$

During the rather dormant time interval,  $[t_s, t_s + \Delta t]$ , we have  $I(e^{-r_1t_s} - e^{-r_1(t_s+\Delta t)})$  people who progress from stage 1 to stage 2. These people are apt to experience no wait in the antibiotics queue, and the fraction of these people who die is  $1 - e_2$ , invoking the  $\mu_A \gg r_2$  assumption that was used

in (33). It follows that

$$D_2 = (1 - e_2)I(e^{-r_1 t_s} - e^{-r_1(t_s + \Delta t)}). \quad (43)$$

We cannot apply the results from §4.2 in the main text to the third time interval,  $[t_s + \Delta t, t_e + \Delta t]$ , because  $Q_2^A(t)$  no longer drops linearly over time, but rather rises and falls somewhat parabolically. The bulk of the people in this time interval start out in  $Q_0^A$  and  $Q_1^A$ . Let  $L_R$  be the number of people who progress from  $Q_1^A$  all the way to  $Q_3^A$  before getting served, let  $S$  denote the number of people who get served from compartment  $Q_2^A$ , and let  $G$  be the number of people who enter compartment  $Q_2^A$ . These definitions imply that  $D_3 = L_R + (1 - e_2)S + (1 - e_1)(1 - e_2)(Q_1^A(t_s + \Delta t) - G)$ , where the last term in  $D_3$  represents those who are served while in stage 1, but the antibiotics are not effective. Because  $G = L_R + S$ , we have

$$D_3 = e_2 L_R + (1 - e_2)G + (1 - e_1)(1 - e_2)(Q_1^A(t_s + \Delta t) - G). \quad (44)$$

We calculate the quantities  $G$  and  $L_R$  from a probabilistic analysis, under the reasonably accurate assumption that  $Q_1^A(t)$  drops linearly to zero throughout this time interval. Given that someone enters stage 2 at time  $t$ , we have a competition between an  $\exp(r_2)$  random variable, call it  $X_2$ , and a  $U[t, t_e + \Delta t]$  random variable denoted by  $U(t)$ . This competition yields

$$L_R = \int_{t_s + \Delta t}^{t_e + \Delta t} r_1 Q_1^A(t_s + \Delta t) \frac{t_e + \Delta t - t}{t_e - t_s} P(X_2 \leq U(t)) dt. \quad (45)$$

Substituting

$$P(U(t) < X_2) = \int_t^{t_e + \Delta t} \frac{e^{-r_2(u-t)}}{t_e + \Delta t - t} du = \frac{1 - e^{-r_2(t_e + \Delta t - t)}}{r_2(t_e + \Delta t - t)} \quad (46)$$

into (45) and integrating gives

$$\begin{aligned}
L_R &= \frac{r_1 Q_1^A(t_s + \Delta t)(t_e - t_s)}{2} + \frac{r_1 Q_1^A(t_s + \Delta t)}{r_2^2(t_e - t_s)}(1 - e^{-r_2(t_e - t_s)}) - \frac{r_1 Q_1^A(t_s + \Delta t)}{r_2} \\
&= I r_1 e^{-r_1(t_s + \Delta t)} \left( \frac{(t_e - t_s)}{2} + \frac{1 - e^{-r_2(t_e - t_s)}}{r_2^2(t_e - t_s)} - \frac{1}{r_2} \right).
\end{aligned} \tag{47}$$

The quantity  $G$  is simply all those who enter stage 2 by progressing from  $Q_1^A$ ,

$$G = \int_{t_s + \Delta t}^{t_e + \Delta t} r_1 Q_1^A(t) dt = \frac{I r_1 (t_e - t_s) e^{-r_1(t_s + \Delta t)}}{2}. \tag{48}$$

Equations (44), (47) and (48) give

$$\begin{aligned}
D_3 &= I e^{-r_1(t_s + \Delta t)} \left[ \frac{r_1(t_e - t_s)(e_1 + e_2 - e_1 e_2)}{2} + \frac{e_2 r_1(1 - e^{-r_2(t_e - t_s)})}{r_2^2(t_e - t_s)} \right. \\
&\quad \left. - \frac{e_2 r_1}{r_2} + (1 - e_1)(1 - e_2) \right].
\end{aligned} \tag{49}$$

By (12) in the main text, (41), (42), (43) and (49), the total number of deaths is approximately

$$\begin{aligned}
\frac{D}{I} &= 1 - C_1 - e_2 C_2 + (1 - e_2) e^{-r_1 \tau} + e^{-r_1(t_s + \Delta t)} \left[ \frac{r_1(t_e - t_s)(e_1 + e_2 - e_1 e_2)}{2} \right. \\
&\quad \left. + \frac{e_2 r_1(1 - e^{-r_2(t_e - t_s)})}{r_2^2(t_e - t_s)} - \frac{e_2 r_1}{r_2} - e_1(1 - e_2) \right].
\end{aligned} \tag{50}$$

Fixing all parameter values except  $\Delta t$  in (50) gives

$$\begin{aligned}
\frac{D}{I} &= 0.634 - 0.361 e^{-0.08 \Delta t} \\
&\approx 0.273 + 0.029 \Delta t \quad \text{for small } \Delta t.
\end{aligned} \tag{51}$$

Note that the coefficient in front of the ring delay parameter  $\Delta t$  in (51) is identical to the coefficient for the time it takes to distribute antibiotics in (63) in the main text. For small  $\Delta t$ , we directly compute

the impact of the ring parameter  $p$ , via  $\frac{dD}{dp} = \frac{dD}{dt_p} \frac{dt_p}{dp} = \frac{bN}{r_1(I_1(0)-pN)}$ , which follows from (24) in the main text, (51) and the fact that  $\Delta t = t_p - t_s$ . Plugging in base values, with  $I_1(0) = 0.5N$  (Table 1), we have  $\frac{dD}{dp} = \frac{0.725}{1-2p} \approx 0.725 + 1.45p$ .

Finally, we note that in the limiting case  $p = 1$ , where only symptomatic people are given antibiotics, the overcongested estimate is simply

$$\frac{D}{I} = 1 - e_2. \quad (52)$$

## 4 Spatial Aggregation

We derive equation (69) in the main text in this section. While we have not been able to integrate (68) in the main text, for a release size less than about eight grams (roughly the amount in all the tainted envelopes in the 2001 postal attack), the first argument in the minimum function in (68) in the main text is not needed, and the total number of infected people is given by

$$I_T = \frac{\theta}{A} \int_0^A \int_0^\infty \int_{-\infty}^\infty \frac{k_1 x^{-2d} \exp(-k_2 y^2 x^{-2d} - k_3 x^{-2d})}{c_1 - c_2 a} dy dx da, \quad (53)$$

$$= \frac{\theta}{A} \int_0^A \int_0^\infty \frac{k_1 x^{-2d} e^{-k_3 x^{-2d}}}{c_1 - c_2 a} \left[ \int_{-\infty}^\infty e^{-k_4 y^2} dy \right] dx da \quad \text{where } k_4 = k_2 x^{-2d}, \quad (54)$$

$$= \frac{\theta}{A} \int_0^A \int_0^\infty \frac{k_1 x^{-2d} e^{-k_3 x^{-2d}} \sqrt{\pi}}{(c_1 - c_2 a) \sqrt{k_4}} dx da \quad \text{by Gradshteyn \& Ryzhik(1980), p.307,} \quad (55)$$

$$= \frac{\theta}{A} \int_0^A \frac{k_1 \sqrt{\pi}}{\sqrt{k_2}(c_1 - c_2 a)} \left[ \int_0^\infty x^{-d} e^{-k_3 x^{-2d}} dx \right] da, \quad (56)$$

$$= \frac{\theta}{A} \int_0^A \frac{k_1 \sqrt{\pi}}{\sqrt{k_2}(c_1 - c_2 a)} \left[ -\frac{1}{2d} \int_0^\infty w^{-\frac{(d+1)}{2d}} e^{-k_3 w} dw \right] da, \quad \text{where } w = x^{-2d}, \quad (57)$$

$$= -\frac{\theta}{A} \int_0^A \frac{k_1 \sqrt{\pi}}{2d \sqrt{k_2}(c_1 - c_2 a)} \left[ \frac{\Gamma\left(\frac{d-1}{2d}\right)}{k_3^{\frac{d-1}{2d}}} \right] da, \quad (58)$$

$$= -\frac{\theta k_1 \sqrt{\pi} \Gamma\left(\frac{d-1}{2d}\right) \log\left(\frac{c_1}{c_1 - c_2 A}\right)}{2A \sqrt{k_2} d c_2 k_3^{\frac{d-1}{2d}}}. \quad (59)$$

## 5 Biosensors vs. Antibiotic Distribution

As an illustration of how the biosensor analysis in §3 of the main text, the analysis of a service zone in §4-5 of the main text, and the spatial aggregation across zones in §6 of the main text can be combined to assess policy tradeoffs, in this section we compare the value of biosensors and rapid antibiotic distribution, under both exponential and log-normal disease progression. We focus on a release of  $10^{15}$  spores, and refer readers to Figure 4 of Wein *et al.* (2003) for an investigation of the impact of the release size on the performance of biosensors. For a region 50 km downwind by  $\pm 10$  km crosswind with a population density of  $\theta = 2000$  people per  $\text{km}^2$  (e.g., a portion of Los Angeles), numerically integrating (68) in the main text leads to  $I_T = 314,425$  infected people out of a total of 2 million in the region. We assume that early symptomatic detection occurs when the  $k = 20^{\text{th}}$  infected person develops symptoms. Although the detection delay via early symptomatics is random in (2) in the main text, we use its expected value and assume  $\tau_s = E[X_{k:I_T}]$ . In the exponential case, we have (e.g., Barlow and Proschan 1975)

$$\tau_s = \frac{1}{r_1} \sum_{i=0}^{k-1} \frac{1}{I_T - i} = 8 \times 10^{-4} \text{ days.} \quad (60)$$

For the log-normal case, Theorem 5.8 of Balkema and de Haan (1978) implies that

$$\tau_s \approx F^{-1}\left(\frac{k}{I_T}\right) = 0.713 \text{ days,} \quad (61)$$

where  $F(x)$  is the cdf of the log-normal incubation period.

To compute the detection delay via biosensors, we fix the detection limit at  $l_b = 10,000$  spores, which is roughly the inhaled dose that would infect half the population. We investigate variations in the time delay to obtain test results,  $\tau_b$ , which is dictated by the frequency and turnaround time of sampling, and the distance between adjacent biosensors,  $w_b$ . The values of  $l_b$ ,  $\tau_b$  and  $w_b$  are classified for current biosensors. By Figure 3 in the main text, we use the small- $w$  approximation for  $w \leq 200$

m, the intermediate- $w$  approximation for  $w \in (200, 10^5]$  m, and the large- $w$  approximation for  $w > 10^5$  m. The computations described thus far in this section allow us to compute the intervention delay  $\tau$  in (2) in the main text. We then use the overcongested approximations (49) in the main text and (66) in the main text to compute the fraction dead under the exponential and log-normal cases.

Figure 1 shows two isocurves, for exponential and log-normal disease progression, that sweep out  $(\tau_b, t_e - \tau)$  pairs (i.e., the time to obtain test results and time to distribute antibiotics) resulting in 20% of the infected population dying (i.e.,  $D/I = 0.2$ ) for the exponential case and  $D/I = 0.1$  for the log-normal case. These curves hold as long as the attack is detectable by biosensors, which occurs if  $w \leq 19.9$  km; if  $w > 19.9$  km, biosensors are unable to detect the attack and the fraction dead is independent of  $\tau_b$ . By (60), detection via symptomatics is essentially instantaneous under exponential disease progression, and is faster than biosensors regardless of the time to obtain biosensor results. Hence, the tradeoff curve in Figure 1 is horizontal in this case. The tradeoff curve is linear with a slope of -1.25 in the log-normal case, up to the point in which the time to obtain biosensor results reaches 0.773 days, which is the symptomatic detection delay in (61). Hence, in this range, a one-hour reduction in the time to obtain biosensor results is approximately 25% more beneficial than a one-hour reduction in distributing antibiotics to the population. However, many additional deaths (i.e., beyond  $D/I = 0.1$ ) can be avoided by reducing the time to distribute antibiotics below 3.9 days.

A more thorough analysis would investigate a variety of release sizes (as is done in Wein *et al.* 2003) and their corresponding likelihoods (which is extremely difficult to predict). As noted in Wein *et al.* (2003), biosensors are of limited value for an anthrax attack: early symptomatics allow for early detection in a large attack and there are not many lives to save in a small attack.

While it would be tempting at this point to introduce costs for antibiotic servers, biosensors and sampling, and derive cost-minimizing choices of  $w_b$ ,  $\tau_b$  and  $n_A$ , a cost analysis is not straightforward for several reasons (see §7 of the main text for a discussion), and is beyond the scope of this paper.

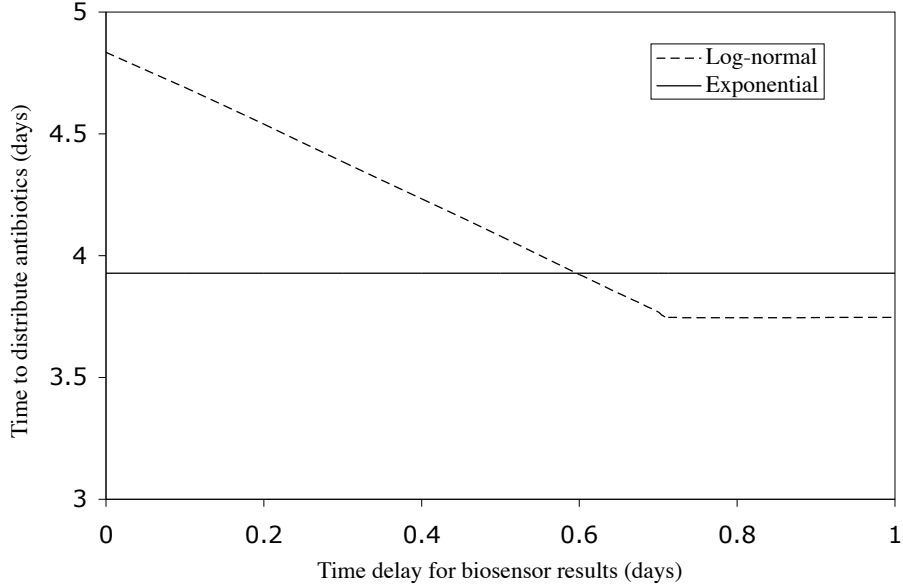


Figure 1: Iso-mortality curves (resulting in  $D/I = 0.2$  for exponential disease progression and  $D/I = 0.1$  for log-normal progression) of time to distribute antibiotics vs. time delay for biosensor results, when the attack is detectable by biosensors (i.e.,  $w \leq 19.9$  km).

## 6 Static Allocation of Antibiotic Servers

In this section, we consider the optimal static allocation of antibiotic servers across service zones. Suppose that post-attack situational awareness is such that the location of the attack and an estimate of the number of infected people in each service zone are known (e.g., Kaplan 2004). Let  $\tilde{I}_k$  be the estimated number of infected people in service zone  $k = 1, \dots, K$ . Adapting the notation in Table 1 in the main text, let  $N_k$  be the population size of zone  $k$  and let  $n_{Ak}$  be our decision variable, which is the number of antibiotic servers allocated to zone  $k$ . Suppose  $\bar{n}_A$  antibiotic servers are available to allocate across the  $K$  service zones. The number of deaths in zone  $k$  is approximately  $\tilde{I}_k$  times the right side of equation (49) in the main text, where by (44) in the main text we replace  $t_e - \tau$  by  $\frac{N_k}{n_{Ak}\mu_A}$ .

Hence, the optimal static allocation is the solution to

$$\min_{\{n_{A1}, \dots, n_{AK}\}} \sum_{k=1}^K \tilde{I}_k \left[ \frac{r_2 C_2 N_k}{2n_{Ak} \mu_A} + \frac{(1-e_1)(1-e_2)C_1 n_{Ak} \mu_A}{r_1 N_k} \left(1 - e^{-\frac{r_1 N_k}{n_{Ak} \mu_A}}\right) \right], \quad (62)$$

$$\text{subject to } \sum_{k=1}^K n_{Ak} = \bar{n}_A, \quad (63)$$

$$n_{Ak} \geq 0 \quad \text{for } k = 1, \dots, K, \quad (64)$$

which can be derived by a straightforward application of the Karush-Kuhn-Tucker theorem. If the time to distribute antibiotics is no more than four days, then  $e^{-\frac{r_1 N_k}{n_{Ak} \mu_A}} \approx 1 - \frac{r_1 N_k}{n_{Ak} \mu_A} + \frac{r_1^2 N_k^2}{2n_{Ak}^2 \mu_A^2}$ , and the solution to (62)-(64) is

$$n_{Ak}^* = \frac{\sqrt{N_k \tilde{I}_k}}{\sum_{k=1}^K \sqrt{N_k \tilde{I}_k}} \bar{n}_A \quad \text{for } k = 1, \dots, K; \quad (65)$$

i.e., antibiotic servers are allocated in proportion to the square root of the product of the population size and the number of infected people.

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