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Risk-Based Decision Making for Reoccupation of Contaminated Areas Following a Wide-Area Anthrax Release

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This article presents an analysis of postattack response strategies to mitigate the risks of reoccupying contaminated areas following a release of *Bacillus anthracis* spores (the bacterium responsible for causing anthrax) in an urban setting. The analysis is based on a hypothetical attack scenario in which individuals are exposed to *B. anthracis* spores during an initial aerosol release and then placed on prophylactic antibiotics that successfully protect them against the initial aerosol exposure. The risk from reoccupying buildings contaminated with spores due to their reaerosolization and inhalation is then evaluated. The response options considered include: decontamination of the buildings, vaccination of individuals reoccupying the buildings, extended evacuation of individuals from the contaminated buildings, and combinations of these options. The study uses a decision tree to estimate the costs and benefits of alternative response strategies across a range of exposure risks. Results for best estimates of model inputs suggest that the most cost-effective response for high-risk scenarios (individual chance of infection exceeding 11%) consists of evacuation and building decontamination. For infection risks between 4% and 11%, the preferred option is to evacuate for a short period, vaccinate, and then reoccupy once the vaccine has taken effect. For risks between 0.003% and 4%, the preferred option is to vaccinate only. For risks below 0.003%, none of the mitigation actions have positive expected monetary benefits. A sensitivity analysis indicates that for high-infection-likelihood scenarios, vaccination is recommended in the case where decontamination efficacy is less than 99.99%.

KEY WORDS: Anthrax; bioterrorism; decision analysis; evacuation

1. INTRODUCTION

In the 2001 "Amerithrax" incidents, in which *Bacillus anthracis* spores were mailed to multiple addresses via the postal service, most of the acute risk was due to the initial exposure to aerosolized spores. However, bioattacks also contaminate surfaces in the environment, which may present long-term reaerosolization risk if not remediated.(1) Because spores are highly persistent in the environment, contaminated areas may need to be decontaminated before being reoccupied.(2,3) Estimates for the decontamination and other direct costs for the 2001 attacks range from approximately $500K for the U.S. Department of Justice mail facility to $200M for the Brentwood and Trenton Mail Processing and Distribution Centers.(4,5) Other studies have estimated the entire cost of decontamination at $320M.(6) Given the high levels of contamination at these sites, the aggressive response appears to have been justified.(7)

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However, a wide-area release of *Bacillus anthracis* spores would likely result in a gradient of contamination from high levels in the immediate area of the release to progressively lower levels as the distance from the release increases. Aggressive response actions cannot be taken at all potentially contaminated locations. Thus, it will be necessary to identify switch-over points where less aggressive actions should be taken, as well as a point below which the risk is considered too small to warrant a response.

Several previous studies have considered the policy decisions that must be made following such an event and, in general, agree that determining the appropriate response to an attack is a difficult task given the complexity of the situation and its inherent uncertainties.[8,9] Fowler *et al.* utilized a decision model to assess the results of prevention and response policies for an anthrax attack in an urban area. The model considered four "postattack" strategies (including no vaccination, vaccination, antibiotics, and vaccination plus antibiotics) and two "preattack" strategies (no vaccination or vaccination). They determined that the optimal strategy from a cost-benefit perspective was the combined administration of postattack antibiotics and postattack vaccination. This is in general agreement with work by Schmitt *et al.*,[10] who determined that postattack antibiotics and vaccination was more cost effective than preattack antibiotics. Baccam and Boechler[11] compared preattack and postattack vaccination strategies following an anthrax attack and found that in either case, a rapid postexposure prophylaxis (PEP) response is critical for reducing the number of casualties. Brookmeyer *et al.* modeled the outcomes of possible response strategies to an anthrax release and concluded that initiation of antibiotic treatment to potentially exposed individuals within six days would prevent at most 70% of cases.[12] The addition of vaccination slightly improved this outcome. Others have modeled the placement of medical dispensing points following an anthrax attack,[13] the importance of prophylactic antibiotics administered quickly following an attack,[14] and the logistics of pharmaceutical deployment.[15,16] Kyriacou *et al.*[17] modeled a hypothetical wide-area anthrax release in Chicago using Markov decision models and compared response tactics that were initiated two days after the attack or five days after the attack. Using guidance from the Anthrax Modeling Working Group,[18] postattack options included (1) antibiotics and (2) vaccination. Tactics that incorporated a preattack measure included (1) preattack vaccination of the entire metropolitan population with postattack antibiotics for everyone exposed, and (2) preattack vaccination of the entire metropolitan population with postattack antibiotics and vaccination of everyone exposed. Results of the analysis were in agreement with the U.S. government's strategy to administer postattack antibiotics and vaccination to all exposed individuals within two days after the detection of the attack.

Research on the postattack recovery process has also been performed by several joint government agency efforts, focusing on developing guidance for different stakeholder groups following a wide-area attack. These include the Interagency Biological Restoration Demonstration (IBRD) project, which ran from 2007 through 2010 as a joint effort between the Department of Defense and the Department of Homeland Security, and the Wide Area Recovery and Resiliency Program (WARRP), which ran from 2011 through 2013.[19] The IBRD project produced guidance that may be useful to a number of stakeholder groups following an attack, including a methodology to select an appropriate form of decontamination and an investigation of the challenges posed by anthrax-contaminated waste.[3,20–23] Another project, the Bio-response Operational Testing and Evaluation (BOTE) project, was undertaken by the EPA in 2011 as a set of field exercises to test sampling and decontamination methods.[24]

While many studies assume evacuation of contaminated areas after an attack, the costs and benefits of evacuation as a response to a bioterrorism incident have been less thoroughly studied than vaccination and antibiotic treatment. However, evacuation has been studied as a response to other (nonbioterrorism) hazards. Sorensen *et al.*[25] evaluated the factors that determine whether evacuation or sheltering in that place is more effective following an airborne hazardous chemical release, considering the characteristics of the chemical released, current weather conditions, the type of buildings near the release, and other factors. It was determined that although the decision is very rarely simple, there are situations in which one option is clearly preferred over the other. The most relevant of these situations to an anthrax release include: (1) evacuation is preferred when it can be completed prior to plume arrival; and (2) when such an evacuation could not be conducted in time, sheltering in place is the default. Even in urban areas that have biosensor networks installed, it seems unlikely that an anthrax release would be detected and verified in enough time to evacuate people near the point of release, and without rapid biosensors, it may be days before the nature of a release is confirmed. This means that in any typical urban area, some people could enter and exit the contamination zone several times before the attack had been detected. Thus, for anthrax the decision to evacuate is not typically driven by the initial human exposure but by the risk presented by reaerosolization of spores.

While these previous studies contribute to understanding appropriate response options, they generally have not explicitly identified switch-over points at which different response actions are warranted. One that did conduct such an analysis was an analysis by Mitchell-Blackwood *et al.*[26] that applied a cost-benefit analysis to three postattack managerial decisions: (a) whether to administer prophylactic antibiotics, (b) whether to vaccinate individuals, and (c) whether to decontaminate the building. A decision model was developed that compared the expected outcome of each response option against the expected outcome of a no-action alternative, as a function of the risk. The point at which the expected values of the action/no-action alternatives were equal was determined and proposed as a potential threshold below which response actions were not justified based on their expense and possible side effects. For antibiotic treatment, this risk threshold was 1 infection per 6,500 people; for vaccination, 1 infection per 7,100 people, and for building decontamination 1 infection per 32 people. The study of Mitchell-Blackwood *et al.* did not consider short-term evacuation as a response option and did not consider combinations of different response options. The analysis presented in this article extends the work of Mitchell-Blackwood *et al.* to include evacuation, and develops an integrated response model that considers the value of evacuation in the context of other possible responses, including antibiotic prophylaxis, vaccination, building decontamination, and combinations thereof. Values for the cost and effectiveness of these options were taken from the literature[27] and the scenarios were analyzed with a decision tree to produce expected values of different options as a function of risk. Preferred responses (i.e., those with the lowest expected cost per person) were identified for different infection-probability levels.

The risk of developing inhalation anthrax due to reaerosolized *B. anthracis* spores is difficult to quantify, and substantial ambiguity regarding the precise health impacts due to reaerosolization remains. Recently, a probable exposure to reaerosolized spores in a Belgian wool-sorting factory caused asymptomatic infection among exposed workers, but no actual cases.[28] In the early 20th century, textile mill employees were likely exposed to hundreds of anthrax spores on a routine basis and few cases of inhalational anthrax were reported.[29,30] Following the contamination of the AMI building during the 2001 Amerithrax attacks, it was estimated that nearly 100 employees were exposed to *B. anthracis* spores while illness was reported in only two employees, possibly due to the evacuation of the building and antibiotic prophylaxis of potentially exposed individuals.[31]

Despite these empirical ambiguities, there is a body of research suggesting that reaerosolization of *B. anthracis* does present a serious health risk. Further, this risk has been taken very seriously and resulted in the long-term closure of facilities and expensive decontamination efforts after the 2001 attacks. Two papers examining the 2001 attacks determined that reaerosolization of spores was associated with active movement in previously contaminated offices[1] and with the operation of a previously contaminated mail-sorting machine.[32] Empirical studies using simulants have showed that spores can infiltrate buildings from outside,[33] and that spores can be reaerosolized in HVAC ductwork.[34] Others have linked the amount of residual contamination within a building to corresponding risk levels.[7] In one recent review article, Layshock *et al.* (2012) concluded that there is evidence that *Bacillus* spp. are "reaerosolized by wind under ambient conditions, by pedestrian or vehicle traffic, and by other types of mechanical action."[35]

The dose-response (DR) relationship for inhalation anthrax is not completely understood, though many competing models have been proposed.[7,11,18,36–41] While it is assumed for this analysis that reaerosolization of anthrax spores is possible and results in a nonzero risk to human health, no assumptions are made regarding the type or nature of a dose-response model for inhalation anthrax. Instead, results are framed as a "what-if" analysis, where the entire spectrum of risk (from 0% chance of infection to 100% chance of infection) is mapped out and corresponding recommendations are made for each risk level. Such a structure means that whatever reaerosolization and dose-response models are judged to be most appropriate may be used in conjunction with this framework.

2. METHODS

2.1. Hypothetical Scenarios Considered

The base case scenario concerns a release of *B. anthracis* spores in a major urban area, resulting in the exposure of some number of people relatively quickly and the possible exposure of others by future reaerosolization of spores that have settled on surfaces in buildings. The attack is assumed to have been quickly detected. Given that previous studies have determined that the rapid administration of antibiotics is the most appropriate response to mitigate immediate risk from a bioattack, this article assumes that antibiotics were administered to residents of the affected region and focuses on subsequent decisions regarding the risk from future reaerosolization of spores.[1,26,27,42,43]

2.2. Response Options and Assumptions

2.2.1. Vaccination

The vaccination strategy assumes the use of Anthrax Vaccine Absorbed (AVA), the only anthrax vaccine currently licensed by the U.S. Food and Drug Administration. The vaccine was initially approved as a preexposure sequence comprising six priming doses (0, 2, and 4 weeks, 6 months, 12 months, and 18 months) with subsequent booster doses every year.[44] Although not licensed for use in children under the age of 18, there is some evidence from other inactivated vaccines indicating that minors may also receive the AVA vaccine if necessary.[45] Therefore, this model does not distinguish between minors and adults in receiving the vaccine. Information on the efficacy of postattack antibiotic and vaccine treatment and the optimum time window for action exists in the literature. In emergency situations, the vaccine can be given in two doses, two weeks apart, providing protection for half the recipients beginning at three weeks following the first dose and for the remaining recipients at four weeks after the first dose.[46] When a full series of six subcutaneous inoculations is followed, the vaccine was reported to be 93– 100% effective at preventing inhalational anthrax.[27]

2.2.2. Decontamination

It is assumed that decontamination of the physical environment is accomplished through a combination of fumigation and the use of sporicidal solutions applied as foam or spray. In controlled experiments, some of these products were demonstrated to be 99.9999% effective (six-log reduction) against anthrax spores on most nonporous surfaces with a contact time of 30 minutes and on porous surfaces with two applications and a contact time of one hour.[47] Previous research has confirmed the possibility of achieving a six-log reduction in spore counts.[48] Costs for decontamination were calculated for an average of 234 square feet of space per occupant scaled from costs reported from the 2001 cleanups.[26] Published data on the length of time that buildings remained closed in 2001 for fumigation reveal an average closure time of approximately 22 months but an actual fumigation time of only approximately four months.[49] We assume for this analysis that advances in sporicidal and fumigation technologies and a better understanding of the application of such technologies to a scenario involving anthrax would require approximately six months of closure for the base case. This value is varied from three months to 24 months in the sensitivity analyses discussed below.

2.2.3. Evacuation

There are two instances in which evacuation is applicable—the first applies to the vaccine only response option; the second applies to the building decontamination response option. In the first case (when evacuation is only undertaken to allow time for the vaccine to become effective) we assume an evacuation duration of two months, as this is considered sufficient for the vaccine to reach full efficacy.[50] In the second case, the evacuation duration is assumed to be longer to allow for decontamination activities to be completed. As discussed above, the duration of evacuation in this second case is assumed to be six months for the base case. The approach taken here is generally in line with the framework suggested by Lesperance *et al.*[51] and the results of the Seattle Urban Area Security Initiative (UASI).

Any discussion of evacuation costs must include reference to the classification of economic costs associated with major disasters. Such costs are commonly broken up into subcategories, including direct, indirect, and induced costs.[52–54] Direct costs include transport, food, lodging, and other miscellaneous items during the actual evacuation, as well as lost earnings and production losses immediately resulting from the attack. In addition to direct costs, more extensive economic models include indirect costs (which may include lost wages and lost business revenue in the affected area) and induced costs (which represent changes in consumer sales due to impacts on residential income). For brevity, indirect and induced impacts are combined under the term "higher-order effects."(55) Several types of models exist to estimate the impact of higher-order effects on a region's economy, including input-output (IO) models, inoperability input-output models (IIMs), and computable general equilibrium (CGE) models.(56,57) Our analysis is focused on the choices private citizens will be faced with concerning the disposition of their real estate assets independent of the regional higher-order effects—therefore, only the direct costs of evacuation and a subsequent period of displacement are considered here. We conceptualize the cost of evacuation as consisting of two separate costs: a one-time cost to perform the evacuation and a monthly cost that reflects government assistance to the individuals displaced. The one-time cost includes a change of shoes and clothing, transportation out of the affected area, and physical decontamination of individuals and their vehicles. The monthly cost consists of unemployment assistance and housing assistance. An estimate of housing assistance costs was derived from Federal Emergency Management Agency (FEMA) assistance to victims of Hurricane Sandy.(58) Unemployment assistance was estimated from data for Pennsylvania published by the Pennsylvania Department of Labor and Industry.(59)

2.2.4. Abandonment

Abandonment, the renunciation of home ownership, represents the most costly response strategy considered. For this article, the base cost of abandonment per person was approximated as the median home price for the greater Philadelphia area.(60) With few valid empirical precedents to draw from, there is significant uncertainty regarding this option and, of course, great variability from home to home and neighborhood to neighborhood. In an economically distressed area, home values would be lower and abandonment would be a more attractive option than it is in the analysis conducted here. There is some evidence that bioterrorism events themselves would push regions toward devaluation of home prices, which would favor abandonment. Dormady *et al.* (2014), using the same postattack framework used in the IBRD effort, assumed a temporary postattack displacement of 75% of the population from the central business district of Seattle and estimated this would result in an overall 33% drop in city-wide residential real estate values and potentially tens of thousands of residential foreclosures. While the current study uses the median home price for Philadelphia in the base case scenario, this value is varied widely in the sensitivity analysis in order to capture the full range of uncertainty associated with this option.

2.3. Decision Model Design

A decision tree was developed[4] to compare the projected cost per person based on different responses following an attack. The analysis is based on risk-neutral decision making in which the preferred outcome is selected by choosing the path with the highest expected value (i.e., the lowest expected cost).(61) As shown in Fig. 1, the tree structure comprises six different branches, with each branch representing a different response strategy. The tree is read by starting at the left and moving right. Following an attack, the choice must be made to evacuate or not. Subsequent choices then depend on which response option (branch) is chosen. Table I summarizes the strategies and the formulae used to compute risk for each. In order of least aggressive to most aggressive (i.e., least costly to most costly), these strategies include:

- Option 1: Do not evacuate and do not vaccinate (antibiotics only). Residents who take no action would be exposed to a risk of infection due to reaerosolizaton, denoted for sake of simplicity as α. However, during "Period 1," the initial 60 days, residents are taking antibiotics as a result of their exposure to the initial release. Based on Hong *et al.* (2010), the initial 60 days is estimated to account for 18% of the reaerosolization risk.(7,62) During Period 1, residents would become ill only if the antibiotics fail (probability denoted by F_a), making their risk of infection $0.18\ \alpha\ F_a$. For the remainder of the time, residents are exposed to 82% of the reaerosolization risk or $0.82\ \alpha$. The risk of infection during either time period is $1 - (1 - 0.18\,\alpha\, F_a)(1 - 0.82\,\alpha)$. Infected individuals may recover (probability of $1 - P_m$) or die (probability of P_m).
- Option 2: Do not evacuate but do vaccinate. The antibiotic administered at the outset of

[4]The decision tree was developed using PrecisionTree (Palisade Software, Ithaca, New York) for Microsoft Excel 2010 (Microsoft, Inc., Redmond, Washington).

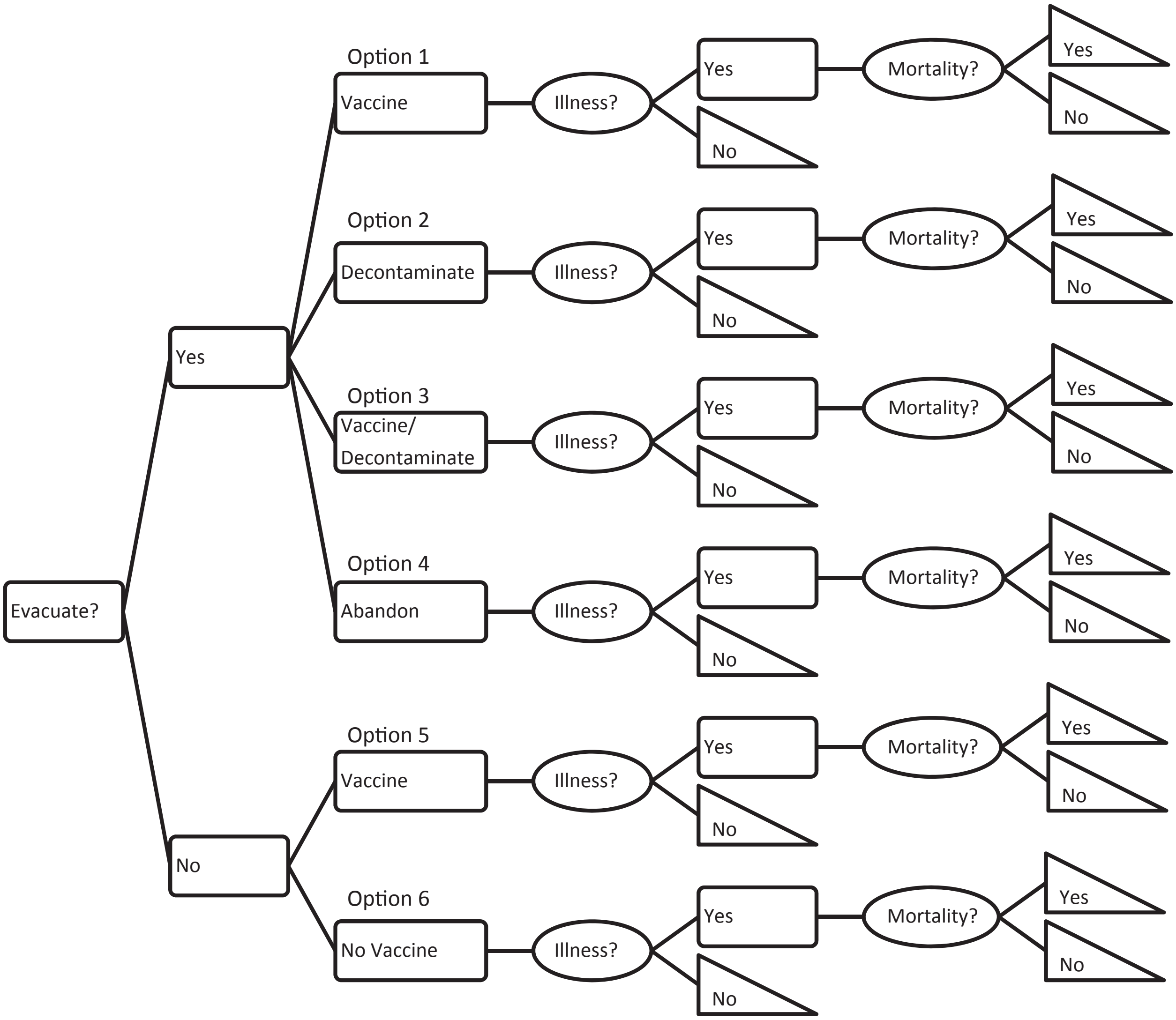

Fig. 1. Decision model structure.

the attack is assumed to offer some protection against residual reaerosolization during the 60 days following the attack until the vaccine becomes effective. Period 1 risk is 0.18 α F_a and Period 2 risk is 0.82 α F_v, where F_v is the risk of failure of the vaccine. It is assumed that nonvaccinated individuals are restricted from accessing the building.

- Option 3: Evacuate and vaccinate. Evacuation provides time for the vaccination to become effective. Risk is α F_v. In scenarios such as this where people are in uncontaminated surroundings during Period 1, we assume that 100% of the applicable risk is restricted to Period 2, as no one is present to reaerosolize spores in the contaminated area during Period 1. It is assumed that nonvaccinated individuals are restricted from accessing the building.
- Option 4: Evacuate and decontaminate buildings. Risk is α F_d, where F_d is the risk of failure of the decontamination.
- Option 5: Evacuate, vaccinate, and decontaminate buildings. Risk is α F_v F_d.
- Option 6: Evacuate and abandon area. This option is modeled as completely effective; reaerosolizaton risk is reduced to zero.

A switch-over analysis was performed to define the risk level at which different options produce equal expected values. One-way and two-way

Table I. Model Parameters and Assumptions for the Cost-Benefit Analysis of Response Strategies for the Base Case and Sensitivity Analysis

Parameter	Symbol	Values[h]			References
		Base	Low	High	
Probability of infection (α)[a]	α	0.2	0	1	
Baseline mortality given infection	P_m	0.45	0.25	0.75	26, 27
Efficacy of antibiotics[b]		0.8			26, 27
Efficacy of vaccination[c]		0.93	0.05	0.99	26, 27
Efficacy of building decontamination[d]		0.999999	0.7	1	45, 46
Probability of antibiotic failure	F_a	0.2			26, 27
Probability of vaccine failure	F_v	0.07	0.95	0.01	26, 27
Probability of decontamination failure	F_d	0.000001	0.3	0	45, 46
Cost of antibiotics (60-day regimen)		$28 ($22) [h]			26, 27
Cost of vaccine		$81 ($64)[h]			26, 27
Cost of anthrax-related illness		$36,396 ($28,731) [h]	$1,000	$30,0000	26, 27
Value of a statistical life	VSL	$9,101,067 ($7.4M) [h]	$1,000,000	$10,000,000	63
Cost of evacuation[e]					
Initial cost (sum of costs below)		$400	$100	$2,000	See footnote e
Replacement shoes and clothing		$100	$25	$200	
Physical decontamination during evacuation		$200	$25	$1,600	
Cost of gas		$100	$50	$200	
Monthly cost (sum of costs below)		$2,125	$584	$2,988	
Housing assistance		$439	$152	$648	
Unemployment assistance		$1,686	$432	$2,340	
Cost of building decontamination[f]		$23,830 ($16,714) [h]	$15,256 ($10,700) [h]	$42,250 ($29,633)[h]	26
Cost of abandonment[g]		$228,200 ($215,100) [h]	$50,000	$350,000	58
Duration of evacuation		6 months	3 months	24 months	See footnote i
Proportion of Period 1 risk	$P1$	0.18			60
Proportion of Period 2 risk	$P2$	0.82			60

[a] α represents the probability of a person being infected given a release as described in Section 2.
[b] It is assumed antibiotic protection is provided by Ciprofloxacin and treatment is started within several days after the release.
[c] It is assumed vaccine protection is provided by the AVA vaccine. Protection is assumed to take effect within two months following the initial dose.
[d] It is assumed that building decontamination would be achieved through the use of spray-on foam and/or fumigation.
[e] Initial cost of evacuation includes change of clothes, shoes, and physical decontamination. Monthly cost includes housing assistance and unemployment assistance. Engineering judgment was used to estimate the costs associated with replacement clothing and physical decontamination.
[f] Cost of building decontamination is per person and assumes each person has an occupant loading factor of 234 square feet.
[g] Cost of abandonment uses median home prices for the Philadelphia area.
[h] Costs have been adjusted to 2013 dollars.
[i] Range was derived from building closure durations resulting from the 2001 anthrax attacks.

sensitivity analyses were then performed on key parameters to characterize the amount of variability in the calculated outcomes based on estimated uncertainty in the input values.

2.4. Decision Model Inputs

Parameter values for the base case of the decision model are presented in Table I. In accordance with the recommendations of Brandeau[(63)] and London,[(64)] uncertainty associated with each of the model parameters was addressed by utilizing a range of plausible values taken from the literature. The probabilities and costs are generally consistent with those of Fowler *et al.* and Blackwood *et al.*,[(26,27)] whose values were based on data from the 2001 letter attacks. The EPA's recommended value for the value of a statistical life was used to calculate costs associated with mortality.[(65)] Costs were adjusted to 2013 dollars using the Consumer Price Index. The individual components of the evacuation cost are outlined in Table II, as are the formulas used to calculate expected values of costs associated with different human health outcomes. The initial risk of infection is represented by the value α and can be interpreted as the probability of exposure and infection given a

Table II. Probability Formulas and Cost Components for Each Response Strategy

Response Option	Strategy and Health Outcome	Probability Formula[a] for Expected Value of Outcome	Base Cost	Cost Components Included in Option
Option 1	Don't evacuate/don't vaccinate			
	Illness/survive	$[1-[(1-(\alpha \times P1 \times F_a)) \times (1-(\alpha \times P2))]] \times (1-P_m)$	−$35,441.51	Antibiotics, treatment
	Illness/death	$[1-[(1-(\alpha \times P1 \times F_a)) \times (1-(\alpha \times P2))]] \times (P_m)$	−$8,871,428.50	Antibiotics, treatment, death
	Health	$(1-(\alpha \times P1 \times F_a)) \times (1-(\alpha \times P2))$	−$106.00	Antibiotics
Option 2	Don't evacuate/do vaccinate			
	Illness/survive	$[1-[(1-(\alpha \times P1 \times F_a)) \times (1-(\alpha \times P2 \times F_v))]] \times (1-P_m)$	−$35,362.51	Antibiotics, vaccine, treatment
	Illness/death	$[1-[(1-(\alpha \times P1 \times F_a)) \times (1-(\alpha \times P2 \times F_v))]] \times (P_m)$	−$8,871,349.50	Antibiotics, vaccine, treatment, death
	Health	$(1-(\alpha \times P1 \times F_a)) \times (1-(\alpha \times P2 \times F_v))$	−$27.00	Antibiotics, vaccine
Option 3	Evacuate/vaccinate			
	Illness/survive	$\alpha \times F_v \times (1-P_m)$	−$39,383.51	Evacuation,[b] antibiotics, vaccine, treatment
	Illness/death	$\alpha \times F_v \times (P_m)$	−$8,875,370.50	Evacuation,[b] antibiotics, vaccine, treatment, death
	Health	$1-(\alpha \times F_v)$	−$4,048.00	Evacuation,[b] antibiotics, vaccine
Option 4	Evacuate/decontaminate			
	Illness/survive	$\alpha \times F_d \times (1-P_m)$	−$69,524.59	Evacuation,[b] antibiotics, decontamination, treatment
	Illness/death	$\alpha \times F_d \times (P_m)$	−$8,905,511.59	Evacuation,[b] antibiotics, decontamination, treatment, death
	Health	$1-(\alpha \times F_d)$	−$34,189.08	Evacuation,[b] antibiotics, decontamination
Option 5	Evacuate/vaccinate/decontaminate			
	Illness/survive	$\alpha \times F_v \times F_d \times (1-P_m)$	−$69,603.59	Evacuation,[b] antibiotics, vaccine, decontamination, treatment
	Illness/death	$\alpha \times F_v \times F_d \times (P_m)$	−$8,905,590.59	Evacuation,[b] antibiotics, vaccine, decontamination, treatment, death
	Health	$1-(\alpha \times F_v \times F_d)$	−$34,268.08	Evacuation,[b] antibiotics, vaccine, decontamination
Option 6	Evacuate/abandon			
	Illness/survive	(No residual risk)	−$226,638.51	Evacuation,[b] antibiotics, abandonment, treatment
	Illness/death	(No residual risk)	−$9,062,625.50	Evacuation,[b] antibiotics, abandonment, treatment, death
	Health	(No residual risk)	−$191,303.00	Evacuation,[b] antibiotics, abandonment

[a]Refer to Table I for explanation of symbols.
[b]"Evacuation" includes both initial cost and monthly displacement costs.

Table III. Preferred Response Options for Different Risk Ranges as a Function of Probability of Infection (α)

Risk Class	Probability of Infection	Preferred Option (1st Choice)	Preferred Option (2nd Choice)
High	$\alpha > 11\%$	Antibiotics, evacuate, and decontamination	Antibiotics, evacuate, vaccinate, and decontamination
Moderate	$4\% < \alpha < 11\%$	Antibiotics, evacuate, and vaccinate	Antibiotics, vaccinate
Low	$0.003\% < \alpha < 4\%$	Antibiotics, vaccinate	Antibiotics, evacuate, and decontamination
Very low	$\alpha < 0.003\%$	Antibiotics only	Antibiotics, vaccinate

release of *B. anthracis*. This parameter is varied in the sensitivity analysis from 0 to 1. We assume that for individuals who have contracted anthrax and received treatment, the mortality rate will be 45%, an estimate drawn from previous studies of the 2001 letter attacks.[27,45,66]

3. RESULTS

The first and second preferred response options for different risk ranges are shown in Table III. Figs. 2(a)–(d) show simplified decision trees with the preferred paths highlighted corresponding to each risk level from Table III. The values for the switch-over points (in terms of risk of infection) in Table III are shown graphically in Fig. 3. A switch-over point occurs whenever two lines intersect each other, thus defining the risk ranges detailed in the bullet points below. The least expensive option (i.e., the line closest to the *x*-axis) represents the preferred option for a given infection probability, α. These switch-over points define ranges for which different responses are preferred, as described below:

- For a probability of infection above approximately 11% (i.e., "high risk," such that more than approximately 1 in 9 people would be infected), the preferred option from an expected value perspective is to evacuate and decontaminate buildings. Under the baseline model assumptions, the "evacuate, decontaminate, and vaccinate" option is not preferred. However, the difference is slight—essentially the cost of the vaccine. If the decontamination is less effective than assumed, then it may make sense to include vaccination, as is discussed in Section 3.1.
- For a probability of infection between 4% and 11% (i.e., "moderate risk," where between approximately 1 in 9 and 1 in 21 people were infected), the preferred option is to evacuate and vaccinate but not decontaminate.
- For a probability of infection less than 4% but greater than 0.003% (i.e., "low risk," where between approximately 1 in 21 and 1 in 33,000 people would be infected), the preferred option is to vaccinate without evacuation. At these infection levels, the additional protection afforded by evacuation is outweighed by its costs.
- For a probability of infection less than 0.003% (i.e., "very low risk," where fewer than approximately 1 in 33,000 people would be infected), the "antibiotics only" alternative (i.e., continuing antibiotics for 60 days after the initial exposure, then ceasing antibiotics) is preferred. This value of α is slightly lower than the values of Mitchell-Blackwood *et al.*, who found that vaccination was not justified at risks below 0.014% (where approximately 1 in 7,108 people were infected). This discrepancy is largely due to using a value of a statistical life (VSL) approach to estimate the value of lost health rather than the quality-adjusted life year (QALY) approach used by Mitchell-Blackwood *et al.* that produced somewhat lower costs associated with fatalities. The VSL approach used here is intended to roughly reflect current U.S. EPA approaches to valuing mortality risk.
- The high cost of evacuation and abandonment prevent it from ever being the preferred option regardless of the probability of infection (α) even though it is considered 100% effective in preventing new anthrax cases.

3.1. Sensitivity Analysis

Sensitivity analyses were performed using the cost and parameter ranges presented in Table I at two different infection probabilities ($\alpha = 5\%$ and 20%) in order to identify the parameters responsible for the greatest effect on the final expected cost for the preferred strategy at each infection probability. These two values of α were selected for two reasons: (1) these values represent two levels of risk, a "high" risk ($\alpha = 5\%$) and a "very high" risk

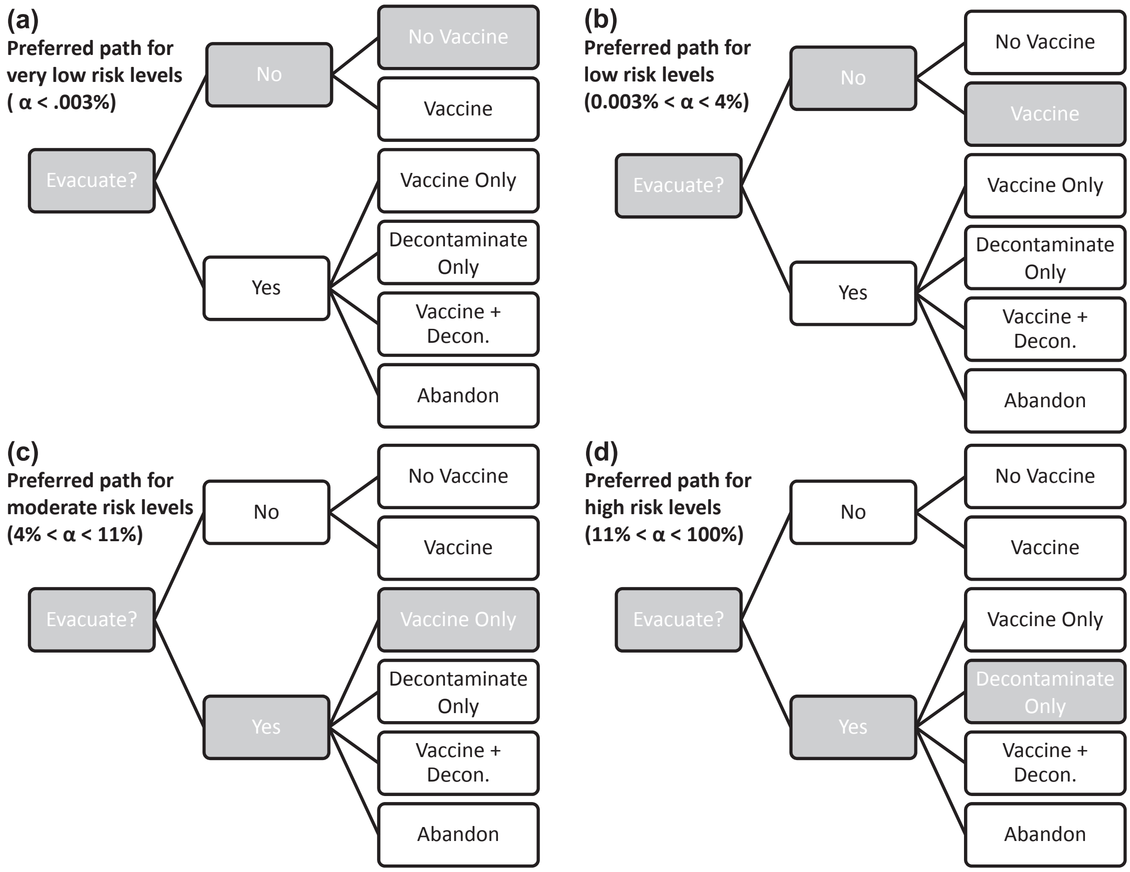

Fig. 2. (a) Preferred path for very low risk levels ($\alpha < 0.003\%$). (b) Preferred path for low risk levels ($0.003\% < \alpha < 4\%$). (c) Preferred path for moderate risk levels ($4\% < \alpha < 11\%$). (d) Preferred path for high risk levels ($11\% < \alpha < 100\%$).

($\alpha = 20\%$), for which the cost of choosing the incorrect response option may be significant, and (2) the optimal response strategy is different for each level (i.e., these values fall on opposite sides of the risk switch-over point for "evacuate and vaccinate" and "evacuate and decontaminate"). To simplify the analysis, only the top two preferred response strategies were considered for each value of α. A one-way sensitivity analysis was performed by varying a select set of parameters and charting the corresponding change in cost difference between the preferred option and second best option for each risk level. For $\alpha = 5\%$, the second best option was "vaccinate only." For $\alpha = 20\%$, "evacuate and vaccinate" (the third most preferred option) was used as the alternative option in the sensitivity analysis instead of the second most preferred option "evacuate, decontaminate, and vaccinate." This is because the only substantive difference between "evacuate, decontaminate, and vaccinate" and the preferred option of "evacuate and decontaminate" was the cost of the vaccine. This variable was considered in a separate one-way sensitivity analysis (see below).

Parameters that were varied in the sensitivity analysis included vaccine efficacy, decontamination efficacy, VSL, cost of decontamination, and duration of evacuation. These analyses revealed that vaccine efficacy and decontamination efficacy had the most significant influence on the overall outcome at both the 5% and the 20% risk levels.

To clarify how changes in vaccine efficacy and decontamination efficacy affect which response option is preferred, we performed a two-way sensitivity analysis using these parameters and generated plots showing which response strategy is preferred for different values of each parameter for $\alpha = 5\%$ and $\alpha = 20\%$. These plots are shown in Fig. 4. These figures offer a useful visual tool to quickly ascertain how the optimal response depends on assumptions regarding both vaccine efficacy and decontamination

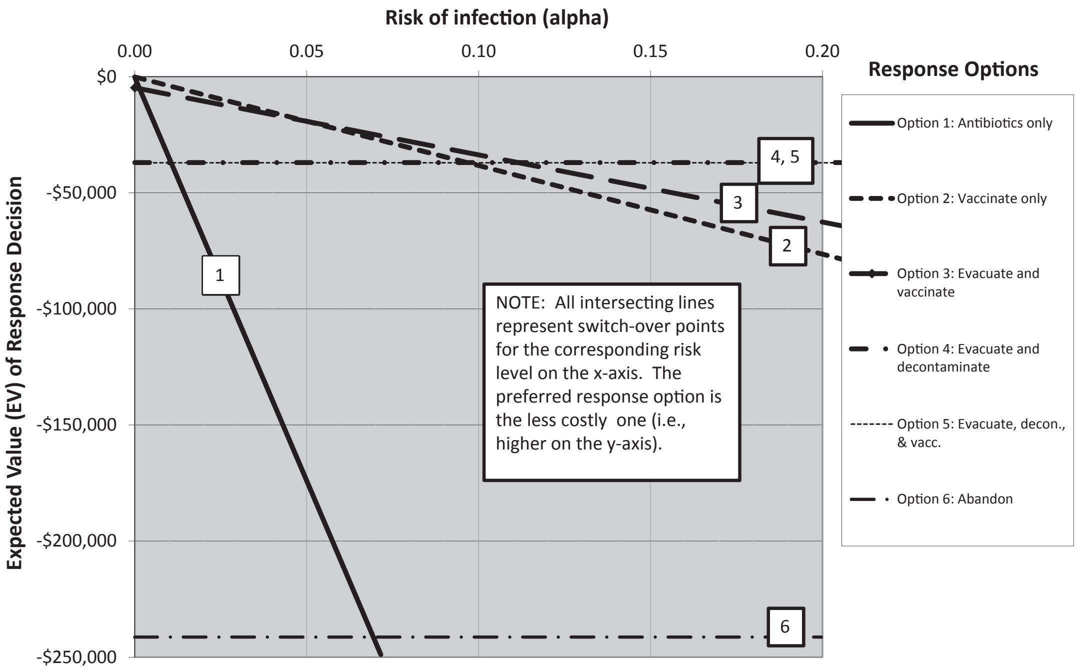

Fig. 3. Risk of infection versus expected value of response option.

efficacy. There may be uncertainty as to the correct values for either of these parameters. In some cases, all of the values in the range of plausible parameter values may have the same preferred response strategy (i.e., the range of values does not cross a switch-over point) and there is no need to further specify the parameter. In other cases different values of the parameter result in different preferred response strategies (i.e., the range of values crosses a switch-over point) and in this case it would be necessary to reduce uncertainty in the parameter value in order to identify the preferred response strategy.

To this point, the analysis has largely assumed that residual risk is known. In reality, it may be very difficult to quantify residual risk, and these uncertainties in risk could lead to inappropriate response strategies. To derive estimates for the penalty of choosing a suboptimal response strategy, a loss function was plotted for each switch-over point (Fig. 5):

$$\text{Loss function} = \text{EV(optimal decision)} - \text{EV(suboptimal decision)}. \quad (1)$$

The x-axis in Fig. 5 shows the actual risk. To the right of each of the three switch-over points, it is assumed that responders believed the risk was below the switch-over point, and the y-axis shows the loss associated with failure to purse the more aggressive response option. To the left of each switch-over point it is assumed that responders believe the risk was above the switch-over point and the y-axis shows the loss associated with unnecessarily pursuing the more aggressive response option. The loss function is symmetric around each switch-over point because all functions are linear. However, for more aggressive (and hence expensive) response strategies at higher risk levels, the slope of the loss function is greater, indicating a greater penalty for not choosing the correct response strategy. While unnecessary vaccination is estimated to have a maximum loss of about \$75 per person, even if provided to those at zero risk, building decontamination decision making has estimated losses of approximately \$2,500 for each percentage error in risk. In responding to an event, decisionmakers may seek to use conservative (i.e., high) estimates of risk and efforts such as this to "price out" the potential cost of under/overresponding could inform risk management efforts.

Key findings from these sensitivity analyses include the following:

- For a risk of infection of 20%, the preferred path using base case values is to evacuate and decontaminate but not vaccinate. The

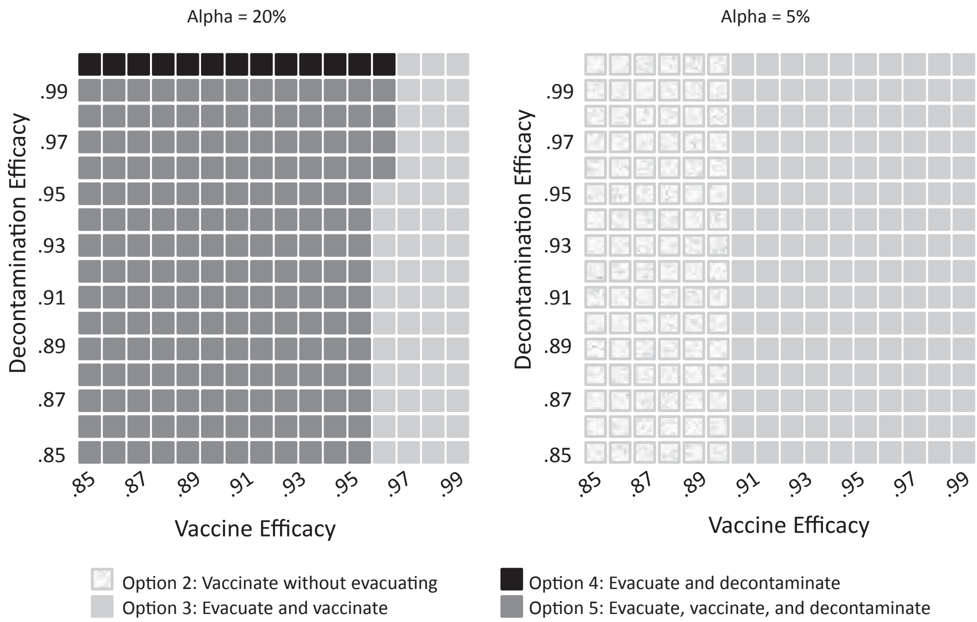

Fig. 4. Two-way sensitivity contour plots showing preferred response option for different values of vaccine efficacy and decontamination efficacy.

second best path is to evacuate, decontaminate, and vaccinate. The sensitivity analysis reveals that if the decontamination is less than 99.99% effective, the second best path (evacuate, decontaminate, and vaccinate) would overtake the dominant path (evacuate and decontaminate) at this probability of infection (with other parameters fixed at their base case values). This suggests that given the inevitable difficulties of ensuring the performance of decontamination measures in a wide-scale field effort, it may make sense to include vaccination in a postattack response in addition to decontamination. Such a policy would be in accordance with both the U.S. government's current response plan, as well as with Kyriacou *et al.*[17]

- Also for a risk of infection of 20%, if the vaccine was considered to be 97% effective or better, the recommended path would be to evacuate and vaccinate but not decontaminate (with other parameters fixed at their base case values). Estimates of actual vaccine efficacy range from 93% to 100%, indicating that in theory the response would depend on the value of this parameter. In reality, decontamination efforts would likely be pursued in an effort to respond aggressively to the incident, as in 2001, and to preserve property values for resale.
- For a probability of infection of 5%, the dominant path in the base case model is to evacuate and vaccinate. The secondary path at this probability of infection is to vaccinate without evacuating. At this 5% probability of infection, the sensitivity analysis shows that if the vaccine is only 92% effective, these two paths become indistinguishable from a cost-benefit perspective. However, the 92% efficacy value lies just outside the 93–100% range of vaccine efficacies assumed in this study, indicating that the decision would not be sensitive to this variable.

It should be noted that for either of these risk levels, different combinations of values for vaccine efficacy and decontamination efficacy will yield different preferred responses (hence the importance of Fig. 4).

As previously discussed, the abandonment option is not preferred at any risk level using the current model. However, were median property values to decrease significantly (to about \$23,800, the cost of decontamination), this option would then become preferred at α levels greater than approximately 11%.

4. DISCUSSION

This analysis used a decision analytic approach to estimate where switch-over points between

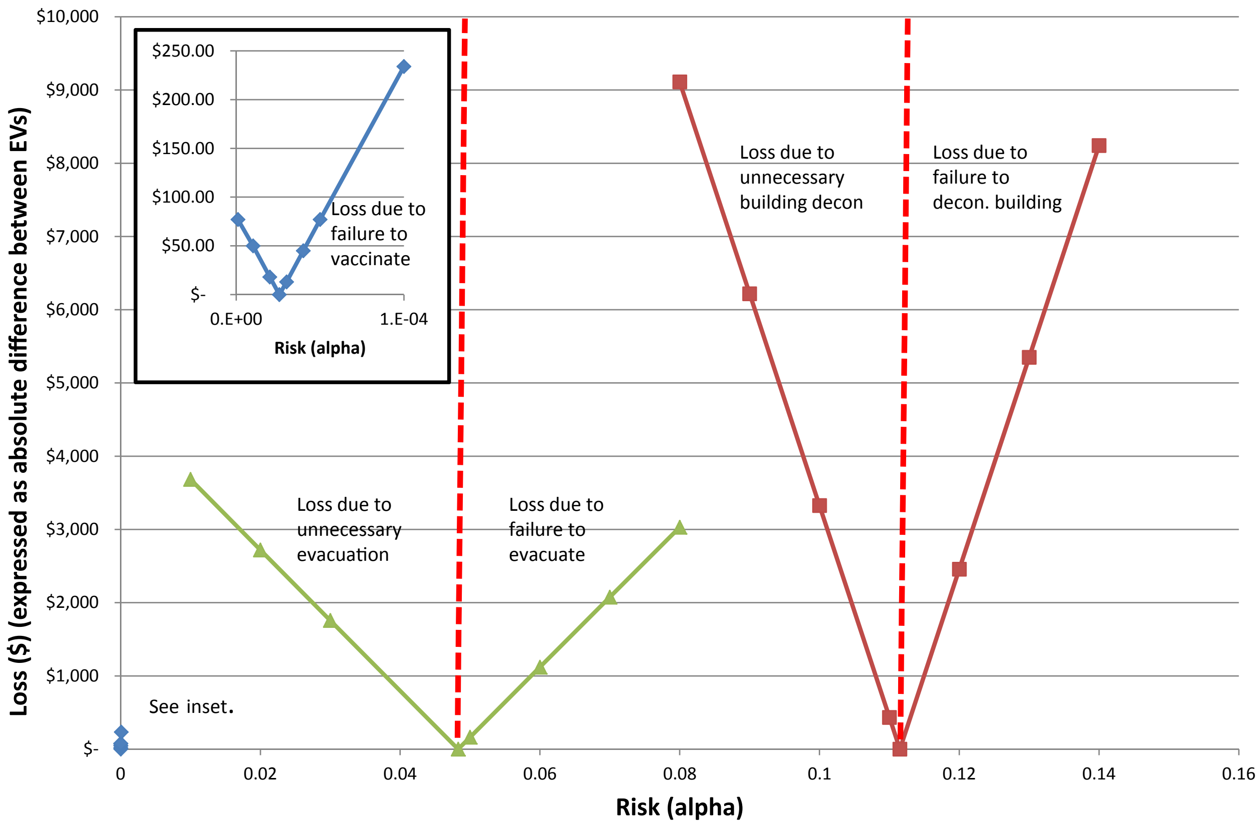

Fig. 5. Loss as a function of alpha. At each switch-over point it is assumed that the model-preferred option is selected. Losses are shown if the less aggressive option is chosen at higher risk levels and if the more aggressive option is chosen at lower risk levels.

response options occur (in terms of risk). Areas deemed to have higher risk would be subject to more intensive (and costly) response strategies while areas of lower risk might receive less rigorous (and less expensive) treatment. There would naturally be a great deal of pressure to respond aggressively to an incident, but there would necessarily be points sufficiently removed from the release where aggressive response actions are not taken. Determining which areas are sufficiently removed from a release to warrant less aggressive action is an important decision. The overall impact of an incident may be substantially influenced by how lower risk areas are treated, as one would expect environmental dispersion to create an area of lower contamination that is much larger than the highly contaminated area of the initial release.

In some cases, benefit-cost analyses function as a test that prospective actions to protect health and the environment must pass in order to be implemented. However, in this case the careful consideration of impacts may lead to more aggressive responses in some areas. In particular, this analysis suggests that vaccination is justified at risks as low as 0.003% (3 in 100,000). Risks this low would likely not be detectable[(67)] and the absence of detectable contamination would seem to argue against action. However, potential contamination might be inferred from dispersion modeling studies. Thus, a combination of modeling and benefit-cost assessment might provide a basis for more aggressive action than would be taken otherwise.

Two of the options considered here (Option 2, vaccinate only, and Option 3, evacuate and vaccinate) would require restricting access to the affected buildings to vaccinated individuals only. Clearly, this would be logistically easier for short time periods. Thus, these options might more realistically serve as short- to medium-term response actions that allow resumption of required functions pending definitive decontamination of affected areas.

Research gaps regarding administration of antibiotics and vaccines to children, the elderly, and the immunocompromised pose a challenge for the modeling performed in this analysis. Because it is unknown whether such groups will experience outcomes that differ markedly than those of normal healthy adults, all groups were modeled in the same manner. This is consistent with a consensus statement of the American Medical Association, which advises administering medical treatment in the same manner to all groups in the absence of more complete information.[45] Regardless, it is possible that these groups may not respond to the disease or the treatment in a similar manner. This could be accounted for in the model by introducing additional inputs for these parameters and generating a different set of results for each subgroup of concern. However, additional data would be required before such adjustments could be made.

This analysis is intended as a framework for decision making, not to direct actual decision making. Public response decisions would need to be arrived at through a deliberative process and benefit-cost assessments, such as this, are only one input into this process.[68] In addition, many decisions might be made privately (i.e., individuals and their doctors would control which medical treatments are used and decisions regarding private property will necessarily involve the property owner). These response decisions should be informed by stakeholders' perceived risk and their values, such as their personal level of risk aversion. These private decisionmakers would not be bound by any sort of benefit-cost assessment, but they may be interested in what guidance benefit-cost assessments can offer.

The way in which such risks are communicated to the public will have a profound impact on its willingness to comply with official recommendations.[63] Such communication becomes particularly important in the case where the risk is high enough so that evacuation is recommended. It will be incumbent upon local, state, and federal authorities to ensure that information is communicated quickly and coherently, and in a manner that is clear, practical, and respectful.[69]

Areas for further research on this topic could focus on individuals' and businesses' willingness to reoccupy a city following a wide-area anthrax release, as well as their willingness to pay for the necessary response actions. There is also a need for a better understanding of the long-term viability of anthrax spores in an urban environment, as well as for the quantitative risk associated with reaerosolization of such particles. Data on these topics would greatly enhance any modeling efforts of a large-scale bioattack.

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