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Earlier Detection in Emergency Response to an Anthrax Attack

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Abstract

Timely detection of a bioaerosol event is emerging as a fundamental step in an effective response against biological weapons[1]. We utilized an enterprise model to examine the impact of detection time and various response strategies on population fatality rates for several attack scenarios. We show that prompt distribution of prophylaxis, best achieved through earlier detection by bioaerosol detectors, is the most gainful strategy for reducing overall numbers of fatalities in an outdoor aerosolized anthrax attack. Maintaining a high level of prophylaxis compliance in the population is also advantageous, while other improvements to hospital surge capacity and treatment efficacy are less critical. A sensitivity analysis on detection time shows that earlier detection by bioaerosol detectors provides a consistent, significant gain in lives saved over all considered attack and response scenarios.

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Earlier Detection in Emergency Response to an Anthrax Attack

1. Introduction

An outdoor attack of aerosolized *Bacillus anthracis* spores on a major urban area could have devastating health consequences for the area population[2]. Using an enterprise model, the Weapons of Mass Destruction — Decision Analysis Center (WMD-DAC) Biological Defense Application, we examined a range of attack scenarios and analyzed the effect of earlier detection and different response strategies on scenario outcomes, namely numbers of fatalities. We show that fatality rates could be reduced significantly if public health officials received indications of an attack early enough to respond aggressively with a mass antibiotic prophylaxis campaign.

2. Materials and Methods

Detection of an anthrax attack through public health surveillance[3] relies on the manifestation of symptoms in the population[2]. The incubation time for anthrax typically ranges from 2 – 11 days, but can be much shorter or longer depending on factors such as a person's cumulative dose and susceptibility[4,5]. Thus, an attack is not likely to be detected through public health surveillance until several days after the initial release[2]. Present day bioaerosol detection systems, such as BioWatch[6], may shorten detection time. For this study, we assumed that a bioaerosol detection system would be capable of detecting an anthrax attack one day after the initial release and a public health surveillance system would detect the attack two days after the initial release[3].

Once detection has occurred, there is a time delay before distribution of prophylaxis may begin. Depending on a city's bio-terrorism response preparedness, delays due to the decision-making process and the logistics of setting up prophylaxis points of distribution (PODs) may be one to two days (according to internal studies by Frederic M. Leykam and Larry C. Madsen for the Department of Homeland Security, Science and Technology Directorate). For this analysis, we assume that this delay is one day. Therefore, in our model, with a bioaerosol detection system in place, mass prophylaxis distribution first begins two days after an anthrax release; with no detection system in place, distribution starts three days after the simulated release.

For this study, the simulated geography is a generic regional grid. As shown in Figure 1, this grid consists of an urban area of approximately 1,100 square kilometers and a rural area of about 6,000 square kilometers. These areas are divided into census tracts that are uniformly populated. The total population is 6.4 million, with 5.8 million people in the urban area and 0.6 million in the rural area. We used a population density that is representative of the densities of the 20 most populated U.S. metropolitan areas per the 2000 U.S. Census.

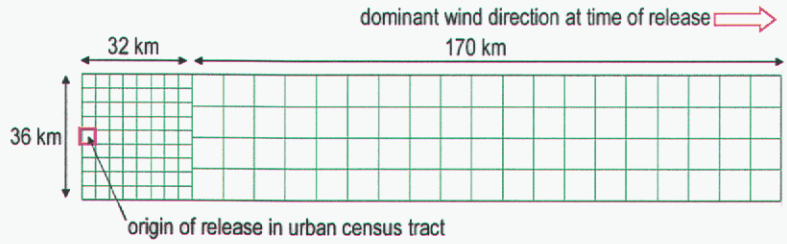

Figure 1. Urban census tracts are 4x4 km and have a population density of 5,000 people/km^2. The rural area is divided into 9x9 km census tracts with a population density of 100 people/km^2.

On the day of the attack, anthrax spores are released from a point source in a central urban census tract. A percentage of these spores are aerosolized and travel downwind. We assumed meteorological conditions that would cause a large area of exposure in the region. The dispersion model, the Hazard Prediction Assessment Capability (HPAC)[7], generates a plume with cumulative dosage contours that is mapped onto the simulated geography. This dosage data is folded into a probabilistic infection model and used to determine whether a simulated individual has been infected based on his exposure. Infections due to the re-aerosolization of deposited anthrax spores were not considered.

Once an attack is detected, one day is required for a public health officer to decide to distribute prophylaxis, alert the population, request and receive supplies from the Strategic National Stockpile (SNS), and activate PODs[8]. People begin receiving antibiotics one day after an attack is detected at a fixed daily rate until there are no longer people in the queue.

In WMD-DAC, people can be in one of six states of disease progression: uninfected, infected, mildly symptomatic, severely symptomatic, dead, and recovered. An infected individual's disease progression is calculated as a probability function based on incubation models that were developed from historical data[9]. The probability of progressing to a different disease stage is altered if a person receives antibiotic prophylaxis or hospital care. Even if antibiotics are made available, some people may not comply with the direction for prophylaxis[10-11,12]. Full prophylaxis compliance is defined as complete adherence to the treatment schedule and completion of the entire course of prophylactic antibiotics. It is assumed that infected people who are fully compliant will not develop symptoms and will eventually recover. In other words, with full compliance, antibiotic prophylaxis is assumed to be 100 percent effective. If an infected person has not received prophylaxis or is non-compliant, he will eventually develop mild nonspecific flu-like symptoms and progress to the severe symptoms (e.g., sudden fever, dyspnea, diaphoresis, and shock) of the fulminant disease stage[2].

It is assumed that people with mild symptoms remain in the antibiotics queue at PODs until they receive prophylaxis or become severely symptomatic. Oral antibiotics are

modeled as not effective in halting the disease progression of people with mild symptoms[2,5]. Mildly symptomatic people are not given hospital care[5].

People experiencing severe symptoms do not seek prophylaxis; instead, they immediately seek a hospital intensive care unit (ICU) bed. In the scenario, each census tract has 10 available ICU beds to start[13]. ICU beds are available on a first-come, first-served basis to severely symptomatic members of the population residing within a hospital's census tract. The maximum ICU residence time for a severely symptomatic hospital patient is 14 days[5]. If a person becomes severely symptomatic at a time when all ICU beds are full, he cannot wait for a bed to become available. Instead, he is given a general bed without critical care resources and eventually dies.

People who are uninfected after an attack still queue at PODs if directed by the public health officer, since they do not know that they are uninfected. They remain in the queue until they receive prophylaxis.

WMD-DAC tracks population states of health, population behavior, and resource utilization statistics on a daily basis for three months following an attack. In this study, the scenario parameters listed in Table 1 were varied to determine their effects on the total number of fatalities.

Table 1. Parameter values varied in this study.

Parameter	Values	
	Baseline	**All Variations**
Prophylaxis distribution strategy	60-day supply distributed by PODs; 3 days to distribute antibiotics; 1 day delay to set up and supply PODs	60-day supply distributed by PODs; 3 days to distribute antibiotics; 1 day delay to set up and supply PODs Unlimited supply of prophylaxis on shelf, distributed before an attack and ready to be taken immediately
Detection date	Day 2 after an anthrax release	Day 0, 1, 2 or 3 after an anthrax release
Attack size	100 grams aerosolized anthrax spores	1, 10, 100 or 1000 grams aerosolized anthrax spores
Infection model	Glassman[1]	Age-dependent model used by Wein *et al.*[2] Glassman
Epidemic model:		
Incubation period	Lognormal model	Exponential model Lognormal model Truncated lognormal model
Prophylaxis compliance rate	90%	80, 90 or 100%

[1] Glassman, H.N., (1966) *Bacteriological Reviews*, **30**, 657-9.
[2] Webb, G. F., & Blaser, M. (2002) *Proc. Natl. Acad. Sci.* USA **10**, 7027-32.

Hospital treatment effectiveness and capacity	55%; 10 available critical care beds per census tract	0, 55 or 100% 10 or 340 available critical care beds per census tract

3. Results

Ensuring that most of the population is able to begin an antibiotic regimen before developing symptoms is expected to mitigate the consequences of widespread anthrax exposure. In the 2001 U.S. anthrax attacks, of the thousands of potentially exposed people who were treated before the onset of symptoms, there were no recorded deaths; of the 11 people who received medical treatment after showing symptoms, six recovered[5]. People who were infected had significantly improved chances of recovery if medical treatment was administered to them before their symptoms appeared. Given that the incubation time for anthrax could be less than two days[4,5], initiating a prophylaxis campaign in the first few days after an attack is critical to reducing fatality rates. In Figure 2, the numbers of fatalities resulting from the baseline attack scenario are shown for varying delays to the start of prophylaxis distribution. For every additional day of delay before prophylaxis distribution begins, the number of fatalities rises at an increasing rate. Likewise, the recovery rate (percentage of infected people who eventually recover) decreases at a greater rate within the first few days following an anthrax release, as shown in Figure 3.

If the bioaerosol detector architecture detects an attack one day earlier than public health surveillance, prophylaxis distribution may begin a day earlier. This is predicted to result in up to a 24 percent reduction in the numbers of fatalities (12,000 fewer fatalities) for the baseline case. It is possible that once an attack is detected, the process of deciding to distribute prophylaxis and setting up PODs may take up to two days[11]. In this situation, earlier detection (i.e., starting prophylaxis distribution three days after an attack, as compared to four days) is predicted to result in a 27 percent decrease in the number of fatalities (19,000 fewer fatalities).

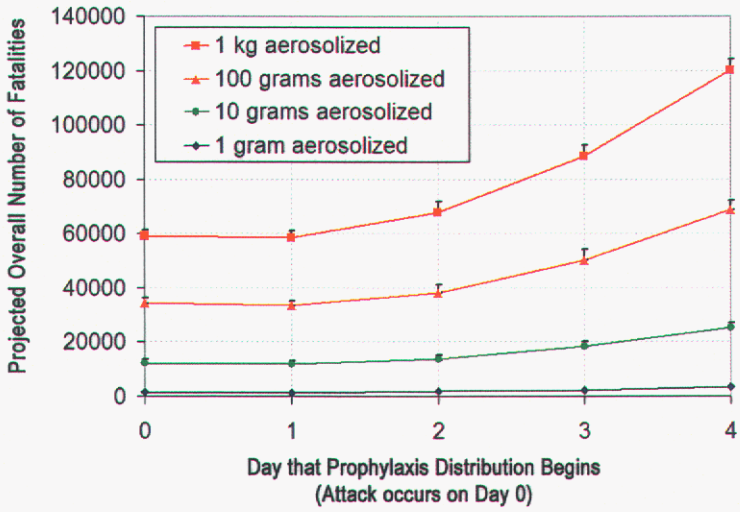

Figure 2. Fatality rates increase with longer delays to prophylaxis distribution: overall number of fatalities vs. day that prophylaxis distribution begins for the baseline case. Prophylaxis distribution prompted by a bioaerosol detection system is expected to start on Day 2.

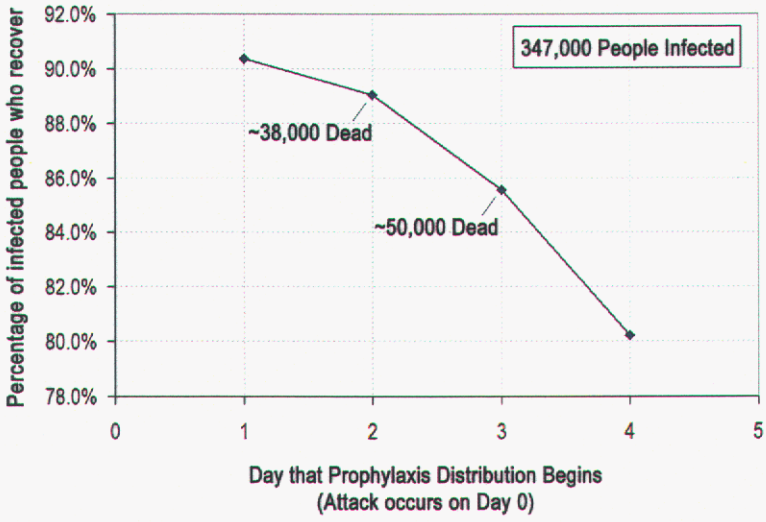

Figure 3. Recovery rate decreases if there is a longer delay before prophylaxis distribution: percentage of people infected with anthrax that recover for the baseline case. Prophylaxis distribution prompted by a bioaerosol detection system is expected to start on Day 2.

These results show that faster detection by present day bioaerosol detector systems can greatly reduce mortality, provided that public health officials have enough information and confidence in the data to decide quickly to conduct a mass prophylaxis campaign. Given the multiple logistical steps that delay the start of prophylaxis distribution, saving

time through earlier detection can be important for reducing the number of fatalities in an anthrax attack. In a scenario in which public health officials are not certain enough in a biosensor alarm to immediately respond with mass prophylaxis, the alarm may be sufficient for lower-regret actions to be taken while the initial detection is being confirmed. By getting a head start on logistical actions like activating the Strategic National Stockpile[14], prophylaxis distribution can begin sooner if the alarm is confirmed and public health officials decide to respond.

In a previous investigation, Wein *et al.* used a mathematical model to compare emergency responses to outdoor airborne anthrax attacks[15]. They concluded that, "modestly rapid and sensitive biosensors, while helpful, produce only second-order improvements [to emergency response]." Wein *et al.* made a fixed assumption that antibiotics are distributed to the population prior to the attack, enabling the entire population to begin prophylaxis immediately in the event of a detected attack. Present-day public health policy is that prophylaxis would be distributed only after an attack is detected[11]. This assumption by Wein *et al.* may have predisposed their conclusion about the value of early detection to be comparatively low, as supported by the data in Figure 2. To estimate the value of early detection by bioaerosol detectors, Wein *et al.* assumed that if detectors are deployed, detection would occur one day after an attack and the entire population would begin prophylaxis on the same day; with no detectors deployed, both detection and prophylaxis would occur two days after an attack.

Comparing these cases using WMD-DAC, the value of detectors is calculated to be approximately 40 percent less for the Wein *et al.* scenario than for our baseline case that includes representative delays. Gains due to earlier detection are less significant in scenarios in which prophylaxis distribution delays are shorter or non-existent. This result also implies that improvements in biosensor technology that further reduce detection time could lead to additional gains in recovery rates.

In addition to rapid initiation of prophylaxis distribution, the population's prophylaxis compliance rate (i.e., the fraction of the population that adheres to the ordered antibiotics regimen) was also found to have a large effect on the number of fatalities resulting from an anthrax attack. In Figure 4, fatalities calculated for the baseline case scenario are shown for three prophylaxis compliance rates: 80, 90 and 100 percent. For the 100-gram release scenario, in which compliance is assumed to be 90 percent, increasing this number to 100 percent causes the number of fatalities to decrease by half. By increasing compliance rates, such as through public education and awareness campaigns, fatality rates resulting from an anthrax attack can be reduced significantly.

Furthermore, by increasing compliance rates, greater gains are achieved by deploying bioaerosol detectors because a larger percentage of infected people would benefit from earlier prophylaxis distribution. Figure 5 illustrates the reduction in fatalities if detectors detect an attack for the three compliance rates considered. If the prophylaxis compliance rate is increased from 90 to 100 percent, the reduction in fatalities from deploying detectors increases from 21,000 to 26,000.

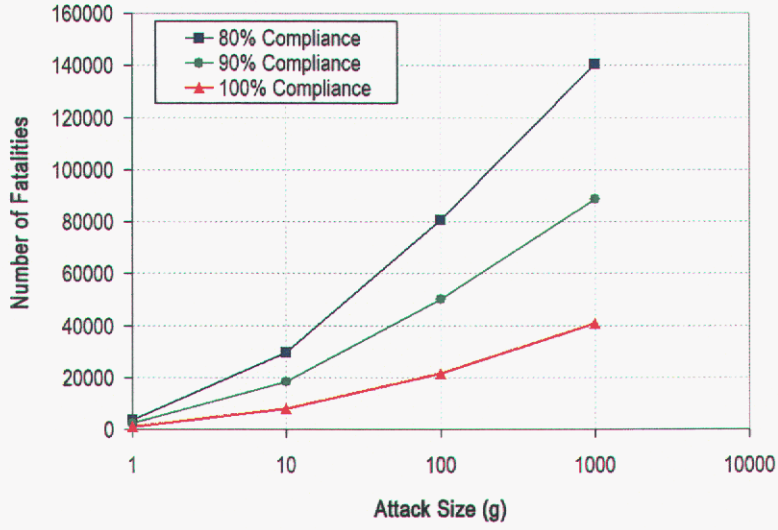

Figure 4. Improving the population's prophylaxis compliance rate can significantly reduce the number of fatalities: numbers of fatalities vs. attack size, for various prophylaxis compliance rates.

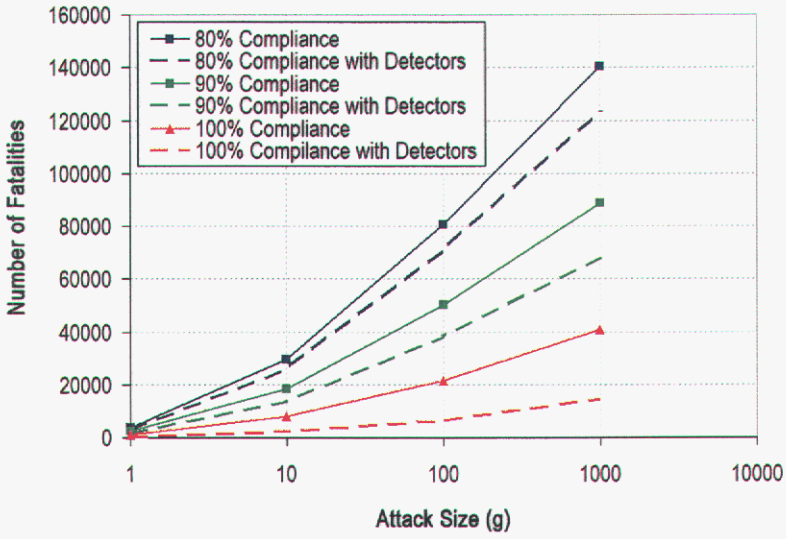

Figure 5. Early detection achieves greater gains when compliance rate is higher: numbers of fatalities vs. attack size, for various prophylaxis compliance rates, for scenarios with and without detectors deployed.

Compared to prophylaxis compliance rates, we found that the effectiveness of hospital intensive care has a low impact of the overall number of fatalities and the calculated value of early detection by bioaerosol detectors in an anthrax release. A small number of intensive care unit (ICU) beds—2.3×10^{-4} per capita—are available for anthrax patients. Furthermore, the average residence time in an ICU bed for an anthrax patient is about 14 days[5]. Thus, only a small fraction of severely symptomatic patients receives intensive care treatment and increasing the hospital treatment effectiveness results in little change to the overall number of fatalities. The relative importance of prophylaxis compliance and hospital treatment effectiveness on the value of early detection is shown in Figure 6. It appears that because orders of magnitude more people can be given prophylaxis than can be treated in hospitals, prophylaxis compliance rate is a much stronger determinant of scenario outcomes than hospital treatment effectiveness.

In most attack scenarios, a large increase in the number of hospital ICU beds is required for the overall number of fatalities to decrease significantly. In the baseline scenario, 30 times more ICU beds in the urban census tracts results in a 17 percent reduction in number of fatalities.

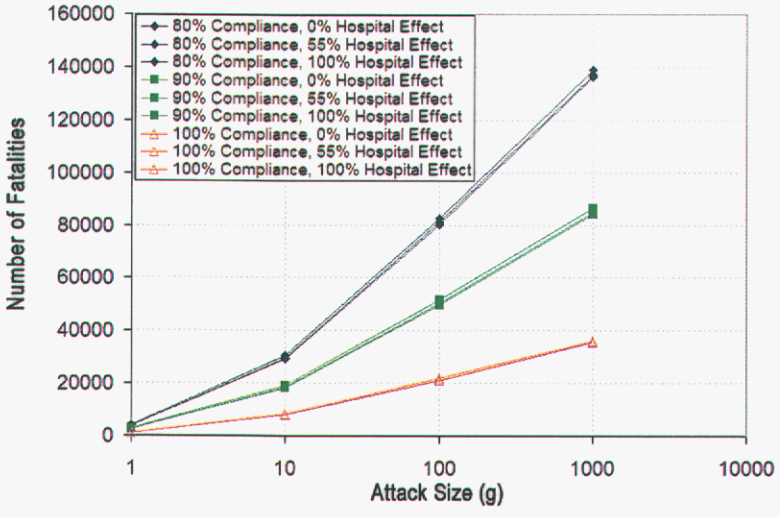

Figure 6. Effectiveness of hospital ICU care has a comparatively low impact on scenario outcomes, because very few people receive hospital care: numbers of fatalities vs. attack size for various compliance rates and hospital effectiveness rates.

4. Discussion

Rapid initiation of prophylaxis distribution, enabled through earlier detection by bioaerosol detectors, along with promotion of prophylaxis compliance in the population are the most effective strategies for reducing overall numbers of fatalities in an outdoor aerosolized anthrax attack. This can be seen in Figure 7, in which the relative effect of different response strategies on total numbers of fatalities in the baseline case scenario is shown. While prophylaxis compliance rate stands out as a key driver in our model, it is difficult to predict with much certainty the impact of educational programs on the population's compliance rate in the event of an attack. In the 2001 U.S. anthrax attacks, of the postal workers that were known to potentially have been exposed to anthrax only 40 percent adhered to the full course of prophylactic treatment[11]. Similarly, it may not be feasible to implement some of the idealized response strategies included in our analysis, such as pre-attack distribution of antibiotics or an order of magnitude increase in ICU resources. Given these infeasibilities and the uncertainty in prophylaxis compliance rate, taking additional response measures, including deployment of bio-detectors, creates a more robust strategy for response.

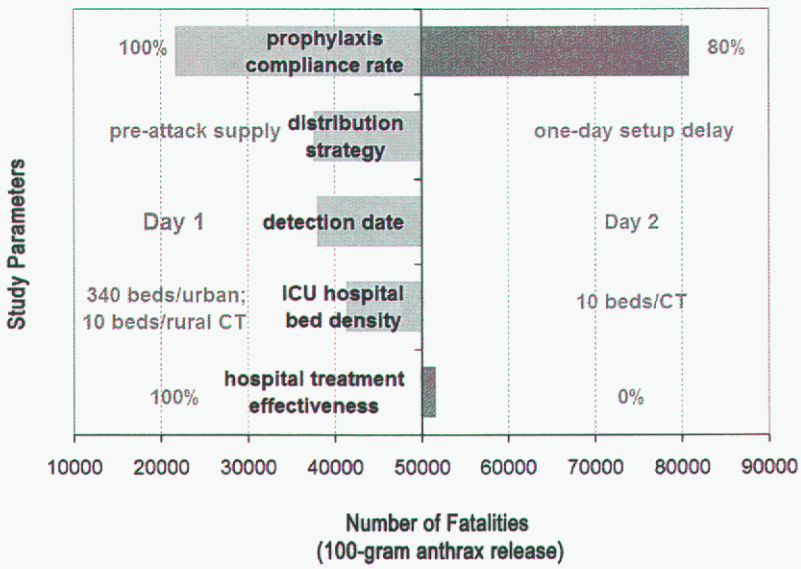

Figure 7. Relative impacts of study parameters on the number of fatalities in the baseline scenario. (CT = census tract)

The value of early detection by bioaerosol detectors was found to be consistently high for the range of scenarios that we considered. In Figure 8, the relative effect of different response strategies and assumptions on this calculated value is shown. The timeliness of prophylaxis distribution and prophylaxis compliance are key factors that determine whether the full benefit of earlier detection is achieved. One important assumption is the

disease incubation time. Although we considered three commonly employed anthrax incubation models, incubation times for people who receive very high or very low doses are not well understood, and need to be studied further. If the onset of symptoms occurs much earlier or later than what is currently known, then this could affect the relative value of early detection by detectors in some cases.

Immediately following an anthrax attack, every additional day's delay to the start of prophylaxis causes the fatality rate to rise at an increasing rate. Detection of an anthrax attack is one of many delays before prophylaxis distribution can begin, and time saved through biosensor detection can significantly reduce fatality rates.

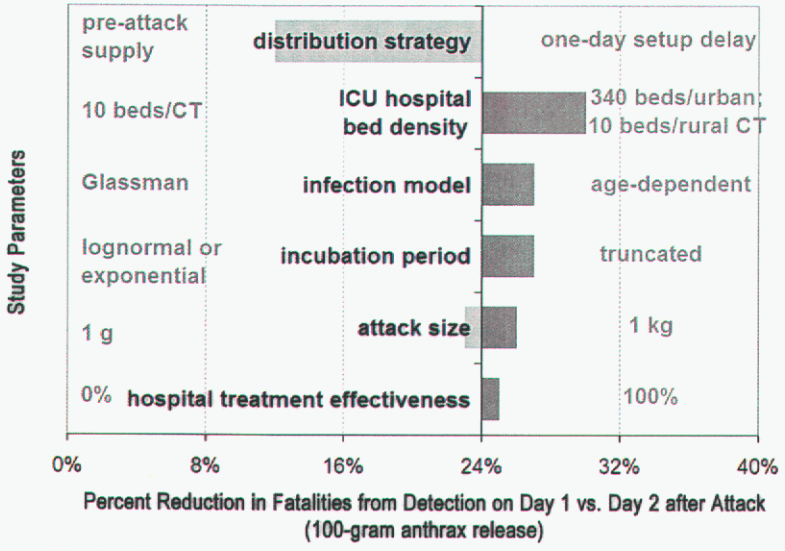

Figure 8. Relative impacts of study parameters on percent reduction in fatalities due to early detection in the baseline scenario. (CT = census tract)

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