Risk-based decision making for reoccupation of contaminated areas following a wide-area anthrax release

ABSTRACT

This paper presents an analysis of post-attack response strategies to mitigate the risks of re-occupying contaminated areas following a ~~wide-area outdoor~~ 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 re-occupying buildings contaminated with spores due to their re-aerosolization and inhalation is then evaluated. The response options considered include: decontamination of the buildings, vaccination of individuals re-occupying 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 re-occupy 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%.

KEYWORDS: Anthrax, bioterrorism, evacuation, decision analysis

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, bio-attacks also contaminate surfaces in the environment, which ~~contributes~~ may presentcontribute to long-term re-aerosolization 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 ~~(6)~~have been justified. (7) 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 switchover 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 which 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 "post-attack" strategies (including no vaccination, vaccination, antibiotics, and vaccination plus antibiotics) and two "pre-attack" strategies (no vaccination or vaccination) were considered. They determined that the optimal strategy from a cost-benefit perspective was the combined administration of post-attack antibiotics and post-attack vaccination. This is in general agreement with work by Schmitt *et al.* (10), who determined that post-attack antibiotics and vaccination was more cost-effective than pre-attack antibiotics. Baccam and Boechler (11) compared pre-attack and post-attack vaccination strategies following an anthrax attack and found that in either case, a rapid post-exposure 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. ~~(12)~~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 which were initiated two days after the attack or five days after the attack. Using guidance from the Anthrax Modeling Working Group (18), post-attack options included (1) antibiotics and (2) vaccination. Tactics which incorporated a pre-attack measure included (1) pre-attack vaccination of the entire metropolitan population with post-attack antibiotics for everyone exposed, and (2) pre-attack vaccination of the entire metropolitan population with post-attack antibiotics and vaccination of everyone exposed. Results of the analysis were in agreement with the US government's strategy to administer post-attack antibiotics and vaccination to all exposed individuals within 2 days after the detection of the attack. Research on the post-attack 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) ~~(19)(20)~~

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 (non-bioterrorism) hazards. Sorensen *et al.* (25) evaluated the factors that determine whether evacuation or sheltering-in-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 re-aerosolization of spores.

While these previous studies contribute to understanding appropriate response options, they generally have not explicitly identified switchover 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 post-attack 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 paper 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 re-aerosolized *B. anthracis* spores is ~~not well characterized in the literature, and many experts disagree on whether or not re-aerosolized spores pose a significant health threat. A lack of empirical data has made this question harder to answer~~difficult to quantify. Recently a~~it has been argued that it is not a problem given that~~ probable exposure to re-aerosolized spores in a Belgian wool-sorting factory caused asymptomatic infection among exposed workers, but no actual cases. (28) ~~Others have made similar arguments by pointing to historical records from~~In the early 20^{th} century ~~and noting that~~ textile mill employees were likely exposed to hundreds of anthrax spores on a routine basis and yet very few cases of inhalational anthrax were reported. (29, 30) In response to a reported inhalation anthrax fatality in New Hampshire in 1957, Dahlgren *et al.* (1960) investigated a goat-hair processing mill and determined that that up to 1300 *B. anthracis* spores may be inhaled over the course of 8 hours without causing illness. (30)

While it may be difficult to quantify, the risk presented by residual contamination *with B. anthracis* spores has been taken very seriously and resulted in the long-term closure of facilities and expensive decontamination efforts after the 2001 attacks. (31)contrast, other analyses have indicated that it is not advisable to ignore risk due to re-aerosolization. In the case of the American Media Inc. (AMI) building (contaminated during the 2001 attacks), an analysis by the National Resource Council noted that the observed outcome was consistent with the re-aerosolization of spores in the building (although fewer cases were reported than models would have predicted, this figure was not outside the distribution of predicted values). (31) Two papers examining the 2001 attacks determined that re-aerosolization 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 re-aerosolized in HVAC ductwork. (34) Others have linked the amount of residual contamination within a building to corresponding risk levels. (7) In a recent review article, Layshock *et al.* (2012) concluded that there is unambiguous evidence that *Bacillus* spp. are "... re-aerosolized by wind under ambient conditions, by pedestrian or vehicle traffic, and by other types of mechanical action." (35)

It is important to note that tThe 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 re-aerosolization of anthrax spores is possible and results in a non-zero risk to human health, no assumptions are made regarding the type or nature of a dose responseDR 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 ~~(26)~~recommendations are made for each risk level. Such a structure means that whatever re-aerosolization and dose response~~DR~~ 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~~n instantaneous~~~~wide-area outdoor~~ release of ~~anthrax~~ *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 re-aerosolization of spores that have settled on surfaces in buildings~~ (via infiltration)~~. 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 bio-attack, this paper assumes that antibiotics were administered to residents of the affected region and focuses on subsequent decisions regarding the risk from future re-aerosolization 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 US Food and Drug Administration. The vaccine was initially approved as a pre-exposure sequence comprising 6 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 post-attack 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% to 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 non-porous surfaces with a contact time of 30 minutes and on porous surfaces with two applications and a contact time of 1 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 ~22 months but an actual fumigation time of only ~4 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 6 months of closure for the base case. This value is varied from 3 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 6 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 include disruptions in trade with businesses outside the affected area) and induced costs (which represent changes in consumer sales due to impacts on residential income). For clarity, it has been suggested indirect and induced impacts be 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 which 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 victim 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 paper, the base cost of abandonment per person was approximated as the median home price for the greater Philadelphia area. (60) With few valid precedents to draw from, there is significant uncertainty regarding this option and of course great variability from home to home and neighborhood to neighborhood. ~~(54)~~

2.3. **Decision Model Design**

A decision tree was developed [1] 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 Figure 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 1 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 re-aerosolizaton, denoted for sake of simplicity as~~of~~ α. However, during "Period 1," the initial 60 days, residents are taking

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

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 re-aerosolization 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 α F_a. For the remainder of the time, residents are exposed to 82% of the re-aerosolization risk or 0.82 α. The risk of infection during either time period is 1-(1-0.18 α F_a)(1-0.82 α). Infected individuals may recover (probability of 1-P_m) or die (probability of Pm).

- Option 2: Do not evacuate but do vaccinate. The antibiotic administered at the outset of the attack is assumed to offer some protection against residual re-aerosolization 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 non-vaccinated 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 re-aerosolize spores in the contaminated area during Period 1. It is assumed that non-vaccinated 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; re-aerosolizaton risk is reduced to zero.

A switchover analysis was performed to define the risk level at which different options produce equal expected values. One-way and two way 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 1. 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 2, 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 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 below in Table 3. Figures 2a through 2d show simplified decision trees with the preferred paths highlighted corresponding to each risk level from Table 3. The values for the switchover points (in terms of risk of infection) in Table 3 are shown graphically in Figure 3. A switchover 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 switchover 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 the section on sensitivity analysis.
- 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 7108 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

S~~equential one-way s~~ensitivity analyses were performed using the cost and parameter ranges presented in Table 1 at two different infection probabilities (α =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 ~~because ~~for two reasons: (1) these values represent two levels of risk, a “high~~moderate~~” risk (α =5%) and a “very high” risk (α =20%), for which the cost for choosing the incorrect response option may be significant, and (2) the optimal response strategy is different for each level (i.e., these values~~y~~ fall on opposite sides of the risk switchover 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 α =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 which 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% 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 contour plots showing which response strategy is preferred for different values of each parameter for alpha=520% and alpha=205%. These contour plots are shown in Figure 4. These figures offer a useful visual tool to quickly ascertain how the optimal response depends on assumptions regarding both vaccine efficacy and decontamination efficacy. When experts may disagree on these values, the figures show where such discord may be problematic and where it will not (i.e., if the range of values crosses a switchover point, there wouldmay be a need for reconciliation of views to determine the preferred option).

To this point, the analysis has largely assumed that residual risk is known. In reality if 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 switchover point (Figure 5):

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

The x-axis in Figure 5 shows the actual risk. To the right of each of the 3 switchover points, it is assumed that responders believed the risk was below the switchover point, and the y-axis shows the loss associated with failure to purse the more aggressive response option. To the left of each switchover point it is assumed that responders believe the risk was above the switchover point and the y-axis shows the loss associated with unnecessarily pursuing the more aggressive response option. The loss function is symmetric around each switchover 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 ~$2500 for each percentage error in risk. In responding to an event, decision makers may seek to use conservative (i.e., high) estimates of risk and efforts such as this to "price out" the potential cost of under/over-responding 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 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 post-attack response in addition to decontamination. Such a policy would be in accordance with both the US 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 93-100%, 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 Figure 4).

4. **DISCUSSION**

This analysis used a decision analytic approach to estimate where switchover points between 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.

~~(63)(68)~~

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 decision makers 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 their 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 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 re-aerosolization of such particles. Data on these ~~two~~ topics would greatly enhance any modeling efforts of a large scale bio-attack.

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