



INSTITUTE FOR DEFENSE ANALYSES

Emerging Infectious Diseases Study

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Executive Summary

Beyond their broad humanitarian and economic costs, emerging infectious diseases (EIDs) have the potential to decrease the effectiveness of United States (U.S.) military forces operating in regions where outbreaks occur. While infectious disease is a longstanding force health protection issue, it is also possible that an adversary could use EIDs operationally or manipulate EID outbreaks in ways that put U.S. forces and objectives at risk. The Joint Requirements Office-Chemical, Biological, Radiological, and Nuclear (CBRN) Defense (JRO-CBRND) asked the Institute for Defense Analyses (IDA) to assess the potential risk to U.S. military forces and objectives posed by EIDs and, based on the outputs of this assessment, to recommend Chemical and Biological Defense Program (CBDP) initiatives to improve our capabilities to mitigate outbreaks of EIDs and to provide insights into the requirements for those capabilities. The IDA research team found that should diseases with certain characteristics emerge in the future, they would indeed pose a risk to U.S. military operations. Moreover, the best opportunities to mitigate that risk start at the point of emergence, and failure to exploit those opportunities would lead to heavy reliance on minimally effective and operationally disruptive restrictions of movement.

Emerging infectious disease is a very broad and non-specific topic. Although the conditions that foster disease emergence are becoming better understood, where and when diseases will emerge, and what the characteristics of these diseases will be, are still largely unknown. It is this element of the unknown that distinguishes “emerging” from “traditional” infectious disease. Prevailing definitions of EIDs in the global and national health communities consider three types: novel pathogens, such as Severe Acute Respiratory Syndrome (SARS); variants of known pathogens, such as seasonal influenza and antibiotic-resistant tuberculosis; and diseases that appear in new geographic areas or populations, such as Ebola in West Africa. All three types of EIDs can be difficult to diagnose—either clinically or via laboratory testing, they may be invulnerable to available medical countermeasures, and the consequences of these diseases may be exacerbated by a lack of understanding of the nature and progression of illness and mode of transmission. While novel pathogens pose the greatest challenges, the 2014 Ebola outbreak showed that even a relatively well-known and understood pathogen can have serious health risks if it emerges in an area where it has not been seen before and is not expected.

The research team considered three broad scenarios in which EIDs could potentially affect military operations and create risk: development of EIDs as biological warfare

(BW) agents and use in aerosolized attacks (“weaponization”); improvised use of pathogen sources as crude biological agents (“improvised biological operations”); and natural outbreaks. These three scenarios span the spectrum of adversary intent, sophistication, and level of effort; each poses different challenges to situational awareness and response. In BW attacks of the type postulated here, most or all of a military force would be simultaneously exposed to high doses of agent, resulting in a large spike in cases of disease, so that the disease outbreak within that population would be relatively easy to detect. However, with mean disease onset times of just a few days and with cases tightly clustered in time, there would be very little time to implement any post-exposure response capable of avoiding combat ineffectiveness. Natural outbreaks, by contrast, evolve much more slowly, providing significantly greater time windows for response. In the natural outbreak scenarios modeled for this task, the time to reach combat ineffectiveness—defined as time to reach a 20 percent casualty rate force-wide—ranged from days to weeks for the diseases considered, and was often much longer for larger force arrays. However, there were very few cases of symptomatic illness early in the outbreak, and those that did appear were often not collocated. To be able to respond effectively, commanders would have to understand that these few cases of disease are correlated, that they are atypical, and that they are harbingers of a much larger problem in weeks to come.

Improvised biological operations with EIDs of concern, generating on the order of 10 to 100 initial infections of contagious disease, would be particularly challenging. In general, modeled outbreaks of this type progressed much more rapidly than did natural outbreaks, but fewer symptomatic cases of disease served as the basis for making decisions.

The research team found that some EID “characteristics of concern” varied by scenario. A review of available literature identified a number of characteristics that diseases must have to be suitable for use in BW attacks. Just as the process of acquisition and use of EIDs for improvised biological operations is different from that in BW attacks, so too are characteristics best-suited to this purpose.

A review of the literature showed that the characteristics used by the United States and the Soviet Union as criteria for selection of pathogens for weaponization were very different, and were closely related to each side’s strategic and operational objectives and concept of use. This suggested that in BW scenarios, the characteristics of agents of concern may depend on the motives of the adversary in question. In addition, the technological sophistication and investment of time and financial resources needed to develop an EID as a BW agent made it unlikely, if not impossible, for an adversary that is not a nation-state and does not have state sponsorship and support. Further, the literature suggested that, given the time and money required, such adversaries would be unlikely to

pursue an EID for weaponization if it did not provide some advantage over a previously weaponized pathogen.

The characteristics of concern for EIDs used in improvised operations and as the causative agents of natural outbreaks were fundamentally influenced by both situational awareness challenges and the availability of effective medical countermeasures. For example, small numbers of cases of illness that are mild and non-specific are less likely to be discernable from the background of infectious disease prevalent among military personnel than those that manifest quickly and with specific or particularly gruesome symptoms. The inability to identify diseases for which diagnostic testing is limited or non-existent may significantly delay the implementation of mitigating capabilities, as there would be limited information available upon which to base the selection and timing of appropriate responses.

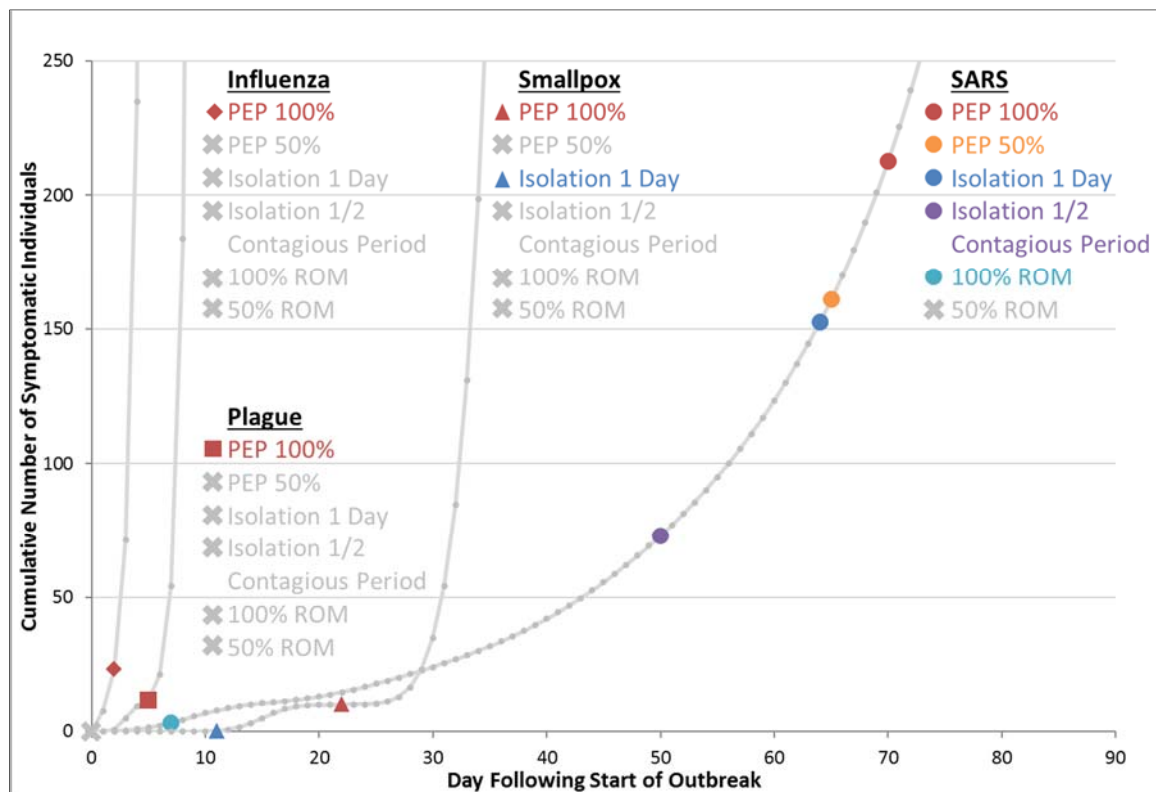
The research team found a clear hierarchy of response capabilities in terms of their effectiveness in mitigating operational impact by all measures considered. Vaccination and other forms of enhanced immunity were clearly the best means of preventing or reducing the operational impact of an EID outbreak. Post-exposure prophylaxis (PEP) proved nearly as effective as immunization in preventing casualties and mitigating outbreaks, even when implemented after a substantial time delay. Moreover, even with efficacies as low as 50 percent, both immunization and PEP will significantly reduce the operational impact of an EID outbreak. Because medical countermeasures were significantly more effective in mitigating the impact of EIDs than other forms of response, the lack of effective medical countermeasures—something that is very likely to be the case for novel pathogens and certain variants of existing pathogens—is a key characteristic of EIDs of concern in natural outbreaks and improvised biological operations.

The modeling results indicate that in general, restriction of movement (ROM) of personnel between units is far less effective than other response measures in preventing casualties. The major reason for this is the speed with which outbreaks spread among sub-populations: in several of the cases examined, disease spread beyond the first sub-population prior to the onset of symptoms in any individual. Further investigation revealed that in cases with more than one initial infection and a high rate of movement, the disease spread is in fact likely to occur prior to symptom onset. This problem is further exacerbated by longer incubation periods. Unfortunately, in the absence of medical countermeasures or rapid and effective means of isolating ill individuals, restricting the spread of disease to the initial sub-population—or to as few sub-populations as possible—becomes critically important to preventing the entire force from becoming combat ineffective. When ROM is the only mitigating capability available, and when the effectiveness of that capability is degraded by both prevailing operational

tempo and the intrinsic characteristics of disease, the operational risk of EID outbreaks will be extremely high.

The relationship between situational awareness and response time was a major theme explored in our research. The modeling conducted allowed the IDA research team to quantify this relationship for the three postulated EID scenarios: natural outbreaks, improvised biological operations, and BW attacks. An understanding of the information available over time, as outbreaks progress, will both underscore the challenges that biosurveillance (BSV) programs face and inform BSV requirements.

The figure below shows the last day on which the various response options (other than immunization) must be implemented to avoid combat ineffectiveness from improvised biological operations, for four diseases used as surrogates of EIDs in the modeling: 1918 influenza, plague, smallpox, and SARS. The figure also shows the number of symptomatic individuals on those days. In the figure, only those options that can prevent combat ineffectiveness are shown in color; if an option could not be effectively used regardless of time of implementation, it is shown in gray text.



Latest Day on Which Response Must Be Implemented to Avoid 20% Casualties (560) over 90 Days: Improvised Biological Operations

In general, the number of symptomatic individuals on which to base a response decision is much smaller in the improvised biological operations scenario than in natural

outbreaks or BW attacks. In the influenza outbreak generated by improvised biological operations, there were 23 symptomatic individuals at the time the response window closed, versus 68 and 77 symptomatic individuals at the time the response window closed in natural outbreaks or BW attacks, respectively. The team observed the same pattern in smallpox outbreaks, with just 10 symptomatic cases at the end of the response window in the improvised biological operations scenario, but 86 and 102 symptomatic cases in the natural outbreak and BW attack scenarios, respectively. These results highlight the challenge posed by improvised biological operations: a short response window, similar to that of BW attacks, but a significantly smaller number of symptomatic cases than in either natural outbreaks or BW attacks that can serve as a response trigger.

The following table summarizes the characteristics of EIDs of concern in the three scenarios examined in this paper.

Characteristics of EIDs of Concern in Different Scenarios

Component of Risk	Natural Outbreaks	Weaponization	Improvised Biological Operations
Producibility	N/A	Stable in storage Feasibly produced on a large scale Similar to classic BW agents	Stable during transport and storage (<i>crude agent</i>) Easily handled (<i>crude agent</i>) Broad host range (<i>animal/insect vectors</i>) Contagious (<i>human vectors</i>)
Employability	N/A	Stable in the environment Stable as an aerosol Easily disseminated as an aerosol Infectious via the aerosol route	Stable/survivable in the environment (<i>crude agent, animal/insect vectors</i>) Easily dispersed (<i>crude agent</i>) Resistant to controls (<i>animal/insect vectors</i>) High infection-to-disease ratio (<i>human vectors</i>)
Effectiveness	Contagious High morbidity and mortality Lack of diagnosis Lack of prophylaxis Lack of treatment Early contagious, non-specific, mild phase Long incubation period	<i>Characteristics depend on adversary objectives but provide some advantage over classic BW agents</i>	Contagious High morbidity and mortality Lack of diagnosis Lack of prophylaxis Lack of treatment Early contagious, non-specific, mild phase Long incubation period High infection-to-disease ratio

The IDA research team's recommendations are intended to ameliorate the key challenges to mitigating operational impact of EIDs of concern, as illustrated in the assessment of operational impact. They focus on development of capabilities, such as medical countermeasures, that would change the overall assessment of a specific EID from being "of concern" to being manageable from the standpoint of risk. The team also recognized that, despite DOD's best efforts, the time between the point of emergence and an operational deployment may be too small a window to develop capabilities needed to support situational awareness and effective response, limiting both the range of response choices and the opportunities to implement them in a timely manner. Several of the

team's recommendations, therefore, focus either on shortening the development timelines for the most effective response capabilities or on hedging against the possibility that such capabilities would be unavailable.

Consistent with the requirements of the JRO's tasking, this paper makes recommendations both for science and technology initiatives within the CBDP and for non-materiel solutions. These recommendations focus on the most significant challenges for mitigating EID operational impact, as identified in this paper, and are organized into two categories of mitigating capabilities: situational awareness and response. Additional recommendations are intended to help rectify identified knowledge gaps and to support prioritization of EID threats.

Situational Awareness Capabilities

Science and Technology Initiatives

- Adopt analytically supported performance targets for the contribution of BSV to the detection of EID outbreaks and triggering of responses.
 - The results of this paper suggest that threshold requirements should focus on the detection of natural disease outbreaks and BW attacks in time to support the use of medical countermeasures. For the scenarios and diseases we considered, these goals can be met if BSV can detect 20 symptomatic individuals among the population at risk within five days of the start of the outbreak.
 - The use of BSV capabilities to trigger procedural controls, or to trigger any response to improvised biological operations, is much more challenging and should be the focus of objective BSV requirements. For the scenarios and diseases we considered, these goals can be met if BSV can detect one to three symptomatic individuals among the population at risk within two days of the start of the outbreak.
- Develop and acquire approved diagnostic assays for EIDs of concern, as quickly as possible after the point of emergence, compatible with the furthest-forward deployed diagnostic systems.

Non-materiel Solutions

- Develop a strategy for far-forward diagnostic testing of individuals with non-specific symptoms of disease. Such a strategy should be supported by an analytically based sampling plan that specifies the size of the sample needed to detect an outbreak under various circumstances. It should also specify criteria for the selection or exclusion of test subjects.

Response Capabilities

When considering potential responses to EID outbreaks, the IDA team found that immunization and prophylaxis were more effective than isolation and ROM in mitigating operational impact. However, there is no guarantee that medical countermeasures would or even can be available to counter currently unknown diseases of concern. There are significant challenges in developing medical countermeasures that are likely to be effective against EIDs, and in having a strategy for using those with limited or unknown efficacy. At the same time, if medical countermeasures are unavailable, procedural controls like ROM may be the only means of containing the outbreak and avoiding significant operational impact. However, significant work remains to understand and implement the most effective use of procedural controls. This includes an assessment of the effectiveness of procedural controls in combination (e.g., isolation plus ROM)—something that could not be explored within the timeframe of this research effort.

Science and Technology Initiatives

- Conduct a cost-effectiveness analysis of different approaches to medical countermeasure development that specifically accounts for the inherent lack of knowledge about EIDs.
 - Emphasize widely applicable antibiotics/antivirals, universal vaccines, and general enhancement of immunity to hedge against unknown future diseases.
 - Take advantage of the time between point of emergence and use of an EID as a weapon to develop targeted responses.
- Support efforts to enhance agility in the acquisition of diagnostics and medical countermeasures.

Non-materiel Solutions

- Develop a strategy and a set of decision criteria for the selection, distribution, and use of medical countermeasures in an EID outbreak, when the efficacy of available countermeasures is unknown or limited.
- Develop doctrine and procedures for the implementation of ROM. This should include decision support for the implementation and relaxation of ROM, including which units should be included. It should also include plans for individual unit sustainment under conditions of ROM.

Although there are many advantages to medical countermeasures, there is a very real possibility that they simply will not be available, and the only means we would have to mitigate operational impact would be through ROM. Therefore, it would behoove us to

do some planning and analysis to figure out the best way to make that as effective as possible under various circumstances.

Additional Recommendation

Invest in research to close knowledge gaps related to the propagation of contagious disease, particularly within a military population. This work would support the background awareness component of situational awareness and is important for understanding the potential risk that a given EID would pose operationally.

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1. Introduction

For the past 20 years, emerging infectious disease (EID) has been a growing concern of the national and international public health community.¹ Once thought on the verge of eradication,² the health risks from EIDs and fears of future epidemics have been driven steadily forward by a host of factors such as climate change, population migration, poverty and war, the globalization of travel and commerce, and the increase in antibiotic resistance. Recent experience has reinforced the concern over EIDs, as the 2014 outbreak of Ebola in West Africa poignantly illustrated the nature of the problem and the limits in the capability of the international community to generate an effective response.

Beyond their broad humanitarian and economic costs, EIDs have the potential to decrease the effectiveness of United States (U.S.) military forces operating in regions where outbreaks occur. While infectious disease is a longstanding force health protection issue, it is also possible that an adversary could use EIDs operationally or manipulate outbreaks in ways that put U.S. forces and objectives at risk. Adversary use of EIDs in these ways would be of concern to the Chemical and Biological Defense Program (CBDP). In FY 2014, the Joint Requirements Office- Chemical, Biological, Radiological, and Nuclear (CBRN) Defense (JRO-CBRND) asked the Institute for Defense Analyses (IDA) to conduct an advanced threat assessment of the potential risk posed by EIDs to U.S. military forces and objectives.

A. Task Objectives

As specified by the JRO, research on the EID study has four objectives. First, it should identify ways that adversaries might use EIDs to disrupt U.S. military operations.

¹ Spurred by the emergence of human immunodeficiency virus (HIV), the persistence of malaria and dengue, and the availability of new genomic research tools, the Institute of Medicine issued a seminal report on emerging infectious disease in 1992. See Joshua Lederberg, Robert E. Shope, and Stanley C. Oaks, Jr., eds., *Emerging Infections: Microbial Threats to Health in the United States*, Institute of Medicine, Committee on Emerging Microbial Threats to Health (Washington, DC: National Academy Press, 1992). This report led the Centers for Disease Control and Prevention to develop and implement the first national strategy for countering the threats to public health posed by EIDs. See US Centers for Disease Control and Prevention (CDC), "Addressing Emerging Infectious Disease Threats: A Prevention Strategy for the United States," *Morbidity and Mortality Weekly Report* 43, no. RR-5 (Atlanta, GA: US Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, April 1994).

² Frank M. Snowden, "Emerging and Reemerging Diseases: A Historical Perspective," *Immunological Reviews* 225 (2008): 10-11.

Second, it should develop scenarios in which adversaries could use or exploit EIDs for operational gain, and determine the measures adversaries would have to take to be successful. Third, it should assess the impact of adversary use of EIDs on U.S. forces and identify associated vulnerabilities, with emphasis on those areas related to the CBDP capability areas and for which the JRO has responsibilities. Fourth, it should provide the JRO with recommendations on ways to reduce the vulnerability of U.S. forces to the operational effects of EIDs.

This paper is one of a series of advanced threat studies conducted by IDA for the JRO. The broad purpose of these studies is to characterize the operational risk associated with new or non-traditional threat agents of various types; most of these potential threats have been identified by the intelligence community as areas of some interest to adversary nations or non-state actors. They are intended to be quick-look assessments, based primarily on reviews of the available literature supplemented as appropriate by modeling, and are therefore largely qualitative in nature. In all of these studies, IDA's first step has been to conduct a search of the literature to determine whether or not sufficient information is available on a given threat agent to make a reasonable assessment of operational risk and then, where necessary, to identify key knowledge gaps that would need to be filled. If IDA finds that a given threat agent could indeed pose an operational risk, the research team seeks to qualify the magnitude of that risk, and to make recommendations for mitigating it. The latter could include recommended actions for the CBDP, suggested priority intelligence requirements, and proposals for science and technology initiatives.

The advanced threat studies consider the operational risk posed by an agent to have three components: *producibility*—the ease with which an adversary could manufacture and store operationally relevant quantities of agent; *employability*—the ease with which an adversary could use the agent to achieve a desired aim; and *effectiveness*—the ability of an agent to overcome current defenses against chemical and biological agents. A given threat agent would pose an operational risk if the available information suggested that agent could meet specified sub-criteria for producibility, employability, and effectiveness. The advanced threat studies commonly illustrate this evaluation concept using the construct shown in Figure 1; they similarly summarize results using this same construct by assigning a qualitative score to each criterion, shown here in the form of one or more plus signs.

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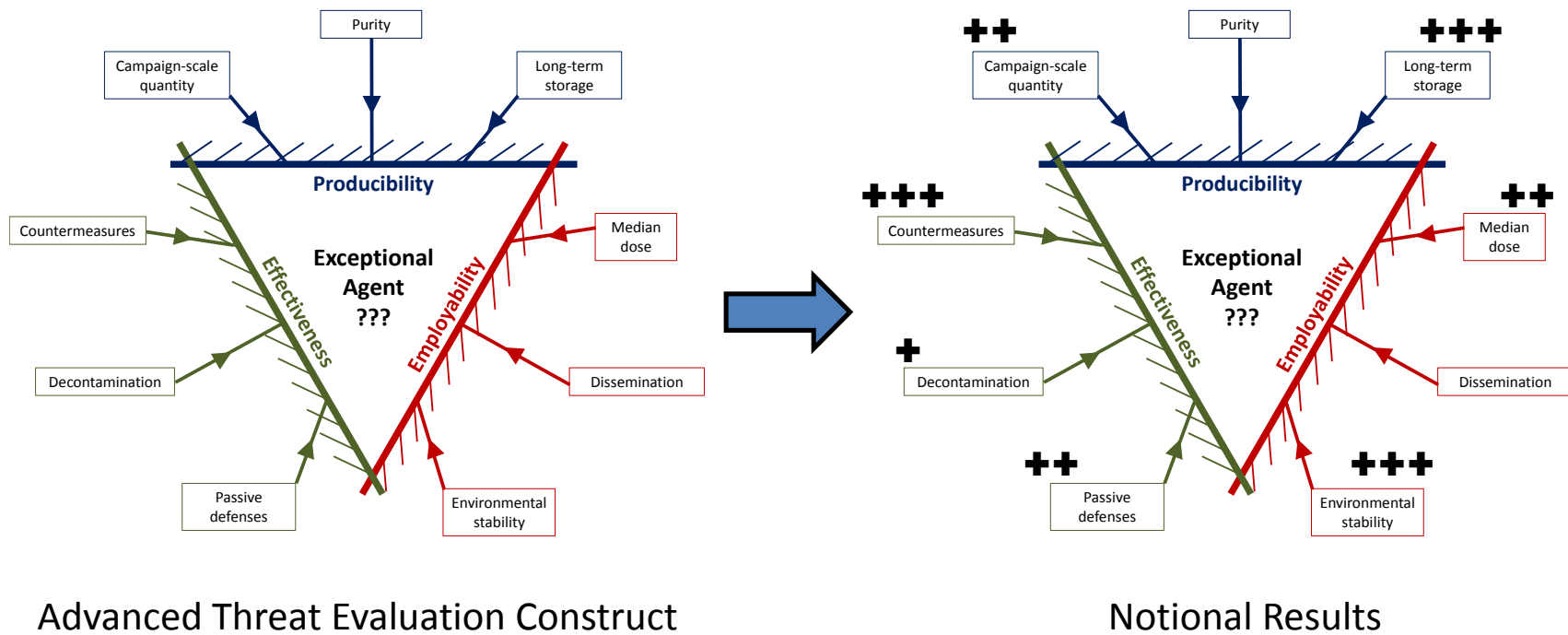


Figure 1. IDA Advanced Threat Study Construct for Assessing Operational Risk

To date, the IDA advanced threat studies have focused on specific compounds or classes of compounds. These may be newly discovered, newly considered as weapons, or produced in a new manner that significantly alters their threat behavior. In general, IDA has found these threats to be well enough characterized and understood in the literature to qualitatively assess their potential operational risk and to gauge whether or not the CBDP should be concerned about them.

The EID advanced threat study differs from previous research in several important respects. First, “emerging infectious disease” is a very broad and non-specific topic. Although the conditions that foster disease emergence are becoming better-understood, where and when diseases will emerge is still largely unknown. Moreover, key characteristics of emerging disease-causing organisms—their pathogenicity and virulence in humans, their behavior in the environment, their vulnerability to countermeasures, their mode of transmission, and the duration and severity of the associated disease—are even more difficult to predict. As is true of well-known infectious diseases, not all EIDs will pose a significant operational risk.

Second, unlike other advanced threats under assessment at IDA, EIDs are already an acknowledged threat with programs in place that could mitigate them. There is a broad and long-standing consensus among the U.S. and global health communities that outbreaks of EIDs can have significant, even devastating, human and economic costs. The International Health Regulations (IHR), an international agreement among nations negotiated under the auspices of the World Health Organization (WHO), is intended to be “the key global instrument for protection against the international spread of disease.”³ Originally signed in 1969 in an effort to control a small number of specific diseases, the member nations of WHO significantly revised and expanded the IHRs over a ten-year period between 1995 and 2005, due to the growth in international travel and trade and the emergence or re-emergence of international disease threats and other public health risks.⁴ No longer limited to specific diseases, the resulting agreement (*IHR (2005)*) requires signatory nations to maintain certain minimum public health capabilities and to notify WHO of events that may constitute a public health emergency of international concern according to defined criteria.⁵ *IHR (2005)* entered into force in 2007; all 194 members of WHO are signatories.

High-level U.S. government concerns over the health risks from EIDs have been manifest since the early 1990s. In 1996, President Clinton issued *Presidential Decision Directive NSTC-7: Emerging Infectious Disease*; this document called for “a series of

³ World Health Organization (WHO), *International Health Regulations (2005)*, 2nd ed. (Geneva: WHO Press, 2008), 3 (hereafter cited as *IHR (2005)*).

⁴ *IHR (2005)*, 1.

⁵ Ibid.

actions to improve our surveillance, prevention, and response capability.”⁶ More recently, in February 2014, the United States and WHO jointly launched the Global Health Security Agenda (GHSA), a commitment by over 40 nations to “accelerate progress toward a world safe and secure from infectious disease threats and to promote global health security as an international priority.” In September 2014, at the height of the Ebola outbreak in West Africa, President Obama and a number of Cabinet-level officials met with senior national and international officials to obtain specific commitments to implement the GHSA.⁷

The Department of Defense (DOD) is one of several federal departments supporting the GHSA. As noted at Health.mil, the official website of the Military Health System,

Preventing, detecting, and responding to infectious disease threats requires holistic solutions through strengthened relationships with health services, other government and industry partners, and academia....Though DOD is in a supporting position, there is a clear and important role to be played by military medicine: the GHSA offers DOD and other militaries a framework to engage and better coordinate with interagency (other ministries) and international partners.⁸

For decades, DOD has worked to protect soldiers from endemic diseases within deployment areas, and from adversary use biological warfare (BW) agents. Historically these efforts have been separate responsibilities, and have focused on pathogens and diseases that are known and well characterized. In recent years, however, EIDs have received both increased attention within DOD and increased collaboration among responsible organizations, reflecting a growing concern about operational risk.⁹ In 2009, the Assistant to the Secretary of Defense for Nuclear, Chemical and Biological Defense Programs (ASD/NCB) issued a memo directing the use of CBDP funds for EID preparedness and response activities, in coordination with the Assistant Secretary of Defense for Health Affairs (ASD/HA). To date, these coordinated activities have largely focused on biosurveillance (BSV) initiatives. At the same time, concerns about EIDs are reflected in other CBDP programs, including research on broad-spectrum medical countermeasures and antibiotic resistance.

⁶ The White House, *Presidential Decision Directive NSTC-7: Emerging Infectious Disease*, 1996.

⁷ The White House, Office of the Press Secretary, “FACT SHEET: Global Health Security Agenda: Getting Ahead of the Curve on Epidemic Threats,” September 26, 2014.

⁸ “Global Health Security Agenda,” Health.mil, <http://www.health.mil/Military-Health-Topics/Health-Readiness/Global-Health-Engagement/Global-Health-Security-Agenda>.

⁹ For a good summary of current DOD organizations and programs that support force health protection and biodefense, while broadly aligning with the objectives of the GHSA, see Robin M. Moudy et al., “Bridging the Health Security Divide: Department of Defense Support for the Global Health Security Agenda,” *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 12, no. 5 (2014): 247–53. doi: 10.1089/bsp.2014.0055.

These differences posed several consequences for IDA's EID advanced threat research. First, the initial focus was less on demonstrating that EIDs have the potential to create operational risk—there is already consensus that this is so, and this consensus is supported by historical experience—and more on determining which EIDs could pose a threat and which ones may not. Given that we do not know what diseases will emerge, or when or where, can we identify specific disease or pathogen characteristics that would generate operational risk? Would these characteristics vary by scenario? For the EID advanced threat research effort, the construct illustrated in Figure 1 was in essence reversed, as shown in Figure 2. Rather than starting with a list of characteristics that would make a non-traditional agent “exceptional” and therefore of concern, a major objective of this research was for IDA to replace the question marks in Figure 2 by identifying characteristics of any EID or pathogen that could contribute to its producibility, employability, and effectiveness. Any future EID displaying such characteristics would be of concern for the risk potential it would present.

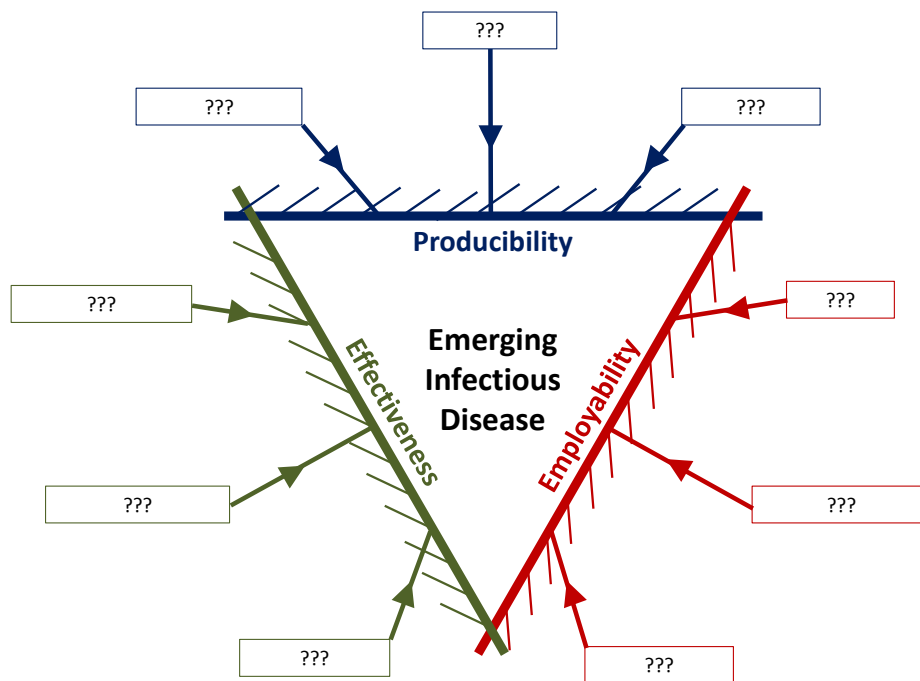


Figure 2. Construct for Evaluating Emerging Infectious Disease

Second, given the breadth of ongoing activity designed to mitigate the health risks of EIDs and to prevent their spread, the potential impact of EIDs cannot be understood without some reference to existing and programmed capabilities that could defend against them. An evaluation of the effectiveness of these capabilities in mitigating EIDs was beyond the scope of this research. However, IDA's research did make assumptions about the types of capabilities that could be brought to bear and how they would function. It

also sought to determine generally when, where, and how they would need to be implemented to be effective against EIDs of various types.

Third, this research could not make recommendations for the CBDP in a vacuum. Any recommended programmatic actions, direction of priority intelligence requirements, or science and technology initiatives need to be undertaken with an understanding of the broad range of capabilities now in place and actions that are underway elsewhere within DOD, across the U.S. government, and within Allied nations and the global health community. At the same time, however, national and international efforts are intended to minimize human health, environmental, and economic risks; they do not specifically address operational military risks. There are certainly overlaps between these types of risk, and these efforts can have obvious benefits for deployed U.S. forces. However, EIDs may pose additional, different risks to operational military forces and objectives that require further or different types of mitigation.

B. Background

1. Definition of EID

The key national and international health organizations have published definitions of EID. WHO considers an emerging disease to be “one that has appeared in a population for the first time, or that may have existed previously but is rapidly increasing in incidence or geographic range.”¹⁰ The CDC uses a consistent but much more detailed definition:

Infectious diseases whose incidence in humans has increased in the past two decades or threatens to increase in the near future have been defined as “emerging.” These diseases, which respect no national boundaries, include

- New infections resulting from changes or evolution of existing organisms
- Known infections spreading to new geographic areas or populations
- Previously unrecognized infections appearing in areas undergoing ecological transformation
- Old infections reemerging as a result of antimicrobial resistance in known agents or breakdowns in public health measures.¹¹

Although these definitions seem clear and comprehensive, they leave room for interpretation when it comes to any specific disease, particularly when differentiating

¹⁰ WHO, Health Topics: Emerging Diseases, http://www.who.int/topics/emerging_diseases/en/.

¹¹ CDC, “EID Journal Background and Goals,” www.cdc.gov/eid/page/background-goals.

“emerging” from “traditional” infectious disease. For example, prior to the 2014 outbreak in West Africa, one might have considered Ebola to be a “traditional” disease, as it was first discovered 40 years ago. Yet given that the 2014 outbreak both occurred in a geographic region where the disease was not previously known and included urban populations for the first time, one would now likely consider Ebola to still be “emerging.” The ambiguity over “traditional” vs. “emerging” in the standard definitions made it difficult to define or restrict the scope of this research. Yet clear boundaries are needed when considering, for example, the range of mitigating capabilities now available or the ways in which adversaries could acquire and use EIDs for operational gain.

Based on the CDC definition, this research considered three types of EIDs:

- Those caused by known pathogens that appear in new geographic areas or populations, such as the Ebola outbreak in West Africa starting in 2014, and the spread of chikungunya to the Western hemisphere in the fall of 2013;¹²
- Those caused by variants of known pathogens, such as seasonal influenza and antibiotic-resistant tuberculosis;
- Those caused by novel pathogens, such as Severe Acute Respiratory Syndrome (SARS), first reported in 2003, and Middle East Respiratory Syndrome Coronavirus (MERS-CoV), first reported in 2012.

This research specifically excluded consideration of deliberately altered pathogens.

All three types of EIDs listed above have some aspects that are unknown, and it is this element of the unknown that distinguishes “emerging” from “traditional” infectious disease. For the purposes of this research, as long as this element of the unknown was present, a disease continued to be characterized as “emerging.” Each type of EID listed in this paper is associated with a different level of knowledge and awareness; this in turn determines the availability of response capabilities and, consequently, is a key factor in determining operational impact.

Well-known pathogens can be identified and diagnosed using existing laboratory equipment and techniques, although the availability, location, and timeliness of such analysis may depend upon correctly anticipating where the pathogen exists. Hence, even when a disease is relatively well known, its emergence in a new geographic region or a

¹² The spread of chikungunya is less well-publicized than the 2014–2015 Ebola outbreak, but illustrates the potential for the astonishing spread of EIDs. Chikungunya is a mosquito-borne viral disease that has become endemic throughout parts of Africa and Asia over the past decade. The first cases in the Western hemisphere due to local transmission (as opposed to travel-related) occurred in the Caribbean in December 2013; by the end of 2014, there had been over a million cases in the equatorial regions of the Western hemisphere, including more than 2,000 in the United States. Ann M. Powers, “Chikungunya Virus Outbreak Expansion and Microevolutionary Events Affecting Epidemiology and Epidemic Potential,” *Research and Reports in Tropical Medicine* 6 (2015): 13–14.

new population can pose significant challenges. In West Africa, the index case in the 2014–2015 Ebola outbreak lived in the Guinea village of Meliandou, some 2,000 miles away from the nearest previous occurrence of Ebola.¹³ Because the symptoms of Ebola mimic those of cholera and malaria, both of which are widespread in West Africa, it took over three months and several dozen deaths before anyone suspected that Ebola virus was the causative agent in the outbreak.¹⁴

Variants of known diseases may have familiar clinical presentations, but depending on the nature of the variation, it may be difficult to confirm clinical diagnosis of these diseases via laboratory testing, or it may be difficult to effectively treat them with standard medical countermeasures.

For novel pathogens, there will be a period of discovery during which virtually nothing is known about the pathogen and the associated disease, including disease characteristics such as incubation period, clinical presentation, mode of transmission, and lethality. Such diseases will be difficult or impossible to diagnose, clinically or via laboratory testing. Medical personnel are unlikely to have drugs and other forms of targeted treatment available, and may not fully understand the requirements for supportive care.

2. Operational Risk from EIDs

EIDs can have both direct and indirect effects on U.S. military operations. Since the immune systems of U.S. military personnel would likely be naïve to the challenge of EID pathogens, the number of casualties expected during EID outbreaks may be greater than those experienced during traditional infectious disease outbreaks; these numbers may well be operationally significant. Difficulties in clinical and laboratory diagnosis, delays in recognition of the disease, and a lack of effective medical countermeasures mean that casualties may be more severe than they otherwise would be, and the associated lost duty time incurred across the force substantially greater.

Outbreaks of EIDs—especially those that have significant morbidity and mortality, and/or are highly contagious—may trigger mitigating actions that themselves affect military operations by limiting force maneuverability, flexibility, and sustainability. Commanders may choose to avoid specific geographic areas where disease outbreaks are ongoing in the indigenous civilian population, or where animal or insect vectors are

¹³ Jeffrey E. Stern, “Hell in the Hot Zone,” *Vanity Fair*, October 2014, accessed at <http://www.vanityfair.com/news/2014/10/ebola-virus-epidemic-containment>. This article provides an excellent popular account of the evolution of the early months of the Ebola outbreak, describing the confluence of circumstances that delayed the first positive laboratory results while contributing to the spread of the disease.

¹⁴ Ibid.

prevalent. They may also choose to implement physical control measures, such as isolation and quarantine of individuals, or restrictions on the movement of personnel between units. Nations outside of the outbreak region may restrict overflight and landing rights, complicating movement of supplies and personnel into and out of the operating area. Contact with local civilians, other host nation personnel, and allied forces may also be restricted, either by command policy or naturally as a consequence of the spread of illness among those populations.

The research described in this paper sought to measure, very broadly, the potential operational impact from both the direct and indirect effects of EID outbreaks on U.S. military forces and operations. Moreover, these direct and indirect effects also influenced our development of “characteristics of concern” for evaluating the operational risk posed by any given EID. Given current mitigation capabilities, what types of diseases could generate large numbers of casualties or fatalities? What types of diseases are most difficult to control, either through physical control measures or medical countermeasures?

C. EID Research Focus Areas

Our research is divided into four parts, each described in a chapter to follow. Chapter 2 presents the research concept—the different component pieces of the EID operational risk problem and how they fit together. It discusses some key overarching themes and issues that emerged during the course of the research; these themes and issues in turn serve as a framework for presenting outputs of the analysis.

The JRO asked IDA to develop scenarios in which adversaries could exploit EIDs for operational gain, and to identify the measures adversaries would have to take to do so. While the range of potential scenarios is great, in terms of both impact and requirements, this problem is bounded on one end by weaponization scenarios, wherein adversaries develop biological warfare agents from an EID, and on the other by natural outbreaks, where there is no adversary intent at all but still the potential for significant operational risk. In the middle are what the research team has termed “improvised biological operations”—adversary shaping and exploitation of EIDs and EID outbreaks in a manner intended to have an impact on U.S. military operations. This type of scenario includes a virtually infinite number of possible low-tech adversary actions, such as dissemination of collected body fluids, attacks on medical facilities that cause contagious patients to flee into the local population, or disruption of disease control efforts. Chapter 3 describes the EID scenarios developed in this research. It also discusses the scenario-driven producibility, employability, and effectiveness characteristics of concern that can be used to assess specific EIDs.

As noted above, this research could not reasonably characterize the operational risk from EIDs or make recommendations for the CBDP without reference to the significant

amount of effort underway globally, nationally, and within DOD to protect against them. Chapter 4 describes current and planned mitigating capabilities, with an emphasis on those underway within DOD to support situational awareness with respect to EIDs or to respond to the threat or occurrence of an EID outbreak.

Chapter 5 presents IDA's assessment of the operational impact of EIDs of varying types under the scenarios described in Chapter 3, including the analytical approach, tools and methods used, quantitative measures, and results. Given the "quick look" nature of this research effort, this assessment is not comprehensive. However, it does provide an indication of the magnitude of the potential operational impact from EIDs of varying types under varying scenarios, and identifies the manner in which mitigating capabilities would have to be brought to bear to be effective, in isolation and in combination. It also provides additional insight into of the characteristics that would make some EIDs a concern from an operational risk standpoint, and thus contributes to the list of EID assessment criteria.

Finally, Chapter 6 contains observations and insights derived from the research and analysis IDA conducted for this paper, and provides recommendations for actions to be taken by the CBDP, the intelligence community, and the science and technology community to mitigate the risk from EIDs.

2. EID Study Concept and Major Themes

Assessing the nature and magnitude of the operational risk posed by EIDs is a complex problem. The initial challenge of this research was to develop a structured, comprehensive approach that addressed the range of EID types, potential adversary pathways for their use, and the associated operational impact. This chapter describes the concept the research team developed to identify the different component pieces of the EID operational risk problem and how they fit together.

Underlying the research concept is the understanding of disease *emergence* as a process that has a defined beginning and continues over time. All three types of EIDs considered in this research—known diseases appearing in new areas or populations, variants of existing diseases, and novel diseases—have some characteristics that are unknown, although the extent to which EIDs are understood varies widely with type. Nonetheless, it is this element of the unknown that distinguishes “emerging” from “traditional” infectious disease. As long as this element of the unknown persists, a disease will continue to be characterized as emerging. By extension, the process of emergence would end when the disease is fully understood, within the constraints of existing technologies.¹⁵

Thus, the research team began with the notion that, at some future point in time, a disease emerges. Then, at a later point in time, U.S. forces deploy to an area of operations (AO). These two points in time are completely independent of each other, but the magnitude of the interval between them is the critical determinant of three major factors: the types of adversary actions that are possible, the types of capabilities that would be needed to mitigate them, and whether or not those capabilities would be available. Moreover, the interval is unknown and unpredictable. Broadly speaking, the disease emergence process can start a long time before an operation begins, a short time before an operation begins, or during an operation. These three possible relationships between the time at which a disease begins to emerge and the time at which forces conduct operations is depicted in Figure 3 by the arrows and green circles shown in the region above the timeline.

¹⁵ The research team did not consider that the end of the emergence process meant that the disease could no longer pose an operational risk, but rather that the associated risk could be well understood and, if deemed necessary, mitigating capabilities could be developed if possible and brought to bear. Even so, there are some traditional diseases—malaria being the canonical example—that continue to be disruptive to military operations despite extensive and heretofore not fully successful efforts to defend against them.

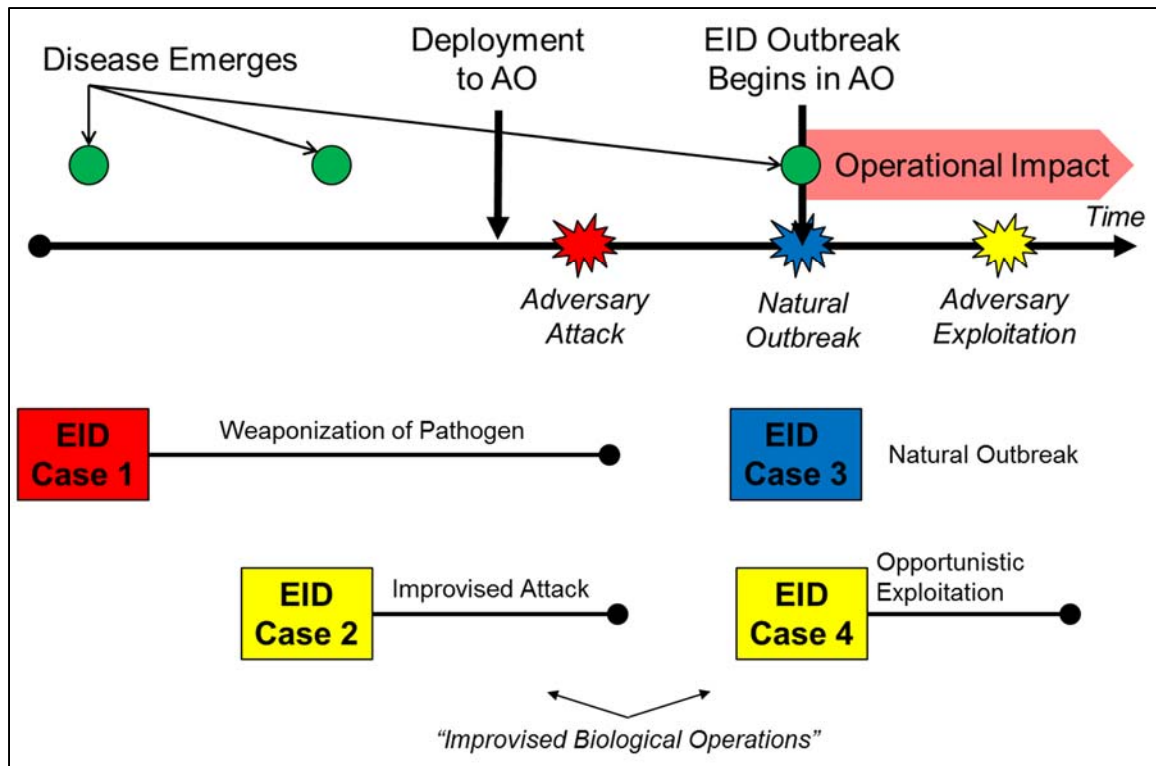


Figure 3. EID Study Concept

Next, imagine that a technologically sophisticated, stable, and well-financed adversary decides to weaponize an EID, eventually using it to attack deployed U.S. forces. As a consequence of that attack, an outbreak of disease begins within the AO, causing some as yet undetermined operational impact. This pathway to adversary use of an EID is illustrated in red (Case 1) in Figure 3.

Traditional biological warfare agent development is a complex and lengthy process, so the interval between emergence of a disease and its availability for use in a BW attack would have to be relatively long. Traditional weaponization is not, however, the only pathway by which an adversary could attack with an EID. Less sophisticated attacks could come from crude weapons made from the bodily fluids of diseased patients, infected animals, or other pathogen sources. In this case (Case 2, illustrated in yellow in Figure 3), the time between emergence and attack could be much shorter.

Of course, naturally occurring outbreaks of disease can occur within the AO, even in the absence of adversary intent. This type of outbreak can occur at any point in time after the disease emerges, but—unlike the first two cases—the outbreak in the AO can be the initial point of emergence. Finally, once an outbreak occurs (whether natural or deliberately induced), an adversary can attempt to exploit it in various ways for operational gain or to meet other objectives. Because this final pathway is very similar to improvised attacks—differing primarily in the timing of execution—it is also illustrated

in yellow (Case 4 in Figure 3). For the assessment of operational impact described in later sections of this paper, Cases 3 and 4 are considered together under the umbrella designation “improvised biological operations.”

Each of these different cases can have multiple adversary pathways, multiple relevant EID characteristics, and multiple operational impacts. The analytic challenge for this research was to determine which, if any, are of concern and the extent to which current and planned mitigating capabilities need to be improved or augmented to deal with them.

The EID operational risk problem has two major underlying themes: time and knowledge. The fact that there are, by definition, aspects of EIDs that are not known directly affects what can be done to mitigate their effects. The longer the interval between emergence of a disease and an outbreak (whether naturally occurring or initiated deliberately by an adversary), the greater the opportunity to learn about the disease and prepare to mitigate it. At the same time, the more deliberate an adversary can be in exploiting an EID, the more sophisticated their attacks can be. For example, adversary attacks with weaponized EIDs could well turn out to be operationally disastrous, but the time it would take an adversary to develop them allows a greater opportunity for the development of mitigating capabilities.

There is a relationship between time and knowledge that is characteristic of the challenges posed by various adversary pathways. As illustrated in Figure 4, this relationship is reflected in the number and timing of cases of disease among the targeted population. Each case poses different challenges to situational awareness and response: in a traditional BW attack, one would expect to see a big spike of cases very early in the outbreak;¹⁶ this would make the outbreak relatively easy to detect, but would allow very little time to implement any response that could avoid casualties and mitigate operational impact. In improvised biological scenarios and natural outbreaks, by contrast, even determining that an outbreak is underway would be a challenge initially. Consequently, as exposed and infected personnel disperse throughout the population at risk, controlling the spread of disease becomes more challenging; restriction of movement (ROM) must be implemented more broadly and the associated operational impact would be greater.

¹⁶ As discussed in subsequent sections of this paper, the research generally considers EIDs of operational concern to be contagious. Otherwise, natural outbreaks and improvised biological operations could not pose operational risk as defined herein. Traditional BW attacks are an exception, however, as such attacks can directly expose large percentages of the population at risk and result in combat ineffectiveness; they do not need to rely on the multiplicative effects of contagion. Nonetheless, the spike in early cases shown in Figure 4 could be expected to result whether or not the causative agent is contagious.

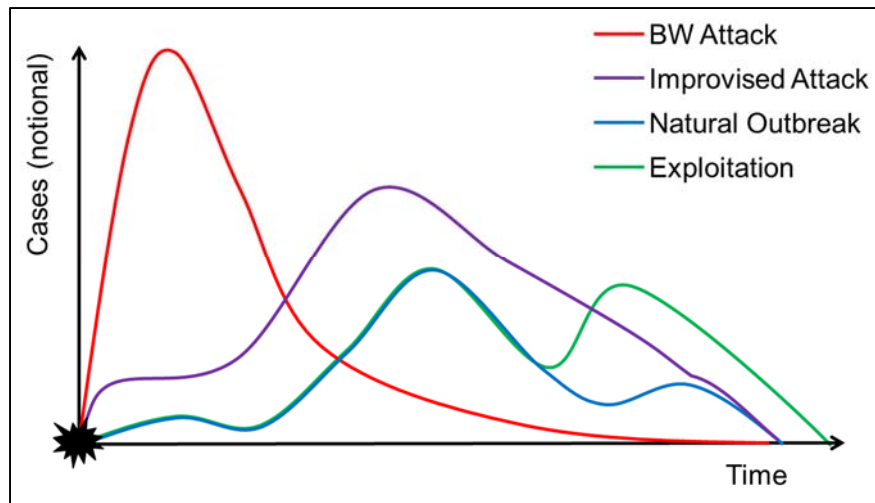


Figure 4. Presentation of Casualties over Time in Different Adversary Use Cases

The operational impact of EIDs and the mitigating effects of response measures can be described in terms of time and knowledge. What knowledge would become available over time as an outbreak progresses? What knowledge is needed that cannot currently be provided? What knowledge is needed more quickly? How does this relationship affect the availability of response capabilities and the ability to apply them in an efficient, effective manner with minimum impact on operations?

The operational impact assessment discussed in Chapter 5 seeks to describe the relationship between time and knowledge in a formal way. *Time* is represented by the days on which milestones occur in the spread of disease; these milestones include the disease spreading from one unit to another, and units individually and collectively reaching combat ineffectiveness. *Knowledge* is represented by the number of cases of manifest illness accumulating within the population by the time these milestones occur.

An evaluation of the contribution of specific capabilities in mitigating EIDs was beyond the scope of this research. The assessment of operational impact does, however, make assumptions about the types of responses that could be brought to bear and how they would function. The assessment then seeks to determine the effectiveness of different types of response; the extent to which that effectiveness changes, given time of implementation; and the knowledge that would be available at those times. This information is then used to describe the challenges that mitigating capabilities must meet to be effective.

3. Adversary Pathways and Characteristics of EIDs of Concern

A. Introduction

The JRO asked IDA to develop scenarios in which adversaries could exploit EIDs for operational gain, and to identify the pathways adversaries would have to take to do so. This chapter describes the EID scenarios and adversary pathways developed for this research. In addition to meeting the requirements of the task, these scenarios were used as a basic input to the assessment of operational impact at the heart of this research.

The postulated scenarios and adversary pathways also support the research objective of developing a set of producibility, employability, and effectiveness characteristics of concern by which any future EID could be evaluated to determine its risk potential. Many of these characteristics are scenario driven, in that they are necessary for an adversary to execute a given pathway or would be associated with increased operational risk relative to other EIDs. Collectively, these characteristics provide a starting point. Based on the results of the research, it is possible that, regardless of the disease, some pathways may not have significant operational impact; hence, even the “worst” EIDs may not pose an operational risk. The assessment of the potential operational impact from EIDs in Chapter 5 was intended, in part, to address this specific issue. The results of the impact assessment were also used to refine the list of disease characteristics postulated in this chapter and, where possible, to determine which are the most important drivers of impact.

EID threat scenarios and adversary pathways can be bounded on one end by weaponization scenarios, wherein adversaries develop biological warfare agents from an EID, and on the other by natural outbreaks, where there is no adversary intent at all but still the potential for significant operational risk. In the middle are what the research team termed improvised biological operations—adversary shaping and exploitation of EIDs and EID outbreaks in a manner that has an impact on U.S. military operations. The postulated adversary pathways vary in technological sophistication, the commitment of time and resources required, and the availability of opportunities for use and exploitation. In addition, as shown above in Figure 4, the use of EIDs in these different scenarios is likely to result in different overall numbers of casualties and a different pattern of manifestation of illness within a military force.

The IDA team began with a literature review, through which they discovered that the history of biological weapons development has been thoroughly documented, to include evidence and speculation regarding decision criteria for the selection of

pathogens for weaponization. Many major natural outbreaks of infectious disease throughout history are similarly well documented. Interestingly, many of the canonical stories of early recorded use of biological weapons fall into the category of improvised biological operations. For example, contemporary accounts describe the Mongols hurling plague-infected cadavers over city walls during their siege of the Crimean city of Caffa in 1346, resulting in an outbreak of disease that, some historians believe, initiated the Black Death plague pandemic in Europe.¹⁷

By contrast, few recent examples in the literature exist of nations or non-state actors attempting to exploit or shape disease outbreaks for military or political gain. The team subsequently conducted broad discussions with subject matter experts (SMEs) in the intelligence and infectious disease communities on the feasibility and potential impact of improvised biological operations, and discovered that these individuals—limited only by their imaginations—could generate any number of possible scenarios. These discussions were reinforced at the time by more lurid speculation in the popular press and social media over nefarious means of exploiting the Ebola outbreak in West Africa. Given the wide-ranging nature of the information gathered through these means, the research team used an inductive approach, discussed in detail below, to categorize components of scenarios of this type and associate them with producibility, employability, and effectiveness characteristics of concern.

B. Disease Characteristics of Concern

A paper recently published by the North Atlantic Treaty Organization (NATO)¹⁸ offers a methodology for evaluating the weaponization potential of emerging diseases, one of the adversary pathways explored in this research. This “Dirty Dozen” methodology was intended for use by policy makers, countermeasure developers, and medical planners to prioritize resources and efforts. The Dirty Dozen methodology scores diseases on a scale of 0 to 3 for each of 12 criteria; it then combines the individual criteria scores to generate an overall score between 0 and 36, with 36 representing an “ideal” BW agent. These criteria, and the meaning assigned to the lowest and highest scoring values, are provided in Table 1. For the purposes of this research, the IDA team assigned these criteria to producibility, employability, and effectiveness categories.

¹⁷ James W. Martin, George W. Christopher, and Edward M. Eitzen, Jr., “History of Biological Weapons: From Poisoned Darts to Intentional Epidemics,” in *Medical Aspects of Biological Warfare*, Textbooks of Military Medicine (Washington, DC: Office of the Surgeon General, US Army Medical Department Center and School, Borden Institute, 2007), 2.

¹⁸ Theodore J. Cieslak et al., *Beyond the Dirty Dozen: A Matrix Methodology for Assessing Future Biowarfare Threats*, STO-MP-HFM-239 Paper NBR 1-1 (NATO Science and Technology Organization, 2014).

Table 1. Dirty Dozen Criteria for Evaluating the BW Potential of Emerging Diseases

Component of Risk	Characteristic	Lowest Score (0)	Highest Score (3)
Producibility	Ease of large-scale production and storage	Nearly impossible to cultivate in quantity	Easy—can be propagated efficiently in artificial media
Employability	Infectivity	Non-infectious (e.g., toxins)	Highly infectious—ID ₅₀ 1-10 organisms ^a
	Predictability	Very low—incubation period very lengthy and/or variable	High—incubation period short and/or very predictable
	Aerosol stability	Very low—impossible to formulate in a homogenous aerosol	High—can be formulated in a homogenous aerosol of 2–3 micron particles
	Atmospheric stability	Very low—decay rates of unstabilized organism in the environment >3%/min	High—relatively impervious to decay under normal atmospheric conditions
	Ease of dispersal	Virtually impossible to disperse in quantity	High—can survive dissemination via ballistic weaponry
Effectiveness	Communicability	Non-contagious	Contagious via droplet nuclei
	Infection-to-disease ratio	Low (1:100)	Certain (nearly 1:1)
	Morbidity and mortality (virulence)	Minimal	High—lethal agents
	Prophylactic countermeasure availability	Countermeasures readily available or unnecessary	No known countermeasures available
	Therapeutic countermeasure availability	Countermeasures readily available or unnecessary	No known countermeasures available
	Ease of detection	Point-of-care assays available	No assays available for detection

Source: Cieslak et al., *Beyond the Dirty Dozen*.

^a The ID₅₀ is the dose required to infect 50 percent of exposed individuals.

Note that of the 12 characteristics discussed in the Dirty Dozen study, three of them are not necessarily inherent to the disease itself, but are determined by mitigating capabilities: prophylactic medical countermeasure availability, therapeutic medical countermeasure availability, and ease of detection. This supports the research team's assumption that the operational impact of an EID cannot be considered without reference to the availability of capabilities to mitigate it. Furthermore, as illustrated in Figure 3 (on

page 14), for EIDs of concern, it will be critical for DOD to use the interval between point of emergence and disease outbreak within an AO to develop mitigating capabilities.

Taking into consideration the assumption that outbreaks of disease manifest differently under different scenarios (Figure 4), this chapter explores the characteristics of those EIDs that could pose an operational risk in these various scenarios. Although focused primarily on medical versus operational impact, and specifically on biological warfare agent development, the set of 12 evaluation criteria proposed in the Dirty Dozen report is a good place to begin development of the producibility, employability, and effectiveness characteristics of concern for this research. In addition, this chapter seeks to identify any relevant characteristics beyond those shown in Table 1 and to determine, from an operational perspective, those that are most important.

C. Natural Outbreaks of Emerging Infectious Disease

1. Background

Even in the absence of an adversary with malevolent intent, outbreaks of EIDs among U.S. or allied military personnel, or among civilian populations in the AO, can generate significant operational risk beyond the levels typically associated with disease and non-battle injuries (DNBI).

Casualty rates among U.S. military forces engaged in combat operations in general have decreased over time. One comparative assessment of sustained U.S. military casualties showed an overall decline in total casualties, defined as fatalities (killed in action, died of wounds, and non-hostile deaths) plus wounded in action, from 13,871 per 100,000 per year during the war in Vietnam to 3,582 per 100,000 per year during Operation Iraqi Freedom (OIF).¹⁹ In the latter conflict, 88 percent of total casualties were nonfatal,²⁰ and these were dominated by DNBI casualties: during the Major Combat Operations phase and Support and Stability phase of OIF, 75 percent of U.S. Marine Corps and Army casualties were DNBI.²¹ Of these, however, only a small percentage were caused by infectious disease. An analysis of DNBI casualty care statistics compiled by an Army Brigade Combat Team during OIF found 1,324 DNBI casualties among a total of 4,122 soldiers, but only 43 of these were attributed to infectious disease, and all

¹⁹ Matthew S. Goldberg, "Death and Injury Rates of U.S. Military Personnel in Iraq," *Military Medicine* 175, no. 4 (2010): 222. Casualty rates for OIF were calculated from data reported 19 March 2003 through 10 January 2007.

²⁰ Ibid.

²¹ James M. Zouris, Amber L. Wade, and Cheryl P. Magno, "Injury and Illness Casualty Distributions among U.S. Army and Marine Corps Personnel during Operation Iraqi Freedom," *Military Medicine* 173, no. 3 (2008): 248.

but 7 were returned to duty.²² In short, infectious disease has not been a significant issue during recent U.S. combat operations.

Although disease has been associated with war and combat since antiquity, by the start of World War I, advances in medicine and public health had reduced the risk that infectious disease in general posed for military forces and operations. Still, this risk did not disappear entirely; although not as debilitating as smallpox and typhoid fever outbreaks had been in the past, malaria created operational and medical problems for U.S. forces operating in tropical regions during the 20th century. It has been estimated that over a half million casualties from malaria occurred in U.S. troops in the Pacific in World War II, more than 35,000 in Korea, and some 65,000 during Vietnam.²³ During and since World War II, DOD has actively sought to develop defensive measures against malaria, including effective vector control and avoidance measures as well as medical countermeasures.²⁴

The operational impact of malaria, however, even during World War II, is dwarfed by the challenges to U.S. military operations posed by influenza at the end of World War I. As cogently stated in the synopsis of one historical treatise:

The American military experience in World War I and the influenza pandemic were closely intertwined. The war fostered influenza in the crowded conditions of military camps in the United States and in the trenches of the Western Front in Europe. The virus traveled with military personnel from camp to camp and across the Atlantic, and at the height of the American military involvement in the war, September through November 1918, influenza and pneumonia sickened 20% to 40% of U.S. Army and Navy personnel. These high morbidity rates interfered with induction and training schedules in the United States and rendered hundreds of thousands of military personnel non-effective. During the American Expeditionary Force's campaign at Meuse-Argonne, the epidemic diverted urgently needed resources from combat support to transporting and caring for the sick and the dead. Influenza and pneumonia

²² LTC Philip Belmont, Jr. et al., "Disease and Nonbattle Injuries Sustained by a U.S. Army Brigade Combat Team during Operation Iraqi Freedom," *Military Medicine* 175, no. 7 (2010): 472. The casualties reported in this study include both those admitted to hospitals and those treated in an ambulatory setting and promptly returned to duty. Consequently, Belmont et al. believe their estimates of DNBI casualties within a defined unit are significantly higher than those officially reported from hospitals and surgical treatment facilities, as such reports only account for individuals who reach those facilities.

²³ Coreen M. Beaumier et al., "United States Military Tropical Medicine: Extraordinary Legacy, Uncertain Future," *Neglected Tropical Diseases* 7, no. 12 (2013): 1–6.

²⁴ C. W. Hays, "The US Army and Malaria Control in World War II," *Parassitologia* 42 (2000): 47.

killed more American soldiers and sailors during the war than did enemy weapons.²⁵

The 1918 influenza pandemic is the most definitive historical example of the impact a natural outbreak of an EID could have on military operations. Pervasive degradation in combat effectiveness would result from direct personnel losses alone, in particular if they occurred in an extreme burst over a very short period of time, as they did in the fall of 1918. In addition, the indirect effects can be significant. The logistics demand for medical care and transport of casualties and fatalities can make it difficult to sustain combat operations in unaffected units. Any movement of personnel and equipment into and out of theater would also be constrained by fears that the disease could be introduced into home nation and host nation populations.

Natural outbreaks of infectious disease can also constrain operations even when U.S. military personnel remain unaffected. During an outbreak of endemic disease in the AO, units may choose to avoid specific geographic regions or minimize contact with the local population. Operation United Assistance was the DOD component of the broader U.S. government response to the 2014 Ebola outbreak in West Africa. In this case, U.S. forces were not engaged in combat operations, so operational impact, in the sense considered in this research, was nil. Moreover, the health risks to military personnel from the Ebola outbreak itself were purposefully limited, as the mission did not include treatment of or direct contact with Ebola patients, focusing instead on building hospitals, training health care workers, and providing laboratory support. Nonetheless, U.S. forces took unusual precautions to prevent exposure to the disease—including proscribed physical contact and a mandated three-foot separation rule when engaged with any host nation personnel, frequent handwashing with chlorine solution, and prohibitions on the consumption of unapproved food and water.²⁶ In addition, personnel underwent twice-daily temperature monitoring during their deployment and were quarantined for 21 days after leaving Africa but before returning to the United States.²⁷ This latter measure was somewhat controversial and, if applied to a larger force redeploying from an operational theater, could well be particularly onerous and disruptive to the normal cycle of unit rotations.

²⁵ Carol R. Byerly, “The U.S. Military and the Influenza Pandemic of 1918-1919,” *Public Health Reports* 125, Supplement 3 (2010): 82.

²⁶ Patricia Kime, “Isolation Pods Will Carry Troops If They Get Ebola,” *Army Times*, October 24, 2014, <http://www.armytimes.com/article/20141024/NEWS04/310240059/Isolation-pods-will-carry-troops-they-get-Ebola>.

²⁷ Under Secretary of Defense (Personnel and Readiness) Memorandum, *Pre-Deployment, Deployment, and Post-Deployment Training, Screening, and Monitoring Guidance for Department of Defense Personnel Deployed to Ebola Outbreak Areas—Change 1*, October 31, 2014.

2. Characteristics of Concern for Natural EID Outbreaks

Since the causative agent of natural disease outbreaks is not deliberately introduced into a population by an adversary, the producibility and employability axes of the EID evaluation construct (Figure 2, on page 6) do not apply. The operational risk of EIDs in this scenario is solely a function of their effectiveness in impacting operations. Of the characteristics listed in Table 1 that relate to effectiveness, three are inherent characteristics of disease: communicability, infection-to-disease ratio, and morbidity and mortality. These three characteristics influence but do not completely determine the direct impact a disease outbreak can have, in terms of overall numbers of casualties and lost duty time. Other characteristics, as noted above, are related to the availability of mitigating capabilities, which can reduce the direct impact of an outbreak but also be an indirect source of impact, from reduced operational maneuverability and flexibility as well as reallocation of resources. Medical countermeasures can also have significant side effects, which, while debilitating for the affected individuals, are unlikely to be so pervasive as to pose any significant risk.²⁸

The communicability of a disease refers to the mechanism by which it spreads among a human population and the ease with which it does so. Contagious diseases pass directly from one human to another via inhalation, ingestion, or physical contact with human bodily fluids, secretions, or hair/skin containing infectious pathogens. Non-contagious diseases are passed to humans through exposure to the pathogen in the environment, through consumption of contaminated food or water, or by contact with an animal or insect vector.²⁹ The ease with which a contagious disease can spread among humans depends on the location and amount of pathogen within the body. Airborne pathogens such as influenza spread more easily within a population than bloodborne pathogens like HIV.

The Dirty Dozen methodology scoring system assigns a higher value—and greater risk—to diseases that are readily contagious among humans. This is consistent with the historical record, as plague, influenza, and smallpox have been associated with the most significant disease outbreaks in recorded history; all would therefore be assigned the highest possible score. Still, non-contagious diseases have also been responsible for significant outbreaks of disease. As the cited experience with malaria shows, non-contagious vector-borne diseases can cause large numbers of casualties and pose an operational challenge of sufficient magnitude to spur urgent development of response

²⁸ Deena S. Disraelly et al., *A Methodology for Examining Collateral Effects on Military Operations during a Chemical, Biological, Radiological, and/or Nuclear Attack—Operational Effectiveness Loss Multiplier (OELM)*, IDA Paper P-5202 (Alexandria, VA: Institute for Defense Analyses, April 2015), 29.

²⁹ These two categories are not mutually exclusive. Most contagious diseases (for example, Ebola and pneumonic plague) are introduced into the human population by animals or insect vectors.

measures. However, several factors limit the operational impact of vector-borne diseases: first, vectors themselves are vulnerable to eradication methods; second, military personnel can use insect repellents, nets, and coverings to effectively avoid contact with vectors; and third, while uncontrolled vectors can be associated with high rates of casualties, these rates are unlikely to reach the threshold required to place an operation at risk of failure within the timeframe of a deployment. Waterborne pathogens can also be responsible for large outbreaks of disease. The worst cholera outbreak in recent history occurred in Haiti, with nearly half a million cases directly resulting from the breakdown of water sanitation in the aftermath of the 2010 earthquake.³⁰ Yet, like vector-borne diseases, waterborne diseases are highly susceptible to eradication or avoidance efforts. While diseases like cholera continue to affect millions of people worldwide each year,³¹ they are now rare in the United States and other developed countries.³² Western armies today have standard procedures for ensuring the quality of water and minimizing risk from waterborne pathogens.³³ However, as vector- and waterborne diseases emerge in the future, it is possible that the causative pathogen or its associated vector would become highly resistant to existing eradication and avoidance measures and pose a greater operational risk than they have in the past, and this bears monitoring. EIDs that are highly contagious would be of even greater concern, as they are much more likely to be capable of generating large numbers of casualties within an operationally relevant timeframe.

Infection-to-disease ratio refers to the probability that infection with a given pathogen will result in illness versus remaining asymptomatic. In general, the higher the infection-to-disease ratio, the greater the concern. However, this concern would only become manifest after a threshold ratio is reached. From an operational perspective, the infection-to-disease ratio determines the upper bound on the percentage of personnel that could become casualties from a given disease. For example, only about half of individuals infected with Eastern Equine Encephalitis Virus (EEEV)—a mosquito-borne pathogen in nature—develop symptoms, and most of those are mild cases of flu-like illness; only about 8 percent of infected individuals develop the severe, encephalitic form of disease.³⁴ In other words, a natural outbreak caused by EEEV that infected everyone within a deployed military population would result in a casualty rate of 8 percent. In reality, it is unlikely that 100 percent of a population would become infected during a

³⁰ CDC, “Haiti Cholera Outbreak,” http://www.cdc.gov/haiticholera/haiti_cholera.htm.

³¹ WHO, “Cholera Fact Sheet,” <http://www.who.int/mediacentre/factsheets/fs107/en/>.

³² CDC, “Cholera in the United States,” <http://www.cdc.gov/cholera/usa/index.html>.

³³ For example, see NATO Standard 2136, *Allied Medical Publication 4-9, Requirements for Water Potability during Field Operations and in Emergency Situations*, promulgated March 21, 2014.

³⁴ Martin Goldfield, James M. Welsh, and Bernard F. Taylor, “The 1959 Outbreak of Eastern Encephalitis in New Jersey #5: The Inapparent Infection: Disease Ratio,” *American Journal of Epidemiology* 87, no. 1 (1968): 35.

natural outbreak. For purposes of comparison, one study of the 2009 influenza A (H1N1) pandemic estimated that 24 percent of the population worldwide had been infected with the virus in its first year of circulation.³⁵ A hypothetical EID with an attack rate comparable to H1N1 and an infection-to-disease ratio comparable to EEEV, then, would generate a maximum casualty rate of about 2 percent and pose little operational risk. At a minimum, EIDs would be of concern only if the infection-to-disease ratio were higher than the rate of casualties a force could sustain before becoming combat ineffective. In practice, this minimum threshold for concern could be adjusted based on the ease with which the disease is transmitted: for diseases with high attack rates, like measles and influenza, the threshold for concern may be a factor of 2 or 3 higher than the minimum sustainable casualty rates, while for other, less contagious diseases it would be higher still.

Morbidity and mortality refer respectively to the severity of illness and the probability that it would result in death. For an EID outbreak to result in casualties, the illness it causes must be severe enough that the affected personnel are lost to their unit. The operational impact of that outbreak would be enhanced if the illness were of long duration, as not only would it cause direct personnel losses for extended periods of time, but would also generate indirect impact from the need to care for and transport casualties within and out of an AO. Finally, diseases that are lethal or debilitating enough to prevent return to duty will cause permanent personnel losses and lost operational capability.

At the same time, diseases that begin with a lengthy period of asymptomatic or mild presentation of illness, during which time the affected individual is highly functional but contagious, would be of much greater concern than those that rapidly become incapacitating. Once individuals become severely ill, they are unlikely to come in contact with large numbers of people outside the medical system. Given that contagious diseases are of greatest concern in natural outbreaks, those that rapidly progress to the point where hospitalization is required would tend to limit opportunities for the disease to spread within the general population.

As considered in the Dirty Dozen methodology, ease of detection refers to the availability of laboratory diagnostic techniques to identify and characterize a disease-causing pathogen. For this characteristic, the lowest score is assigned to those diseases for which point-of-care assays are available, meaning diagnostic testing can be done in a clinical setting, such as forward-deployed medical treatment facilities (MTFs). Highest scores are assigned to diseases that cannot be identified, even in the most capable laboratories. At the point of emergence, novel pathogens by definition would be

³⁵ Maria D. Van Kerkhove et al., “Estimating Age-Specific Cumulative Incidence for the 2009 Influenza Pandemic: A Meta-analysis of A(H1N1)pdm09 Serological Studies from 19 Countries,” *Influenza and Other Respiratory Viruses* 7, no. 5 (2013): 878.

impossible to identify. On the other hand, known diseases presenting in new geographic regions or populations could be identifiable fairly quickly if point-of-care assays or laboratory assays already exist, as seems likely for diseases that are otherwise of significant concern. The availability of assays for variants of such diseases would depend on the nature of the variation and the target of the assay, although at a minimum they would be identifiable at high-level laboratories with sophisticated genomic sequencing techniques.

Identification of the pathogen responsible for an outbreak is essential before effective and efficient treatment and infection control measures can be initiated. Clinicians may suspect an illness is viral or bacterial in origin, but without confirmatory laboratory diagnosis, they may not prescribe appropriate therapy drugs, understand the prognosis of the illness, or recognize a need for extraordinary disease containment measures. Even when laboratory diagnostic techniques are available, however, their use must be triggered by suspicious health care providers. For diseases with symptoms that are non-specific in their early phases, or that share symptomology with other endemic diseases, such suspicions may not exist at the start of an outbreak, resulting in delays in the initiation of response measures. As noted above, the similarity in early clinical presentation between Ebola, malaria, and cholera was a significant contributor to the delay in identifying Ebola as the causative agent of the 2014 outbreak in West Africa and the consequent failure to contain the spread of the outbreak throughout the region. This problem was exacerbated by the fact that Ebola had not previously been observed in the region, so clinicians were not familiar with the disease presentation and diagnostic assays were not locally available. One cluster of Ebola patients was initially diagnosed with cholera, a diagnosis that was apparently confirmed with point-of-care cholera assays with high false positive rates.³⁶ Ultimately, the first Ebola-positive tests of clinical samples from the outbreak were conducted in a laboratory in Lyon, France. Moreover, even at the height of the outbreak, when point-of-care diagnostic testing was routinely provided in Ebola treatment centers, diagnosis and treatment were complicated by the high incidence of malaria infections and co-infections in those presenting with illness, and the need to quickly differentiate and segregate malaria-only patients from those with Ebola.³⁷

Prophylactic and therapeutic medical countermeasures can minimize the susceptibility of a population to a given disease and reduce the severity, duration, and probability of death or long-term disability among those who become ill. In the absence of such countermeasures, outbreaks of contagious disease must be controlled exclusively through physical means, such as isolation and quarantine, and treatment is limited to

³⁶ Stern, "Hell in the Hot Zone."

³⁷ CDC, "Recommendations for Managing and Preventing Cases of Malaria in Areas with Ebola," <http://www.cdc.gov/vhf/ebola/outbreaks/malaria-cases.html>.

supportive care. While both physical controls and supportive care are potentially effective, they can also be operationally restrictive, comparatively resource intensive, and less predictable in their outcome. Consequently, diseases that can be readily prevented or quickly and effectively cured via medical countermeasures would be of less concern than those that cannot.

In summary, for naturally occurring outbreaks, EIDs of greatest concern would have the following effectiveness characteristics:

- Contagious and easily transmitted among humans;
- Mild, non-specific, and contagious in early phases;
- Lethal or significantly debilitating in later phases with little or no possibility of return to duty;
- Not identifiable using available diagnostic testing; and
- Lacking effective prophylaxis or treatment.

Outbreaks of such diseases would generate large numbers of casualties and lost duty time and would be difficult to mitigate, as they would be challenging to detect initially and much harder to control.

D. Weaponization of EIDs

1. Background

This research assumed that any EID weaponized by an adversary would be of concern to the United States, as any use of BW agents in a military context can be expected to pose significant operational risk. The disease characteristics of concern for weaponized EIDs, then, are those that would lead an adversary to pursue weaponization. This research also assumed that weaponization of an EID would take the same form as a traditional BW agent and follow the same development and production processes. In other words, it would be produced in large quantities (hundreds or thousands of kilograms); formulated to be stable in storage, survive dissemination, and remain viable in the environment; and weaponized for delivery over large geographic areas.

The IDA research team relied heavily on the rich historical record on BW agent programs in the United States, the United Kingdom, and the Soviet Union, both classified and unclassified, to understand the weaponization process and the decision criteria used to select pathogens for development. While an assessment of the technological, financial, and infrastructure requirements of BW development was beyond the scope of this research, this is obviously a sophisticated, lengthy, and expensive process requiring a stable, well-funded, and dedicated adversary.

The time it would take to weaponize an EID and the prospects for success of such an endeavor—both of which affect risk assessment—depend on the status of an adversary's existing BW program. For nations that have previously had weaponization programs, certain steps in the development process may be easier as a consequence of their experience. In order to assess the impact of that supposition, the steps associated with weaponizing a pathogen could be enumerated, and each step judged as easier/quicker/unnecessary given the depth of a given adversary's experience. If estimates of the time associated with each step for both a new and ongoing program could be provided by SMEs, the total time from discovery of a pathogen to tested weapon could be estimated for different types of EIDs.

2. Producibility and Employability Characteristics of Concern for Weaponized EIDs

The producibility and employability characteristics that would allow a pathogen to be effectively weaponized are well defined in the literature and generally the same in all major historical BW programs. Not all pathogens are suitable for production in large quantities, with the percentage of the final product that remains viable diminishing as the scale of production increases from bench processes in a laboratory to pilot plant and, eventually, industrial scale. This problem is not trivial and has led to the rejection of certain pathogens as BW agents in the past. Unfortunately, the general factors that support or prohibit production of a pathogen appear to be largely unknown, which suggests that the feasibility of mass production for any specific EID is unpredictable and may not, in fact, be known until an EID has progressed fairly far down the path of weaponization.

Once produced, BW agents must be stable in storage, either in bulk form or stockpiled in filled munitions. The specific requirements for storage stability are heavily influenced by an adversary's concept for BW use, which would include consideration of the population and geographic size of the intended target, the amount of viable agent that would have to be delivered, and, in turn, the extent to which degradation of stored agent can be tolerated. Unless agent production is intended to support near-term use, in general the greater the stability in storage the better.

To be effectively employed, a BW agent must be sufficiently stable in the environment to expose the target population to sufficient quantities of viable organisms to cause illness and have the intended operational effect. This means that the pathogen itself, in combination with stabilizing additives and via production processes such as freeze-drying, milling, and encapsulation, must survive in a range of temperatures and relative humidity and be resistant to the effects of ultraviolet light.

While a few BW agents have been produced for delivery via insect vectors, the great majority were developed for aerosol dissemination. There are many reasons for this,

among them the greater predictability of effects with aerosols, the greater confidence in the exposure of specific target populations, and the much larger number of pathogens suitable for use as BW agents that are infectious as aerosols compared to those that can be effectively transmitted via vectors. Assuming that an adversary would exhibit a similar preference for aerosol delivery of a weaponized EID, required employability characteristics would also include, by definition, the ability to engender disease via inhalation of the pathogen, as well as the ability to survive the process of dissemination itself.

3. Effectiveness Characteristics of Concern for Weaponized EIDs

Despite the apparent consensus regarding which producibility and employability characteristics are desirable for BW agents, different nations have historically selected very different sets of agents for inclusion in their weaponization programs. These differences reflect very different views of effectiveness characteristics, which appear to have been closely associated with differences in national strategic and operational objectives.

When assessing the apparent merits of an EID as a weapon against U.S. forces, it is critical to consider the adversary's intended objective, as different weapons are better for different objectives and scenarios. A highly lethal pathogen with no known medical countermeasures may be an ideal weapon for an adversary attacking U.S. forces far from the front line of combat, but a poor choice of weapon for use against U.S. troops in close proximity to adversary forces as the attacking forces themselves would be affected.

4. Additional Considerations for Weaponization

a. EID Weaponization and Adversary Capabilities

Adversaries intending to weaponize any EID pathogen have a strong incentive to keep their intentions and the development program itself covert. Detection of a weaponization program could lead the United States to seek destruction of production and storage facilities and means of delivery. Given enough time, the United States could also successfully develop and deploy detection systems and medical countermeasures to mitigate the operational effectiveness of the weaponized EID.

National sovereignty or the consent and coordination of a sovereign government are critical to successfully concealing the infrastructure associated with a BW development program. Governments are very likely to detect and destroy unauthorized weaponization programs conducted by non-state actors on their territory. Non-state actors operating independently from a government body, even if well-funded, are therefore unlikely to choose the weaponization pathway on their own, without government consent, given the likelihood and consequences of detection. Therefore, any group operating with the

consent and cooperation of a governing body was, for the purposes of this research, considered to be a state actor.

The assumption that a rational non-state actor would not engage in weaponization of an EID because of the higher likelihood of detection should not be construed as a justification for the United States or its allies to stop monitoring the activities of such groups. U.S. intelligence should continue to monitor non-state groups for signs that a weaponization program has been initiated so that necessary mitigating responses can be undertaken. Observation of ties between nations and known terrorist groups operating within their borders is essential to detecting any signs of weaponization.

b. Weaponization of Different Types of EIDs

1) Known Pathogens that Appear in New Geographic Areas or Populations

The characteristics of a known pathogen that would persuade a nation to weaponize it would almost certainly be known prior to the pathogen's emergence in a new geographic area or population. If a nation assessed the pathogen to be an attractive candidate for weaponization, it could be expected to acquire environmental or medical samples from which to develop the weapon from a location where the disease is endemic. The emergence of that pathogen elsewhere (even within the nation's borders) is unlikely to trigger efforts to weaponize that particular pathogen. Therefore, there is little additional operational risk to U.S. forces from a nation observing the emergence of a known pathogen in a new geographic area or population and then deciding to weaponize it.

In order for the emergence of a known pathogen to increase the risk of its weaponization, a nation would need to have previously assessed that pathogen to be a desirable candidate but have lacked ready access to the pathogen itself. An example for which this might be the case is smallpox, to which access is extremely restricted. If a smallpox outbreak were to occur, adversary nations may attempt to acquire samples in the hopes of adding this disease to their BW arsenals. In contrast, an outbreak of plague—a disease now common in many regions of the world—in a new area or population is less likely to prompt an adversary to collect samples.

2) Novel Pathogens and Variants of Known Pathogens

The likelihood of an EID becoming a weaponized threat depends on an adversary's assessment of the benefits of an EID weapon versus the substantial costs of development. A perceived benefit would logically exist only if the EID possessed characteristics that made it better suited to meeting a given objective than other pathogens already weaponized. While known pathogens in new geographic areas or populations, with the potential exception of smallpox, are unlikely to pose additional risk for weaponization,

newly emerging diseases caused by novel pathogens and variants of known pathogens cannot be assessed a priori; DOD will need to compare each of these EIDs to known BW agents to assess whether they are better suited to meeting some adversary objective.

Many of the characteristics that would be discovered quickly after a pathogen's emergence would be related to effectiveness, while information about the producibility and employability of a novel pathogen may not be known until research has progressed. For an adversary to see merit in pursuing weaponization of an EID, the pathogen would likely have to be demonstrably better at one of the effectiveness measures or reasonably suspected to be more producible or employable than known BW agents. Variants of an existing pathogen that are resistant to countermeasures or passive defenses, for instance, could be demonstrably better for meeting some objectives than the original pathogen.

The degree to which an EID could be expected to "outperform" the current best weapon for a given objective in large part determines the extent to which it should be considered a risk from a weaponization standpoint. The Soviet Union emphasized "improvement of the characteristics of agents already adopted in to the inventory rather than searching for completely new agents,"³⁸ implying that they found it easier to work with a variant of a previously weaponized pathogen than a new pathogen. EIDs that behave like previously weaponized pathogens would likely present fewer barriers to weaponization than completely novel pathogens. Thus, even a marginal improvement over existing weapons might justify the investment in weaponizing an EID similar to a current BW agent. A more significant improvement over existing pathogens may be needed for a nation to justify the weaponization of pathogens dissimilar to current BW agents.

Therefore, novel pathogens and variants of known pathogens that possess no advantage over the best current BW agent for a given objective pose little additional operational risk to U.S. forces in weaponized form, but those pathogens that do have such advantages could potentially pose significant risk. This risk is higher for EIDs that are similar to previously weaponized agents than for those that are dissimilar, due to the increased likelihood of success and the potential savings in time and effort to successfully weaponize them.

5. Summary

Future EIDs of greatest concern as candidates for adversary weaponization are those that are:

- Feasibly produced in large quantities,

³⁸ *Logic and Selection Criteria for Soviet Offensive Biological Weapons Program*, 1996: 2.

- Stable in storage,
- Stable in aerosol form and in the environment,
- Infectious via the aerosol route, and
- Readily disseminated as an aerosol.

These producibility and employability characteristics are consistent with the list generated by the Dirty Dozen study provided in Table 1. These characteristics—associated with the physical properties of a pathogen—can be considered prerequisites for weaponization as defined in this paper. Because knowledge of these characteristics is independent of a pathogen’s behavior vis-à-vis humans and the disease that results, it can be established fairly quickly after emergence.

An adversary’s decision to pursue weaponization of a specific EID will be heavily influenced by its strategic and operational objectives. Effectiveness characteristics—those related to communicability, lethality, duration and severity of disease, and availability of medical countermeasures and treatment—can be derived from these objectives. While these characteristics are, in general, the same as those identified in the Dirty Dozen study, the associated scoring scheme and relative importance of various characteristics may be very different, as adversaries may be less interested in maximizing medical impact than in achieving some other goal.

Finally, weaponization of EIDs, as discussed in this section, is far more likely to be undertaken by nations and state-sponsored actors than by non-state actors operating without the support or acquiescence of a host nation. EIDs are more likely to be weaponized if (1) adversaries perceive the EIDs provide an advantage over BW agents they already possess, and/or (2) the EIDs are variants of known diseases that are currently weaponized. Known pathogens in new areas or populations are unlikely to be weaponized if they have not been previously.

E. Improvised Biological Operations

1. Background

As defined in this research, improvised biological operations encompass improvised attacks with crude biological weapons and exploitation of disease outbreaks within an AO for operational gain. Such operations require both adversary intent and opportunity. They would be challenging to plan and execute, but would not require the technical sophistication or resources associated with weaponization. Preparations for improvised attacks using stolen or crudely developed biological material are unlikely to have many observable indicators, but would also be limited in scale.

The challenge for this research was to understand how improvised operations differ from natural outbreaks and weaponization scenarios, and whether the EIDs that would be of greatest concern in these operations would have different characteristics. In addition, the research team sought to understand whether the operational impact and associated risk from improvised biological operations using EIDs were more like those from natural outbreaks, or those from the use of weaponized EIDs.

As noted, the research team found that the first historical accounts of BW involved exploitation of natural outbreaks for operational gain. The team also found a few examples in the literature of terrorists and criminals attempting, with mixed results, to acquire and use pathogens or toxins. The manufacture and release of botulinum toxin and anthrax spores in failed terrorist attacks by Aum Shinrikyo in the early 1990s are well-documented. The cult also attempted to acquire samples of other pathogens, including Ebola virus.³⁹ In another famous example, in Wasco County, Oregon in 1984, the Rajneeshee cult attempted to influence local elections by contaminating restaurant salad bars with salmonella bacteria, sickening an estimated 751 people in the hopes of preventing them from voting.⁴⁰

These well-known examples, as well as other instances of individuals using pathogens and toxins (such as ricin) for criminal purposes,⁴¹ show that committed adversaries would likely be able to acquire EIDs in a form allowing them to be used on a small-scale, tactical level. Nonetheless, the IDA team's literature review did not uncover any documented modern instances of nations or non-state actors conducting improvised biological operations in a manner that affected military operations. SMEs in the infectious disease and intelligence communities, however, proved to be rich sources of speculation on the feasibility and potential impact of improvised biological operations. The research team used discussions with these individuals to develop a framework for thinking about scenarios of this type; the team then used that framework to derive producibility, employability, and effectiveness characteristics for EIDs of concern in improvised biological operations.

³⁹ Kyle B. Olson, "Aum Shinrikyo: Once and Future Threat?" *Emerging Infectious Diseases* 5, no. 4 (July-August 1999): 514.

⁴⁰ W. Seth Carus, *The Illicit Use of Biological Agents Since 1900*, Center for Counterproliferation Research, National Defense University (February 2001): 7. Discussion of the Rajneeshee case includes reference to FBI testimony before the Congress that described this as the only bioterrorism incident in the United States in which human illness has been verified.

⁴¹ For documentation of numerous such examples, see Carus, *The Illicit Use of Biological Agents Since 1900*.

2. Approach and Framework

Throughout its discussions, the research team found innumerable plausible scenarios for improvised biological operations, limited only by the imaginations of the individuals postulating them. Upon review, the team found that although these scenarios encompassed a wide variety of adversary means, motives, and opportunities, they all shared three core elements: a means of attack, an adversary objective, and a target. In addition, each of these core elements could be related to broad categories of EID characteristics or operational impact. These relationships, illustrated in Figure 5, collectively form a framework for considering the types of EIDs that could pose operational risk if used to conduct improvised biological operations.

Means of attack refers to the form of the disease-causing pathogen, how it is acquired, and the manner in which it is used. Like weaponized EIDs, these aspects of the scenarios determine the producibility and employability characteristics that an EID would have to possess in order for it to be used in the manner postulated and to achieve an operational effect. Also like weaponized EIDs, effectiveness characteristics of concern are derived from *adversary objectives*. *Target* refers to the population the adversary intends to harm or the geographic area it intends to encompass. Operational impact is determined by the intersection of these characteristics and the adversary's target.

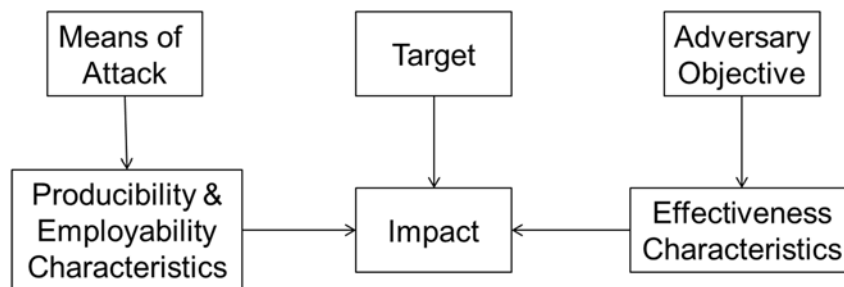


Figure 5. Framework for Deriving Characteristics of EIDs of Concern for Improvised Biological Operations

In its discussions with SMEs, the research team encountered many postulated scenarios for EID use where adversary objectives could be met without generating operational impact as considered in this research. For example, rebel forces could seek to instill fear in the local population or foster distrust in national governments through improvised biological operations. Such objectives are strategic and political in nature, and achieving them could indeed change the broad strategic objectives of US military forces, leading to changes in the presence and composition of forces, missions, etc. This research, however, was concerned only with the use of EIDs in ways that could risk the ability of US forces to execute their missions and achieve their operational objectives; Chapter 5 discusses at length the potential operational impact of adversary use of EIDs.

The impact of EIDs on the nature of those objectives, or whether U.S. forces are even deployed in the first place, was outside the scope of this research.

3. Producibility and Employability Characteristics Derived from Means of Attack

Adversaries wishing to engage in improvised biological operations can acquire and use EIDs in three possible forms: organic material or solutions that contain viable EID pathogens and can serve as crude biological agents; animal or insect vectors; and human vectors. These forms are not mutually exclusive, and one can be an intermediary form en route to adversary acquisition of another. For example, crude biological agents can be used to create human vectors, who then disseminate disease through contact with the target population. Alternatively, human vectors can be used as sources for pathogen-containing bodily fluids that can be sprayed, exploded, added to food or water, or be otherwise used as a crude weapon. However, not all diseases will be amenable to acquisition and use in all three forms, limiting the ways in which any given EID can be used in improvised operations. In addition, different producibility and employability characteristics are associated with each means of attack. Scenarios involving acquisition of one form of EID and generation and use of a second form would require a disease to have both sets of characteristics to be a threat.

The Dirty Dozen criteria listed in Table 1 were developed with specific reference to manufactured BW agents, and the single producibility characteristic—ease of large-scale production and storage—is not relevant to improvised biological attacks. Moreover, the process of BW agent production and storage includes procedures, equipment, and facilities that would promote sustained pathogen viability and safe handling; all of these are assumed to be absent in improvised biological operations. For crude biological agents, “production” would include purchase, theft, or isolation and growth of pathogens on a small scale and/or in crude fashion. Many of the scenarios postulated during the research team’s discussions involved acquiring pathogen samples or vectors from regions where natural disease outbreaks were underway and transporting them to other regions for use as improvised weapons. Producibility in this context requires pathogens that are stable during transportation and storage, with a minimal need for handling requirements such as refrigeration and humidity controls. Adversaries would also need to be able to transport and deliver crude biological agents safely. Equipment and procedures for safe transport and handling of dangerous pathogens are pervasive in medical research settings and presumably would be readily available to potential adversaries of all types. Any pathogens considered too dangerous for handling despite available precautions would be less likely to be used.

Many of the employability characteristics discussed above for weaponized EIDs also apply to EIDs used as crude biological agents in improvised operations; indeed, in many instances they are even more important. Weaponized agents typically include

additives and stabilizers to enhance survivability during dissemination and in the environment; crude biological agents would not. To be viable for operations of this type, pathogens would have to be hardy enough to survive spraying or explosive dissemination, and survive long enough as an aerosol or surface contaminant to expose targeted personnel and cause disease. On the other hand, a pathogen's stability in aerosol form, scored in Table 1 on the basis of the feasibility of formulation as a homogenous, respirable aerosol, is less relevant for small-scale operations of this type involving small quantities of material than it would be for canonical BW attacks.

For improvised operations, animal and insect vectors must be easily acquired and survivable both during transport and handling and within the environment of the target area. Diseases with a broad natural host range would be better suited to this purpose than those with a more limited host range. For example, although chikungunya has spread wildly in the Western hemisphere over the past two years, the disease has been largely restricted to equatorial regions because mosquitoes that thrive in colder climates have not (so far) proven to be viable hosts for the virus.⁴² In addition, vector-borne diseases with hosts that are resistant to control measures such as insecticides and insect repellent would pose a greater threat.

The creation and use of human vectors as a means of attack by definition requires that the disease with which they are infected be contagious. The disease characteristics of concern regarding the employability of humans as a means of attack are those that would engender the largest number of secondary cases per primary human vector. Diseases that are highly transmissible via aerosol droplets would be of concern. So, too, would diseases that begin with a lengthy contagious period of non-specific, mild symptoms. Human vectors with these diseases would be difficult to detect and would be physically capable of engaging with the target population for extended periods of time before worsening symptoms allowed them to be identified.

Note that these producibility and employability characteristics for human vectors were listed above among the effectiveness characteristics associated with natural outbreaks of EIDs. This overlap is not surprising, as the disease characteristics that allow humans to serve as initiators of disease outbreaks—whether deliberately or inadvertently—would also trigger disease outbreaks among a military population and generate operational impact. One important difference, however, is that in improvised biological operations, a high infection-to-disease ratio is much more important than it is in natural outbreaks. For diseases with very low ratios, it would be harder to generate human vectors to begin with, and subsequently those vectors would have a more difficult time causing illness in the target population. Adversaries would be more likely to engage

⁴² Roger S. Nasci, "Movement of Chikungunya Virus into the Western Hemisphere," *Emerging Infectious Diseases*, 20, no. 8 (August 2014): 1394–5.

in improvised biological operations using diseases with high infection-to-disease ratios, as they are much more likely to generate the desired impact. Natural outbreaks, on the other hand, may occur eventually, regardless of infection-to-disease ratios, as any number of asymptomatic infections can occur before a cluster of symptomatic cases causes a disease to spread and fosters a larger outbreak.

During the 2014 Ebola outbreak, populations in many nations—including in the United States—feared that individuals in the early stages of illness would travel from West Africa to other countries and foster widespread disease around the world. Within DOD, questions arose regarding whether adversary nations and terrorist groups could effectively use humans as vectors for spreading disease generally, and Ebola specifically. One white paper-like presentation that circulated widely, entitled the “Typhoid Mary Brief,” attempted to address the question of whether adversaries could use human vectors successfully.⁴³ This presentation concluded that adversaries would have to overcome a number of barriers to do so, but that assuming willing vectors could be found and successfully infected, the primary challenges were related to the characteristics and limitations of specific, known diseases. The assessment criteria used in the Typhoid Mary brief to evaluate these known diseases—transmissibility, infection-to-disease ratio, severity of illness during the contagious period, and the degree of native immunity in the target population—are the same as those proposed in this paper; from the perspective of the Typhoid Mary brief, future EIDs that met the producibility and employability characteristics postulated above for human vectors would certainly be of concern.

The Typhoid Mary brief assumed that adversaries would create human vectors by recruiting healthy individuals and subsequently causing them to become ill with contagious disease by some means. In its discussions, the research team found this to be just one of many scenarios for adversary acquisition and use of human vectors. Table 2 lists the many possibilities discussed with SMEs, in the popular press, and among research team members. It is included here partly for reader interest, but also to illustrate the broad range of possible scenarios the team found, related to just this one means of attack in improvised biological operations.

⁴³ *Typhoid Mary: Could An Adversary Use Humans to Act As BW Vectors?*, presentation provided to IDA by JRO-CBRND, January 2015.

Table 2. An Example: How Can Patients Become Vectors of Disease?

With Evil Intent on Patients' Part	Of Patients' Own Will But Without Evil Intent	Against Patients' Will/ Without Their Knowledge
Bribe families/individuals to send dying family members into target population to infect enemies (external motivation)	Flee an attack on a health care facility and unintentionally risk infection in the target population	Kidnap patients and leave them among the target population
Intentionally expose individuals in target population because of ideological/political beliefs (internal motivation)	Fearing systematic persecution of infected individuals in the community, they leave the area however they can	Threaten/blackmail/pay families to get them to give up patients
Volunteer for a relief organization and expose oneself through contact with existing patients	Seek medical care within the target population	Set up fake health care centers and prescribe treatment in location of target population
Intentionally contract the disease through contact with contaminated materials		Acquire agent through voluntary medical samples to "doctors"

4. Effectiveness Characteristics Derived from Adversary Objectives

To derive effectiveness characteristics for EIDs of concern in improvised biological operations, the research team began with the notion that, like weaponized EIDs, those characteristics would be a function of adversary objectives. Based on its discussions, the team identified seven broad potential objectives:

- Cause casualties among U.S. and coalition military forces;
- Disrupt or delay deployment of U.S. and coalition forces to the AO;
- Restrict U.S. and coalition forces from operating in a specific area;
- Impede U.S. and coalition force maneuverability and flexibility;
- Cause panic within the local population;
- Impose a socio-economic burden on the host nation; and
- Destabilize the host-nation government.

The last three of these objectives are political in nature. As noted above, they are largely outside the scope of this research; they are mentioned here for completeness. While an adversary's pursuit of these objectives could cause the United States to alter its operational objectives, and indirectly affect U.S. military operations, they are not likely to have sufficient impact in an operationally relevant timeframe to result in combat ineffectiveness or mission failure. If achieved, however, the first four of these objectives have the potential to place U.S. operations at risk.

a. Adversary Objective: Cause Casualties among U.S. and Coalition Military Forces

Improvised biological operations, as conceived in this paper, are limited in scale; any single improvised attack would directly affect a relatively small number of individuals compared to those that could be exposed during an attack with aerosolized BW agents. To generate casualties among U.S. forces in numbers sufficient to degrade operations, adversaries would have to either conduct multiple successful operations or rely on the multiplicative effects of contagion. EIDs that are readily transmitted among humans would therefore be of greater concern in this context. Since those initially infected via adversary operations then serve as unwitting human vectors, the same employability characteristics that support the use of human vectors would apply here: a high infection-to-disease ratio and a lengthy, early contagious phase of illness characterized by mild, non-specific symptoms. In addition, since operational impact from direct casualties is a function of not only the overall number of casualties, but also the length of time they are lost to their unit, diseases that have high degrees of morbidity and mortality in later stages would be of greater concern than those that do not.

As with natural outbreaks, an inability to diagnose a disease in a clinical setting or via laboratory testing would delay detection of an outbreak and the implementation of outbreak control measures in response. For contagious diseases, this delay would serve to perpetuate the spread of disease, resulting in even greater numbers of casualties. Moreover, if prophylactic or therapeutic medical countermeasures were not available, casualties would be more difficult to prevent and those who survive would be lost to their unit for longer periods of time.

b. Adversary Objective: Disrupt or Delay Deployment of U.S. and Coalition Forces to the AO

To accomplish this objective, adversaries must meet the challenge of attacking those forces at their mustering locations and causing symptomatic illness prior to deployment. Alternatively, attacks on the first units to arrive within an AO could lead commanders to consider delaying the deployment of healthy follow-on forces or reconfigure the flow of forces to give a higher priority to medical units and supplies. In either case, disruption and delay may not require large numbers of casualties, and hence contagious diseases are less advantageous in this context. Moreover, the window of time available to adversaries to affect deployment schedules is fairly narrow, on the order of days to weeks, and does not allow for multiple generations of infection to achieve the desired impact. Indeed, for this objective, the shorter the incubation period, the better; therefore, diseases with significant morbidity and mortality manifesting quickly—particularly those associated with novel pathogens that cannot be diagnosed or readily identified—would encourage commanders to proceed with an abundance of caution as the health risks to the force from

maintaining a brisk deployment schedule would appear to be high, and the ability to manage those risks would be unknown. As above, the lack of prophylaxis or treatment would exacerbate health risks and decision-making challenges.

c. Adversary Objective: Restrict U.S. and Coalition Forces from Operating in a Specific Area

Completely preventing U.S. forces from operating in specific areas would be difficult to accomplish with improvised biological operations. Area denial is typically accomplished by creating hazards that are more difficult to manage than to avoid. From a CBRN perspective, persistent chemical agents are most often considered in this context, not because they cause casualties, but because they force U.S. forces to operate in burdensome protective equipment and buttoned up within combat vehicles equipped with collective protection. The rapid physiological response to and detectability of persistent chemicals support area denial because the adoption of protective measures requires that the transiting forces be aware of the presence or risk of a hazard. Large-scale BW attacks could have similar effects, by forcing troops within a hazard area to don protective masks and follow procedures to minimize contamination of clothing and equipment. Even so, the hazard associated with BW agents is typically aerosolized and hence transitory. Some pathogens, such as anthrax and Q fever, can persist in the environment for extended periods of time and could therefore pose a re-aerosolization hazard if ground contamination is particularly heavy in areas where U.S. forces are transiting. However, very large quantities of these agents would have to be delivered to accomplish this effect. The crude EID agents associated with improvised biological operations would not, as considered here, be available in sufficient quantities to accomplish this objective, and adversaries with limited quantities of material available are not likely to use them for this purpose.

Adversaries might be more successful in discouraging U.S. forces from operating in a specific area by initiating an outbreak of contagious disease among the local civilian population. Under such circumstances, U.S. forces could minimize risk by adopting strict procedures that limit interaction with civilians in the area. Some contact is nearly inevitable, however, and if the disease in question were highly transmissible, U.S. forces might choose to avoid the area altogether rather than risk exposure. As with the adversary objective of disrupting deployment schedules, diseases that have significant morbidity and mortality would encourage commanders to proceed cautiously.

d. Adversary Objective: Impede U.S. and Coalition Force Maneuverability and Flexibility

Finally, adversaries may seek to use improvised biological operations to disrupt ongoing operations and interfere with the maneuverability and flexibility of friendly

forces. Operations with this objective would maximize the indirect operational impacts associated with efforts to contain and mitigate disease outbreaks. Imposition of isolation, quarantine, and the restriction of movement of personnel between and among U.S. and allied/coalition units, within the AO, and into and out of the AO, could pose serious challenges. Diseases most suited to this objective must, first and foremost, be contagious. In addition, when prophylactic medical countermeasures are not available, disease spread can be disrupted only through procedural controls that physically limit contact between healthy and ill individuals. Finally, as with natural outbreaks, diseases that begin with an extended contagious period of non-specific, mild illness can spread widely in the population at risk before they are recognized to be a concern.

5. Summary

In the absence of relevant examples from the literature, the research team relied on discussions with SMEs, speculation in the popular press, and internal discussions to develop a set of plausible scenarios that could be used to assess the characteristics of concern for EIDs in improvised biological operations and better understand their operational impact. From the wide range of scenarios postulated, the research team developed a framework that could be used for this purpose (Figure 5), focusing on three core scenario elements: means of attack, adversary objectives, and target population. Within this framework, the producibility and employability characteristics of EIDs of concern are derived from the means of attack, effectiveness characteristics are derived from adversary objectives, and impact is determined by the exposure of a target population to a disease with these identified characteristics. The characteristics derived from this framework are summarized in Table 3 and Table 4, while impact is discussed at length in Chapter 5.

Table 3. Producibility and Employability Characteristics of EIDs of Concern for Improvised Biological Operations

	Means of Attack		
	Crude Agent	Animal/Insect Vectors	Human Vectors
Producibility	Stable during transport and storage Easily handled	Broad host range	Contagious
Employability	Stable in the environment Easily dispersed	Survivable in target AO Resistant to controls	Easily transmitted Early contagious, non-specific, mild phase High infection-to-disease ratio

Table 4. Effectiveness Characteristics of EIDs of Concern for Improvised Biological Operations as a Function of Adversary Objective

Characteristic	Adversary Objectives			
	Cause Casualties	Disrupt or Delay Deployment	Area Denial	Restrict Force Maneuverability and Flexibility
Contagious	x		x	x
Short incubation period		x		
Early contagious, non-specific, mild phase	x			x
High morbidity and mortality	x	x	x	x
High infection-to-disease ratio	x	x		
Lack of diagnostic tests	x	x		
Lack of prophylaxis	x	x	x	x
Lack of treatment	x	x	x	x

F. Summary

The EID research concept presented in Chapter 2 identified three possible pathways by which adversaries could affect U.S. military operations and create risk through the use of EIDs: natural outbreaks, weaponization, and improvised biological operations. This chapter has discussed these pathways and the diseases that would be of greatest concern in each case, and as expected found that the characteristics would vary by pathway.

For improvised biological operations, effectiveness characteristics are those associated with the first objective, causing casualties. There are two reasons for using this objective as the basis for selecting effectiveness characteristics: first, because this objective had the largest number of characteristics, this list is somewhat conservative, as fewer diseases would meet them; and second, because the number of casualties is the means by which this paper measures direct operational impact. Nonetheless, it should be noted that other diseases could well generate sufficient, albeit indirect, impacts as adversaries pursue other objectives.

Note that this research made no attempt to assign relative weights to characteristics associated with different adversary pathways. However, one of the objectives of the impact assessment presented in Chapter 5 was to determine whether any of the disease characteristics identified in this chapter tend to be particularly important drivers of impact.

4. Capabilities for Mitigating the Operational Risk from EIDs

The concept underlying this research, presented in Chapter 2, highlights the relationship between time and knowledge as a core aspect of the challenges that EIDs pose for developing effective mitigating capabilities. In this context, mitigating capabilities fall into two categories: situational awareness capabilities, which provide knowledge regarding EIDs and EID outbreaks, and response capabilities, which are triggered by situational awareness and must be developed and implemented in a timely fashion to be effective.

This chapter describes the types and functions of situational awareness and response capabilities, and provides information on current and planned DOD capabilities that could be employed in this context. It also discusses major challenges for the development of mitigating capabilities, as identified through literature review and discussion with SMEs.

A. Mitigating Capability Types and Functions

1. Situational Awareness Capabilities

The process of disease emergence, as considered in this research, is to a great extent a process of acquiring knowledge—eliminating the element of the unknown that is characteristic of emerging diseases and developing an understanding of the disease and its causative pathogen. This knowledge is necessary for determining whether a specific EID poses a health or operational risk to military personnel; whether and what type of medical countermeasures exist or can be developed against it; whether investment should be made in such countermeasures given the costs, risks, and priorities of DOD; and whether actions should be taken proactively—such as immunization—to protect military personnel. Some of the required knowledge can only be gained via happenstance, as the human response to the pathogen and the transmission, symptoms, progression, and resolution of the disease cannot be fully understood absent actual human cases. Some of the required knowledge, however, can be acquired through dedicated efforts, independent of outbreaks of disease, and that available from human cases must be actively collected. *Background awareness* capabilities provide knowledge of emerging pathogens that exist in the environment and are capable of causing disease in humans or animals and where they are located. *Disease characterization* is the process of determining the

epidemiology, phenotype, and composition of a disease-causing pathogen and its subsequent pathogenesis in humans or animals. As a mechanism for collecting information from environmental sampling and human or zoonotic cases of disease, *diagnostic testing and laboratory analysis capabilities* are the important tools supporting disease characterization. Background awareness and disease characterization activities are an ongoing, world-wide effort, collaboratively driven by government agencies, academia, and industry, and collectively hastening the discovery of diseases and understanding of the pathogens involved.

Once an EID outbreak begins within an AO, the acquisition of knowledge is also a prerequisite for implementation of effective response. *Detection* of naturally occurring or adversary-generated outbreaks⁴⁴ must happen before any post-exposure response actions can be taken. While some response measures are broadly applicable to any disease outbreak, others are disease-specific. Diagnostic testing and laboratory analysis capabilities provide specific information on the disease-causing pathogen and support selection of the most appropriate countermeasures.

a. Background Awareness

The objectives of background awareness are to (1) establish a global map of disease, including emerging infectious disease, (2) continuously monitor ongoing disease outbreaks throughout the world, and (3) improve the capability to predict the emergence of new or altered pathogens. Background awareness supports ongoing assessments at the international, national, and DOD levels of the health, economic, security, and operational risks posed by EIDs. From the point of emergence forward, background awareness supports the development of passive defenses and medical countermeasures against identified EIDs. It also serves as the basis for health risk assessments conducted in the planning and execution phases of military deployments.

Background awareness is generated in a broad sense by a number of activities within DOD. The National Center for Medical Intelligence (NCMI) collects and analyzes foreign disease surveillance information from a wide range of sources. The Armed Forces Health Surveillance Branch (AFHSB) of the Defense Health Agency monitors the health

⁴⁴ Response actions can also (and preferably would) be triggered by detection of adversary EID attacks, of whatever level of sophistication. The same systems used to detect traditional aerosolized BW attacks could be used to detect aerosolized attack with a weaponized EID, assuming the EID was recognized as a threat and included in the systems' list of detectable agents. However, assessments of these capabilities exist elsewhere and are generally outside the scope of this research. Improvised biological operations, as described in Chapter 3, are unlikely to have any common, readily detectable or characteristic signature, and detection is likely to be highly dependent on the specifics of the attack. Overall, this research assumes that sentinel cases of disease will provide the earliest indicator of an EID attack, but notes that if an attack were detected, implementation of response actions could commence earlier.

of military and military-associated populations, to include reported cases of infectious disease. The Services maintain a number of forward-deployed laboratories and conduct medical outreach initiatives in many locations throughout the world. At many levels, DOD engages and collaborates with other agencies and organizations, such as the CDC and WHO, that are major contributors to the collective understanding of EIDs. During operational deployments, Service preventive medicine, veterinary, public health, and medical treatment units conduct environmental, animal, vector, and human health surveillance, the outputs of which directly support situational awareness of EIDs in the theater of operations.

b. Disease Characterization

The primary objective of EID characterization is to understand the nature and behavior of disease pathogens such that their impact on human populations can be mitigated. This includes basic research to support development of vaccines and therapeutics, characterization of the clinical manifestations of disease and the development of effective treatment protocols, and identification of natural reservoirs and means of transmission to support decisions on physical control measures.

Characterization of diseases is a multifaceted endeavor, undertaken in research institutes, academia, and industry throughout the world. Although the magnitude of DOD's role in this endeavor overall is relatively small, certain DOD organizations play a unique and critical role in the characterization of the most dangerous pathogens and associated diseases. The U.S. Army Medical Research Institute for Infectious Diseases (USAMRIID) is among the world leaders in basic and applied medical research in Biosafety Level 3 and Level 4 pathogens. Both the Army and the Navy maintain a number of overseas laboratory facilities to support medical countermeasure development, conduct disease surveillance, and provide medical diagnostic capabilities for host-nation civilians.

c. Diagnostic Testing and Laboratory Analysis Capabilities

Diagnostic testing refers to clinical samples taken from humans, while laboratory analysis more broadly includes environmental samples from a variety of sources. These technical capabilities are critical components of ongoing efforts to both detect outbreaks and characterize emerging diseases. The key difference between these capabilities is that, because diagnostic testing is used to inform medical treatment decisions, the associated tests, techniques, and personnel certifications are governed by Food and Drug Administration (FDA) regulations, while laboratory analysis of environmental samples is

not.⁴⁵ In practice, this means that organizational differences often exist between the systems and facilities where these capabilities are embedded and the personnel who use them.

At present there are four fundamentally different ways to identify EIDs through technical testing and analysis: (1) traditional phenotyping/serological methods, such as cell culturing, staining, serology, and urinalysis; (2) immunoassays, a presumptive diagnostic technique⁴⁶ based on the reactivity of known and pathogen-specific antigens; (3) polymerase chain reaction (PCR) assays, a more sophisticated and more broadly applicable presumptive diagnostic technique involving amplification of pathogen DNA; and (4) next-generation sequencing (NGS) techniques. These capabilities exist in varying systems and at varying levels of sophistication throughout deployed military medical and non-medical forces and within fixed medical and laboratory facilities.

d. Outbreak Detection

Detection of disease outbreaks typically begins with the recognition of an anomalous rise in the number of cases of disease, or cases of disease with an unusual presentation of symptoms, by comparison with an established baseline. This initial awareness would be followed by identification of the disease-causing pathogen and investigation into the source of the outbreak, in order to estimate its potential scope and to implement the most appropriate outbreak response measures.

Opportunities for detection of outbreaks within these varied populations depends on the individuals and organizations responsible for monitoring them. Detection may occur at the tactical or local level, by medical personnel directly observing clustered cases of illness, or at higher levels by organizations, such as NCMI and AFHSB, able to correlate disease reports from a variety of sources across the AO.

2. Response Capabilities

EID response capabilities are measures taken to prevent or control disease outbreaks and to limit their impact on operations. Some measures can be implemented proactively to minimize the susceptibility of personnel, by strengthening the general health and immune systems of military personnel, by *enhancing immunity* to specific pathogens through vaccination or pre-exposure prophylaxis, and by minimizing the opportunities for

⁴⁵ For the Services, this means adherence to the Clinical Laboratory Improvement Program (CLIP). CLIP is a modification of Clinical Laboratory Improvement Amendments (CLIA) for the Services, which aims to regulate the environment in which clinical samples are collected and processed.

⁴⁶ The term *presumptive diagnostics* refers to the requirement that prior knowledge of the pathogen is needed to develop assays that are specific to that pathogen. Presumptive diagnostics are contrasted by *de novo* techniques, which do not require prior knowledge for pathogen identification.

infection through public health and hygiene practices. Additional measures would be implemented after an attack or following the start of an outbreak. These measures are of two general types: *physical controls* that prevent exposure of personnel through area avoidance, movement controls, and barrier precautions for infection control; and *medical controls* that prevent manifestation of illness in exposed personnel, limit the course and severity of illness, and prevent death through prophylaxis and treatment.

a. Enhancing Immunity

The objectives of DOD efforts to enhance immunity against infectious disease are to provide military personnel with protection from infectious disease, to avoid disease-related reductions in force readiness, and to minimize risk to operational objectives. The primary programmatic means of accomplishing this is through the development, procurement, and administration of vaccines, as available and as judged appropriate based on strategic and deployment-specific health risk assessments.

Vaccine development is a long and expensive process, heavily regulated in the United States by the FDA.⁴⁷ Not all vaccine development programs are successful, but for those that are, it can take 10–15 years for a vaccine to go from basic research through FDA approval. Because of the time and cost involved, the pharmaceutical industry may be reluctant to pursue vaccines for diseases like anthrax that are serious threats in weaponized form but do not pose a general risk to public health. Consequently, DOD maintains vaccine research, development, testing, and evaluation programs for diseases of military concern that are not generally acquired from other sources, including those caused by BW agents and those that have historically proven difficult to manage in military operations, such as yellow fever and malaria. USAMRIID is the locus of these efforts within DOD.

b. Physical Outbreak Control Measures

Physical outbreak control measures are procedural in nature, intended to limit contact between healthy individuals and those who are ill, thus preventing exposure and spread of contagious disease. Equipment and procedures for standard infection control and more stringent barrier precautions are well-established methods for preventing the spread of disease within MTFs.⁴⁸ In addition, ROM is a major means of outbreak control, and includes isolation of infectious personnel, quarantine of personnel suspected of being

⁴⁷ “Guidance for Industry: General Principles for the Development of Vaccines to Protect Against Global Infectious Diseases,” FDA-2011-D-0855, U.S. Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research, December 2011.

⁴⁸ Although these procedures are well-established, personnel must be regularly trained to use them effectively. Personnel must also be provided with the necessary personal protective equipment and trained to use it safely.

exposed to disease, and limitations on the movement of personnel into and out of military facilities.

Roles and responsibilities for public health emergency management within DOD are delineated in Department of Defense Instruction 6200.03.⁴⁹ This instruction assigns the ASD/HA responsibility for developing policy and guidance for quarantine and isolation within DOD. Military commanders have the authority to establish ROMs for all types for military personnel on installations and in operating areas within their control, in coordination with local, state, and federal agencies for installations within the United States, and in coordination with host nation governments overseas.

c. Medical Outbreak Control Measures

The objectives of medical outbreak control measures are the same as those of enhanced immunity: protecting personnel from infectious disease and minimizing risk to operational objectives. Antibiotics and antiviral drugs can be administered to personnel at risk of infection or already manifesting illness; unlike vaccines, many of these drugs are effective against multiple pathogens to a greater or lesser degree. The primary role of DOD is to determine which drugs are most effective against diseases of particular interest, and subsequently to conduct the research and development necessary to achieve FDA approval for use of those drugs as either post-exposure prophylaxis or therapeutics in an operational setting.⁵⁰ Much of this work is being conducted by the Joint Science and Technology Office-Chemical and Biological Defense (JSTO-CBD), together with a number of industry partners.

The rapid pace of antibiotic resistance has led to a critical need for novel antibiotics. Unfortunately, the pace of antibiotic discovery has slowed significantly in recent decades, and the infrastructure and financial incentives no longer exist to support industry investment in programs with such high levels of technical risk.⁵¹ The potential for medical countermeasures to become increasingly ineffective against BW agents has garnered attention to this problem within DOD and fostered both basic research and procurement initiatives. For example, the Joint Program Executive Office-Chemical and Biological Defense (JPEO-CBD) recently established a Countermeasures for Multi-Drug

⁴⁹ Department of Defense Instruction 6200.03, *Public Health Emergency Management within the Department of Defense*, March 5, 2010, incorporating changes effective October 2, 2013.

⁵⁰ JRO-CBRND, "Modernization Plan for Chemical, Biological, Radiological, and Nuclear (CBRN) Defense," January 2012.

⁵¹ Anthony R. M. Coates, Gerry Halls, and Yanmin Hu, "Novel Classes of Antibiotics or More of the Same?" *British Journal of Pharmacology* 163 (2011).

Resistance-Bacterial Medical Countermeasures Acquisition Program to identify and procure therapeutics for drug-resistant BW agents.⁵²

B. Planned Mitigating Capabilities

As noted above, the threat from EIDs has received growing attention within DOD, with organizational roles and responsibilities for developing mitigating capabilities evolving. One advantage of ongoing cooperation between ASD/HA and the CBDP is that it leverages the commonalities in mitigating the effects of traditional infectious disease, EID, and BW agents. Thus, many of the capabilities currently available or in development for providing situational awareness of and response to traditional infectious disease and BW agents are applicable to the EID problem as well. Capabilities of this type that exist or are being developed within DOD are discussed in the sections that follow, with particular attention given to the amount of disease-specific knowledge that would be required to trigger their use in an EID scenario.

Other capabilities, such as vaccines, are disease-specific. While these capabilities in and of themselves may not be directly applicable to EIDs of the future, understanding the process for developing them—with the associated timelines, technical challenges, and information requirements—can indicate what response capabilities are likely to be available should an EID outbreak occur within an AO. In addition, for those diseases that are considered “emerging” because they appear in new locations, or those that are a variant of well-characterized diseases, these capabilities may be directly applicable, albeit less effective,⁵³ and they may not be readily available when needed.

1. Situational Awareness Capabilities

The NCMI is tasked with continuously monitoring foreign health threats, both prior to and during operations. DOD also uses publicly available information from resources such as the CDC, WHO, Médecins Sans Frontières (MSF), and the Gates Foundation to monitor outbreaks of disease worldwide. In addition, DOD is developing a BSV concept and infrastructure, with the objective of providing consolidated, accessible disease and

⁵² DOD CBDP, “2014 Department of Defense Chemical and Biological Defense Annual Report to Congress,” March 2014.

⁵³ For example, in the United States in the winter of 2014–2015, the seasonal influenza vaccine was well matched to the dominant strain of circulating virus (influenza A (H3N2)). Normally in these circumstances, observed vaccine efficacy is high. However, in this period, the opposite was the case: the CDC estimated an overall vaccine effectiveness of 23 percent, a relatively low value that the CDC attributed to antigenic and genetic drift—in other words, a variant of the disease that the vaccine was designed to prevent. Nonetheless, the CDC continued to recommend vaccination because it prevented a still-significant number of cases and reduced the severity of illness in others. See Brendan Flannery et al., “Early Estimates of Seasonal Influenza Vaccine Effectiveness – United States, January 2015,” *Morbidity and Mortality Weekly Report* 64, no. 1 (January 16, 2015).

pathogen surveillance databases, with the planned capability to cross information domains (Internet/NIPR/SIPR/JWICS) when appropriate.

Table 5 lists major current and planned DOD programs and initiatives supporting situational awareness of EIDs.

Table 5. Selected Programs and Initiatives Supporting EID Situational Awareness

	Current	Future
Concept	“Comprehensive Health Surveillance” Case reporting supplemented by occupational and environmental surveillance, medical intelligence, collaboration with other federal agencies and international organizations, open-source information	“Biosurveillance” - All sources, all hazards - Unified, integrated datasets
Information management	GEIS, ESSENCE, GEMS, DRSi	BSV Ecosystem, Global BSV Portal, Constellation
Laboratory capabilities	Analytical Laboratory System (ALS) Joint Biological Agent Identification and Detection System (JBAIDS)	Common Analytical Laboratory System (CALS) Next Generation Diagnostic System (NGDS)
Supporting technology	Traditional laboratory techniques, immunoassays, PCR assays, next-generation sequencing	Current + more capable and further forward next-generation sequencing

2. Response Capabilities

In addition to actively funding vaccine development, DOD has established the Medical Countermeasures Advanced Development and Manufacturing (ADM) program with the goal of rapidly developing and producing medical countermeasures for potential CBRN threats, including EIDs.⁵⁴ A center was selected in 2013 to support the goal of this program.⁵⁵

⁵⁴ Medical Countermeasures ADM, Joint Program Executive Office for Chemical and Biological Defense, <http://www.jpeocbd.osd.mil/packs/Default.aspx?pg=300>, accessed February 13, 2015.

⁵⁵ Medical Countermeasures Advanced Development and Manufacturing (MCM ADM) Capability, https://www.fbo.gov/?s=opportunity&mode=form&id=f9b23a6ce17386b96b40d969a2ee827d&tab=cor e&_cview=1, accessed February 4, 2015; DOD CDBP, “2014 Department of Defense Chemical and Biological Defense Annual Report to Congress.”

The ADM contract will provide DOD with centralized manufacturing and testing, regulatory, and FDA non-clinical and clinical trial support for the ADM of medical countermeasures against traditional CBRN threats and EIDs.⁵⁶ The new ADM center is still in development; therefore, the reduction in manufacturing time for producing campaign quantities of a vaccine to protect military personnel from an EID is unknown. The Department of Health and Human Services (HHS) has a similar program to improve the manufacturing turn-around time of vaccines with a focus on public-health-related diseases.⁵⁷

⁵⁶ T. Belski, “Overview of the Department of Defense’s Vision for the Advanced Development and Manufacturing (ADM) Capabilities,” presentation to the Chemical and Biological Defense Acquisitions, Initiative Forum, September 9, 2014.

⁵⁷ US Department of Health and Human Services (HHS), “HHS Creates New Centers to Develop, Manufacture Medical Countermeasures,” HHS News Division, June 18, 2012.

5. Assessment of EID Operational Impact

This research was motivated by concerns within DOD that EIDs have the potential to harm U.S. military forces and prevent the accomplishment of mission objectives. One of the research team's primary objectives, therefore, was to determine whether the nature and potential magnitude of operational impact from EIDs is sufficient to generate operational risk. If so, the team was to further describe operational impact in terms that support the selection, development, and application of mitigating capabilities.

EIDs can directly affect operations by generating casualties among military forces and reducing unit combat power. Increased numbers of casualties of any type will indirectly affect operations by generating requirements for individual or unit replacement and by increasing the burden on the military medical system, leading to reprioritization and reallocation of transportation assets and supplies needed to manage those casualties. In addition, for infectious disease casualties, many of the measures taken to prevent casualties and mitigate direct impacts can themselves have indirect impact. The use of post-exposure prophylaxis, for example, requires logistics support and can cause adverse health effects in some portion of the population. Even the implementation of unusual personal hygiene or social distancing measures can be time-consuming and distracting. For contagious diseases, the potential for indirect operational impact is even greater still. Outbreak control measures such as area avoidance, ROM between units, isolation of infected personnel, and quarantine of potentially exposed personnel may significantly reduce force maneuverability and flexibility. Contagious disease outbreaks can originate among or extend to host nation civilians as well, reducing host nation support capability. Finally, contagious disease outbreaks can exacerbate political, economic, and social disruption in a host nation, broadly increasing the difficulty of conducting military operations.

This chapter assesses the direct impact of EIDs by estimating the number of casualties expected in a set of notional scenarios, with and without the implementation of various outbreak response measures at various points in time. It also assesses the indirect impact of response measures where possible, albeit in a more qualitative manner. For example, the research team investigated the degree to which movement between units must be restricted to be effective; that was in turn compared to typical movement patterns to provide a sense of the extent of disruption of normal operations. Other possible response activities, such as the use of unusual personal hygiene measures, would be highly dependent on the specific characteristics of diseases that are currently unknown.

Because the nature of such measures is also unknown, this research made no attempt to evaluate either their potential benefits or their potential impact.

The research team found a number of knowledge gaps that had significant implications for its approach to assessing EID impact. First, as often noted, the characteristics of future EIDs are unknown, and indeed it is this element of the unknown that is the defining characteristic of emerging vs. traditional infectious disease. This lack of knowledge extends to many factors that would influence operational impact, such as the behavior of any potential EID within an infected individual and within a population, the effectiveness of available medical countermeasures, and the feasibility of developing targeted vaccines or therapies. To provide a more concrete basis for the conduct of analysis, the team derived the disease-related inputs to the impact assessment from known diseases that are either in the process of emerging, such as SARS, or that would be considered emerging if they appeared in a population, such as smallpox. In addition, rather than evaluating the effectiveness of response capabilities against an unknown disease, the research team defined response effectiveness parametrically. This alleviated some of the analytical challenges posed by the lack of knowledge about EIDs and at the same time, led to an enhanced general understanding of how effective response capabilities need to be to mitigate operational impact.

Second, the research team could not fully establish the nature and timeliness of the information that current situational awareness capabilities would make available during an EID outbreak. Moreover, as discussed in Chapter 3, the literature review conducted during this research found that, historically, outbreak detection, pathogen identification, and disease characterization generally have not followed a predictable, consistent process. Yet the availability of information during a disease outbreak—especially information supporting detection of the outbreak, identification of the associated pathogen, and understanding of the potential behavior of disease within a population—is critically important to making decisions and implementing responses in a timely manner. Consequently, the research team considered response implementation times parametrically, and assumed that the required information would be available within those time parameters.

Third, the factors that affect the propagation and cessation of disease outbreaks within a population are not fully understood, which made it difficult to assess the progression of disease outbreaks and the extent to which various response measures might influence disease transmission.⁵⁸ The research team used a model of contagious

⁵⁸ Note that this problem is not unique to this research, but was observed during the Ebola outbreak as efforts to use modeling and analysis to predict the course of the outbreak were generally unsuccessful and occasionally misleading. See Declan Butler, “Models Overestimate Ebola Cases,” *Nature* 515 (November 2014): 18.

disease dynamics that incorporates disease transmission rates derived from historical outbreak data and is heavily influenced by prevailing epidemiological circumstances. These epidemiological circumstances, though, are essentially “black boxes” that encompass all factors that influenced disease transmission at the population level in the modeled outbreak, without requiring that these factors be defined or measured. While convenient, the results of this model can be of limited applicability for scenarios that deviate from historical outbreaks. This is particularly true in the later stages of a modeled outbreak, as over time epidemiological circumstances would include both overt outbreak control measures and subtler adaptive behaviors on the part of the affected population. Therefore, the research team’s confidence in the assessment results is highest early in the modeled disease outbreaks.

A. Approach

1. Measures of Operational Impact

This research used two primary measures of operational impact:

- Time to reach combat ineffectiveness. For the purposes of this research, combat ineffectiveness was assumed to occur when casualties reached 20 percent of the population at risk (PAR).
- Time until a disease outbreak reaches a specified unit, location, or sub-population.

The effectiveness of response capabilities was measured by:

- Casualties avoided by the response;
- Delay in the time to reach combat ineffectiveness; and
- Delay in the time until a disease outbreak reaches a specified unit, location, or sub-population.

Although EIDs directly affect military operations through the generation of casualties, the research did not use total numbers of casualties as a primary measure. In general, without intervention, the modeled disease outbreaks eventually affected all personnel within the PAR, for a casualty rate of 100 percent. It also generally took hundreds of days for this to happen. These results are highly unrealistic—interventions of some type are likely, unit rotation policies limit the length of time personnel are deployed, and outbreaks do, eventually, die out on their own due to factors that are not well understood and are not captured in the model. Consequently, the team felt that for the purposes of the research, total casualties was not useful as a measure of impact.

This research used a 20 percent casualty rate to define combat ineffectiveness; this value was chosen to be consistent with other IDA advanced threat research that uses the

same value. The time to reach combat ineffectiveness was measured in days, and for the entire PAR. Although individual units or sub-populations could experience much higher casualty rates, or reach their own state of combat ineffectiveness at earlier times, the impact on individual units was not described in the outputs.

At the same time, the research team did consider that even when combat ineffectiveness could not be avoided for the population as a whole, commanders may choose to protect specific high-value units long enough for them to execute their missions. For this reason, the time until an outbreak reached a specific unit was a measure of interest.

2. Enhanced IDA Model of Contagious Disease Dynamics

This research evaluated the operational impact from EIDs using an enhanced IDA model of contagious disease dynamics. This model was originally developed in 1999 by Dr. John Bombardt to support the U.S. Army Office of the Surgeon General in its efforts to develop a standardized means of estimating biological agent casualties across NATO.⁵⁹ Evolving instantiations of the model are regularly used at IDA to estimate contagious disease casualties. Appendix A provides more detailed information on the evolution of the Bombardt model, its underlying methodology, recent revisions, and current capabilities.

The choice of this specific model for assessing impact implies an assumption that EIDs of greatest concern will be contagious. As discussed in Chapter 4, natural outbreaks and improvised biological operations will generate small numbers of initial infections. Without the multiplicative effects of contagion, these adversary pathways are not likely to generate casualty rates sufficient to cause combat ineffectiveness in an operationally relevant timeframe. By contrast, adversaries capable of weaponizing EIDs are also assumed capable of delivering those weapons in a manner that exposes a large percentage of the population at risk and results in combat ineffectiveness via initial infections alone. In such cases, the marginal contribution of the effects of contagion on operational impact would be of less significance. Even so, the contagious disease model is used in this research to represent the effects of a large-scale BW attack, in order to allow consistent comparison with the other two pathways.

⁵⁹ John N. Bombardt, Jr., *Contagious Disease Dynamics for Biological Warfare and Bioterrorism Casualty Assessments*, IDA Paper P-3488 (Alexandria, VA: Institute for Defense Analyses, February 2000). The model described in IDA P-3488 and subsequent IDA papers was used in the development of NATO STANAG 2476, *AMedP-8(B): Medical Planning Guide of NBC Battle Casualties (Biological)* (2005), and NATO STANAG 2553, *AMedP-8(C): NATO Planning Guide for the Estimation of CBRN Casualties* (2011).

a. Basic Methodology

The contagious disease model used in this analysis begins with a traditional Susceptible, Exposed, Infected, and Removed (SEIR) epidemic modeling approach, in which each individual within the population at risk is assigned to one of these cohorts in each time period, and moves from one cohort to another as the outbreak progresses. The SEIR model is then combined with a time-varying disease transmission rate based on historical outbreak data for specific diseases of interest. Currently, the model allows IDA to estimate casualties for four contagious diseases: smallpox, plague, 1918 influenza, and SARS.⁶⁰ All of these disease models share a common methodological flow, shown in Figure 6.

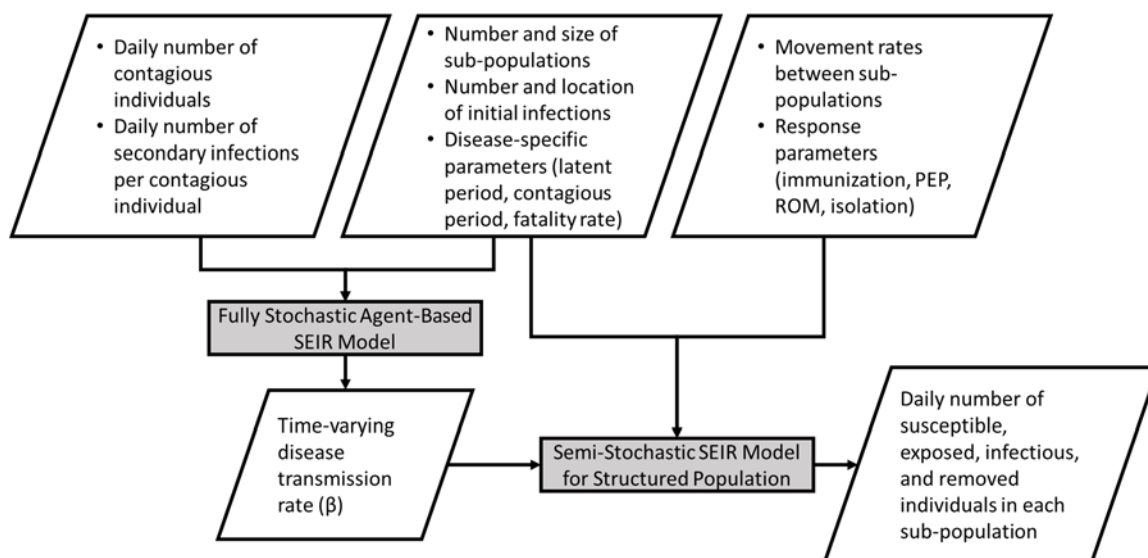


Figure 6. Basic Contagious Disease Model

The methodology begins with the collection and assessment of data from a historical outbreak of a contagious disease and information on the characteristics of that disease. The historical outbreak would ideally serve as a basis for the following model input parameters: the daily number of contagious individuals and the daily number of secondary infections per contagious individual. The historical outbreak data are then combined with other disease-specific parameters (the duration of the latent period, the duration of the contagious period, and the case fatality rate) as well as parameters that describe the population to be modeled (the number and size of sub-populations and the number and locations of initial infections). All of the aforementioned parameters serve as

⁶⁰ The 1999 proof-of-concept model was based on an outbreak of Ebola in Kikwit, Zaire. The IDA research team believes that to generate reasonable estimates of Ebola casualties, the parameter values used in this model need to be updated to reflect the behavior of the disease in the much larger 2014 outbreak of Ebola in West Africa.

inputs to a fully stochastic agent-based SEIR model that is used to calculate the time-varying disease transmission rate, β .

In the fully stochastic, agent-based SEIR model, every aspect of the disease progression within each individual and the propagation of the disease through the population is modeled as a random event. In other words, the latent period, contagious period, and the number of new infections caused by each infected individual are determined by random draws from probability distributions that were derived from the aforementioned input parameters. Results from the fully stochastic agent-based SEIR model are used to then generate a time-varying disease transmission rate for each population and number of initial infections for use in the analytic scenario.

Once the time-varying disease transmission rates are known for each of the sub-populations in the scenario, the semi-stochastic SEIR model for structured populations can be run in order to model the spread of the disease across spatially or organizationally separated sub-populations, as well as the mitigating effects of implementing various response measures. In addition to the time-varying disease transmission rates, the semi-stochastic SEIR model for structured populations also requires an analytic representation of the movement between sub-populations as well as an analytic representation of response measures to be modeled (e.g., the efficacy of post-exposure prophylaxis and the day on which it is implemented). The results of the semi-stochastic SEIR model for structured populations are the daily number of individuals in each cohort (susceptible, exposed, infectious, and removed) in each sub-population.

b. Structure and Movement

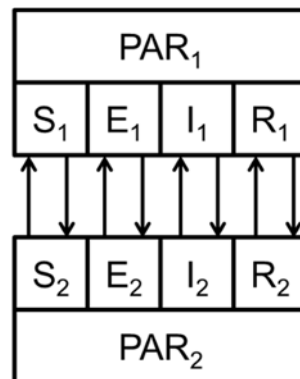
A typical contagious disease model considers a single PAR, where interactions and mixing are assumed to be homogenous. Military populations, however, are highly structured, and the patterns of movement between units are different from those within them. Restricting movement between subsets of a population is one of the means by which the spread of disease can be curtailed. For the purposes of this research, a contagious disease model that allows for the consideration of structure and movement within the population was used.

In lieu of a single PAR, the model subdivides the population into multiple sub-PARs, each of which can be thought of as a military unit, organizationally and/or geographically distinct from others. Each of these sub-PARs is assumed to be evenly mixed, and outbreaks of disease are evaluated separately for each sub-PAR.

The rate at which the disease spreads within a sub-PAR is determined by a set of β values calculated for that specific sub-PAR.⁶¹ Outputs are then summed over all sub-PARs for the population as a whole. This division of the population into sub-PARs is the way in which the model now represents *structure*.

Movement in the model is now represented by the removal of an integer number of individuals from one cohort in one sub-PAR, and insertion of those individuals into the same cohort in another sub-PAR. Movement between sub-PARs can be defined in terms of rates or absolute numbers of individuals. These individuals are randomly selected from within a sub-PAR and can be from any cohort; the probability that an individual will be pulled from a given cohort at any given time is determined by the proportional representation of that cohort within the sub-PAR at that time.

Figure 7 provides a notional representation of population structure and movement as now considered for military populations. Each of the two large rectangles represents an evenly mixed sub-PAR, while the arrows represent the specified movement between the two sub-PARs. As suggested by Figure 7, this model allows individuals from any of the four cohorts (S, E, I, or R) to move from one sub-PAR to another, with the exception of those who died due to their infection (i.e., fatalities).



Note: The cohorts are designated as S (susceptible to infection), E (exposed but non-contagious), I (infectious/contagious), and R (removed as source of infection).

Figure 7. Notional Depiction of Population Structure and Movement

⁶¹ The methodology used to calculate the β values for any population assumes that the infection is introduced into the population at a single point in time (day zero) in the form of a number of initial infections, all of whom are on the first day of their latent period. However, each sub-PAR in the SEIR model will experience the arrival and departure of members of both the E and I cohorts on days following the start of the outbreak. These arrivals and departures are not accounted for in the methodology used to calculate the β values, and it is not clear how this inconsistency will affect the results of the model. Additional development of the model, namely the manner in which the β values are calculated, and employed, would be necessary in order to fill this knowledge gap.

3. Notional Force Arrays

To measure operational impact and the effectiveness of different responses, the research team needed to develop an analytic representation of a military PAR that could be used with the enhanced IDA model. Ideally, this representation would be based on real-world data, would be amenable to division into organizationally and/or geographically distinct sub-PARs, and would provide information on the daily movements of individuals from one sub-PAR to another.

For this research, the IDA team used data on the location of U.S. military personnel deployed in Afghanistan during calendar year 2012.⁶² This dataset, acquired from the U.S. Army Training and Doctrine Command (TRADOC), was gathered via SPOT-JAMMS (Synchronized Predeployment and Operational Tracker—Joint Asset Movement Management System). SPOT-JAMMS captures location information for U.S. military personnel, government civilians, and contractors at data collection points established in operational theaters; these data collection points are typically the locations where personnel swipe identification cards to gain access to specific facilities, such as a dining hall. SPOT-JAMMS used the identification card swipes to record the daily location of each individual Service member while he or she was deployed in Afghanistan.

TRADOC provided IDA with SPOT-JAMMS data in the form of twelve separate Excel spreadsheets, one for each calendar month in 2012. Each spreadsheet provides unique individual swipes—one per person per day—for each of the 28 most populous locations in theater during that month. Movement among these locations could be derived from these data by tracking changes to the swiping locations of individual Service members.

Although the data obtained from SPOT-JAMMS provide a detailed account of personnel locations and movements, they do have several limitations. First, while SPOT-JAMMS avoids double-counting of individuals by reporting only one swipe per person per day, the rules by which a swipe is selected for reporting are unclear (e.g., first swipe of the day, last swipe of the day, or some other swipe). Consequently, a significant amount of individual movement could be unreported in the dataset.

Second, the location names used in the dataset were often vague and ambiguous. Some of the locations were part of the same larger installation, for example dining facilities on an airbase. The IDA team made an effort to identify all such colocated data collection points. Some were found simply by the name used in the dataset but some required a review of open-source literature. In some cases, location names were too

⁶² These data were originally acquired under the auspices of IDA task CA-6-3079 with the assistance of the U.S. Army Office of the Surgeon General. See Julia K. Burr et al., *The Application of Contagious Disease Epidemiological Models to Known Population Structure and Movement*, IDA Document D-5225 (Alexandria, VA: Institute for Defense Analyses, March 2016).

ambiguous, and associating the name with an actual facility proved impossible. All locations that could not be associated with a larger facility were assumed to be independent.⁶³

Finally, and most importantly, the SPOT-JAMMS dataset that IDA acquired is incomplete. SPOT-JAMMS data collection points were not present at all troop locations in theater in 2012; therefore, the actual percentage of deployed personnel locations captured by the system on a daily basis is unknown. Moreover, although the data provided included personnel locations for the entire year, only about a third of all locations gathered by SPOT-JAMMS—the 28 most populous—were included for each month. In addition, the locations included in each month’s dataset varied from month to month. Due to the incompleteness of the dataset, IDA was able to determine the total number of people present at only some of the locations for each day. Finally, the only personnel movements that IDA could track were those between the 28 most populous SPOT-JAMMS collection locations. Movements to other locations—including many that collected SPOT-JAMMS data and all that did not—are not captured in the dataset.

Even with these limitations, IDA was able to derive a notional representation of a military population from the SPOT-JAMMS dataset by identifying all unique locations named over the 12-month reporting period, and then collapsing those that were included in the same installation (e.g., “Camp Leatherneck #1” and “Camp Leatherneck #2”) into a single location; this resulted in a total of 27 separate locations. These locations were culled further by eliminating any location that could not be linked by movement patterns to others in the dataset.⁶⁴ Figure 8 shows the resulting representation of structure and movement, including 13 locations that could be linked, based on movement rates and patterns, into a networked force array.⁶⁵ Each rectangle in the figure represents a location, with its average daily population shown numerically; the total population across all locations is 27,800 personnel. The arrows and numbers between the rectangles represent

⁶³ “RSOI” was among the more ambiguous locations identified in the SPOT-JAMMS dataset. The term “RSOI” refers to the Reception, Staging, Onward-movement, and Integration process by which military units enter an AO and move to their assigned positions; it is not typically used to refer to a fixed location. However, although the SPOT-JAMMS dataset does not contain geographic coordinates, each swipe location has a unique identifier, one of which is “RSOI.” As discussed below, since the representation of structure and movement in a military population used in this research is notional and used for analytic purposes, the IDA team felt comfortable including RSOI as a node within the network of locations between which personnel moved.

⁶⁴ In other words, there were some locations where, no personnel movements were recorded to other locations in the dataset; all movements were to unidentified locations. Because these locations would be completely isolated from disease within the model, they would have no impact on the outcome; consequently, the IDA team excluded them from consideration.

⁶⁵ Although based on recorded movements of deployed military personnel, because of the significant limitations of the available SPOT-JAMMS dataset, in no way should this representation be construed as a complete or realistic depiction of U.S. forces deployed in Afghanistan in 2012.

the movement between the locations and the number of people moving each day.⁶⁶ In order to ensure that the population of each location was constant during the modeled outbreak, it was assumed that the daily number of people departing any location was exactly equal to the daily number of people arriving at the same location. Furthermore, it was assumed that these movement rates were constant during the course of the outbreak unless ROM was explicitly modeled. For simplicity, the IDA team excluded movement between locations of fewer than 10 people per day.

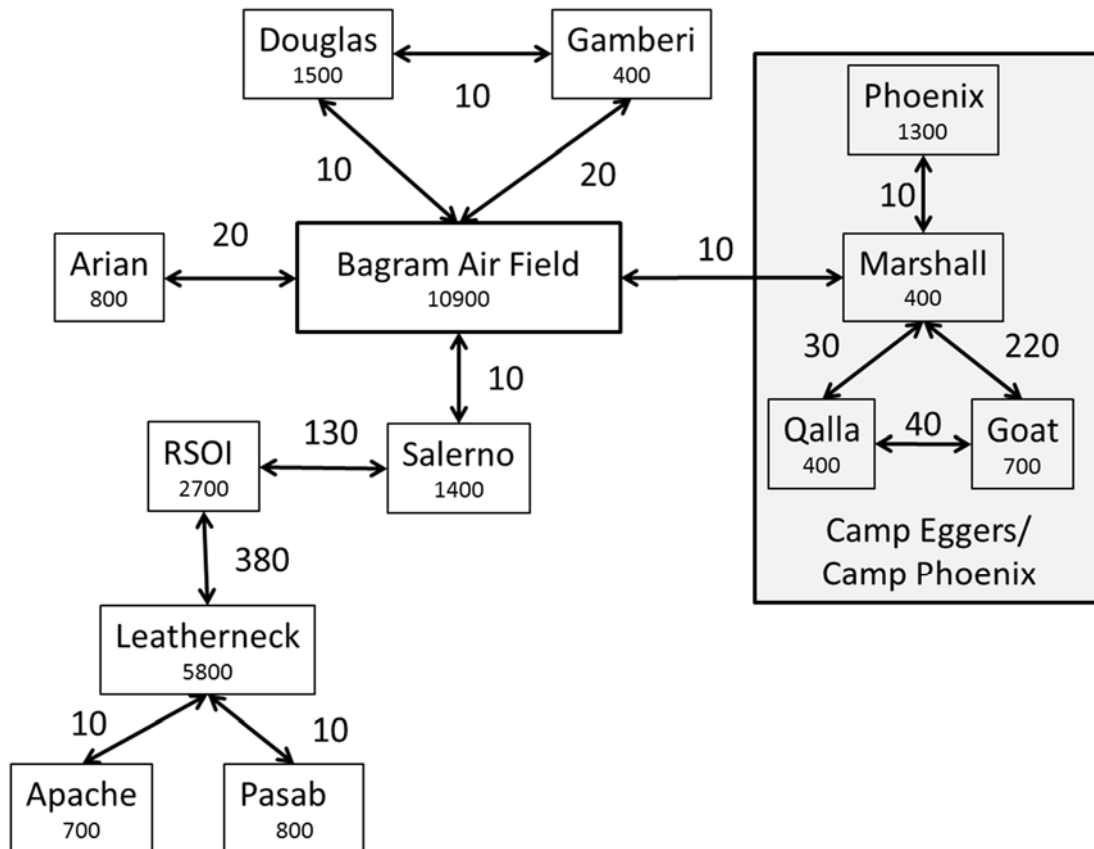


Figure 8. Analytic Representation of a Military Population Derived from SPOT-JAMMS Data

As the research progressed, it became clear that using a force array of this complexity for the entire assessment was not practical within the research timeframe. Given that the model selects individuals randomly from different cohorts for movement from one location to another, the more locations considered, the longer the model run

⁶⁶ In reality the number of individuals present on a day at any one location will change with time. For the purpose of the present analysis, it was assumed that the population at each location is constant over the duration of the outbreak. To achieve constant populations, the number of people leaving one location for another is equal to the number of people returning to the location as shown with the double sided arrows in Figure 8.

time. Additionally, the stochastic nature of the model required that numerous trials be conducted to establish confidence in the resulting outputs.

Based on considerations, the research team chose to use a subset of the force array for the bulk of the assessment, whenever the measure of interest permitted. The major exception was the time it takes for an outbreak to reach a given unit, as the team felt this could be quite sensitive to the number of units in the array and the degree of separation between the unit of interest and the unit in which the outbreak started. For this particular measure, the assessment considered both the force array in its entirety and a subset.

The portion selected for use in the research is the outlined and shaded Camp Eggers/Camp Phoenix area shown in Figure 8 and reproduced in generic form in Figure 9. This area comprises four separate units with a total population of 2800—approximately the size of a modern Brigade Combat Team—with an average of 280 people moving each day.⁶⁷ The research team chose this subset of units because, collectively, they were relatively isolated, and linked to the main body of the array by a small number of individuals moving between Marshall and Bagram Air Field. In addition, there was a range of unit population sizes and a range of daily movement rates between them. Finally, the pattern of movement between units was simple—which would facilitate interpretation of results—but not trivial. Because disease outbreaks can follow multiple paths to reach a given unit, this array could be used to assess the sensitivity of model results to unit population sizes and movement rates. In the end, this feature of the smaller array proved to be an advantage over the bigger, more complex array.

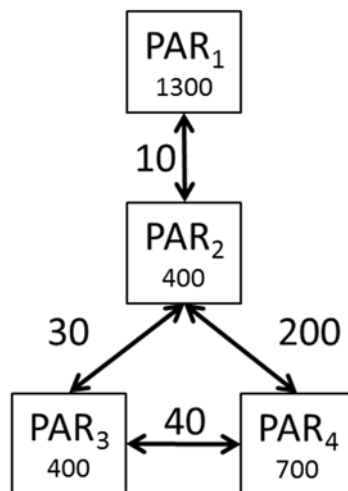


Figure 9. Notional Force Array with Four Sub-PARs

⁶⁷ For purposes of analysis, the research team modified the movement between PAR₂ and PAR₄ from 220, observed in the SPOT-JAMMS dataset, to 200. This resulted in a constant movement rate of 10 percent of the population, a more convenient value for assessing sensitivity of results to movement rates and patterns.

Although the basic structure, unit populations, and movement rates and patterns are derived from real-world troop location data for U.S. forces in Afghanistan, in the notional form shown in Figure 9 this force array can represent a variety of potential scenarios—a civilian population interacting with military units, an air or sea port of disembarkation from which forces move to interior deployment locations, a main operating base and forward units, etc. This flexibility allowed IDA to consider various contexts and objectives when evaluating the effectiveness of a given type of response. For example, if PAR₁ in the notional array represents a host nation population in which a natural EID outbreak is occurring, from an operational perspective, the primary objective of the response could be to prevent the outbreak from reaching PAR₂, PAR₃, and PAR₄, with the objective of preventing casualties within PAR₁ a secondary objective. Conversely, if PAR₁ represents the main route of entry into an operational theater, the primary objective could be to limit the impact on PAR₁ so as to not disrupt the flow of incoming forces.

4. Additional Model Inputs

The three basic adversary pathways discussed in Chapter 3 are represented in the contagious disease model very simply as 1, 10, and 100 initial infections.⁶⁸ At the lower end of the spectrum, naturally occurring outbreaks of contagious disease, with no adversary intent, can often be traced to a single index case. Hence in this assessment, natural outbreaks were represented as one initial infection. Improvised biological attacks—small-scale, rudimentary attacks and exploitation of natural outbreaks—are considered to be of a type that would generate small numbers of initial infections, perhaps ranging from five to 20. For this research, improvised biological operations were represented by 10 initial infections. Finally, at the other extreme, attacks with weaponized EIDs were represented as 100 initial infections. Traditional aerosol attacks with BW agents are certainly capable of covering large geographic areas and exposing thousands of individuals, rapidly leading to combat ineffectiveness. In the smaller force array (Figure 9) used as a baseline, combat ineffectiveness would be automatically reached if a weaponized EID attack generated 520 infections, whether or not the agent was contagious. The research team's primary objective in selecting a number of initial infections to represent weaponized EID threats—in this model assumed to be contagious—was to generate impacts similar to those observed with larger non-contagious aerosol attacks. At the same time, the team wanted to both minimize the model's run time and generate results that could be meaningfully compared to the two other cases.

⁶⁸ The model assumes that the initial infections occur both simultaneously and at the same location. This study did not investigate scenarios in which infections were introduced to the population at various points in time or in multiple locations.

As described in Appendix A, different versions of the IDA contagious disease model have been developed over time, each focused on a specific disease. The model development effort conducted as part of this research consolidated the features of these different versions into a single model, which now provides the capability to consider any of four different diseases: smallpox, plague, the 1918 variant of influenza, and SARS. Key parameters used to characterize these diseases within the model include:

- Incubation period, or time spent in the E cohort, typically represented as a distribution;
- Contagious period, or time spent in the I cohort, typically represented as a distribution; and
- Case fatality rate, or percent of individuals who are removed from the I cohort because of death.

Within the model, these parameters are combined with historical outbreak data to derive disease- and outbreak-specific time-varying disease transmission rates. Values for these parameters were derived through literature review and are provided in Table 6.

Table 6. Modeled Disease Parameters

Parameter	SARS ^a	1918 Influenza ^b	Smallpox ^c	Plague ^d
Incubation Period (days)	Triangular distribution ($\mu=8.5$, $\sigma=3.1$)	Lognormal distribution ($\mu=1$, $\sigma=1$)	Normal distribution ($\mu=15$, $\sigma=2.0$)	Normal distribution ($\mu=3$, $\sigma=0.66$)
Contagious Period (days)	Triangular distribution ($\mu=9.3$, $\sigma=2.3$)	Lognormal distribution ($\mu=5$, $\sigma=1$)	Normal distribution ($\mu=11$, $\sigma=2.23$)	Normal distribution ($\mu=3$, $\sigma=0.83$)
Case Fatality Rate	0.18	0.06	0.35	0.92

^a John N. Bombardt, Jr., personal communication with Professor Ying-Hen Hsieh, China Medical University, Taiwan, 2007.

^b John N. Bombardt, Jr. and Heidi E. Brown, *Potential Influenza Effects on Military Populations*, IDA Paper P-3786 (Alexandria, VA: Institute for Defense Analyses, December 2003), 28.

^c John N. Bombardt, Jr., *Smallpox Transmission and BW Casualty Assessments*, IDA Paper P-3550 (Alexandria, VA: Institute for Defense Analyses, October 2000), 29.

^d John N. Bombardt, Jr., *Primary Pneumonic Plague Transmission and BW Casualty Assessments*, IDA Paper P-3657 (Alexandria, VA: Institute for Defense Analyses, December 2001), 45.

Obviously the values of these characteristics for future EIDs are unknown. It would be useful to have the capability to systematically vary parameter values in order to determine which parameters and/or which range of values produce the greatest operational impact. This would certainly support the development of characteristics of concern for assessing the risk posed by any specific EID. Unfortunately, the close link between disease parameter values and calculated, historically based disease transmission

rates in the IDA model means these values cannot be varied without rendering the associated disease transmission rates meaningless.

Instead, this assessment used each of the four available disease models to evaluate at least one measure of effectiveness. These diseases show considerable variation in incubation period, duration of illness, and case fatality rate. For those parameters defined in terms of time, these diseases cluster into two basic categories: long (SARS and smallpox) and short (influenza and plague). The research team hoped that use of all four diseases would generate trends that could be used to associate disease characteristics with operational impact, at least to some extent.

5. Response Parameters

The assessment that follows considers four types of response to EID outbreaks: immunization, post-exposure prophylaxis (PEP), ROM between units, and isolation of contagious individuals (those in the I cohort). It evaluates the extent to which these responses could mitigate the operational impact of EIDs, given assumptions about the scope of implementation, the trigger or time at which implementation occurs, and the effectiveness of the response.

Immunization was considered in this research to mean the administration of medical countermeasures to individuals in order to reduce or eliminate their vulnerability to a given pathogen. Given this functional definition, it would include both vaccination and pre-exposure prophylaxis. Immunization was assumed to have occurred prior to the start of the modeled outbreak. To assess the effectiveness of immunization as a response measure, the research assumed two different levels of efficacy, 90 percent and 50 percent. In other words, 90 percent and 50 percent of individuals given the postulated vaccine or prophylaxis would subsequently be immune to the disease. The 90 percent efficacy level is comparable to that sought for vaccines against BW agents,⁶⁹ and represents the product of a medical countermeasure development program targeted against a specific pathogen. The 50 percent efficacy level is intended to represent EIDs that are variants of known diseases against which military personnel are already immunized, where the nature of the variant is such that existing immunity is degraded. For example, in any given year, the

⁶⁹ See, for example, P. F. Fellows et al., "Efficacy of a Human Anthrax Vaccine in Guinea Pigs, Rabbits, and Rhesus Macaques against Challenge by *Bacillus anthracis* Isolates of Diverse Geographical Origin," *Vaccine* 19 (2001): 3241–7; and discussion of anthrax vaccine efficacy in Curling et al., *Technical Reference Manual: NATO Planning Guide for the Estimation of Chemical, Biological, Radiological, and Nuclear (CBRN) Casualties, Allied Medical Publication-8(C)*, IDA Document D-4082, Institute for Defense Analyses, August 2010: 201-2.

circulating strain of seasonal influenza is often an evolved or re-emergent strain against which individuals vaccinated in prior years will retain some residual level of immunity.⁷⁰

Note that when considering immunization, the postulated numbers of initial infections are still 1, 10, and 100. The underlying assumption is that these infections either came from a non-immunized population, such as host nation civilians or allied military personnel, or that the adversary adjusted its actions so as to generate these numbers of initial infections in the immunized population. An alternative approach would be to assume that the adversary pathways remained the same and the resulting numbers of initial infections were decremented in accordance with efficacy. In other words, if the efficacy of immunization is 90 percent, the numbers of initial infections would be 10, 1, and 0.1. The problem with this is that it would be more difficult to compare the modeling results with those for other response types if the absolute number of initial infections changed.⁷¹

Like immunization, PEP is the administration of medical countermeasures to individuals to reduce their vulnerability to a given pathogen. However, the countermeasures are given after the start of an outbreak, not before, and are intended to prevent individuals in the E cohort from transitioning to the I cohort. In addition, the effects of PEP are often of limited, finite duration. This research assumed that PEP would be provided to all individuals not showing symptoms of illness; this would include individuals in both the S and E cohorts. From a modeling perspective, this means that members of the S and E cohorts were removed from consideration in the model for as long as the PEP was effective; afterwards, all of these individuals were returned to the S cohort.

As with immunization, the research considered two levels of efficacy: 100 percent, consistent with that estimated for non-resistant strains of BW agents,⁷² and 50 percent, chosen to represent a degraded efficacy of medical countermeasures against new pathogens or those that have evolved a natural resistance.

Implementation of PEP in an operational setting is assumed to be the consequence of a decision triggered by some level of knowledge provided via situational awareness capabilities. Of particular interest to the research, then, was the extent to which the

⁷⁰ Huong Q. McLean et al., "Influenza Vaccine Effectiveness in the United States During 2012-2013: Variable Protection by Age and Virus Type," *The Journal of Infectious Disease* 211 (2015): 1538.

⁷¹ As discussed below, immunization (as expected) proved the most effective among the various means considered of preventing operational impact from EIDs. Under the alternative approach, with fewer numbers of initial infections, the relative effectiveness of immunization would be greater still. The programmatic implications of the results would be largely the same in either case.

⁷² For example, see Arthur M. Friedlander et al., "Postexposure Prophylaxis against Experimental Inhalation Anthrax," *Journal of Infectious Diseases* 167, no. 5 (1993): 1239-43.

effectiveness of PEP changes over time, as this in turn determines the available window of decision and implementation time. To explore this question, the research team considered the effectiveness of PEP implemented at 5, 10, 20, or 40 days after the start of the outbreak.

As discussed above, the research team added a representation of unit structure to the IDA contagious disease model because individuals in the same unit or location are assumed to mix more uniformly than they are with those in other units or locations. At the same time, individuals regularly move between units and locations; in the median sub-PAR in the Afghan SPOT-JAMMS dataset, 20–25 percent of personnel changed locations every day (see Figure 10).⁷³ This movement is an obvious means by which a disease spreads from one sub-PAR to another; restricting this movement could theoretically reduce disease spread among units.

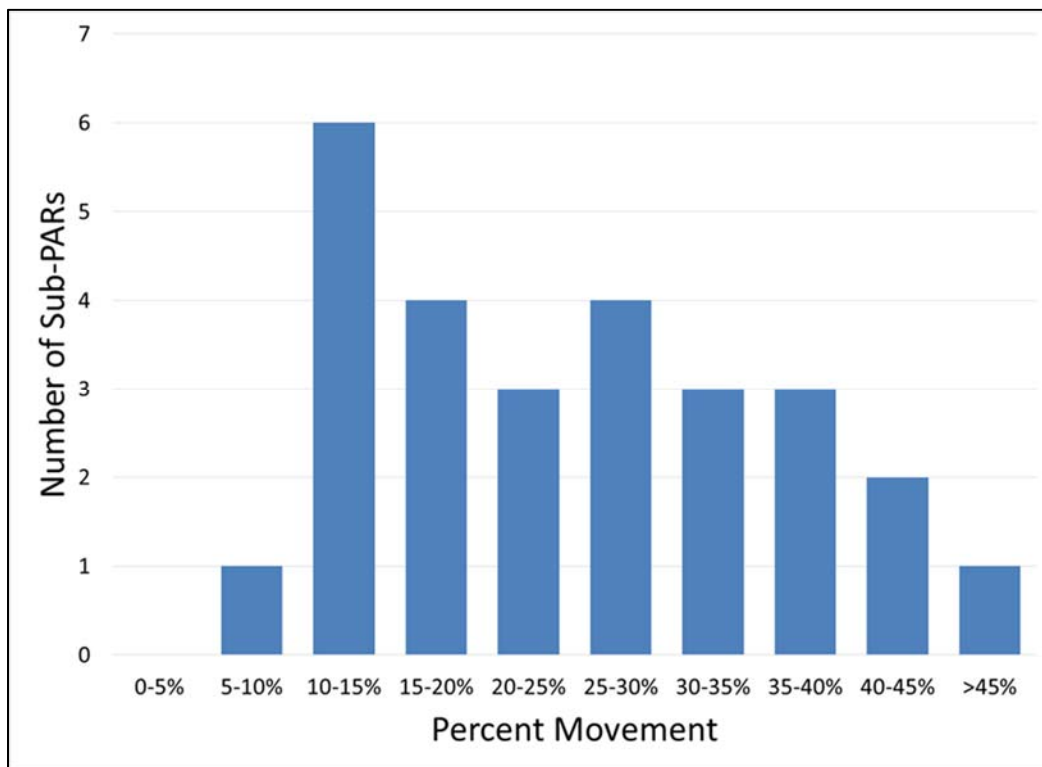


Figure 10. Histogram of Percent Movement for All Sub-PARs in Afghan Troop Movement Dataset

⁷³ Note that Figure 10 shows movement rates for all 27 sub-PARs in the SPOT-JAMMS dataset, not just those shown in Figure 8. Recall that the research team excluded 14 locations from the force array depicted in Figure 8 because they were not linked by personnel movement to other locations in the dataset. However, daily movement rates between these sub-PARs and other, unknown locations could be determined simply by noting the presence or absence of individuals from one day to the next.

The study team was interested in exploring how much movement needed to be restricted to effectively mitigate impact, and how sensitive this effectiveness was to the time it was implemented relative to the start of the outbreak. To do so, the assessment tested restriction of 50 percent and 100 percent of normal movement, implemented at 5, 10, or 20 days.

The fourth response measure actively considered in this research was isolation of contagious personnel. This response is a standard means of disease control,⁷⁴ and can occur through deliberate policy vis-à-vis symptomatic individuals, or incidentally if the disease is severe enough to warrant hospitalization of casualties at some point.⁷⁵ To a great extent, the decision to implement this type of response is tied to specific disease characteristics. Diseases that are contagious prior to the onset of symptoms, or that present initially with non-specific symptoms that are not clinically differentiable from routine infections, would be difficult to control via isolation. Moreover, even when contagious individuals are readily identified and rapidly isolated, there is no guarantee they will not continue to spread disease. The mechanism of transmission and requirements for containment in a medical setting may not be well understood for EIDs, and those put in place initially could well be inadequate. Three years after the first known case of MERS-CoV in humans, the preponderance of infections in the recent MERS-CoV outbreak in South Korea were acquired in hospitals.⁷⁶ Finally, full compliance with this measure is unlikely, as some cases may be misdiagnosed if they show atypical symptoms, and others may simply be overlooked.

Still, because this response measure would remove most of the I cohort from the PAR, it promises to greatly mitigate the impact of a disease outbreak. Because the duration of the contagious period is a key driver of disease spread, the research team chose to explore the effect of truncating this period through isolation. Two cases were assessed: one in which individuals were isolated at the time of symptom onset plus one day, to represent diseases that are more readily diagnosed, allowing identification of contagious individuals; and one in which individuals were isolated at the time of

⁷⁴ For a brief overview, see “Quarantine and Isolation” on the CDC website, <http://www.cdc.gov/quarantine/index.html>.

⁷⁵ Steven Riley et al., “Transmission Dynamics of the Etiological Agent of SARS in Hong Kong: Impact of Public Health Interventions,” *Science* 300, no. 5627 (June 2003): 1964.

⁷⁶ WHO, Summary and Risk Assessment of Current Situation in Republic of Korea and China, June 19, 2015. http://www.who.int/csr/disease/coronavirus_infections/risk-assessment-19june2015/en/. At the time of this report, there had been 166 laboratory-confirmed cases in South Korea. As stated, “The outbreak in the Republic of Korea has been associated with health care facilities and have thus far involved 72 health care facilities which have treated patients. To date, 6 health care facilities have documented nosocomial transmission. All cases reported so far include healthcare workers caring for confirmed cases, patients who were being cared for at the same healthcare facilities as confirmed patients, and family members of confirmed patients or of patients.”

symptom onset plus one-half of the contagious period. This second case could, for example, represent a disease that is non-specific and difficult to diagnose in its early stages, but then becomes severe enough to warrant hospitalization in its later stages. For simplicity, all members of the I cohort were assumed to be isolated, and once isolated, individuals were assumed to be no longer capable of transmitting disease.

Quarantine of healthy individuals suspected of being exposed to contagion is yet another procedural control measure that could be used to prevent the spread of disease. Such individuals are typically identified by tracing the contacts of contagious disease patients, which can conceivably number several hundred per individual.⁷⁷ Within the IDA contagious disease model, quarantine would normally be represented by removing members of the S and E cohorts in numbers proportional to the number of individuals in the I cohort. However, the study team quickly realized that at historically experienced ratios of quarantined to contagious individuals, this response would result in entire units being removed from the four-PAR structure as soon as two or three individuals became ill, rapidly leading to combat ineffectiveness. Moreover, the basic principle of quarantine—segregating one or more portions of the population from the other—was explored in depth in the consideration of ROM. For these reasons, quarantine is not further discussed in the assessment of EID impact.

Table 7 summarizes the modeled response parameters used in this research.

Table 7. Modeled Response Parameters

Response	Scope	Trigger	Assumed Effectiveness
Immunization	Force-wide	Pre-deployment	50% and 90% efficacy
Post-exposure prophylaxis (PEP)	Force-wide	Implemented at 5, 10, 20, or 40 days	50% and 100% efficacy
Restriction of movement between units	50% and 100% of normal movement	Implemented at 5, 10, or 20 days	N/A
Isolation of individuals in I cohort	100% compliance	Symptom onset + 1 day, + ½ contagious period	100%

⁷⁷ John N. Bombardt, “Congruent Epidemic Models for Unstructured and Structured Populations: Analytical Reconstruction of a 2003 SARS Outbreak,” *Mathematical Sciences* 203 (2006): 179–80.

6. Modeling Assumptions and Limitations

Although specific assumptions made in the assessment of EID operational impact are discussed at relevant places in the sections above, three broader assumptions and limitations should be noted. First, the start of the outbreak (day zero) was defined as the day on which the initial infections are exposed. All reported time measurements are relative to this point. In other words, the outbreak was considered to have begun prior to the appearance of the first symptomatic individual.

Next, within each sub-PAR, the progression of the disease was considered at a population level, meaning people are considered as fractional numbers. The implication of this assumption is that the progression of disease within any individual cannot be known. Since individual disease progression is not known, every exposed but non-contagious individual (member of the E cohort) and every contagious individual (member of the I cohort) is considered to be on the first day of their latent or contagious period, respectively, upon moving to a new sub-PAR. Therefore, the average duration of the latent and/or contagious period of each individual who moves is longer than that of an individual who remains in a single sub-PAR. The impact of this modeling limitation on the dynamics of the overall outbreak is exacerbated by higher movement rates.

The historically based time-varying disease transmission rates (β) are limited in their applicability to scenarios with different epidemiological circumstances compared to those of the historical outbreak on which they were based. The β values derived from a single sub-PAR cannot account for the variation in the epidemiological circumstances that might be expected to alter the duration of the outbreak, such as contact with a previously uninfected population. Therefore, the IDA team has less confidence in the accuracy of modeling results at late times, specifically concerning the cessation of the outbreak.

Finally, this research would have ideally considered all possible combinations of agents and force arrays in investigating the measures of operational impact and the effectiveness of various responses. The enhanced contagious disease model used in this research, however, was developed and implemented in Mathematica and was not, at the time of this research, optimized for large-scale production of results. Consideration of structure and movement added stochastic elements to the model and generated an associated requirement for multiple trials of each case. Model run times, particularly for the larger SPOT-JAMMS force array, took several days and even weeks, which severely limited the number of combinations of inputs that could be investigated. Consequently, the results of this assessment should be seen only as an indication of the nature and magnitude of the operational impact of EIDs, and further analysis would be needed to support definitive conclusions.

B. Model Results

The research team conducted 100 trials for each combination of inputs. The model outputs discussed in the remainder of this chapter are those from the 90th percentile case, defined as the case that is worse than 90 percent of the trials for the specific measure of interest (e.g., the median reduction in casualties or the median time to reach combat ineffectiveness). For some scenarios, such as that depicted in Figure 11, the distribution of results was quite broad. In that scenario, a SARS outbreak with 10 initial infections, the 50th percentile or median time to reach combat ineffectiveness was 105 days, shown in red. In comparison, the times to reach combat ineffectiveness for the 90th percentile case (the case worse than 90 percent of the trials, shown in blue) and the 10th percentile case (the case worse than 10 percent of the trials, shown in green) were approximately 15 percent shorter and 25 percent longer, respectively. For other scenarios, such as the 100 initial infections case shown in Figure 12, the distribution of results is fairly narrow. The median time to reach combat ineffectiveness was 47 days, and the times for the 90th and 10th percentile cases were 46 and 47 days, respectively.

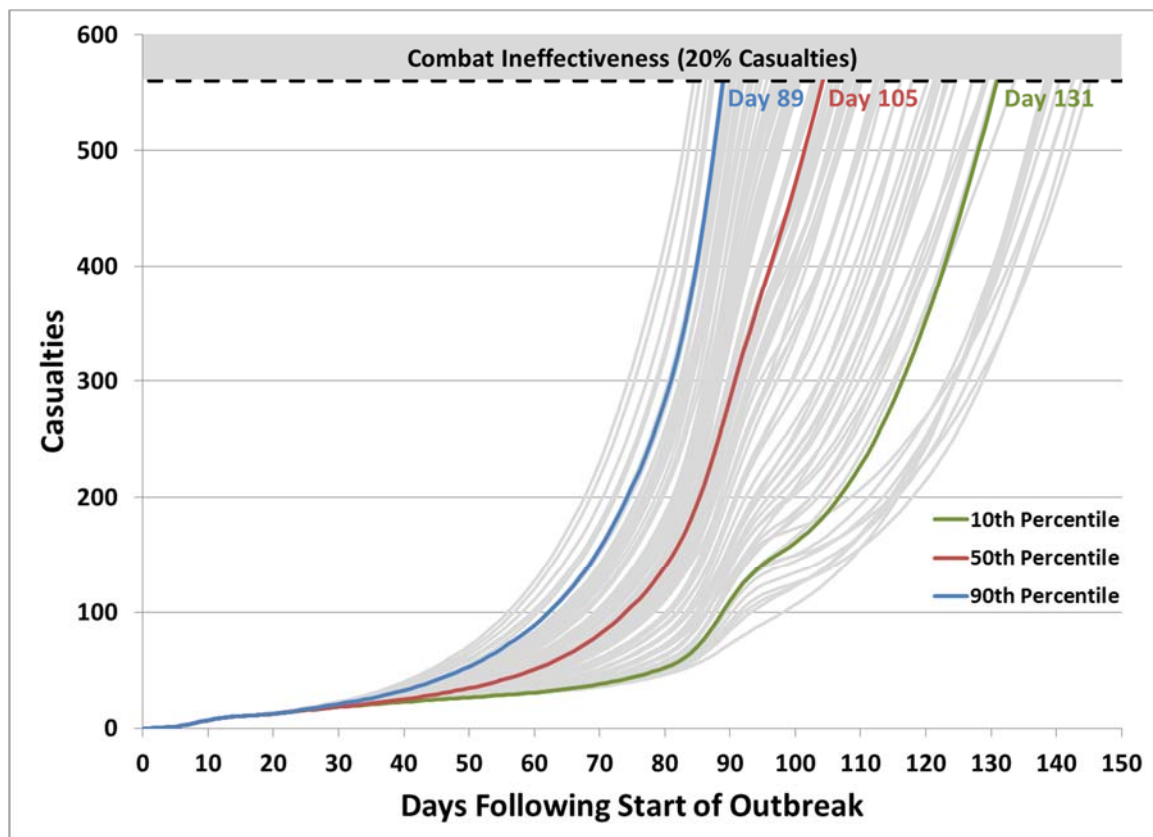


Figure 11. Example Distribution of Model Results: 100 Trials, Time to Reach Combat Ineffectiveness in Four-Sub-PAR System from 10 Initial Infections in PAR₁

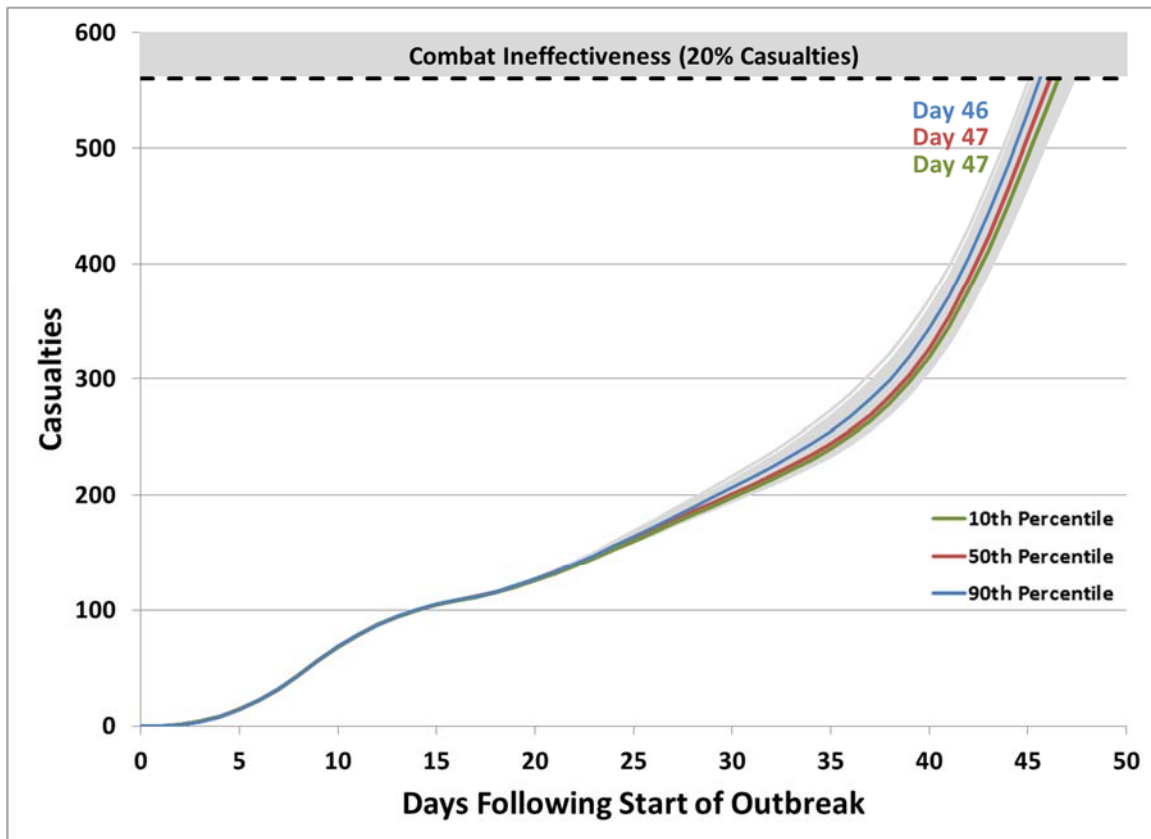


Figure 12. Example Distribution of Model Results: 100 Trials, Time to Reach Combat Ineffectiveness in Four-Sub-PAR System from 100 Initial Infections in PAR₁

1. Baseline Measurement of Operational Impact

In order to assess the effectiveness of various response measures in mitigating the operational effect of an EID outbreak, the IDA research team modeled a series of baseline scenarios. In each of these baseline scenarios—modeled without intervening response measures (e.g., immunization or ROM)—the team assessed two measurements of operational impact: time to reach combat ineffectiveness and time until the outbreak reaches a specified unit, location, or sub-population.

a. Time to Reach Combat Ineffectiveness

The following section provides modeling results showing the time to reach combat ineffectiveness for four diseases: SARS, 1918 influenza, smallpox, and plague. Results for all four diseases are presented for the four-sub-PAR force array depicted in Figure 9 on page 63. The total PAR included 2,800 individuals; therefore, the 20 percent casualty level used as a surrogate of combat ineffectiveness corresponded to 560 casualties.

These four baseline cases did not consider any active interventions or any personnel actions—no return to duty, no individual replacement, no unit replacement. Many of the

modeled outbreaks continued for hundreds of days, obviously an unrealistic outcome. As discussed previously, confidence in modeling accuracy is lower at the end of the outbreak than the beginning. Therefore, these results focus on the early stages of the outbreak, specifically the time from the start of the outbreak to the time when casualties among the overall population reaches 20 percent and becomes combat ineffective.

Figure 13 through Figure 16 show the number of casualties for the SARS, smallpox, 1918 influenza, and plague baseline scenarios described above, in the 90th percentile case. Each of the modeled scenarios shown below resulted in the population becoming combat ineffective. That is to say, in the absence of any response control measures, even a single initial infection eventually infected over 20 percent of the population. For 1918 influenza and plague, this occurred very rapidly; with even one initial infection, 1918 influenza generated 20 percent casualties within a week of the start of the outbreak, and plague within two weeks. For smallpox and SARS, it takes several weeks for the population to become combat ineffective, even with 100 initial infections. Therefore, depending on the duration of an operation, the introduction of an infectious disease might not pose a serious risk to the mission. However, there will eventually be hundreds or thousands of casualties if no measures are taken in response.

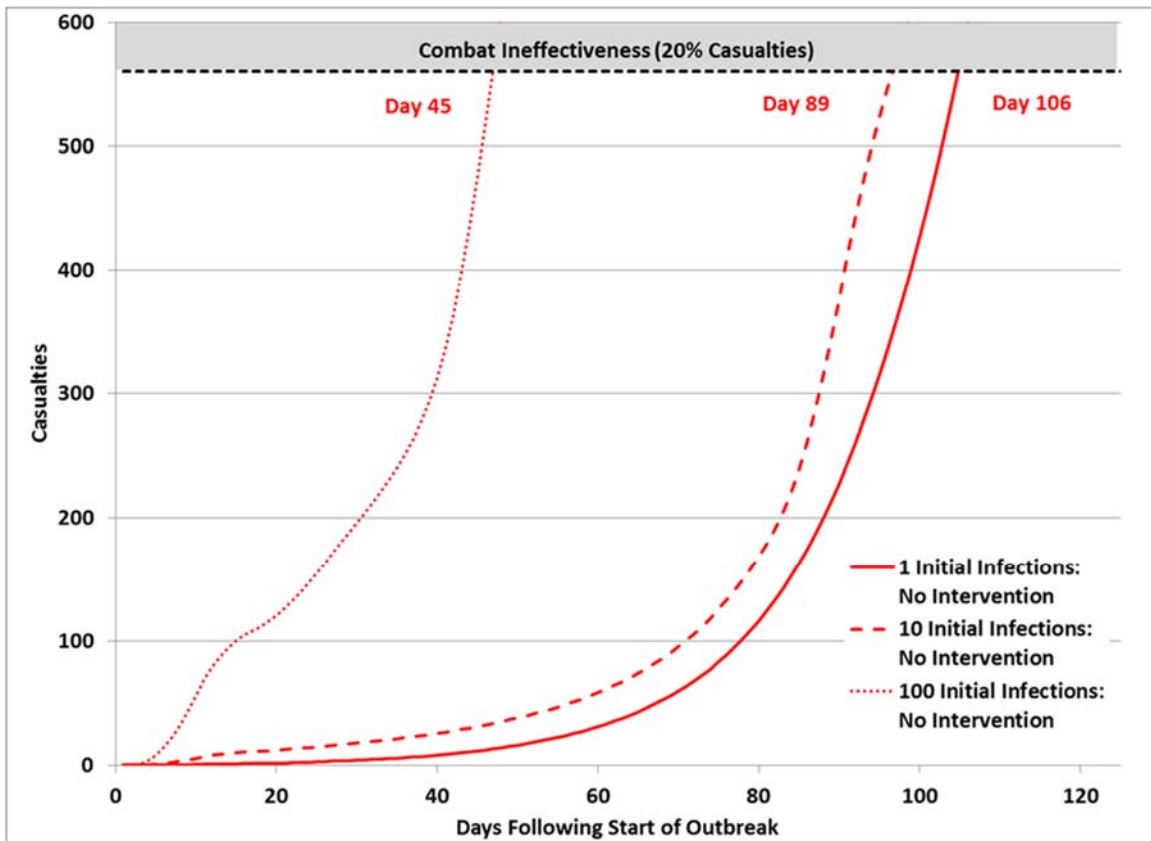


Figure 13. Casualties over Time for 1, 10, and 100 Initial SARS Infections, Baseline Case, Four-Sub-PAR System

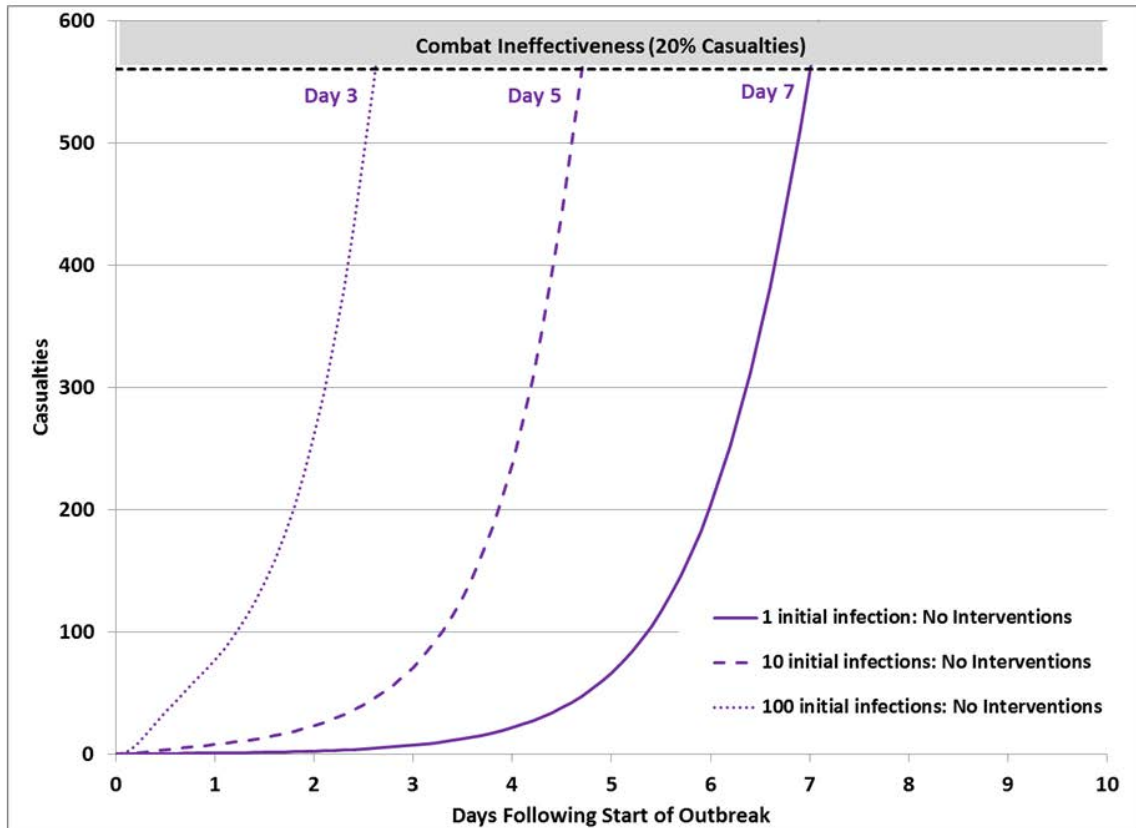


Figure 14. Casualties over Time for 1, 10, and 100 Initial Influenza Infections, Baseline Case, Four-Sub-PAR System

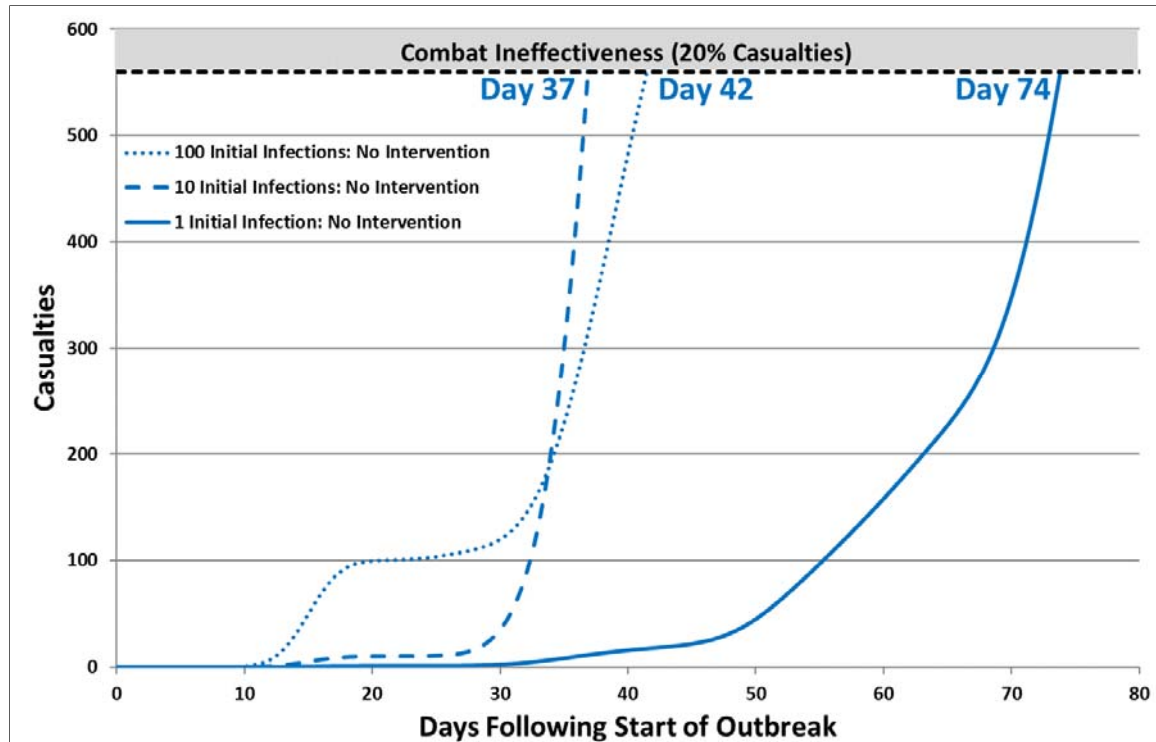


Figure 15. Casualties over Time for 1, 10, and 100 Initial Smallpox Infections, Baseline Case, Four-Sub-PAR System

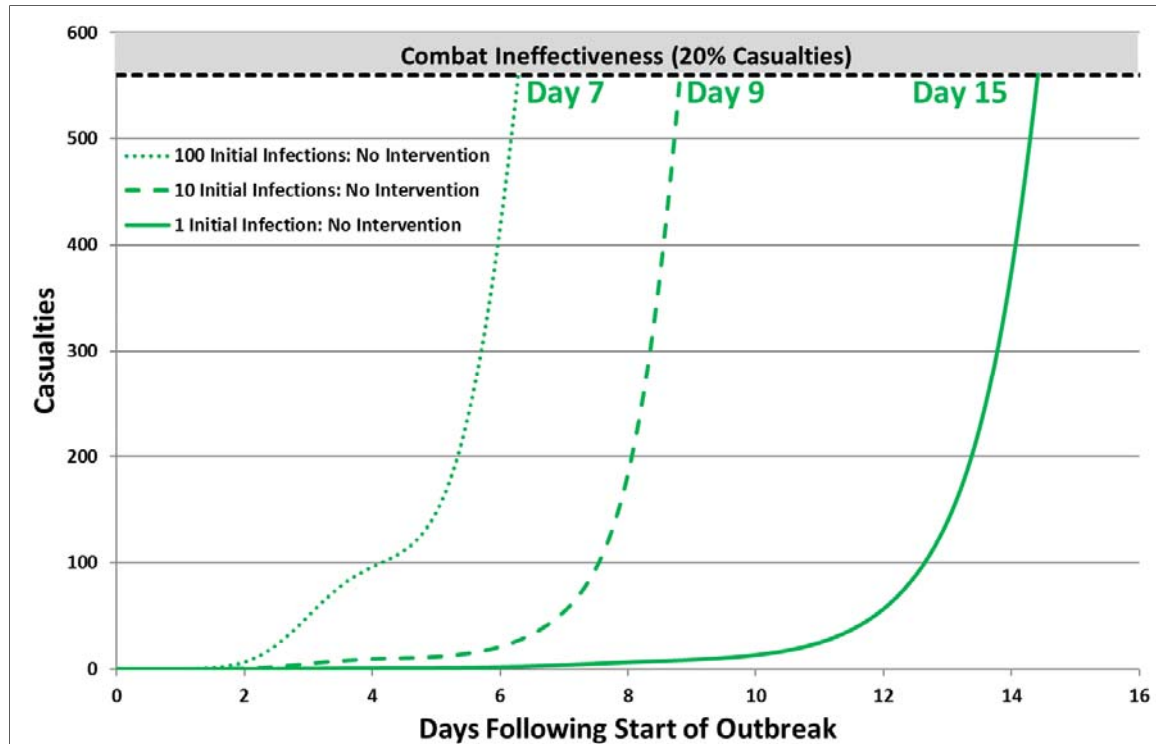


Figure 16. Casualties over Time for 1, 10, and 100 Initial Plague Infections, Baseline Case, Four-Sub-PAR System

While each of the above scenarios resulted in the population becoming combat ineffective, there was substantial variation in the amount of time before the population became combat ineffective when compared across diseases and the number of initial infections. As expected, a greater number of initial infections resulted in the population become combat ineffective sooner. Regardless of the number of initial infections, modeled outbreaks of 1918 influenza and plague consistently caused the population to become combat ineffective sooner than those of smallpox or SARS. This is likely attributable to 1918 influenza and plague having shorter incubation periods.

As discussed above, in the interests of time, the research team chose to use the smaller four-sub-PAR force array for much of the modeling. However, the team also expected that diseases would propagate much more quickly in smaller, less structurally complex arrays. For purposes of comparison, the team estimated the time to reach combat ineffectiveness in the larger, 10-sub-PAR force array, shown in Figure 8, for 1, 10, and 100 initial infections with smallpox and plague. The total size of the population was 27,800; therefore, the 20 percent casualty threshold corresponded to 5,560 individuals. The results for these two cases are provided in Figure 17 and Figure 18.

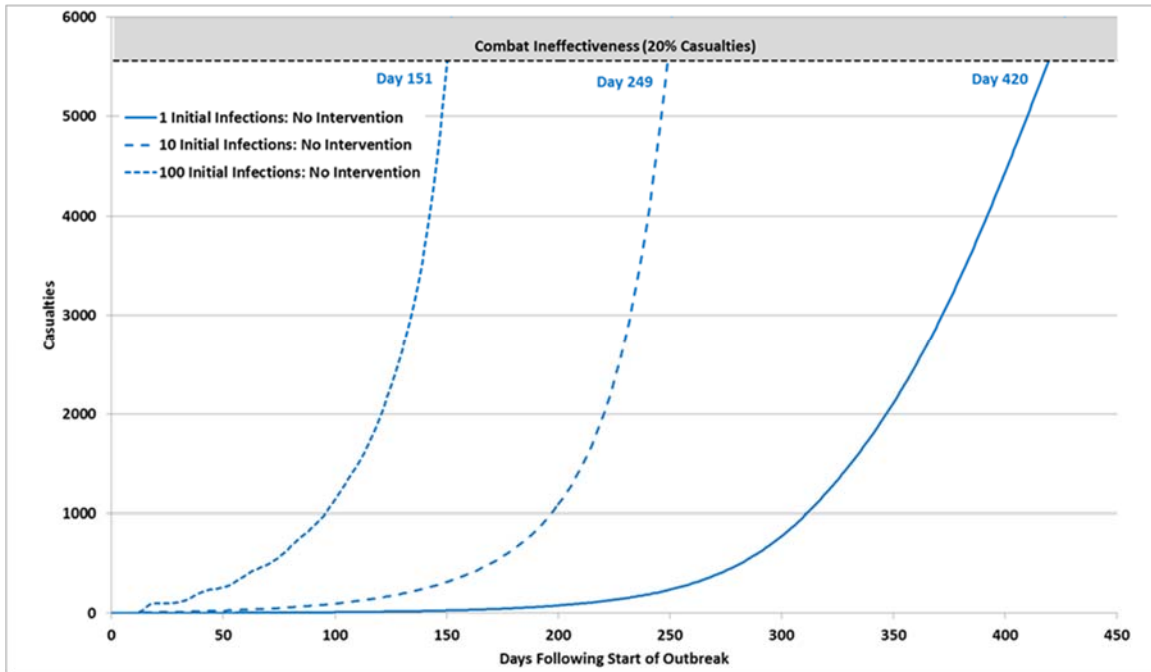


Figure 17. Casualties over Time for 1, 10, and 100 Initial Smallpox Infections, Baseline Case, 10-Sub-PAR System

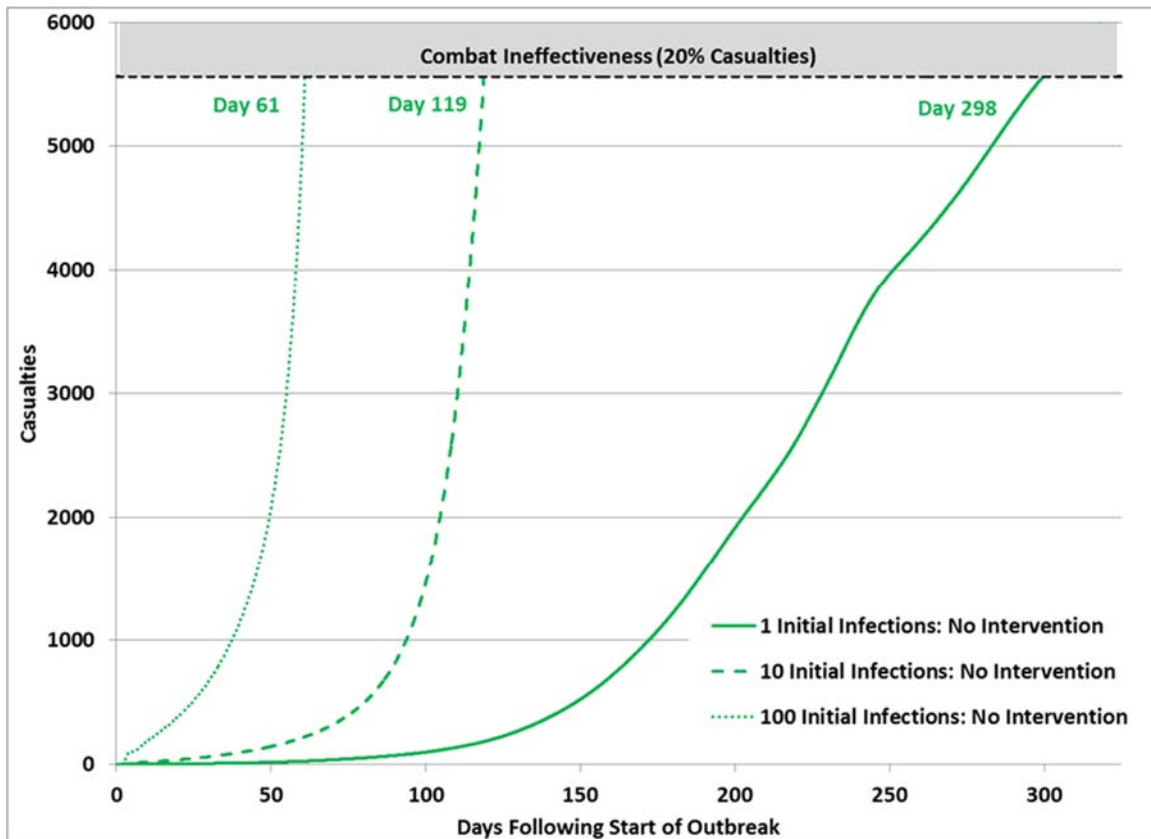


Figure 18. Casualties over Time for 1, 10, and 100 Initial Plague Infections, Baseline Case, 10-Sub-PAR System

As expected, the time to reach combat ineffectiveness consistently proved significantly longer in the larger force array, for both diseases and all numbers of initial infections. The relationship, however, was not linear: although in the larger array, combat ineffectiveness required 10 times as many casualties as in the smaller array, it did not consistently take 10 times as long to do so. For a single initial plague infection, and for all numbers of smallpox initial infections, time to combat ineffectiveness was, proportionally, more rapid in the larger array, while for 10 and 100 initial plague infections it was, proportionately, much slower. One possible explanation is that perhaps outbreaks that spread very rapidly in a relatively well-mixed population may be curtailed by structure in the population more than outbreaks that grow more slowly.

Note that for these results, infections began in the Bagram Air Field sub-PAR, the largest of the sub-PARs considered in the 10-sub-PAR array and that with the most direct connections with other sub-PARs. To gain some insights into the effect of different sub-PAR structures, additional modeling runs were conducted to assess the sensitivity of the time to reach combat ineffectiveness to the location of the initial infections. In these runs, outbreaks with 1, 10, and 100 initial smallpox and plague infections began in the RSOI and Apache sub-PARs. RSOI is of intermediate size and connected to two other sub-

PARs; Apache is among the smallest sub-PARs, is connected to only one other sub-PAR, and is the most remote from Bagram and the bulk of the overall population. The resulting times to reach combat ineffectiveness are shown in Table 8.

Table 8. Time to Reach Combat Ineffectiveness from Smallpox and Plague in 10-Sub-PAR Array (Days)

	Outbreak Start Location		
	Bagram	RSOI	Apache
Smallpox			
1 initial infection	420	396	414
10 initial infections	249	220	239
100 initial infections	151	136	166
Plague			
1 initial infection	298	328	312
10 initial infections	119	111	156
100 initial infections	61	48	130

Similar trends are observed over all starting locations of the outbreak. More initial infections resulted in the population becoming combat ineffective sooner than fewer initial infections, and outbreaks of plague consistently caused the population to become combat ineffective earlier than outbreaks of smallpox with the same number of initial infections. Overall, the time at which the population became combat ineffective was insensitive to the starting location of the outbreak. For a given disease and number of initial infections, no one starting location consistently correlated with earlier or later times to reach combat ineffectiveness, and the differences in results are generally quite small.

The research team used the smaller four-sub-PAR system, shown in Figure 9 (on page 63), to investigate the sensitivity of the time to reach combat ineffectiveness to various movement rates and patterns between these four sub-PARs. SARS outbreaks of 1, 10, and 100 initial infections were started in three variants of the four sub-PAR system. The first variant was exactly as depicted in Figure 9. In this population the majority of the movement between the sub-PARs was between PAR₂ and PAR₄. This pattern of movement among the four sub-PARs will be referred to as *skewed 2-4*. The second variant of movement patterns is the same as skewed 2-4, except that the movement rates between PAR₁ and PAR₂ were switched with the movement rates between PAR₂ and PAR₄. This pattern of movement is referred to as *skewed 1-2* since the largest rate of movement, 200 individuals per day, occurs between the first two sub-PARs. The third and final movement variant involves all the movement rates shown in Figure 9 being the same—70 individuals per day. This third pattern is referred to as *balanced*. In addition to varying the relative rates of movement between the sub-PARs, the movement rates

themselves were also varied. The rates were either left unchanged, (referred to as *medium*), halved (referred to as *low*), or increased by 50 percent (referred to as *high*). Between the three movement patterns (*skewed 2-4*, *skewed 1-2*, and *balanced*) and the three movement rates (*low*, *medium*, and *high*), there were a total of nine scenarios for which 1, 10, and 100 initial SARS infections were modeled. A schematic depiction of each of the nine combinations of movement pattern and rate is shown in Figure 19.

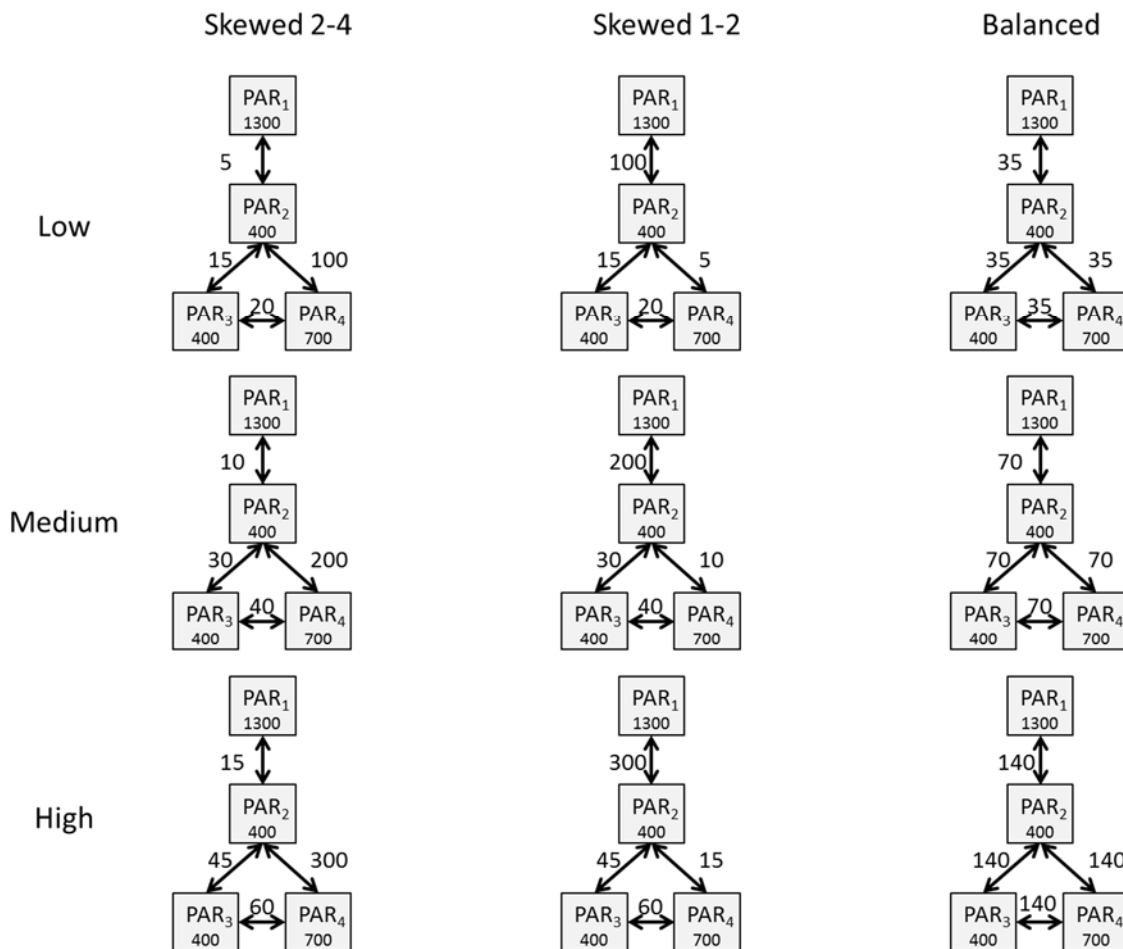


Figure 19. Nine Combinations of Movement Patterns and Rates for the Four-Sub-PAR Population Structure

Figure 20 shows the time to reach combat ineffectiveness for each of the nine combinations of movement patterns and rates for 1, 10, and 100 initial SARS infections. Many of the same trends mentioned previously are observed below. Overall, the factor that most influences when a population will become combat ineffective is the number of initial infections. With a couple of exceptions, the time to reach combat ineffectiveness for a given number of initial infections is relatively insensitive to both the movement

pattern and rate. For example, for 1 initial infection, the time to reach combat ineffectiveness for the balanced low scenario is similar to that of the skewed 2-4 scenario.

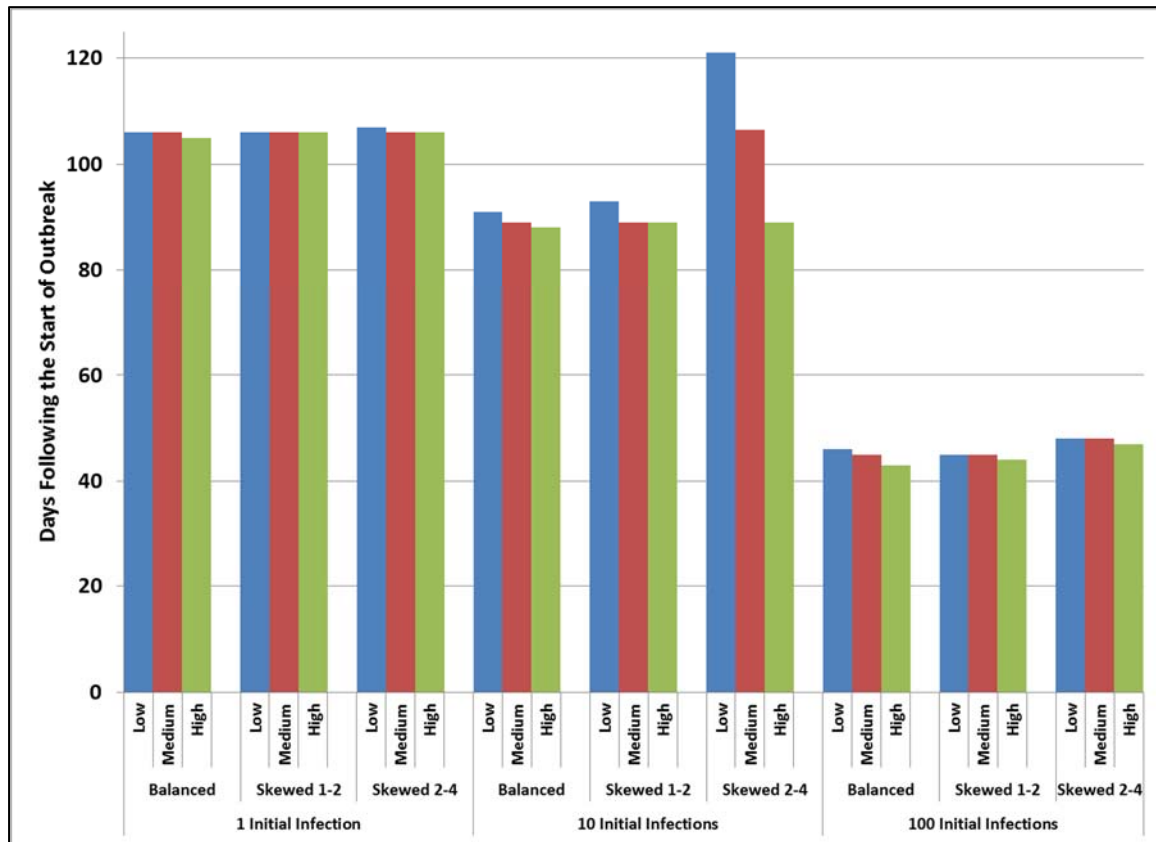


Figure 20. Time to Combat Ineffectiveness for Different Movement Rates and Patterns

b. Time It Takes a Disease Outbreak to Reach a Specified Unit, Location, or Sub-population

In addition to the time to reach combat ineffectiveness, the time it takes a disease outbreak to reach a specific unit, location, or sub-population was also assessed for the baseline no-response scenarios. In the context of the structured populations used in the present analysis, this second measure of operational impact was assessed as the number of days following the start of the outbreak until the appearance of an infected individual in a sub-PAR that previously had none ($I = 0$). Here infected individuals include both exposed but non-symptomatic individuals (members of the E cohort), as well as symptomatic and contagious individuals (members of the I cohort), since both will eventually generate new infections and cause the outbreak to spread. An analysis of when previously uninfected sub-PARs become infected provides insight into the spread of the disease through the population structure, the requisite timeliness of implementing certain

responses, and the amount of knowledge available at the time a response would need to be implemented.

Results from modeling SARS using the smaller four-sub-PAR population structure are used to illustrate the utility of this second measurement of operational impact. Figure 21 illustrates the time it took the disease outbreak to spread from the original sub-PAR to all other sub-PARs in the population structure for 1, 10, and 100 initial SARS infections. In the figure, the length of the green bar shows the number of days during which the outbreak was contained within the sub-PAR where it began. The length of the yellow bar represents the number of days during which the outbreak had spread beyond the starting sub-PAR, but had not spread to all four sub-PARs. Finally, the point at which the red starts is the day at which the disease reached all sub-PARs in the population structure. In addition to revealing information concerning the timing of disease propagation across sub-PARs, Figure 21 also shows the available knowledge at the aforementioned times. The numbers located within the green and yellow bars represent the cumulative number of symptomatic individuals at that time. For example, in the 1 initial infection scenario, there were a total of two symptomatic individuals on day 24, when the infection first appeared outside of the starting sub-PAR.

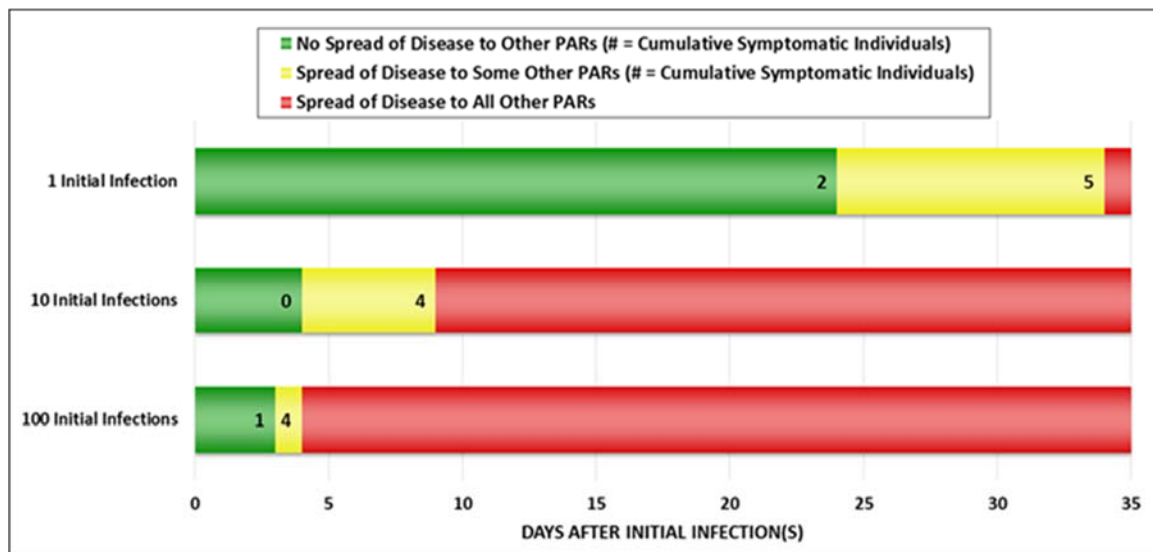


Figure 21. Day of SARS Spread from PAR₁ to PAR_n and Cumulative Number of Symptomatic Individuals at Time of Spread

Just as was the case when considering the time required for the population to become combat ineffective, outbreaks with greater numbers of initial infections progress rapidly relative to those starting with fewer initial infections. This can be seen in Figure 21; the time for the disease to spread from the first sub-PAR to the second (i.e., the length of the green bar) decreases with increasing numbers of initial infections. This

trend is also observed with the time for the outbreak to reach all four sub-PARs (where the red bar begins).

Figure 21 also provides insight into the time available to implement certain response measures. In the event that the only response measure available is to restrict the movement between the sub-PARs, the figure illustrates not only the amount of time one would have to make the decision to restrict movement, but also how much information would be available to make that decision, represented by the total number of individuals presenting symptoms. For example, for a single initial infection, as long as movement out of the first sub-PAR was halted prior to day 24, the disease would not have spread to the other sub-PARs. While 24 days may seem like a substantial amount of time in which to decide whether to restrict movement, observe that there would have been only two symptomatic individuals by that time. In other words, one would have to make the decision to restrict movement based on identifying two symptomatic individuals, who may or may not present simultaneously, in a population of 1,300. This issue of identifying a small number of individuals who are symptomatic with an EID in a large population, some of whom may be symptomatic with diseases not of operational concern, represents a substantial challenge to responding to an EID outbreak.

The research team investigated the sensitivity of the results presented in Figure 21 to the nine combinations of movement patterns and rates outlined in the previous section (e.g., balanced low or skewed 1-2 high). Figure 22 shows the time at which the disease outbreak spread beyond the initial sub-PAR—the same measure illustrated by the green bars in Figure 21—for 1, 10, and 100 initial infections for the nine combinations of movement patterns and rates. Additionally, the length of time for the outbreak to spread from the first sub-PAR to all four sub-PARs—the same measure illustrated by the length of the yellow bars in Figure 21—is similarly shown in Figure 23.

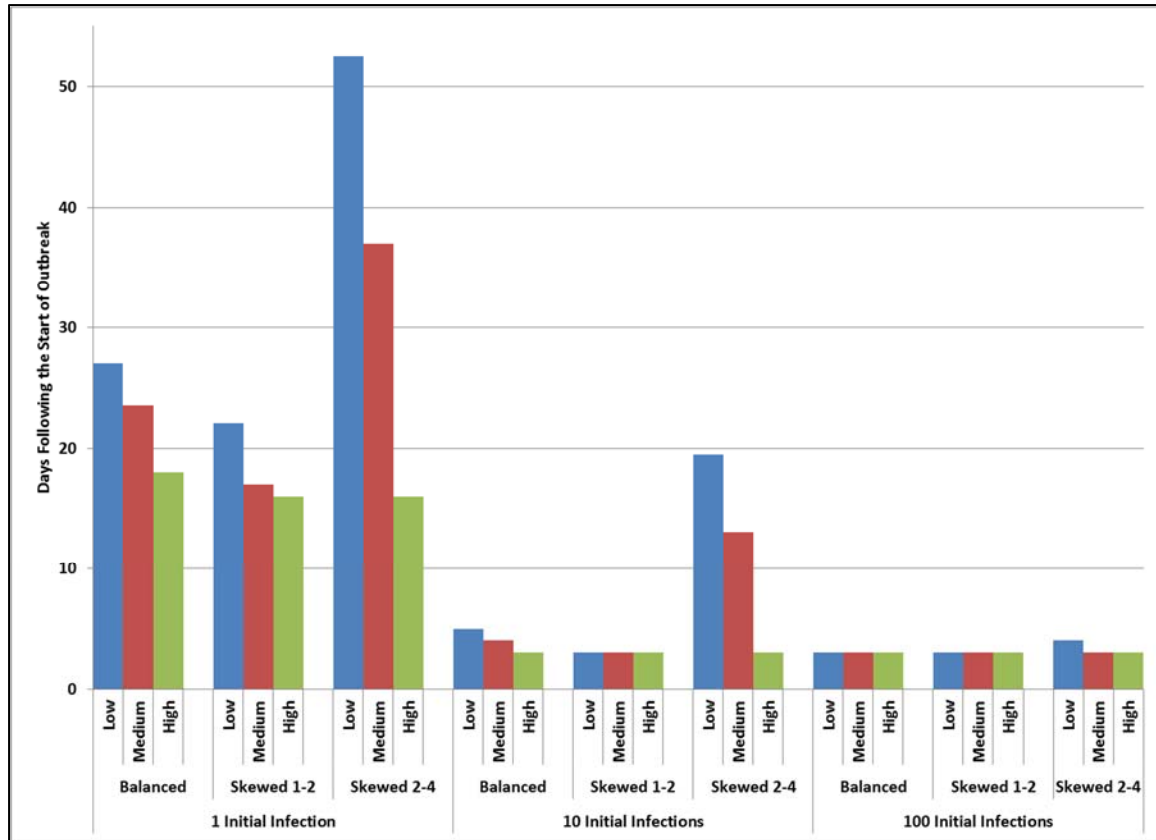


Figure 22. Time at Which Outbreak Spreads beyond Initial Sub-PAR for Different Movement Rates and Patterns

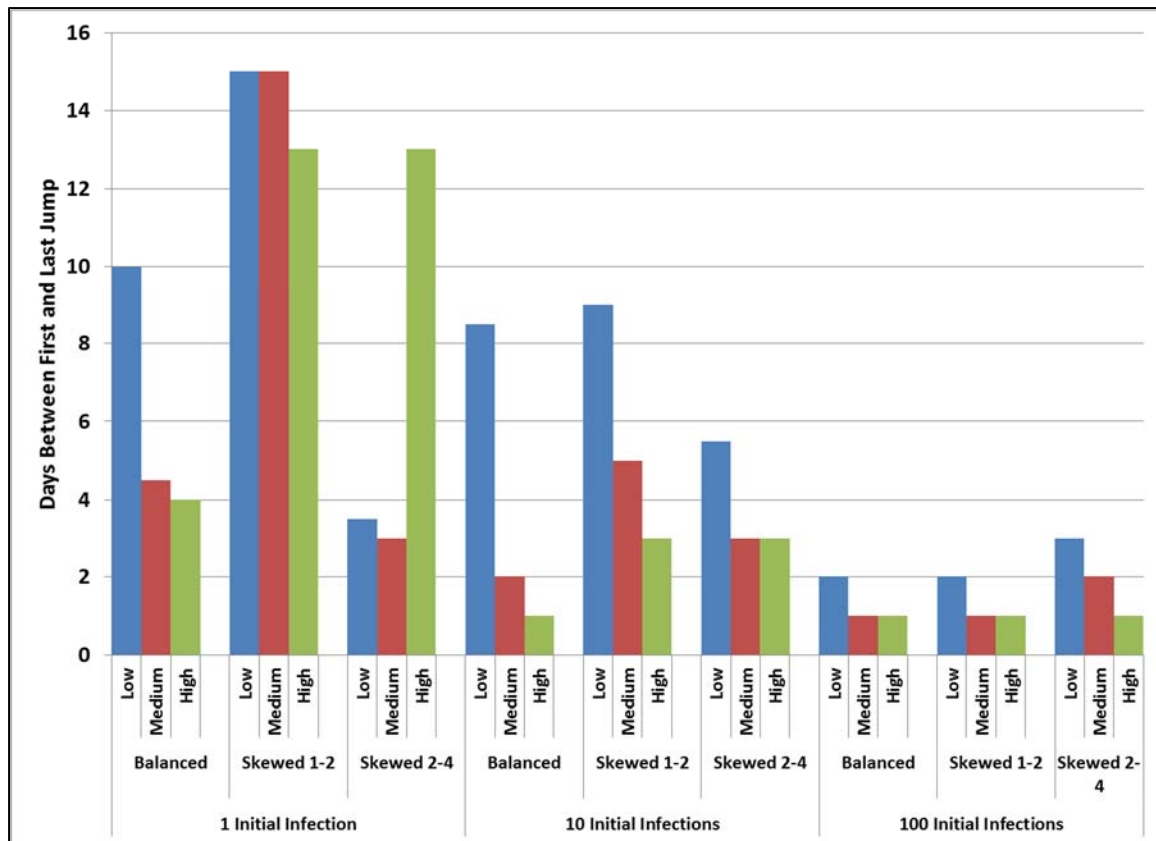


Figure 23. Time between First and Last Jump between Sub-PARs for Different Movement Rates and Patterns

For low numbers of initial infections, the time it takes the outbreak to spread to beyond the first sub-PAR is dependent on the rate of movement out of the first sub-PAR—the higher the rate of movement, the faster the outbreak will spread. The same is not true for larger numbers of initial infections. For 100 initial infections, the outbreak spreads from the first sub-PAR independent of the movement rate or pattern. Similar trends can be observed in Figure 23. Overall, scenarios with greater movement rates tended to have the outbreak spread across all four sub-PARs at a faster rate. This was seen in both the time it took to leave the first sub-PAR and the time until all four sub-PARs became infected. This outcome was as the IDA team expected. With more people moving between sub-PARs, the probability of at least one of those individuals being infected increases.

The scenario with 10 initial infections depicted in Figure 21 warrants further consideration. In the scenario, the disease spreads from the first sub-PAR on day 4, as shown by the length of the green bar, but there are no symptomatic people at that point. This means that at least one of the 10 initial infections moved from the first sub-PAR before any of the initial infections developed symptoms. In other words, there would

have been no way to restrict movement based on identifying symptomatic individuals since the disease had already spread by the time anyone presented symptoms.

Recall that the model used in the analysis was stochastic, and the results presented in Figure 21 correspond to the median trial. Therefore, the number of symptomatic individuals at the time the disease spread from the first sub-PAR was not always the same in each trial. The distribution of the number of symptomatic individuals at the time the disease spread from the first sub-PAR is shown in Figure 24 for 10 initial infections. The most likely number of symptomatic individuals at the time the disease spreads from the first sub-PAR is zero. This means that almost 70 percent of the time, one would expect the disease to spread prior to the appearance of the first symptomatic individual in the population. Approximately 20 percent of the time, there would have been a single symptomatic individual in the population at the time the disease spread beyond the first sub-PAR.

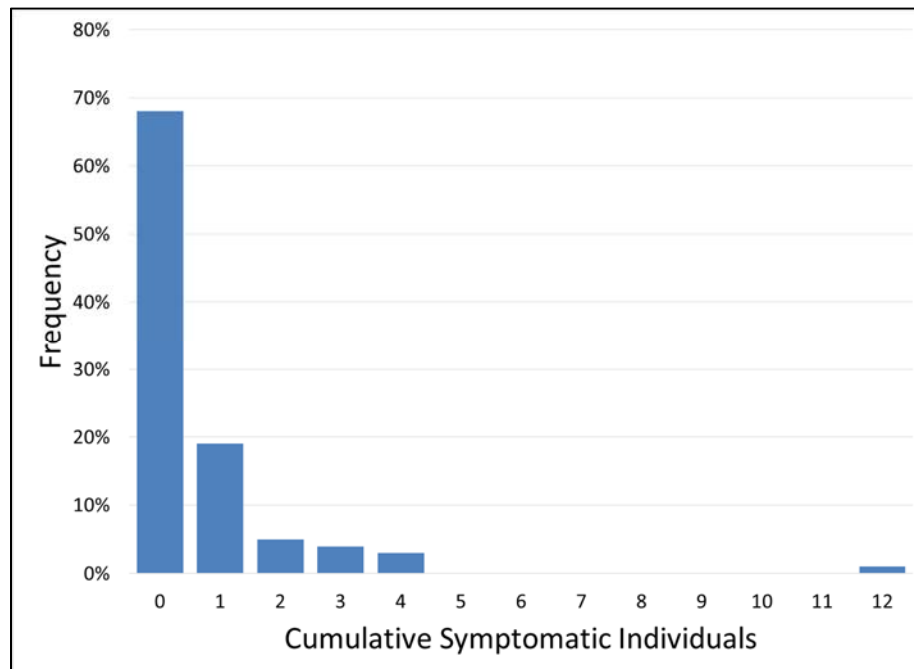


Figure 24. Distribution of Cumulative Number of Symptomatic Individuals at Time Outbreak First Spreads from PAR₁ to PAR_n: SARS 10 Initial Infections Case

The fact that it is possible (and perhaps, as shown above, even likely) for a disease to spread from one sub-PAR to another prior to the onset of symptoms may have serious implications for a surveillance program that depends entirely on identifying symptomatic individuals, as it may not be possible to prevent the disease from spreading in certain scenarios. In order to explore this concept beyond the scenarios analyzed here, the research team performed a simple excursion to identify the scenarios for which an outbreak would be likely to spread before any individuals manifested symptoms.

For this excursion, the team reduced the problem to a simple probability calculation to determine the day at which a disease was likely to spread from one sub-PAR to another. Scenarios were defined by two values: the percentage of the sub-PAR initially infected and the percentage of the PAR moving each day. First, for each scenario, the team calculated the day on which at least one of the initially infected individuals would have moved to a new PAR with 50 percent probability (i.e., in half the cases, the disease would have spread by that day). Second, the team assumed that for a disease of interest, there exists a minimum latent period within which no initial infections would manifest symptoms. Within that minimum latent period, the total number of infected individuals remains constant, since no secondary infections can be generated until the initial infections enter the contagious period. As a result, the probability of an infected individual moving within the minimum latent period is independent of the rate at which a disease spreads among a population, and the excursion results can be decoupled from any particular disease. Finally, a comparison of the minimum latent period to the day on which the disease is likely to spread can identify the scenarios for which symptom-based surveillance could trigger intervention in time to prevent the spread of disease to another sub-PAR.

For scenarios in which there are few initial infections and a low movement rate, the spread of disease to another sub-PAR is likely to occur after the end of the minimum latent period (and therefore after the appearance of symptomatic individuals). In these cases, the exact day on which the spread occurs cannot be calculated without knowing the disease-specific rate of secondary infection and duration of illness. All that can be said with confidence is that 50 percent of the time, the first infected personnel will move sometime after the minimum latent period. At the other extreme, for scenarios with a large number of initial infections and a high rate of movement, the disease is likely to spread prior to symptom onset. This means that if the objective is to prevent the spread of disease outside the population in which it initially appears, the time in which to intervene is less than the minimum latent period. Moreover, in most cases with a high number of initial infections and a high rate of movement, the disease will spread outside the sub-PAR on the first day. Figure 25 illustrates the boundary between these two types of scenarios for three assumed latent periods (two, three, and four days, which are typical minimum latent periods for diseases of concern).

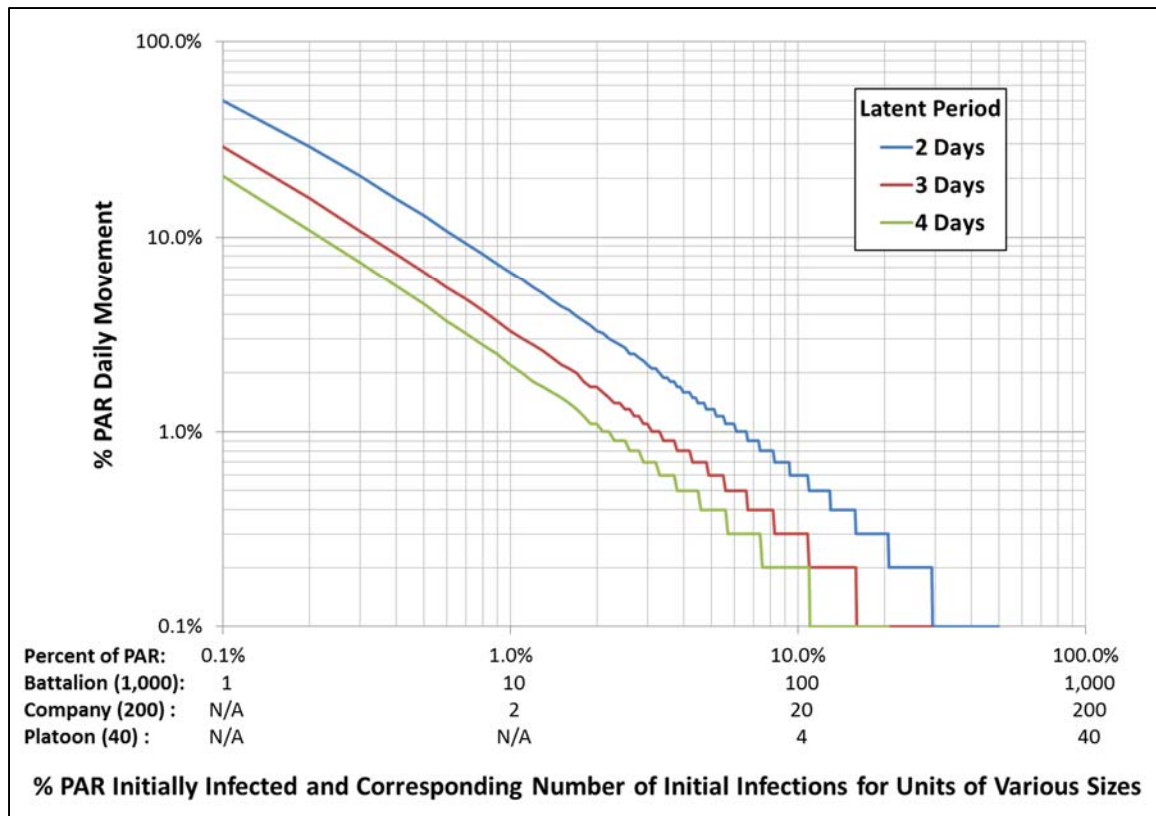


Figure 25. Scenarios for Which Spread of Disease Can Be Prevented 50 Percent of the Time for Various Minimum Latent Periods

Each curve in Figure 25 corresponds to the scenarios for which there is a 50 percent probability that the first jump will have occurred by the corresponding minimum disease latent period. Above the curve are the scenarios for which there is a greater than 50 percent probability that the first jump will have occurred by the corresponding minimum disease latent period, meaning there will likely be no symptomatic individuals to trigger intervention. Below the curve, however, are the scenarios for which intervention based on observing a symptomatic individual could be effective at preventing the spread of disease, as there is a less than 50 percent probability that the first jump will have occurred by the corresponding minimum disease latent period. As a result, if the acceptable level of risk is 50 percent, the space below the curves represents situations that allow for action based on observing symptomatic individuals. Although these curves are shown as continuous, they are applicable only when the values along the axes are integers. Along the x-axis, we have indicated the numbers of individuals corresponding to various values of the percent of the sub-PAR for a notional battalion (1000 personnel), a notional company (200 personnel), and a notional platoon (40 personnel).

In the Afghan SPOT-JAMMS dataset used in this research, the median sub-PAR movement rate was 20–25 percent of the population per day, and in no case was the movement rate less than 5 percent (see Figure 10). Together with the curves shown in

Figure 25, this suggests that during normal operations, with normal rates of personnel movement, any outbreak of contagious disease will likely spread beyond the sub-PAR in which it starts before the first symptomatic case occurs. If the first indicator of an EID outbreak—naturally occurring or otherwise—is the presence of disease symptoms in an individual, preventing the spread of disease outside the initial sub-PAR will be challenging if not impossible the majority of the time.

The implication of this depends on the availability and effectiveness of response measures that can protect the susceptible cohort and limit the spread of disease within a sub-PAR, such as medical countermeasures, isolation of ill individuals, and extraordinary public health measures. If such measures are available, highly effective, and readily implemented force-wide, the need for new measures to prevent disease spread among sub-PARs may not be particularly urgent. On the other hand, in the absence of such measures, restricting the spread of disease to the initial sub-PAR—or to as few sub-PARs as possible—becomes critically important to preventing the entire force from becoming combat ineffective. In addition, even if an outbreak can be controlled despite its spread, the burden on a unit of managing even a few cases of contagious disease may be onerous and cause degradation beyond the immediate loss of ill individuals. Alternatively, commanders may wish to isolate sub-PARs whose operational effectiveness is particularly critical to mission success. Thus, even if it proves impossible to prevent the spread of disease beyond the sub-PAR where it began, the rate at which that disease spreads further through all sub-PARs will be of interest.

The research team therefore conducted an additional excursion to investigate the time it takes the disease outbreak to reach specified sub-PARs. This excursion analyzed results generated using the larger 10-sub-PAR population structure (Figure 8) starting in three different locations: Apache, RSOI, and Bagram. Figure 26 depicts the times at which a plague outbreak caused by 10 initial infections would spread from one sub-PAR to each of the others. The squares on each of the timelines correspond to the time at which the disease first appears in a previously uninfected sub-PAR.

Regardless of starting location, the spread of the modeled plague outbreak to the final sub-PAR occurs almost simultaneously with the cumulative number of symptomatic infections reaching 20 percent of the total population (see Table 8) and the population as a whole reaching combat ineffectiveness. However, in the case described above in which response measures are absent and the disease can be expected to affect all individuals within an exposed sub-PAR, the research team was also interested in determining the time at which the population within exposed sub-PARs exceeded 20 percent, even though they would not all have yet become ill. This is illustrated in Figure 26 by a yellow triangle on each timeline, indicating the time at which the disease has spread to enough sub-PARs that the total population of individuals who are at risk of becoming ill is greater than 20 percent. For times to the left of the yellow triangles, even if the entire

population of each sub-PAR where the outbreak has reached were to become infected, the entire force would not become combat ineffective. The number contained within the yellow triangle is the cumulative number of symptomatic individuals across all sub-PARs on that day. In other words, if the only available response to the outbreak is to restrict movement between sub-PARs, then in order to guarantee that the total population does not become combat ineffective, movement would have to be restricted by the day under each yellow triangle, based on the knowledge of a certain number of symptomatic individuals, as shown by the number within the triangle.

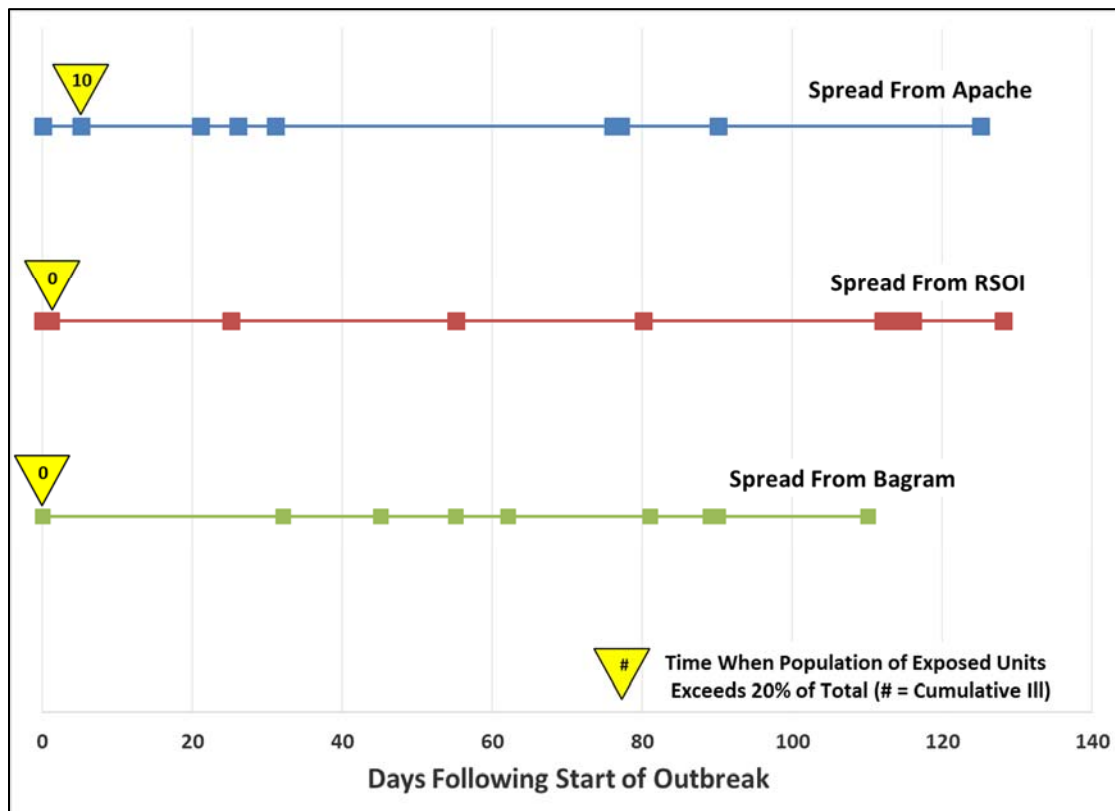


Figure 26. Points in Time When Disease Spreads to Successive Sub-PARs in the 10-Sub-PAR Force Array: Plague with 10 Initial Infections

For the scenarios in which the outbreak starts in the RSOI or Bagram locations, the outbreak spreads to the point of being able to infect over 20 percent of the population before a single individual presents symptoms. For the Bagram scenario, this is due to the fact that the population of the Bagram sub-PAR itself includes well over 20 percent of the total population. In the RSOI scenario, the population of the sub-PAR plus either of the two with which it is connected is greater than 20 percent, so the outbreak needs only to move outside of the RSOI sub-PAR for 20 percent of the population to be at risk. When the outbreak starts in Apache, however, a few days go by before the outbreak reaches a large enough population. Over the course of those few days, symptoms develop in 10

individuals. As discussed previously, the rate at which the disease spreads to different sub-PARs is largely due to the populations of and movement rates between the sub-PARs. Therefore, the location of the initially infected sub-PAR as well as the immediately surrounding sub-PARs strongly influences when the total population could be at risk of becoming combat ineffective.

Although the spread of disease beyond the initial sub-PAR to adjacent sub-PARs is very rapid, it then slows. In the plague example, it takes three to four months to reach the sub-PARs furthest removed from the sub-PAR in which the outbreak starts, by which point a significant fraction of the population would have become ill. This does suggest that it would be physically possible to isolate some units from the risk of exposure to the disease, and for information to support the decision to be available.

The same assessment was conducted with smallpox, and similar trends were observed. For both diseases, there were scenarios in which the outbreak reached enough sub-PARs to infect at least 20 percent of the population prior to the appearance of symptomatic individuals. The only major difference was an increase in the time required to reach subsequent sub-PARs. This is likely due to smallpox's longer incubation period, and is consistent with other observed results.

2. Effectiveness of Outbreak Response Capabilities

The decision to implement any type of outbreak response requires (1) recognition that an outbreak is underway, and (2) selection of the most appropriate response, given the current understanding of the outbreak and the response choices available. As seen in the previous section, the available knowledge on which to base this decision may well be very limited, and depending on the disease, the available response options may be few. This portion of the assessment of operational impact examines the potential mitigating effects of responses of various types. The objective is to provide some initial indication of the benefits of each type of response, both overall and relative to each other. The insights gained can support both efforts to develop response capabilities and decisions to implement them. Within the context of the research, the results can help identify the characteristics of diseases that make them particularly easy or difficult to mitigate; these in turn can be incorporated into the list of characteristics of concern by which future EIDs can be evaluated.

Each type of response was evaluated using three measures of effectiveness: casualties avoided by the response, delay in the time to reach combat ineffectiveness, and delay in the time it takes a disease outbreak to reach a specified unit, location, or sub-population. For the purpose of the present analysis, the delay in time until a disease outbreak reaches a specified unit, location, or sub-population was measured as the number of days it took for the outbreak to infect all sub-populations in the four-sub-PAR force array. In other words, the time at which the last sub-PAR became infected served as

the third measure of effectiveness. The assessment was limited to one disease, SARS. Since the structure and movement of the population in the analysis was largely notional, conclusions are drawn from overall trends, which are expected to hold true for various analytic scenarios, instead of individual scenario results.

For each of the four modeled responses, a series of three bar charts will be presented, each illustrating one of the aforementioned measures of effectiveness. The first bar chart shows the reduction in the total number of casualties due to the response. In these figures, a 100 percent reduction in casualties indicates that there were no casualties, and a 0 percent reduction in casualties indicates that the response had no effect on the number of casualties. The second bar chart shows the absolute number of days for each scenario to reach combat ineffectiveness. A white asterisk (*) on a bar in these figures indicates that combat ineffectiveness was never reached in that scenario. The final figure shows the time required for the outbreak to infect the last sub-PAR. In these figures, a white asterisk (*) on a bar indicates that the response prevented the disease from spreading to the last sub-PAR in that scenario.

For the second and third bar charts in each section, the results from the corresponding scenario without interventions are shown in black. The no-intervention scenarios are not shown in the first figure, reduction in casualties, since the data being illustrated are already calculated relative to the corresponding no-intervention scenario.

a. Immunization

The results from the immunization scenarios are shown in Figure 27 through Figure 29. An immunization with an efficacy as low as 50 percent was adequate to reduce casualties to the point that the population never became combat ineffective for all numbers of initial infections. However, immunization was only able to prevent or delay the spread of the disease to the last sub-PAR when there was a single initial infection; a 90 percent efficacious immunization prevented the disease from reaching all sub-PARs, while a 50 percent efficacious immunization delayed the time required to infect all sub-PARs.

Immunization of personnel against disease can be effective at mitigating the operational impact of an EID. For some types of EIDs—particularly those that are known but emerging in a new population or location, or those that are a variation of a known pathogen—immunizations may be readily available and serve as a viable option. Furthermore, the modeling results presented below indicate that an immunization with a reduced efficacy (e.g., 50 percent) is still highly effective at mitigating the impact of an outbreak. However, existing vaccines may offer little to no protection against truly novel pathogens.

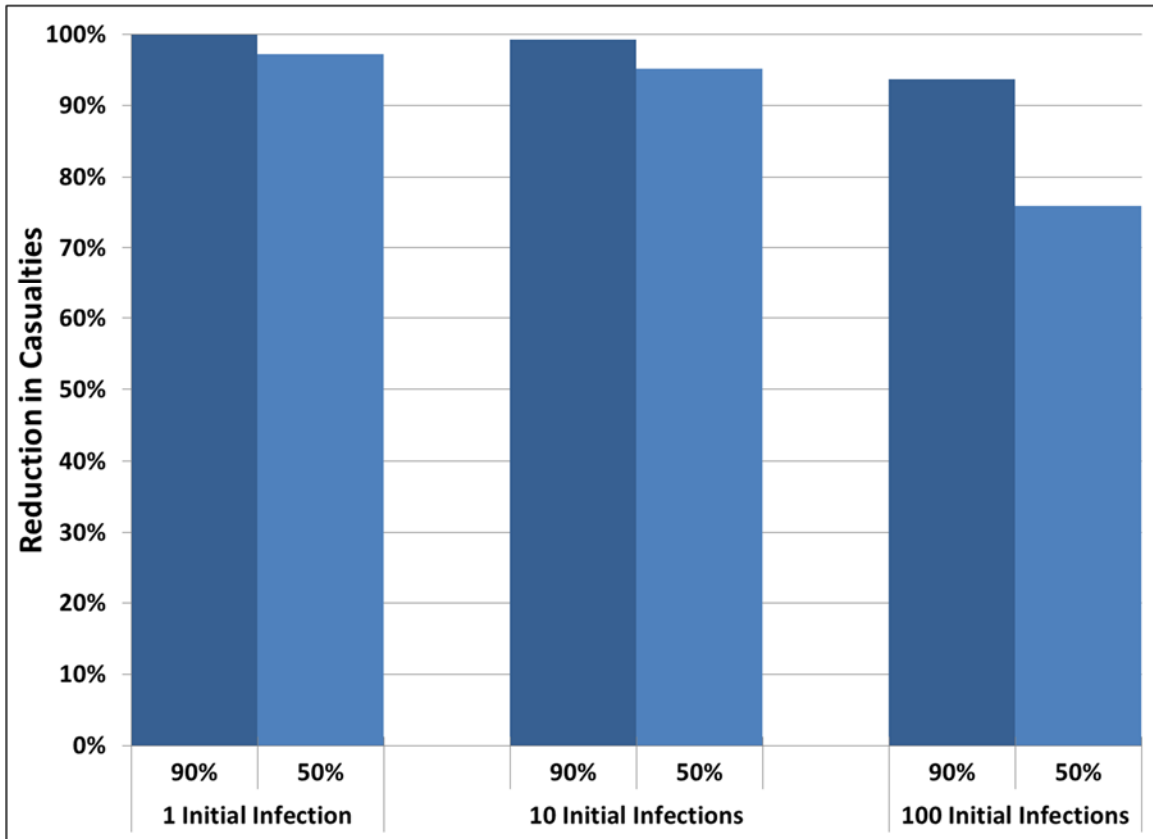


Figure 27. Reduction in SARS Casualties Due to Immunization

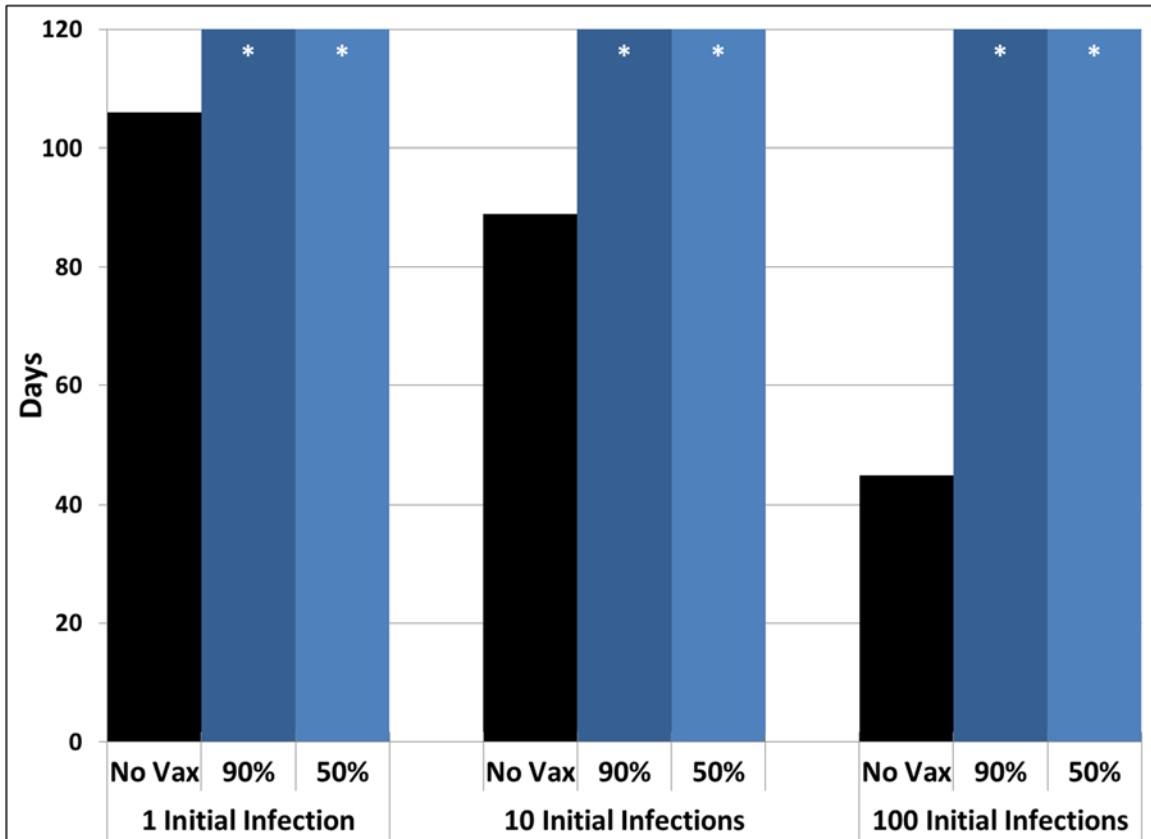


Figure 28. Effect of Immunization on Time to Reach Combat Ineffectiveness
(* = Combat Ineffectiveness Never Reached)

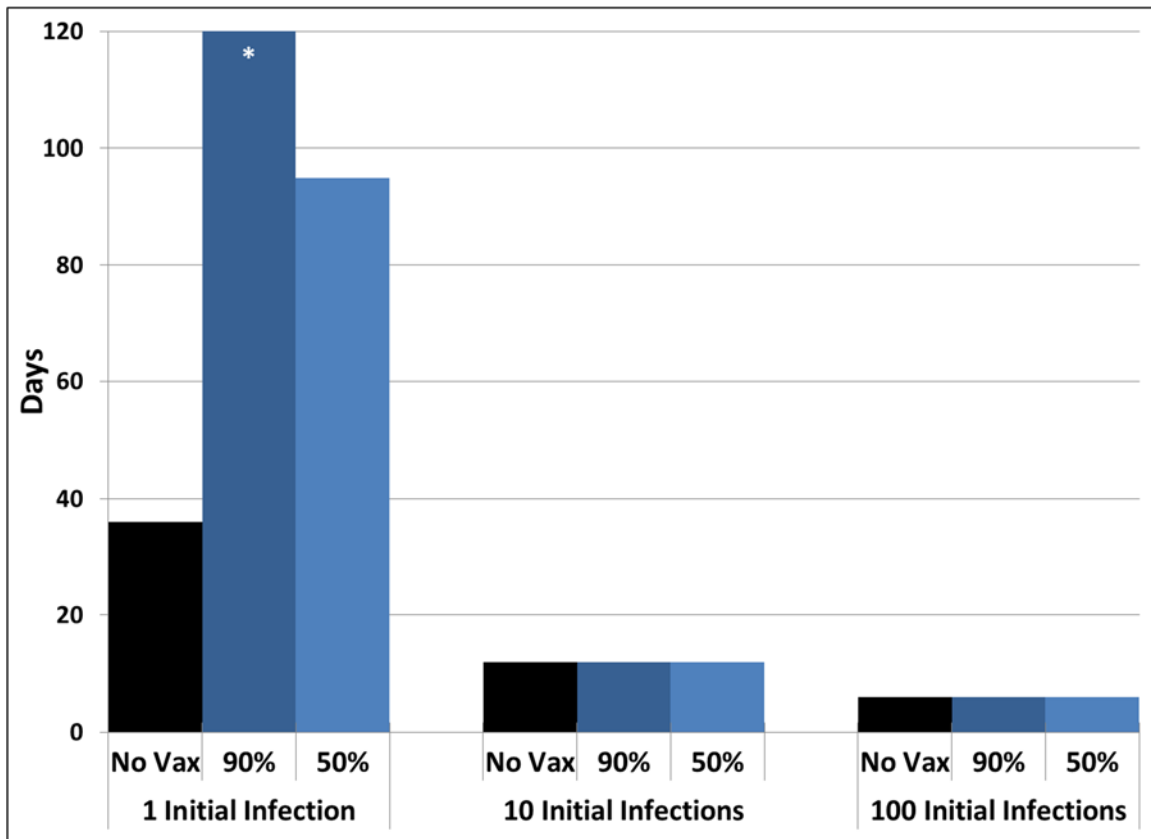


Figure 29. Effect of Immunization on Time for SARS Outbreak to Spread to Last Sub-PAR
(* = Outbreak Never Spread to Last Sub-PAR)

b. Post-Exposure Prophylaxis (PEP)

The results from the PEP scenarios are shown in Figure 30 through Figure 32. Overall, PEP was effective at reducing casualties—all modeled PEP scenarios reduced the total number of casualties by at least 33 percent. As long as it was administered within 10 days of the start of the outbreak, a PEP with an efficaciousness as low as 50 percent was adequate to prevent the population from becoming combat ineffective. If it was administered 20 or 40 days after the outbreak, a 50 percent efficacious PEP still reduced the total number of casualties by at least 64 percent and 33 percent, respectively. PEP was less effective at delaying or preventing the spread of the disease to the last sub-PAR. The 50 percent efficacious PEP was never able to prevent the spread of the disease to the last sub-PAR, and it was able to delay the spread of the disease to the last sub-PAR only for outbreaks with a single initial infection. For scenarios with 10 and 100 initial infections, the only way to delay the spread of the disease to the last sub-PAR was by administering a perfectly efficacious PEP by day 10 or day 5, respectively.

In much the same way as immunization, PEP can be effective at mitigating the effects of an EID outbreak, but there is no guarantee that an efficacious PEP will be

available. However, even a PEP with a reduced efficacy is still able to reduce the operational impact of an EID outbreak. Furthermore, there is a relatively long window of time, in some circumstances up to 40 days, in which an effective PEP can be implemented and still reduce the operational impact of the disease.

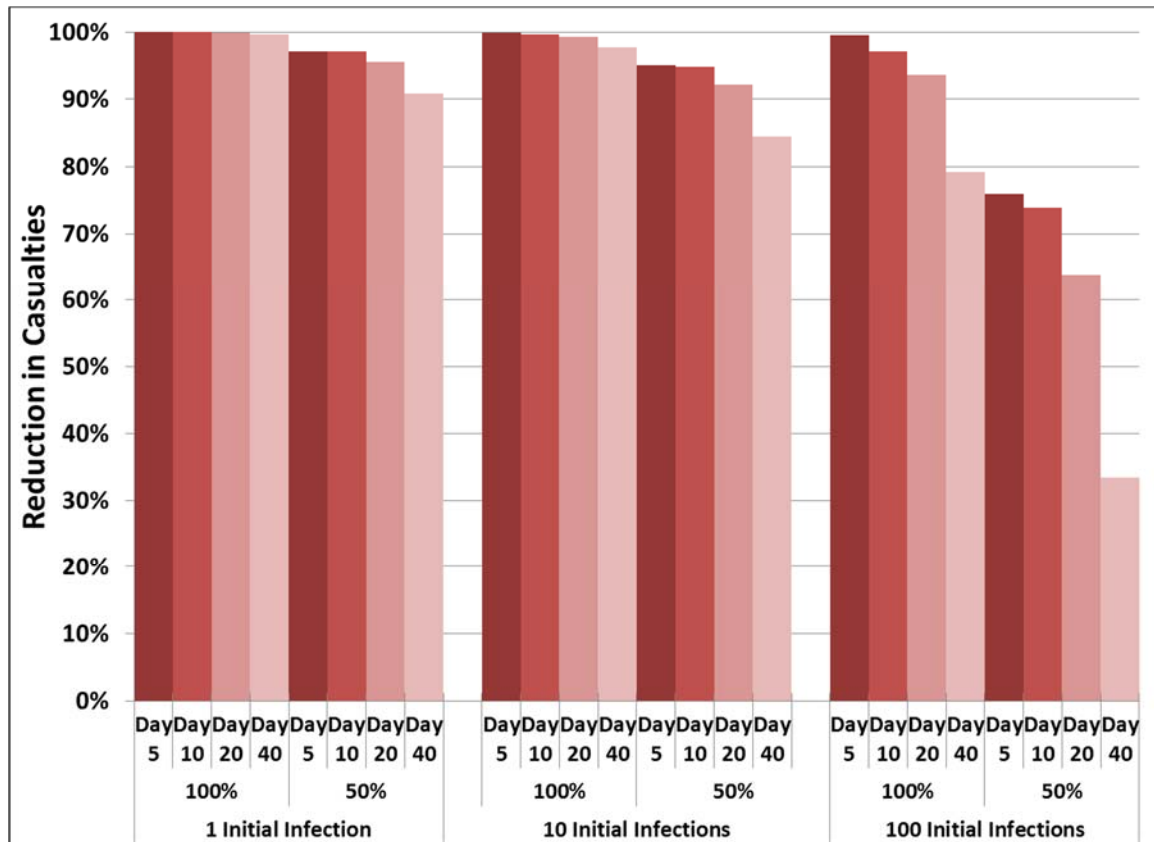


Figure 30. Reduction in SARS Casualties Due to PEP

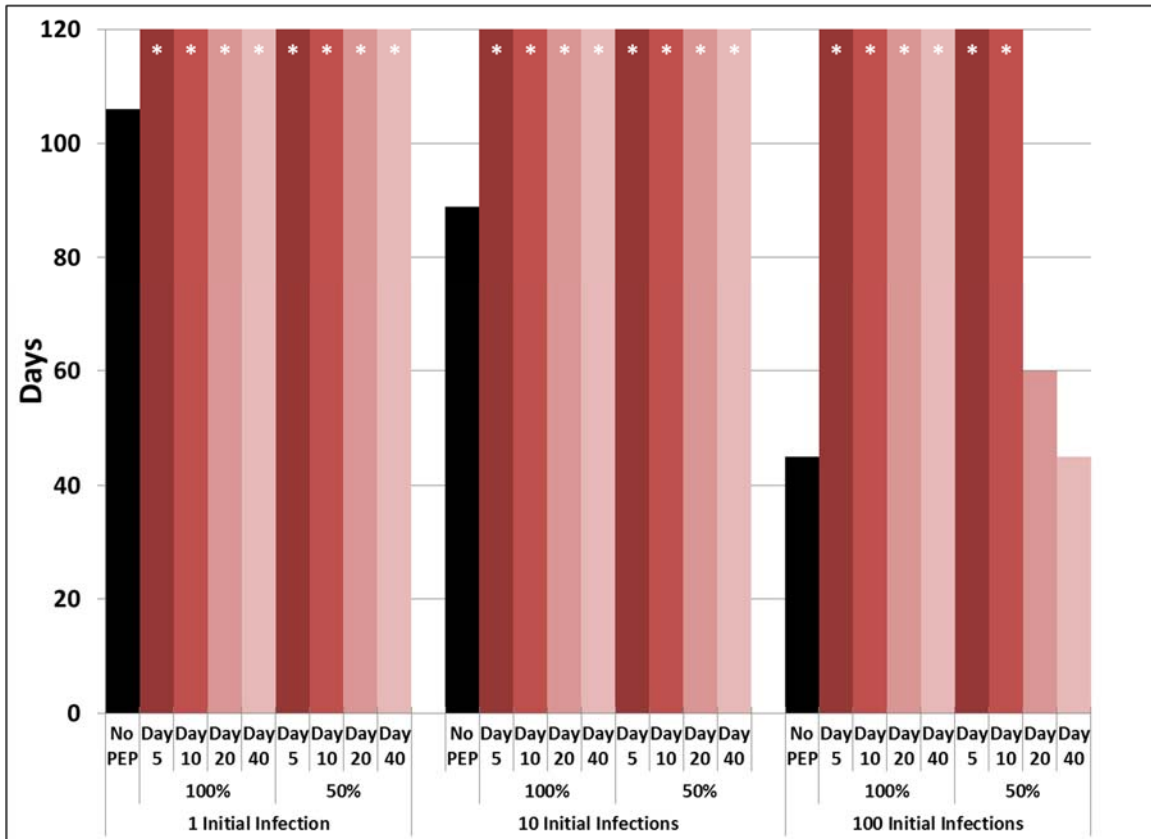


Figure 31. Effect of PEP on Time to Reach Combat Ineffectiveness
 (* = Combat Ineffectiveness Never Reached)

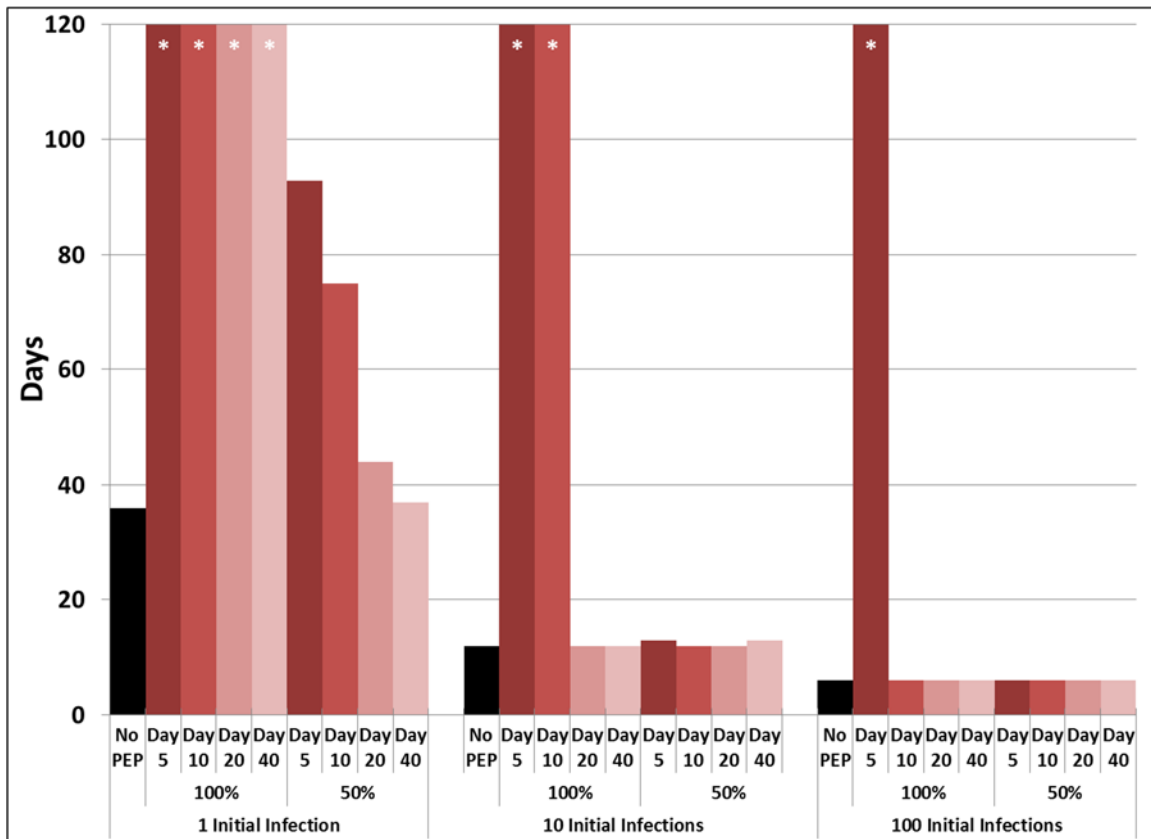


**Figure 32. Effect of PEP on Time for SARS Outbreak to Spread to Last Sub-PAR
(* = Outbreak Never Spread to Last Sub-PAR)**

c. Restriction of Movement (ROM)

The results from the ROM scenarios are shown in Figure 33 through Figure 35. ROM was effective at reducing casualties only when movement was completely prohibited between the sub-PARs (100 percent ROM) for scenarios with 1 and 10 initial infections. Even in these scenarios, ROM was unable to delay the time at which combat ineffectiveness was reached. Complete ROM was able to prevent the disease from reaching the last sub-PAR for scenarios with 1 and 10 initial infections if it was implemented by day 20 or day 10, respectively. ROM was unable to delay the spread of the disease to the last sub-PAR in scenarios with 100 initial infections.

In order to mitigate the operational impact of an EID to any degree, ROM must be total and must be implemented early. For the scenarios analyzed here, partial ROM was shown, by all three measures of effectiveness, to be ineffective at reducing the effects of the outbreak. Furthermore, the process of restricting the movement between sub-PARs will in itself create a substantial operational impact. That being said, unlike the medical countermeasures mentioned above, ROM requires no specific knowledge of the disease characteristics to be implemented.

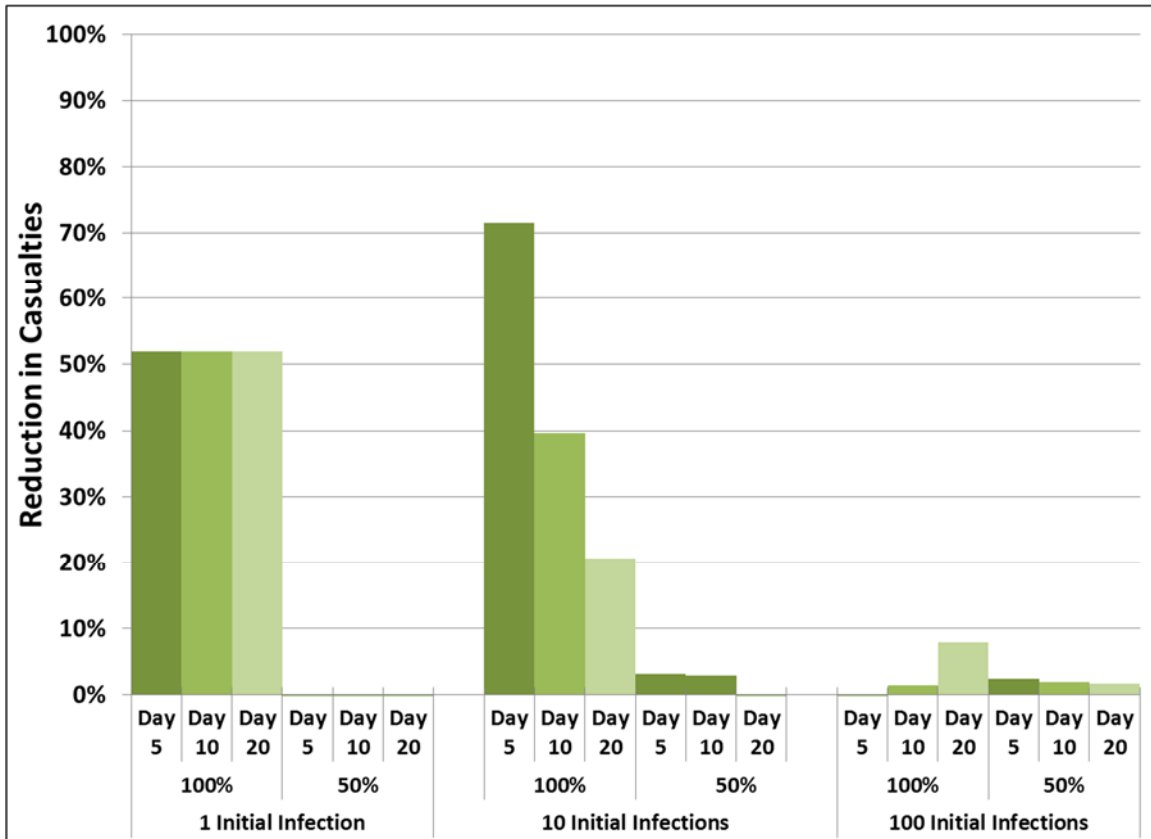


Figure 33. Reduction in SARS Casualties Due to ROM

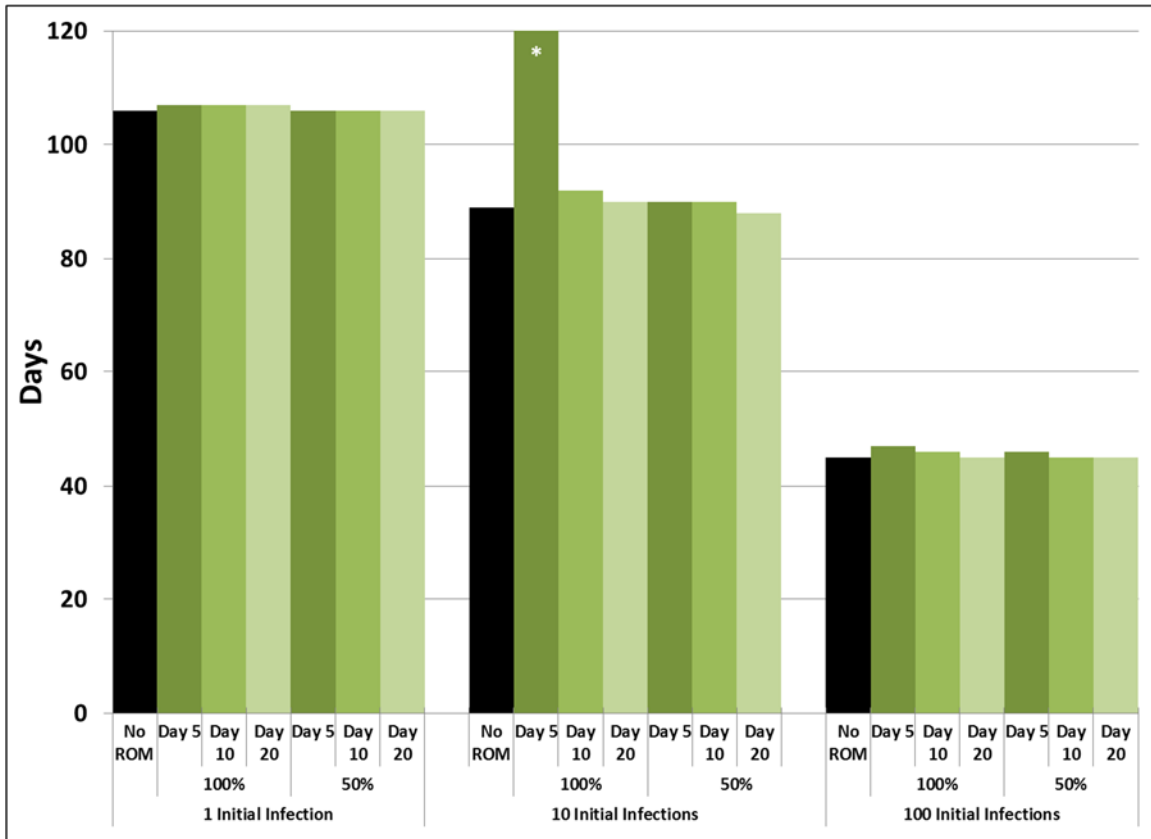


Figure 34. Effect of ROM on Time to Reach Combat Ineffectiveness
 (* = Combat Ineffectiveness Never Reached)

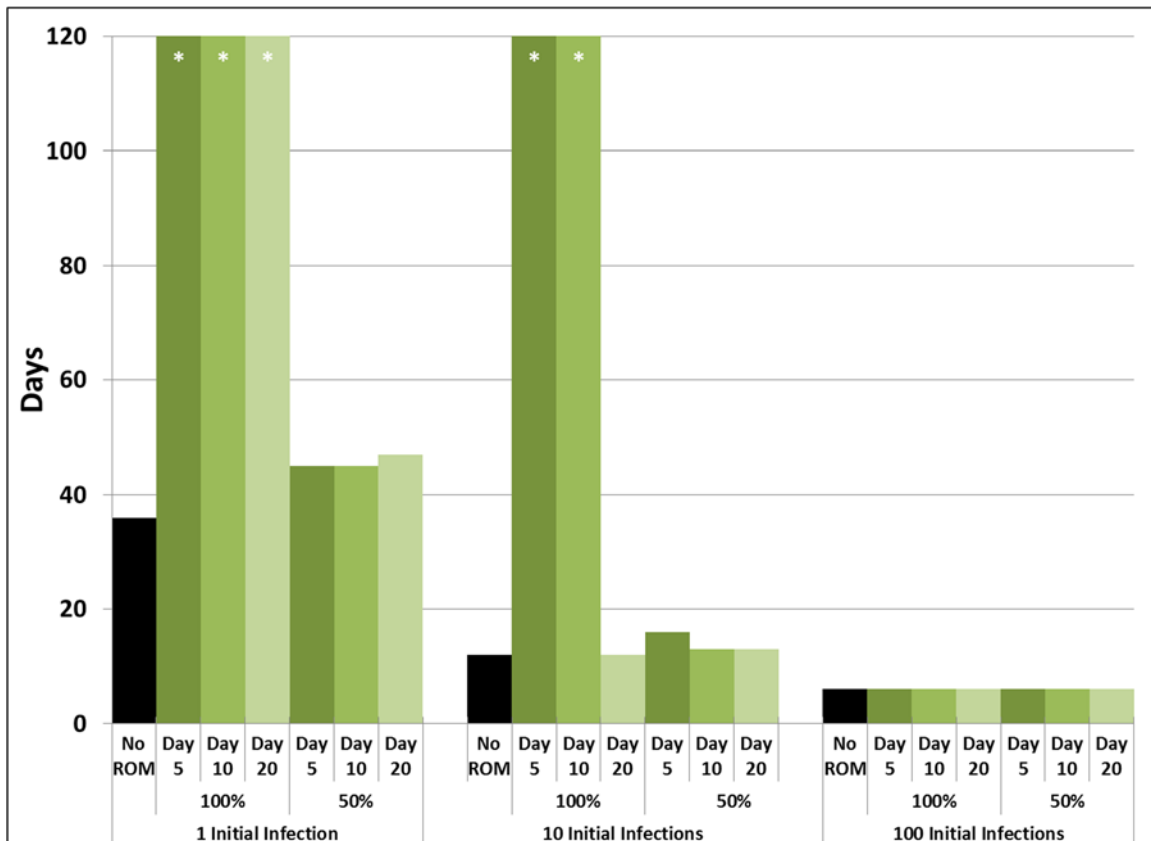


Figure 35. Effect of ROM on Time for SARS Outbreak to Spread to Last Sub-PAR
 (* = Outbreak Never Spread to Last Sub-PAR)

d. Isolation of Contagious Individuals

Results from the scenarios involving isolation of contagious individuals are shown in Figure 36 through Figure 38. Isolation of infectious individuals was effective at reducing casualties in all scenarios. For both 1 and 10 initial infections, both modeled forms of isolation (after 1 day and after half the contagious period) were able to prevent combat ineffectiveness. For 100 initial infections, if the isolation regime was implemented by day 10, combat ineffectiveness was prevented or delayed for both the 1-day isolation and the half-contagious-period isolation. Isolation was largely ineffective at delaying the spread of the disease to the last sub-PAR for scenarios with 10 or 100 initial infections. If implemented by day 10, isolation delayed or prevented the spread of the disease to the final sub-PAR for scenarios with a single initial infection.

Based on the modeling results shown here, the isolation of contagious individuals can be an effective method to reduce the casualties caused by an EID outbreak. However, the response is less effective at curtailing the spread of the disease across sub-PARs. In much the same manner as ROM, the process of isolating contagious individuals in itself causes some operational impact. Depending on the contagiousness of the disease and the

available resources, the complete isolation of a contagious individual may be burdensome, if not impossible. However, the additional time afforded by the response technique may buy time to implement a more effective response (e.g., medical intervention or unit replacement).

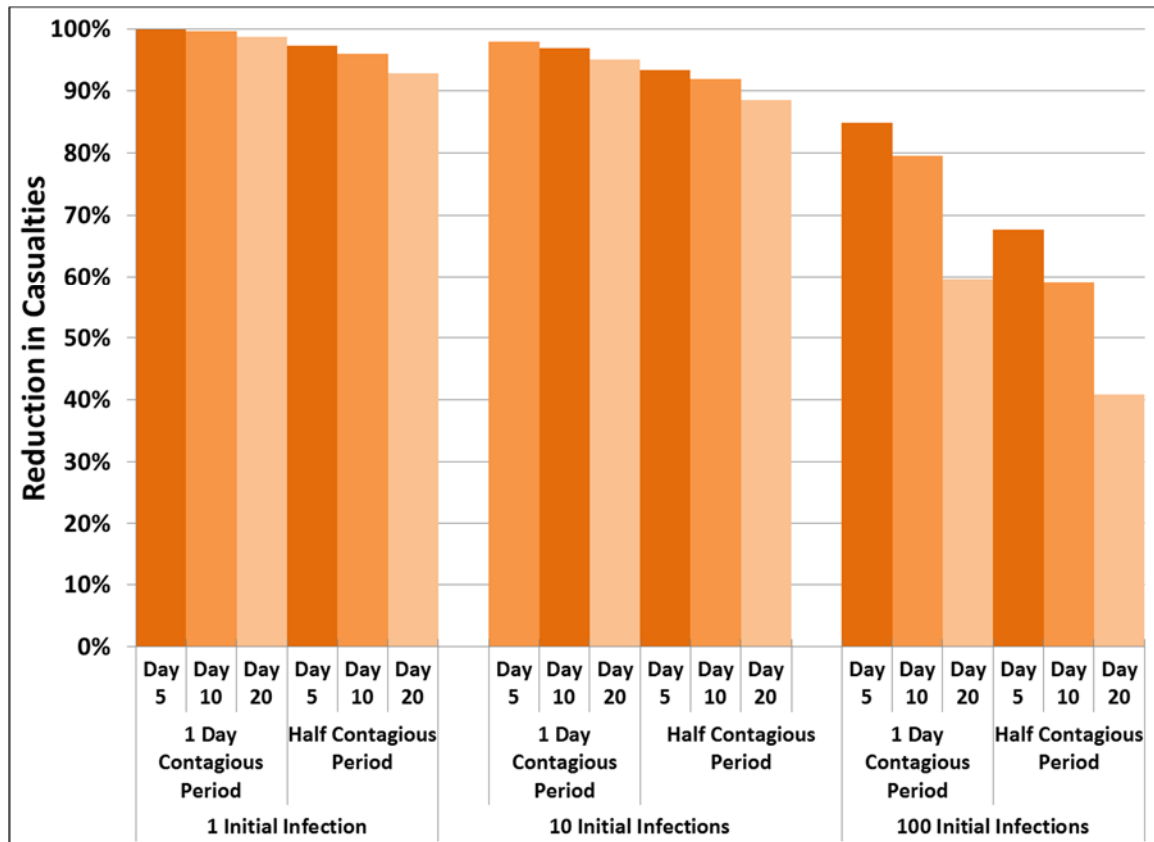


Figure 36. Reduction in SARS Casualties Due to Isolation

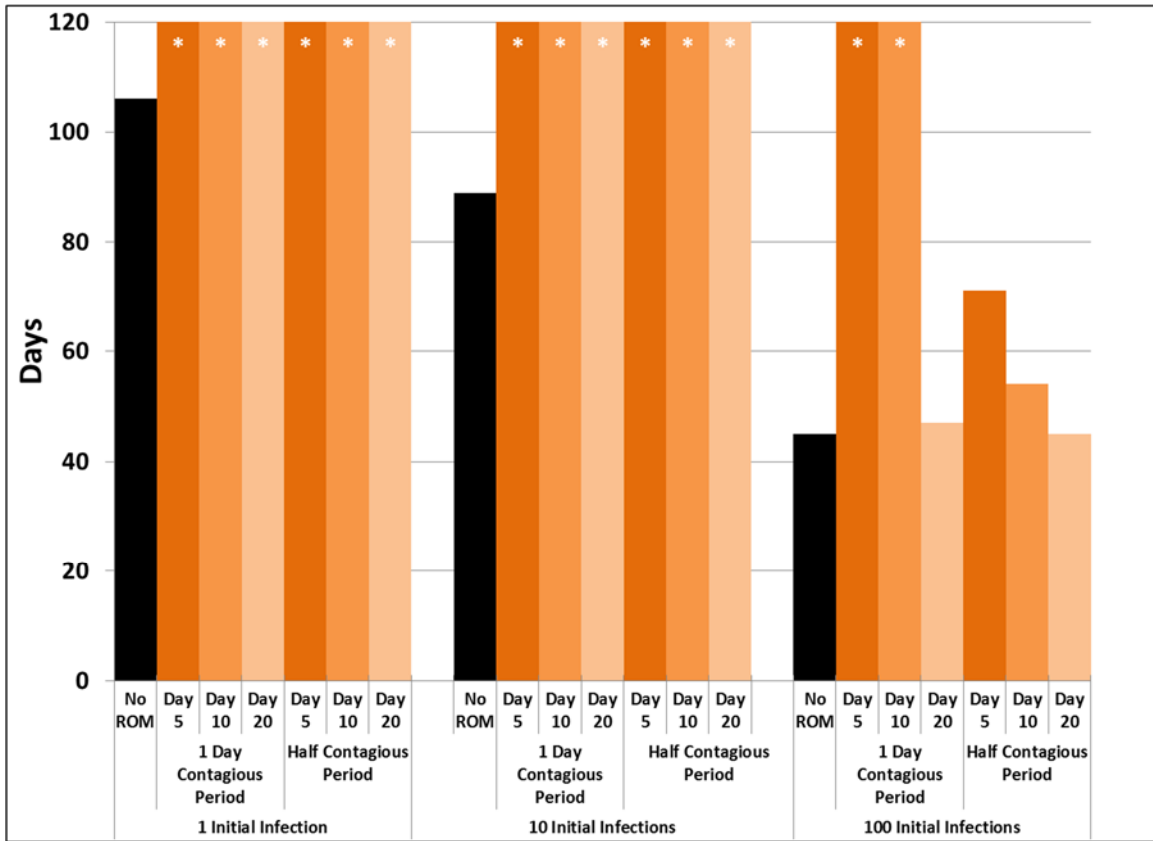


Figure 37. Effect of Isolation on Time to Reach Combat Ineffectiveness
 (* = Combat Ineffectiveness Never Reached)

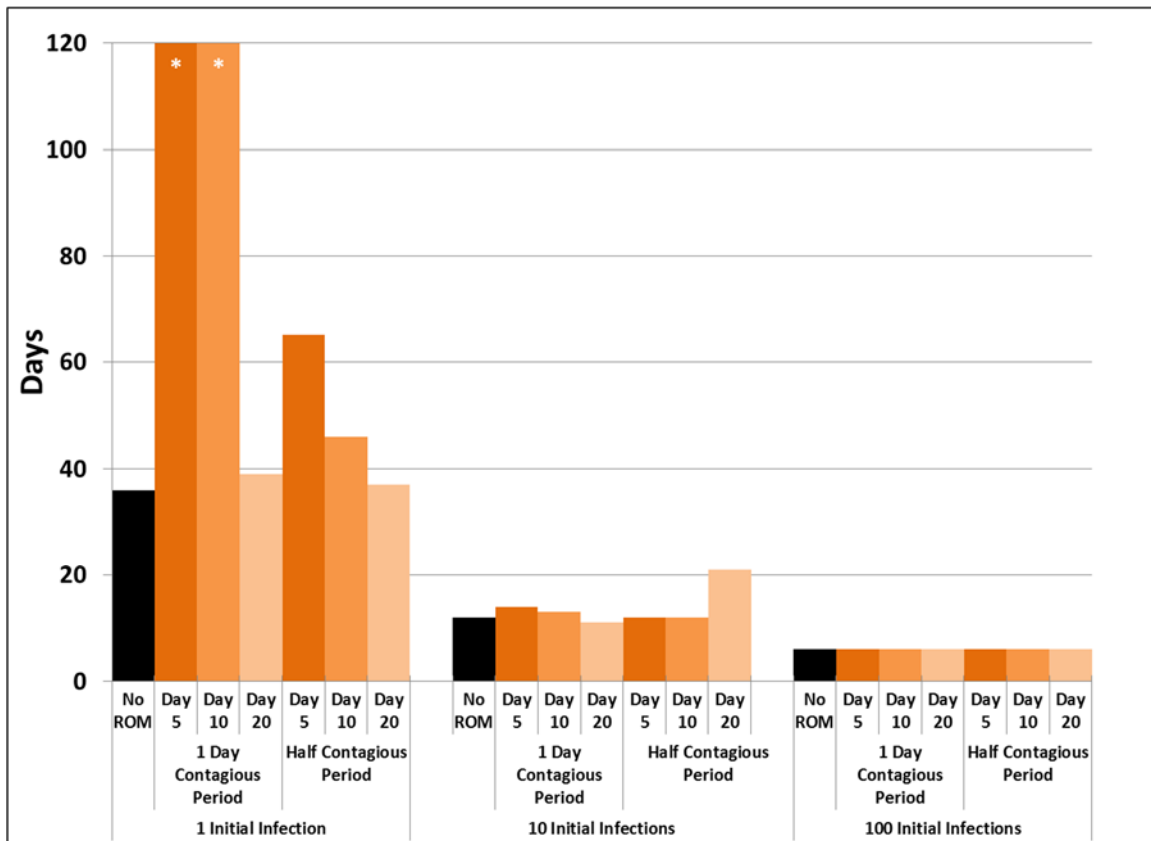


Figure 38. Effect of Isolation on Time for SARS Outbreak to Spread to Last Sub-PAR
 (* = Outbreak Never Spread to Last Sub-PAR)

e. Comparison of Response Capabilities

Figure 39 through Figure 41 compare the effects of the various response capabilities on the reduction of casualties. All modeled responses were able to substantially reduce the number of casualties for 1, 10, and 100 initial infections, with a couple of exceptions. Partial ROM (i.e., 50 percent) never reduced casualties, and total ROM (i.e., 100 percent) reduced casualties for only 1 and 10 initial infections. In general, all responses other than ROM tended to reduce the number of casualties by similar amounts.

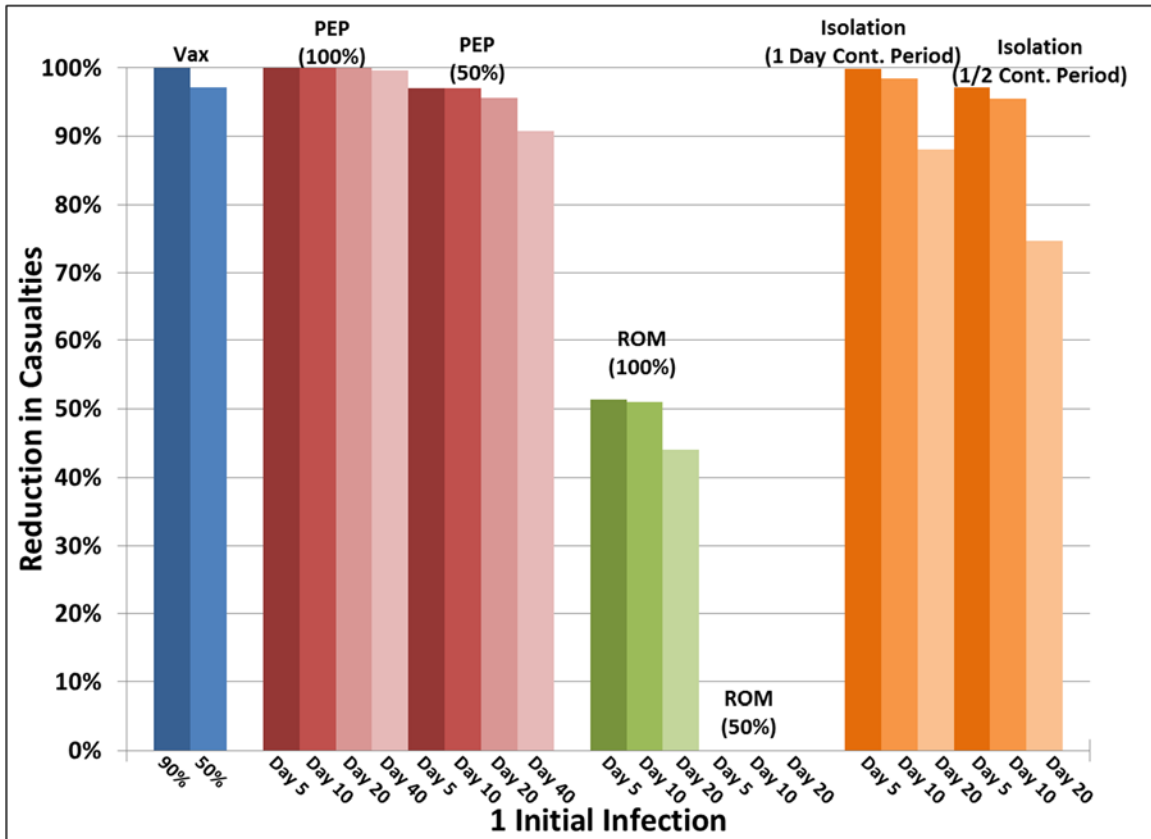


Figure 39. Reduction in SARS Casualties Due to Various Response Capabilities, 1 Initial Infection

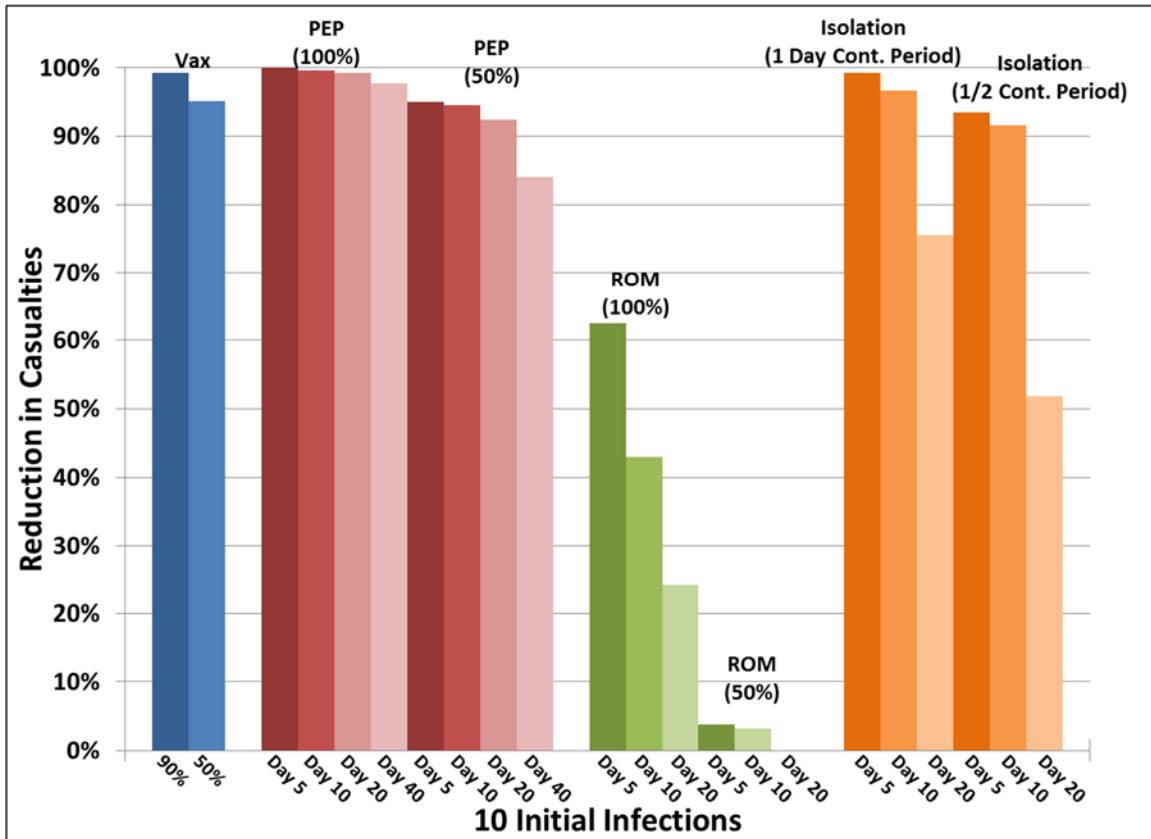


Figure 40. Reduction in SARS Casualties Due to Various Response Capabilities, 10 Initial Infections

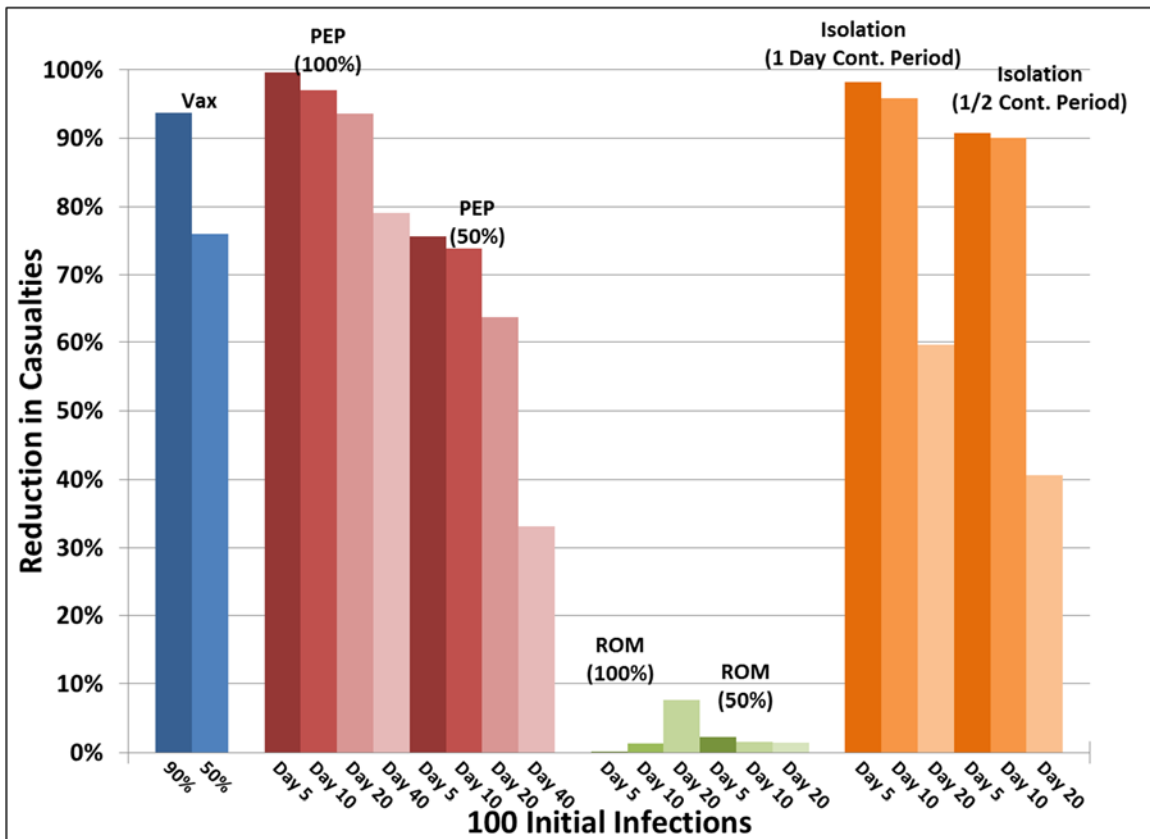


Figure 41. Reduction in SARS Casualties Due to Various Response Capabilities, 100 Initial Infections

Figure 42 through Figure 44 compare the effects of the various response capabilities on the time it took for the population to reach combat ineffectiveness in the four-sub-PAR array. As expected, medical countermeasures (immunization and PEP) were the most effective at preventing the population from becoming combat ineffective. With regard to procedural responses, the isolation of contagious individuals tended to prevent or delay combat ineffectiveness better than ROM. For scenarios with 1 and 10 initial infections, all responses, with the exception of ROM, were able to prevent the population from reaching combat ineffectiveness.

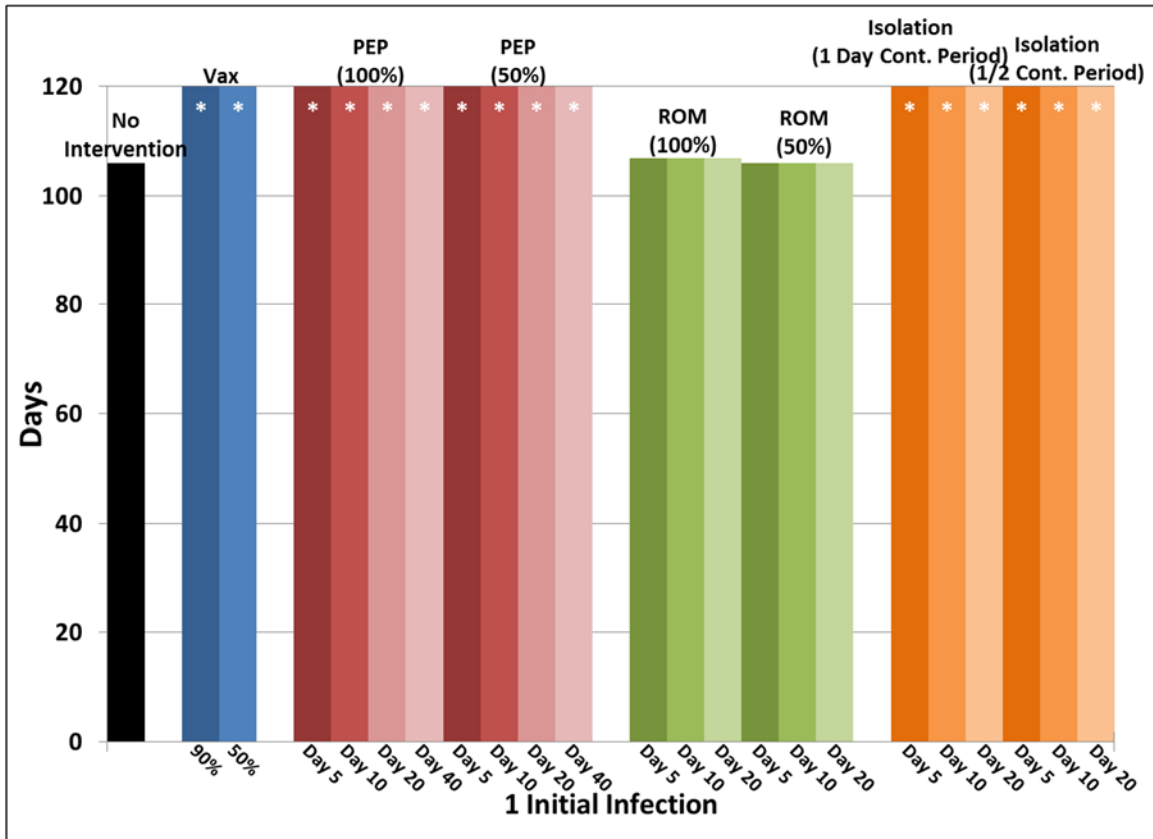


Figure 42. Effect of Various Response Capabilities on Time to Combat Ineffectiveness, 1 Initial Infection
 (* = Combat Ineffectiveness Never Reached)

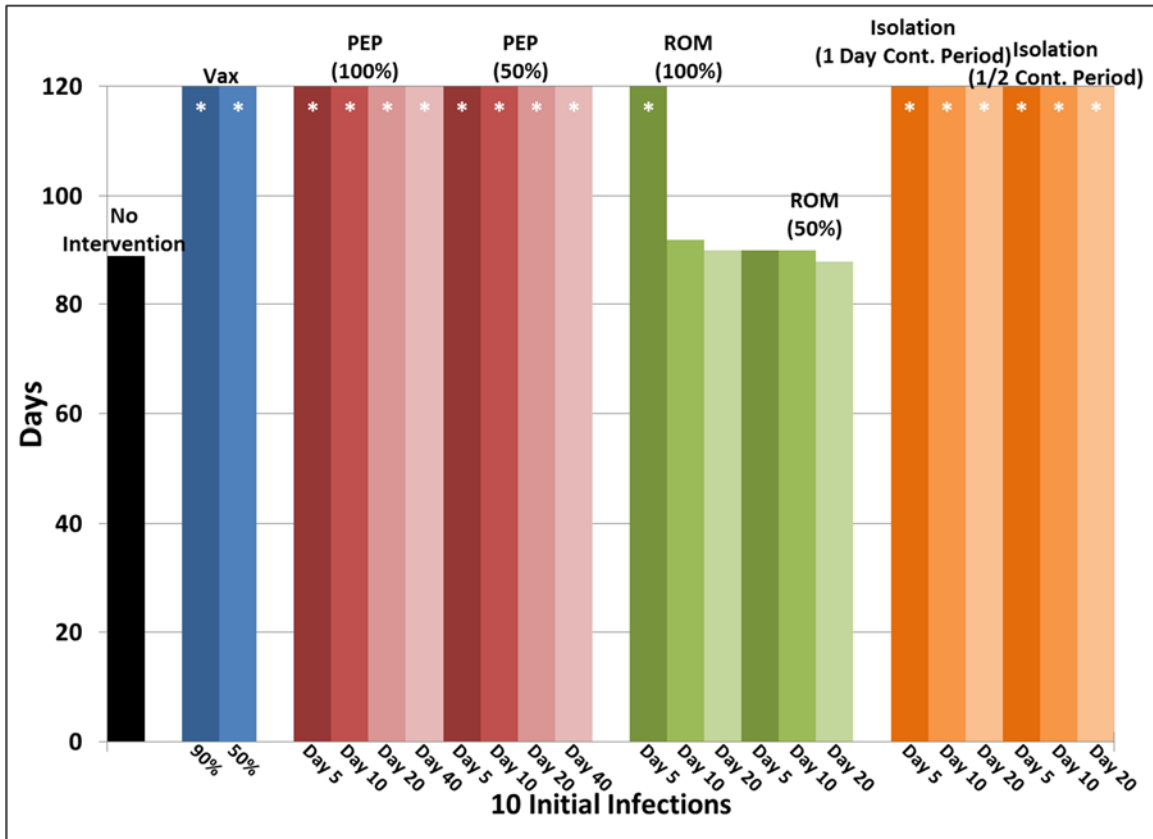


Figure 43. Effect of Various Response Capabilities on Time to Combat Ineffectiveness, 10 Initial Infections
 (* = Combat Ineffectiveness Never Reached)

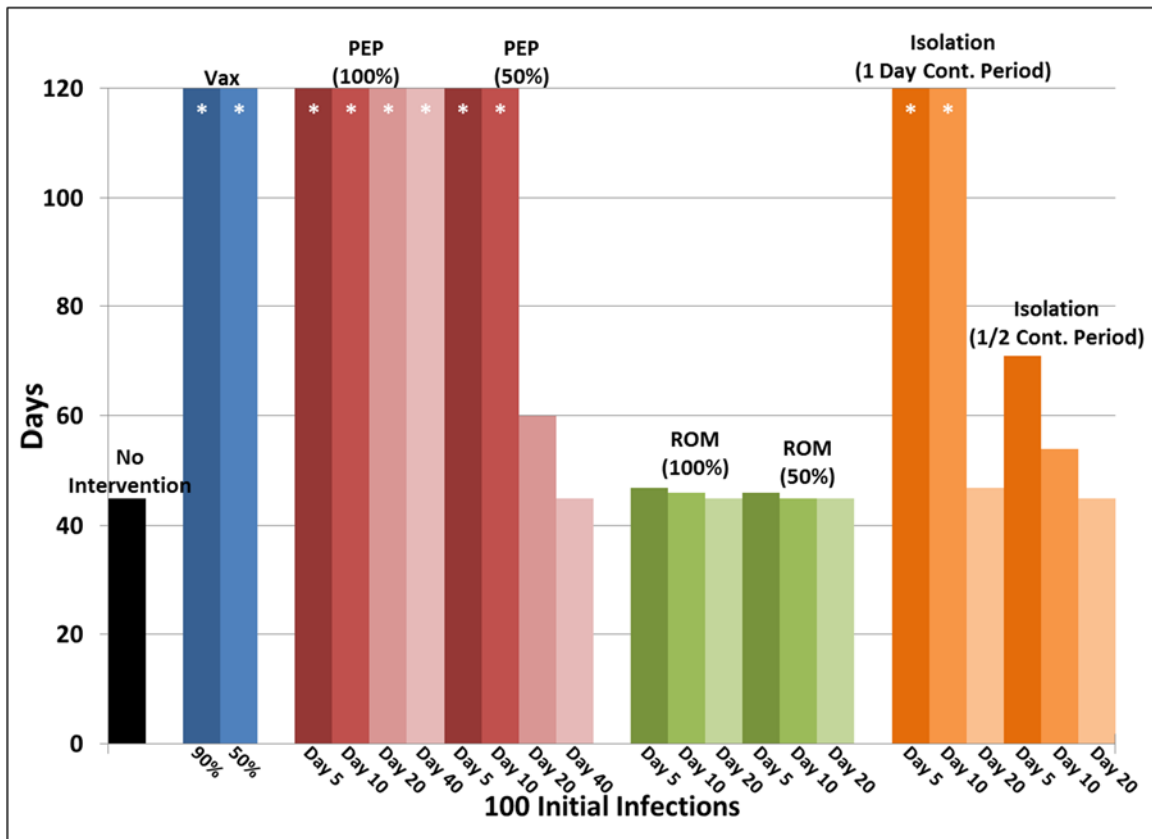


Figure 44. Effect of Various Response Capabilities on Time to Combat Ineffectiveness, 100 Initial Infections
 (* = Combat Ineffectiveness Never Reached)

Figure 45 through Figure 47 compare the effects of various response measures on the time required for the last sub-PAR to become infected. The distinction between the medical responses (immunizations and PEP) and the procedural responses (ROM and isolation) is not as apparent when considering the time for the infection to reach the last sub-PAR as compared to the other two measures of effectiveness (reduction in casualties and time to combat ineffectiveness). For scenarios with 10 and 100 initial infections, most response implementations were unable to delay or prevent the last sub-PAR from becoming infected.

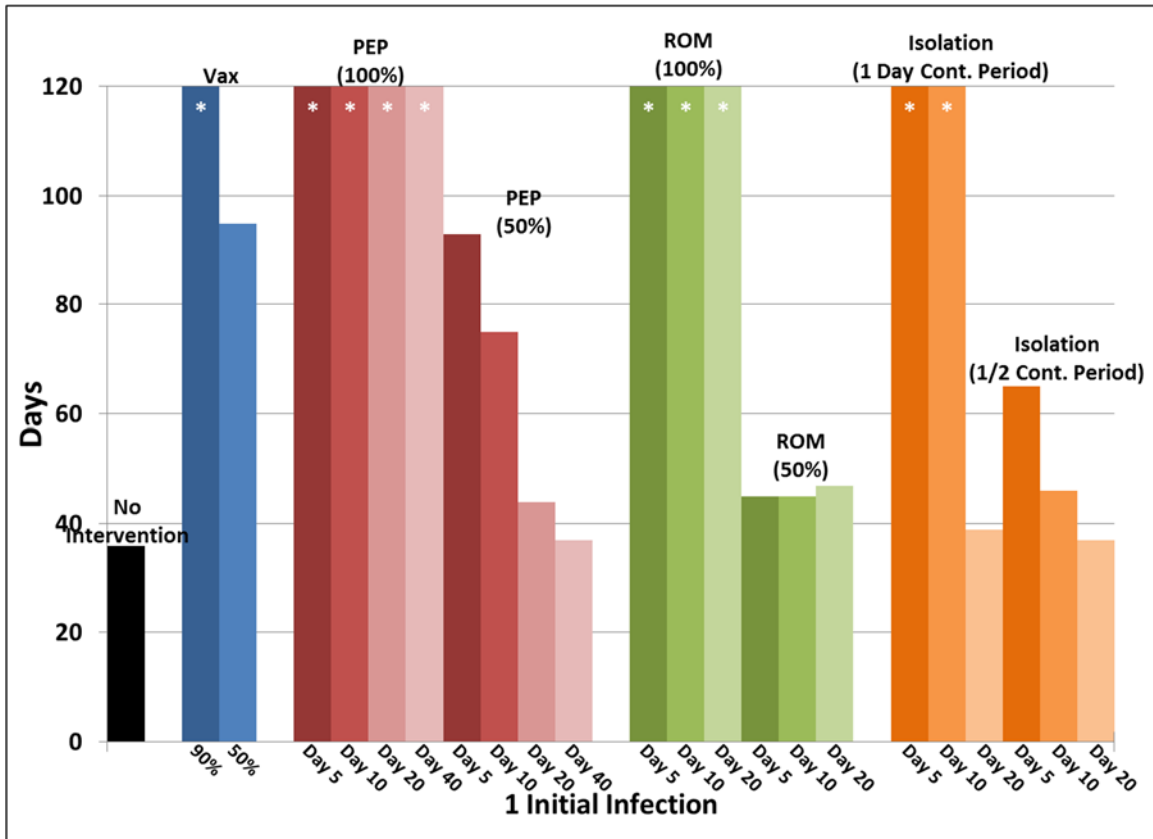


Figure 45. Effect of Various Response Capabilities on Time for SARS Outbreak to Spread to Last Sub-PAR, 1 Initial Infection
 (* = Outbreak Never Spread to Last Sub-PAR)

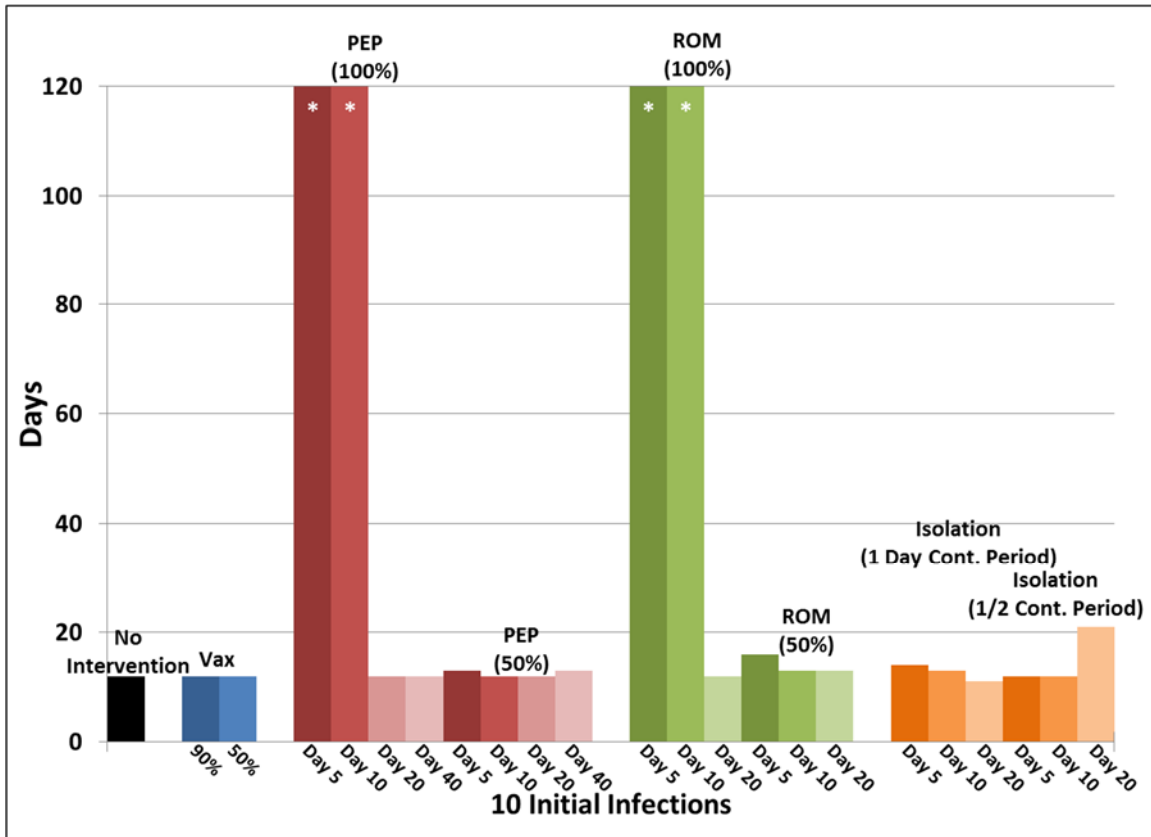


Figure 46. Effect of Various Response Capabilities on Time for SARS Outbreak to Spread to Last Sub-PAR, 10 Initial Infections
 (* = Outbreak Never Spread to Last Sub-PAR)

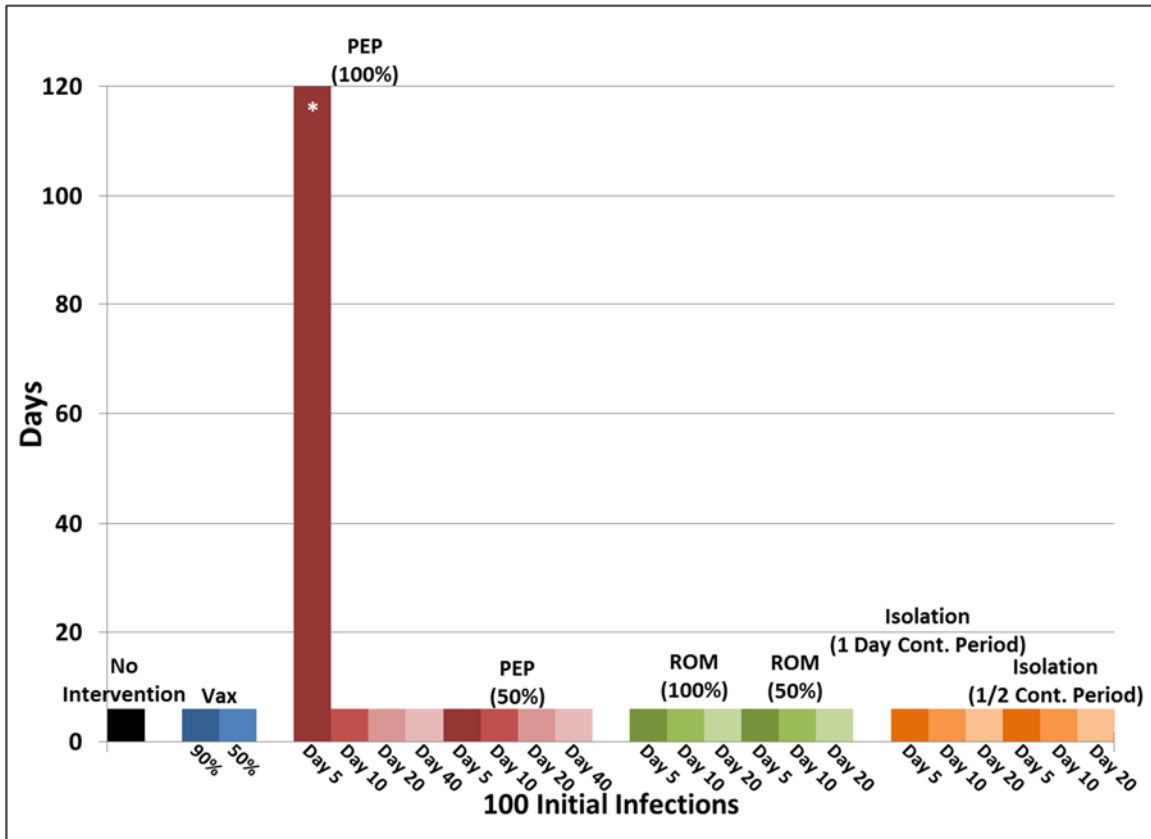


Figure 47. Effect of Various Response Capabilities on Time for SARS Outbreak to Spread to Last Sub-PAR, 100 Initial Infections
(* = Outbreak Never Spread to Last Sub-PAR)

6. Observations and Recommendations

A. Observations on Modeling Results

1. The Potential for EIDs to Have Operational Impact

a. EID Outbreaks Can Lead to Combat Ineffectiveness

The operational impact assessment in this research found that in the absence of any intervention, all cases modeled resulted in the overall population at risk eventually reaching a 20 percent casualty level, thereby becoming combat ineffective. In relatively small force deployments, the time it took for this to occur was extremely short for diseases with short incubation times like 1918 influenza and plague, but somewhat longer for those with lengthy incubation periods like SARS and smallpox. In larger deployments, the time to reach combat ineffectiveness ranged from weeks to months. This suggests that (1) if mitigating capabilities are available, and (2) if those capabilities can be brought to bear in a timely fashion, combat ineffectiveness can often be avoided in both natural outbreaks and improvised biological operations, with larger deployments at less risk than smaller ones. The time at which combat ineffectiveness would be reached following larger attacks involving weaponized EIDs, where large percentages of the overall force are exposed at once, would be much shorter—likely just a few days. In such a case, even if mitigating capabilities are available, mounting an effective response would be extremely challenging.

The modeling results showed that larger numbers of initial infections invariably caused overall force to reach the 20 percent casualty level and hence become combat ineffective sooner than did fewer initial infections, but this relationship is not linear. The time to reach combat ineffectiveness for 10 initial infections was typically closer to that for 100 initial infections than it was for a single initial infection. Considering the postulated adversary pathways, this suggests that outbreaks generated by improvised biological operations would pose a much greater threat than natural outbreaks.

Outbreaks of 1918 influenza and plague consistently caused the population to reach combat ineffectiveness sooner than outbreaks of smallpox and SARS, given the same number of initial infections. 1918 influenza and plague have significantly shorter incubation periods than smallpox and SARS (Table 6); since infected individuals would become ill more quickly, the disease would be expected to spread more quickly. On the other hand, 1918 influenza and plague also have a significantly shorter contagious period,

so each contagious individual would have fewer contacts over time and less opportunity to spread disease. Based on the modeling results, of these two characteristics, incubation period appears to be a greater driver of time to reach combat ineffectiveness than duration of the contagious period.

In the larger 10-sub-PAR force array (Figure 8), sub-PAR populations and patterns of movement were quite varied. In such circumstances, it might be expected that an outbreak's progression across the overall population at risk would be sensitive to the sub-PAR in which the outbreak began. The results of the modeling, however, proved insensitive to the starting location of the outbreak. For a given disease and number of initial infections, no one starting location consistently correlated with longer or shorter times to reach combat ineffectiveness, and the differences in results were generally quite small.

The research team used the four-sub-PAR force array to conduct a detailed investigation into the sensitivity of results to the patterns and rates of movement between sub-PARs. With a couple of exceptions, the time to reach combat ineffectiveness for a given number of initial infections proved relatively insensitive to both the movement pattern and rate.

b. EID Outbreaks Spread Rapidly but Commanders May Have Opportunities to Protect Some Units

Results from modeling SARS using the smaller four-sub-PAR force array provided insight into the spread of the disease, the requisite timeliness of implementing certain responses, and the amount of knowledge available at the time a response decision would be needed. As observed in the time to reach combat ineffectiveness, outbreaks with larger numbers of initial infections progress more rapidly than those starting with fewer initial infections. This trend was also observed with the time for the outbreak to reach all four sub-PARs.

The research found that for small numbers of initial infections, the time at which an outbreak spreads beyond the first sub-PAR is dependent on the rate of movement from the first sub-PAR—the higher the rate of movement, the sooner the outbreak will spread. This did not prove to be the case for larger numbers of initial infections. For 100 initial infections, the outbreak spreads from the first sub-PAR independent of the movement rate or pattern. Overall, scenarios with greater movement rates tended to see the outbreak spread across the sub-PARs at a faster rate. This was seen when measured both by the time to leave the first sub-PAR and the time it took for all four sub-PARs to become infected.

One of the most important insights of this research was that, in several of the cases examined, a disease was observed to spread beyond the first sub-PAR prior to the onset

of symptoms in any individual. Further investigation revealed that in cases where there were few initial infections and a low movement rate, the spread of disease beyond the initial sub-PAR was likely to occur after the appearance of symptomatic individuals. At the other extreme, for scenarios with a large number of initial infections and a high rate of movement, the disease spread is likely to occur prior to symptom onset. This means that if the objective is preventing the spread of disease outside the population in which it initially appears, has authorities have less time than the minimum latent period within which to intervene.

In the Afghan SPOT-JAMMS dataset used in this research, the median sub-PAR movement rate was 20–25 percent of the population per day, and in no case was the movement rate less than 5 percent. Together with the curves shown in Figure 25, this suggests that during normal operations, with normal rates of personnel movement, any outbreak of contagious disease will likely spread beyond the sub-PAR in which it starts before the first symptomatic case occurs. If the first indicator of an EID outbreak—naturally occurring or otherwise—is the presence of disease symptoms in an individual, preventing the spread of disease outside the initial sub-PAR will be challenging if not impossible the majority of the time.

The implications of this observation depend on the availability and effectiveness of response measures that can protect the susceptible cohort and limit the spread of disease within a sub-PAR, such as medical countermeasures, isolation of ill individuals, and extraordinary public health measures. If such measures are available, highly effective, and promptly implemented force-wide, the need to prevent disease spread among sub-PARs may not be particularly urgent. On the other hand, in the absence of such measures, restricting the spread of disease to the initial sub-PAR—or to as few sub-PARs as possible—becomes critically important to preventing the entire force from becoming combat ineffective. In addition, even if an outbreak can be controlled after it has spread throughout the force structure, the burden on a unit of managing even a few cases of contagious disease may be onerous and cause degradation beyond the immediate loss of ill individuals. Alternatively, commanders may wish to isolate sub-PARs whose operational effectiveness is particularly critical to mission success. Thus, even if it proves impossible to prevent the spread of disease beyond the sub-PAR in which it initially occurs, the rate at which that disease spreads further through all sub-PARs remains of interest.

Although the spread of disease beyond the initial sub-PAR to adjacent sub-PARs is very rapid, it then slows. In the baseline case of plague in the 10-sub-PAR force array, it takes three to four months to reach the sub-PARs furthest removed from the sub-PAR in which the outbreak started, by which point a significant fraction of the population would have become ill. This suggests that it might be physically possible to isolate some units

from the risk of exposure to the disease, and that information upon which to base the decision to do so would be available.

The same assessment was conducted with smallpox in the 10-sub-PAR force array, and similar trends were observed. For both diseases, there were scenarios in which the outbreak reached enough sub-PARs to be able to infect at least 20 percent of the overall population prior to the appearance of symptomatic individuals. The only major difference between plague and smallpox was an increase in the time required to reach subsequent sub-PARs. This is likely due to smallpox's longer incubation period, and is consistent with other observed results.

2. Effectiveness of Outbreak Response Capabilities in Mitigating Impact

The research team found a clear hierarchy of response capabilities in their effectiveness in mitigating operational impact, by all measures.

Vaccination and other forms of enhanced immunity were clearly the best means of preventing or reducing the operational impact of an EID outbreak. Even vaccines with relatively low efficacy could still have significant effects. For example, the research team found substantial reduction in operational impact with a 50 percent efficacy. Thus, even if the EID in question is a variant of a disease for which a vaccine is available but less efficacious, it should still be used. The concept is much the same as that behind population-wide immunization against childhood diseases or influenza, where vaccines with relatively low efficacy can still generate herd immunity.

PEP proved nearly as effective as immunization in preventing casualties and mitigating outbreaks, even when implemented after a substantial time delay. As with immunization, even PEP with reduced efficacy will significantly reduce operational impact. In some of the cases modeled, and by some measures of effectiveness, PEP with 50 percent efficacy was as effective as immunization.

In the absence of available medical countermeasures, commanders must rely on physical control measures to mitigate outbreaks. The operational impact assessment demonstrated that isolation could be effectively used to reduce overall numbers of casualties and delay their presentation. However, unlike medical countermeasures, it did not hinder the spread of disease across sub-PARs.

Implementation of isolation requires knowledge that an outbreak is occurring and the ability to identify contagious individuals. As discussed in Chapter 3, diseases that are non-specific in early phases and for which no field or laboratory diagnostic capability is available would be of particular concern as, among other things, they would inhibit acquisition of the knowledge required to trigger this response. In addition, isolation requires significant infrastructure and support to be effective; for highly transmissible diseases, this may mean a requirement for high-containment care for large numbers of

individuals, which might be extremely burdensome and perhaps even impossible in an immature overseas theater. Moreover, for novel pathogens, the transmissibility and behavior of a disease within a population may not be well understood. Consequently, early attempts to isolate individuals may not be effective.

Finally, in the absence of both medical countermeasures and an effective means of identifying and isolating contagious individuals, the only available means of disrupting disease transmission within an AO is the implementation of ROM between units. The modeling results in this research indicated that in general, ROM was far less effective than other response measures in preventing casualties. While ROM proved moderately effective in some of the cases examined, they all assumed that all movement between sub-PARs was completely stopped. Given the degree of movement typical of normal military operations, halting this movement completely would, in and of itself, have a huge operational impact.

3. Biosurveillance as a Trigger for Outbreak Response

Implementation of any response capability after the start of an outbreak—in other words, any response other than immunization—requires knowledge that an outbreak is underway. This research found that at many key milestones in disease progression, the requisite knowledge would be difficult or even impossible to acquire. For example, during normal operations, diseases are likely to jump from the initial sub-PAR to others before any individuals become symptomatic. The research team found that many response capabilities can still be effective if implemented after this jump occurs. However, at all the implementation times considered in this research, there were very few symptomatic cases to trigger such a response. Moreover, these individuals must be differentiated from the background of ordinary infectious disease and assessed to be the precursors of a larger disease outbreak with significant operational risk. For novel pathogens with non-specific symptoms, this is an incredibly challenging problem for situational awareness capabilities.

The relationship between situational awareness and response time was a major theme explored in this study. The operational impact assessment modeling allowed the IDA research team to quantify this relationship for the three postulated EID scenarios: natural outbreaks, improvised biological operations, and BW attacks (represented as 1, 10, and 100 initial infections, respectively). An understanding of the information available over time, as outbreaks progress, will both underscore the challenges that BSV programs face and inform BSV requirements.

Figure 48 shows the last day on which the various response options (other than immunization) must be implemented to avoid combat ineffectiveness from 1 initial infection, for all four diseases (1918 influenza, plague, smallpox, and SARS) in the four-sub-PAR force array, and the number of symptomatic individuals on those days. In the

figure, only those options that can prevent combat ineffectiveness are shown in color; if an option could not be effectively used regardless of time of implementation, it is listed in gray text. Note that for this discussion, the research team established a 90-day period of operational interest, assuming that outbreaks that could not cause combat ineffectiveness within that time frame would not be a risk. This adds a dimension to the assessment that was not present in the baseline cases discussed in Chapter 5, wherein the research team observed that in some of those cases, it took several months to reach combat ineffectiveness. Since it seemed unrealistic to assume that commanders would not adjust their operational plans in response to an outbreak over such an extended period of time, the team chose to focus on those cases where outbreaks progressed more rapidly and offered less time to respond.

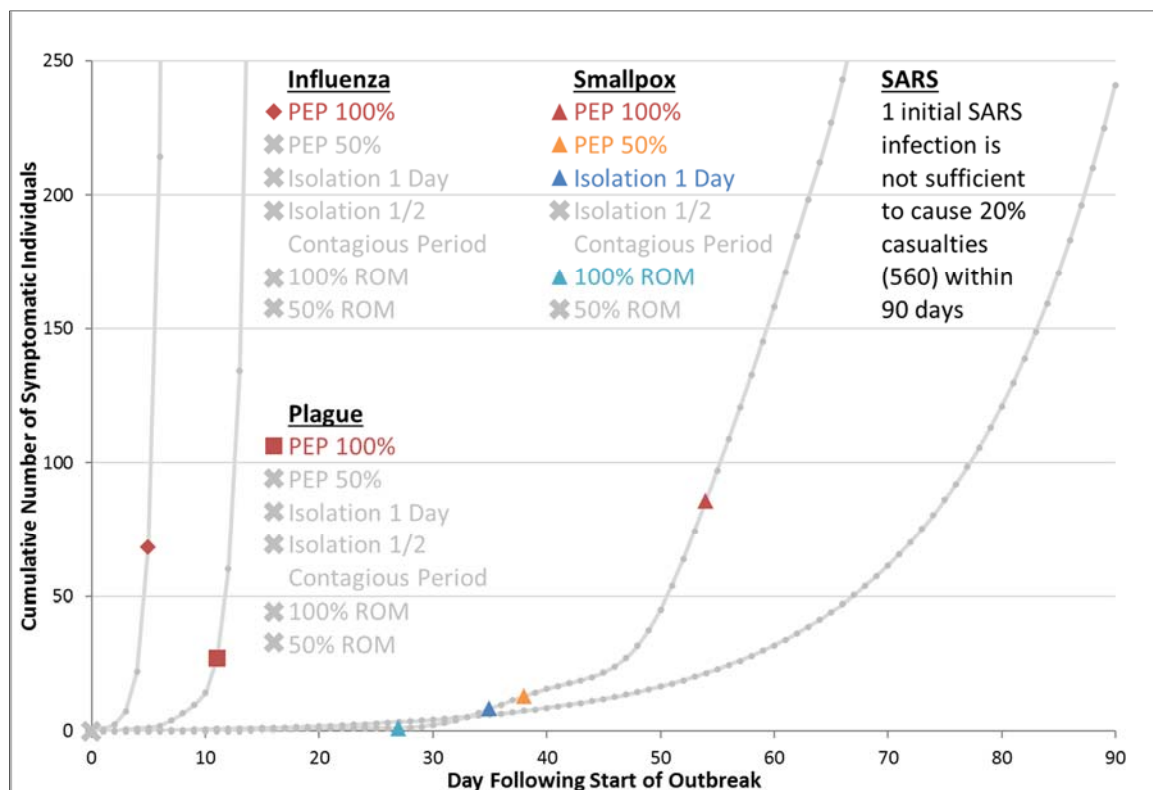


Figure 48. Latest Day on Which Response Must Be Implemented to Avoid 20 Percent Casualties (560) Over 90 Days: 1 Initial Infection

The 1 initial infection scenario—representing natural outbreaks of disease—is less challenging than those with more initial infections. SARS does not generate sufficient casualties to reach the 20 percent threshold for combat ineffectiveness in this scenario, and smallpox takes over two months to do so. Nonetheless, even in this scenario response, options can be limited. For influenza and plague, PEP with 100 percent efficacy is the only response option that could be used to avoid combat ineffectiveness. The time

at which PEP needed to be implemented was also very short—5 and 11 days—but by that time there were relatively large numbers of symptomatic individuals—68 and 27, respectively.

For smallpox, more response options could be effective, to include ROM and isolation, and the window of time for their implementation extended to weeks rather than days. PEP with 100 percent efficacy could be implemented at 56 days and still be effective, by which time there would be 86 symptomatic individuals to trigger a response decision. However, for all other effective responses, the number of symptomatic individuals present in the population was quite small at the time a response had to be implemented: 13 for PEP with 50 percent efficacy, 8 for isolation within 1 day of symptom onset, and just 1 symptomatic individual for ROM. Since the early stages of smallpox are nonspecific, detection of an outbreak solely on the basis of the first symptomatic individual is highly unlikely.

Figure 49 and Figure 50 show the same information for 10 and 100 initial infections, respectively, representing improvised biological operations and BW attacks.⁷⁸ Unlike the 1 initial infection scenario, here SARS can generate sufficient casualties to cause combat ineffectiveness within 90 days. At the same time, the progression of SARS outbreaks is such that a wide range of response options can be effective, and in most cases these options have a lengthy window of time for implementation and large numbers of cases on which to base a response decision. For smallpox, too, both PEP and isolation within one day of symptom onset can be used to avoid combat ineffectiveness. However, for both 10 and 100 initial infections, isolation of contagious individuals must be implemented on the basis of a single symptomatic individual.⁷⁹ For the two diseases with short incubation periods, influenza and plague, PEP with 100 percent efficacy is the only response option that can effectively prevent combat ineffectiveness, and for plague, only in the scenario with 10 initial infections.

These figures show that in general, the response window for 10 and 100 initial infection scenarios is roughly the same, and typically much shorter than that available in the 1 initial infection scenario. In influenza outbreaks, for example, PEP with 100 percent efficacy must be implemented by Day 1 in the 100 initial infections scenario, by Day 2 in the 10 initial infections scenario and by Day 5 in the 1 initial infection scenario. In

⁷⁸ Note that the time scale on the x-axis in Figure 50 is different from those in Figure 48 and Figure 49; because the outbreaks from 100 initial infections progress so rapidly, the team found it difficult to portray the relevant information on a 90-day scale, so chose to use a 30-day scale instead.

⁷⁹ Figure 50 also shows that 100 percent ROM can be effective at mitigating combat ineffectiveness for 100 initial infections, although not for 10 initial infections. This anomalous result is driven by the selection of a specific trial—the 90th percentile case—to generate the S-curves shown in these figures, and in this specific trial 100 percent ROM could be effectively implemented two days after the start of the outbreak with a single symptomatic case.

outbreaks of smallpox, with its longer incubation period, these time windows are extended to 24, 22, and 54 days in the 1, 10, and 100 initial infections scenarios.

However, in general the number of symptomatic individuals on which to base a response decision is much smaller when there are 10 initial infections versus when there are either 1 or 100 initial infections. In the influenza outbreaks with 10 initial infections, there were 23 symptomatic individuals at the time the response window closed, versus 68 and 77 symptomatic individuals at the time the response window closed when there were 1 and 100 initial infections, respectively. The research team observed the same pattern in smallpox outbreaks with just 10 symptomatic cases at the end of the response window in the 10 initial infections scenario, but 86 and 102 symptomatic cases in the 1 and 100 initial infections scenarios, respectively. These results highlight the challenge posed by improvised biological operations: a short response window, similar to that of BW attacks, but a significantly smaller number of symptomatic cases than in either natural outbreaks or BW attacks that can serve as a response trigger.

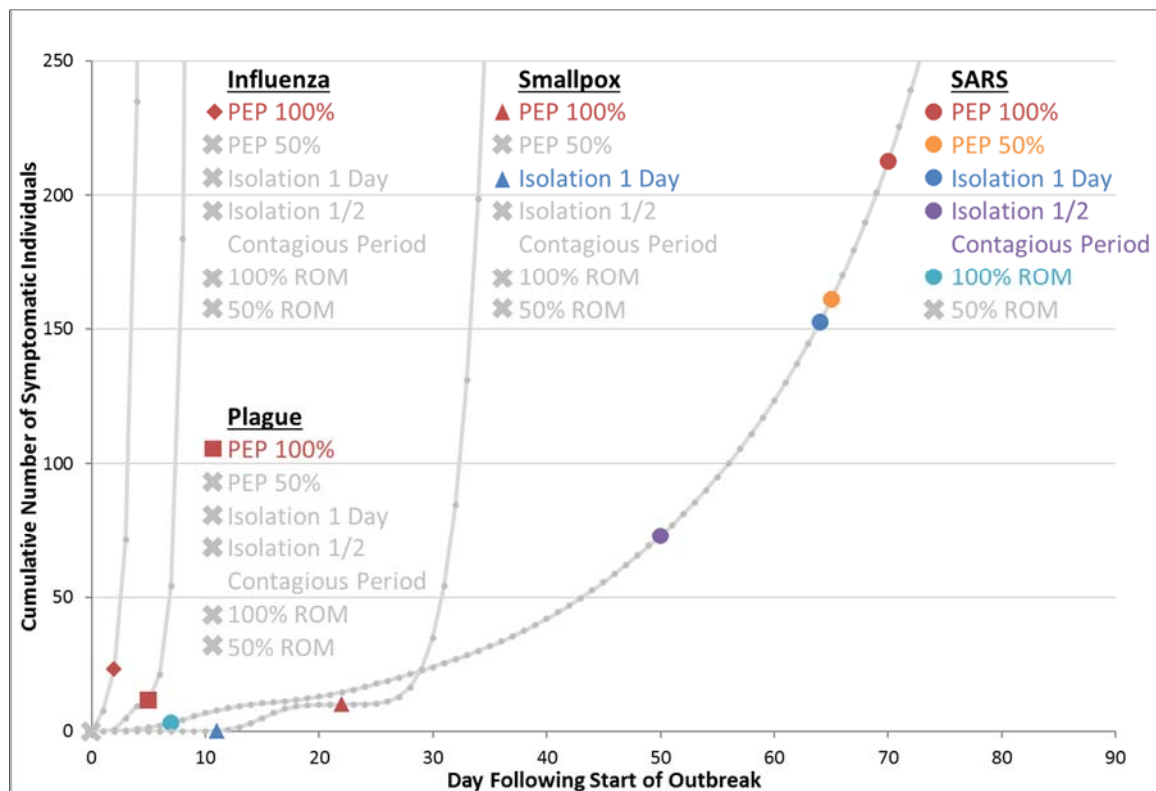


Figure 49. Latest Day on Which Response Must Be Implemented to Avoid 20 Percent Casualties (560) Over 90 Days: 10 Initial Infections

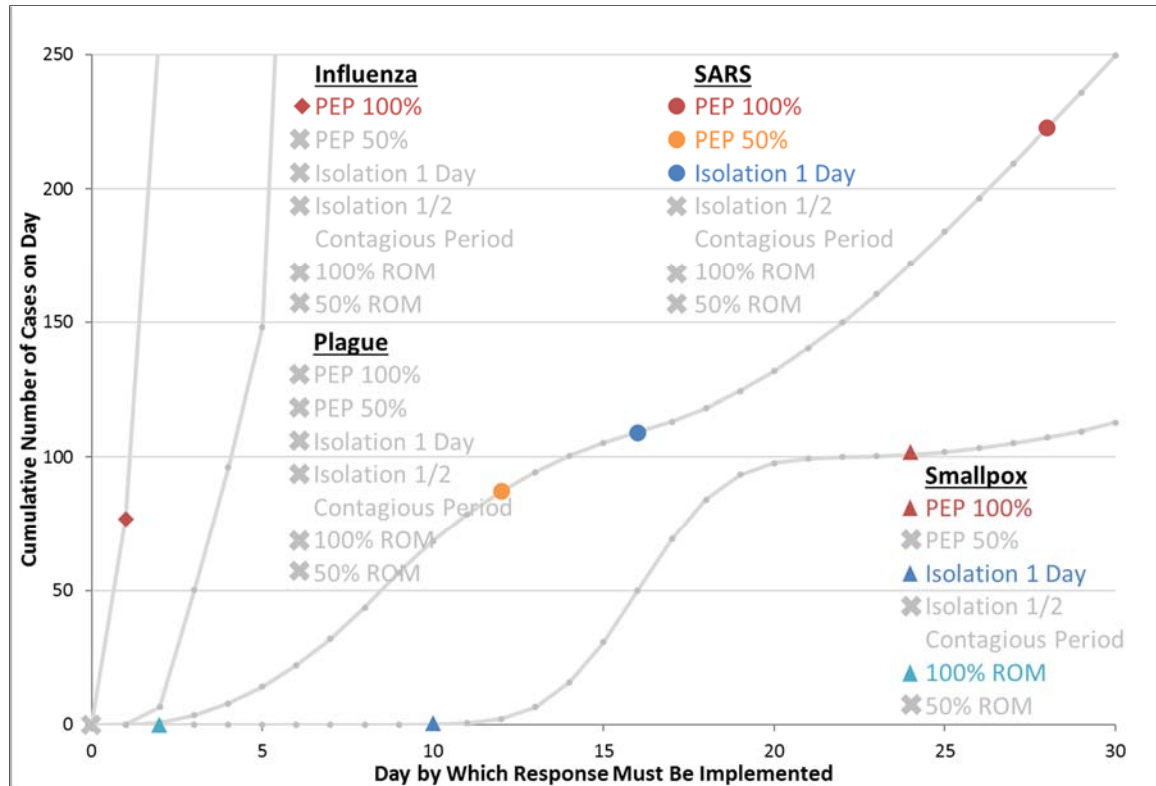


Figure 50. Latest Day on Which Response Must Be Implemented to Avoid 20 Percent Casualties (560) Over 30 Days: 100 Initial Infections

These results have implications for the establishment of BSV requirements, considered here as requirement to detect a disease outbreak, based on the presence of symptomatic individuals in a population, in time to mount an effective response. First, when medical countermeasures are available, the requirements for BSV are significantly less stringent, particularly for diseases with relatively long incubation periods. Second, improvised biological operations pose a much greater challenge for BSV than either natural outbreaks or BW attacks. Indeed, the requirements to detect outbreaks on the basis of symptomatic individuals within the population in time to institute effective procedural controls are so rigorous that they may be impossible to meet in the absence of both other indicators that heighten the index of suspicion and a rapid laboratory diagnostic capability to support the identification of disease in its early phases.

4. Summary Observations

The results of the modeling reinforce the discussion in Chapter 3, where EID characteristics of concern were derived from various adversary pathways. For natural outbreaks and improvised biological operations, these characteristics of concern included a lack of diagnostic capability, a lack of prophylactic medical countermeasures, and a lack of therapeutics. None of these characteristics are inherent properties of EIDs

themselves; hence, they may be amenable to negation through a commitment of resources to developing medical response capabilities. Doing so, however, requires prompt exploitation of the window of time between the point of disease emergence and the initiation of military operations where forces may be at risk.

The modeling results suggest that improvised biological operations with EIDs of concern will be challenging to defend against. Early on, the research team hypothesized that capabilities developed to mitigate natural outbreaks would have comparable effects against improvised biological operations, and that there was very little difference between a single initial infection and a handful of initial infections. In both cases, the team thought it likely that while there might be very little knowledge available to trigger a response, there would be a lengthy window of time in which to respond effectively, during which (it could be assumed), some indication of the outbreak was likely. The assessment of impact, however, suggests this is untrue: as with natural outbreaks, there is very little knowledge available in improvised biological operations, but unlike natural outbreaks, there is often very little time to respond. As seen above in Figure 49 and Figure 50, this contrasts, too, with more sophisticated attacks with weaponized EIDs, where although the response time is comparatively limited, large numbers of casualties at the outset would likely indicate that something has happened. Thus, in many respects, improvised biological operations are a worst case.

B. Characteristics of Concern for Assessing Specific EIDs

A summary list of EID characteristics of concern is provided in Table 9. As described in Chapter 4, the research team derived producibility and employability characteristics of concern from available literature and through discussions held with SMEs and internally at IDA. Characteristics of concern for assessing effectiveness, also derived in this manner, were postulated in Chapter 4 as being largely a function of adversary objectives. In addition, the research team found that these characteristics would vary by scenario.

While the operational impact assessment described in Chapter 5 focused on the consequences of an adversary's actions, independent of their objectives, it did provide additional insights into effectiveness criteria. Specifically, it found that incubation period was a key driver of many aspects of operational impact. In the absence of control measures, shorter incubation periods fostered faster spread of disease throughout a population, and led to shorter times to reach combat ineffectiveness. Conversely, diseases with longer incubation periods were more likely to spread beyond the initial sub-PAR before symptomatic cases of disease occurred, significantly compounding the problem of mounting an effective response.

Table 9. Summary: Characteristics of EIDs of Concern in Different Scenarios

Component of Risk	Natural Outbreaks	Weaponization	Improvised Biological Operations
Producibility	N/A	Stable in storage Feasibly produced on a large scale Similar to classic BW agents	Stable during transport and storage (<i>crude agent</i>) Easily handled (<i>crude agent</i>) Broad host range (<i>animal/insect vectors</i>) Contagious (<i>human vectors</i>)
Employability	N/A	Stable in the environment Stable as an aerosol Easily disseminated as an aerosol Infectious via the aerosol route	Stable/survivable in the environment (<i>crude agent, animal/insect vectors</i>) Easily dispersed (<i>crude agent</i>) Resistant to controls (<i>animal/insect vectors</i>) High infection-to-disease ratio (<i>human vectors</i>)
Effectiveness	Contagious High morbidity and mortality Lack of diagnosis Lack of prophylaxis Lack of treatment Early contagious, non-specific, mild phase Long incubation period	<i>Characteristics depend on adversary objectives but provide some advantage over classic BW agents</i>	Contagious High morbidity and mortality Lack of diagnosis Lack of prophylaxis Lack of treatment Early contagious, non-specific, mild phase Long incubation period High infection-to-disease ratio

C. Recommendations

This paper's recommendations are based primarily on the operational impact assessment presented in Chapter 5, subject to its limitations, with further consideration of the EID characteristics of concern derived in Chapter 3. As discussed in Chapter 4, the research team also recognized that despite DOD's best efforts, the time between the point of emergence and an operational deployment may provide too small a window to develop capabilities needed to support situational awareness and effective response, limiting both

the range of response choices and the opportunities to implement them in a timely manner. Several of this paper's recommendations, therefore, focus either on shortening the development timelines for the most effective response capabilities or on hedging against the possibility that such capabilities would be unavailable.

Consistent with the requirements of the JRO's tasking, this paper makes recommendations both for science and technology initiatives within the CBDP and for non-materiel solutions. These recommendations focus on the most significant challenges for mitigating EID operational impact, as identified in this research, and are organized into two categories of mitigating capabilities: situational awareness and response. Additional recommendations are intended to help rectify identified knowledge gaps and support prioritization of EID threats.

1. Situational Awareness Capabilities

Situational awareness has two primary functions: (1) in general, to support development of response capabilities that will be effective against EIDs of concern, and (2) during an EID outbreak, to provide early recognition of an EID outbreak and support response decision making. The research team found that the signal-to-noise problem in the early stages of an outbreak is the major challenge for situational awareness capabilities, and one that can significantly limit the ability of U.S. forces to respond effectively and mitigate operational impact. The recommendations provided below are intended to address various aspects of this challenge.

a. Science and Technology Initiatives

- Adopt analytically supported performance targets for the contribution of BSV to the detection of EID outbreaks and triggering of responses.
 - The results of this research suggest that threshold requirements should focus on the detection of natural disease outbreaks and BW attacks, in time to support the use of medical countermeasures. For the scenarios and diseases considered in this research, these goals can be met if BSV can detect 20 symptomatic individuals among the population at risk within five days of the start of the outbreak.
 - The use of BSV capabilities to trigger procedural controls, or to trigger any response to improvised biological operations is much more challenging and should be the focus of objective BSV requirements. For the scenarios and diseases considered in this research, these goals can be met if BSV can detect 1–3 symptomatic individuals among the population at risk within two days of the start of the outbreak.

- Develop and acquire approved diagnostic assays for EIDs of concern, as quickly as possible after the point of emergence, compatible with the furthest-forward deployed diagnostic systems.

b. Non-materiel Solutions

- Develop a strategy for far-forward diagnostic testing of individuals with non-specific symptoms of disease. Such a strategy should be supported by an analytically based sampling plan that specifies the size of the sample needed to detect an outbreak under various circumstances. It should also specify criteria for the selection or exclusion of test subjects.

2. Response Capabilities

When considering potential responses to EID outbreaks, the IDA team found that immunization and prophylaxis were more effective than isolation and ROM in mitigating operational impact. However, there is no guarantee that medical countermeasures would or even can be available to counter currently unknown diseases of concern. There are significant challenges in developing medical countermeasures that are likely to be effective against EIDs, and in having a strategy for using those with limited or unknown efficacy. At the same time, if medical countermeasures are unavailable, procedural controls like ROM may be the only means of containing the outbreak and avoiding significant operational impact. However, significant work remains to understand and implement the most effective use of procedural controls. This includes an assessment of the effectiveness of procedural controls in combination (e.g., isolation plus ROM), something that could not be explored within the timeframe of this research.

a. Science and Technology Initiatives

- Conduct a cost-effectiveness analysis of different approaches to medical countermeasure development that specifically accounts for the inherent lack of knowledge about EIDs.
 - Emphasize widely applicable antibiotics/antivirals, universal vaccines, and general enhancement of immunity to hedge against unknown future diseases.
 - Take advantage of the time between point of emergence and use of an EID as a weapon to develop targeted responses.
- Support efforts to enhance agility in the acquisition of diagnostics and medical countermeasures.

b. Non-materiel Solutions

- Develop a strategy and decision criteria for the selection, distribution, and use of medical countermeasures in an EID outbreak, when the efficacy of available countermeasures is unknown or limited.
- Develop doctrine and procedures for the implementation of ROM. This should include decision support for the implementation and relaxation of ROM, including which units should be included. It should also include plans for individual unit sustainment under conditions of ROM.

Although there are many advantages to medical countermeasures, there is a very real possibility that they just will not be available, and the only means we would have to mitigate operational impact would be through ROM. Therefore, it would behoove us to do some planning and analysis to figure out the best way to make that as effective as possible in various circumstances.

3. Additional Recommendation

Invest in research to close knowledge gaps related to the propagation of contagious disease, particularly within a military population. This work would support the background awareness component of situational awareness and is important for understanding the potential risk that a given EID would pose operationally.

Appendix A. Enhanced IDA Model of Contagious Disease Dynamics

A. Background

1. Evolution of Bombardt Contagious Disease Modeling at IDA

The model of contagious disease used in the present research is adapted from a set of models developed by Dr. John Bombardt and now in general use at IDA for a variety of studies and analyses. These models combine a traditional Susceptible, Exposed, Infected, and Removed (SEIR) approach with a time-varying disease transmission rate (colloquially referred to by its variable name, β). In 1999, Bombardt developed a proof-of-concept contagious disease dynamics model of Ebola that introduced his concept of a time-varying disease transmission rate derived from historical outbreaks of disease. He subsequently published a series of papers, each of which calculated β for a new disease, again based on historical outbreaks, while simultaneously enhancing the model's functionality in various ways. The conceptual progression of the Bombardt methodology is depicted in Figure A-1.

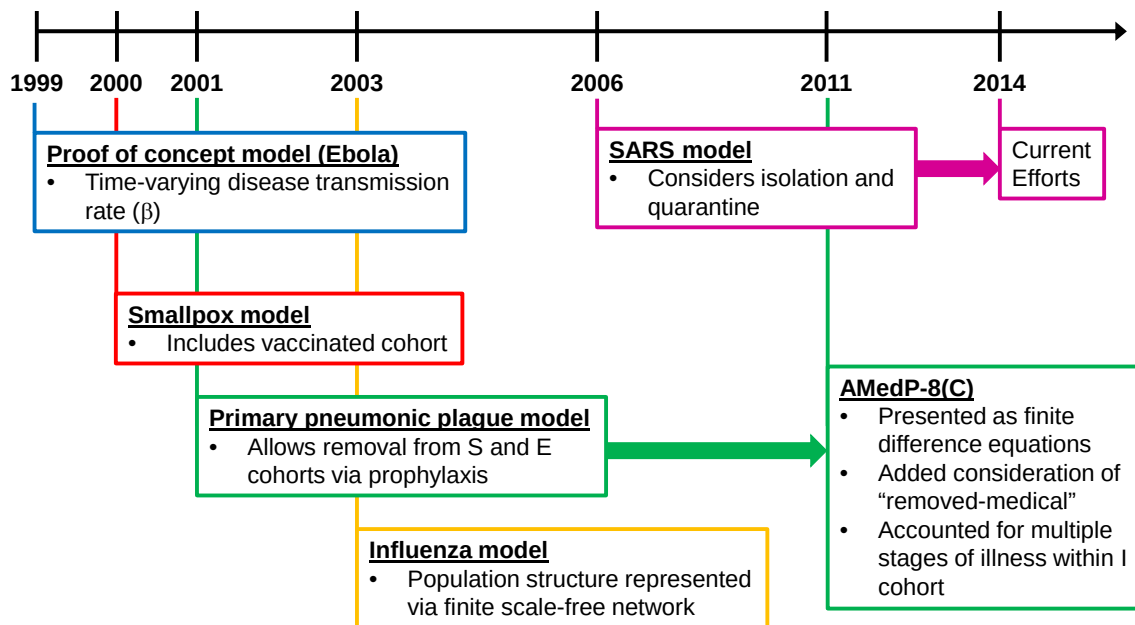


Figure A-1. Evolution of Bombardt Contagious Disease Models

The proof-of-concept Ebola model¹ is the foundation for all subsequent contagious disease models shown in Figure A-1. This work introduced the concept of a time-varying disease transmission rate, demonstrated the derivation of β from historical outbreak data, and incorporated it within the SEIR framework for purposes of retrospective outbreak investigation and prediction of the dynamics of future outbreaks. The β parameter describes the number of new infections caused by each contagious person for each day of their contagious period and strongly influences the overall behavior of the outbreak. The parameter represents both the inherent infectivity of the disease as well as the “epidemiological circumstances” present during the course of any outbreak:

Certain epidemiological circumstances surround any outbreak of a disease and these (along with disease characteristics) virtually determine the rate at which the disease is transmitted from person to person. These circumstances encompass factors such as physical profiles of the susceptible cohort, frequency and types of possible contacts between infectious and susceptible individuals, prevailing health care practices, health care system capacity, and disease awareness levels.²

Bombardt’s smallpox model, published in 2000,³ is almost identical to the Ebola model presented in his first paper on contagious disease dynamics. In addition to the derivation of smallpox-specific β values for two well-documented historical outbreaks, this model also introduces a vaccinated cohort, V; individuals in the V cohort are considered to be removed from the population of susceptible individuals.

Bombardt’s 2001 plague model⁴ is the first model to include a cohort for individuals who have either received chemoprophylaxis and/or chemotherapy, termed the X cohort. Individuals who have received prophylaxis move from the S cohort to the X cohort for the duration of the effectiveness of the medication, then return to the S cohort. Individuals in the E cohort who are given prophylaxis remain in the X cohort indefinitely and are considered to be mitigated, non-fatal casualties. The paper discusses two non-homogenous population mixing methods, although these methods are only briefly introduced and are not fully incorporated into the model presented in the remainder of the paper.

¹ Bombardt, *Contagious Disease Dynamics for Biological Warfare and Bioterrorism Casualty Assessments*, IDA Paper P-3488 (Alexandria, VA: Institute for Defense Analyses, February 2000).

² Ibid., 3.

³ John N. Bombardt, Jr., *Smallpox Transmission and BW Casualty Assessments*, IDA Paper P-3550 (Alexandria, VA: Institute for Defense Analyses, October 2000).

⁴ John N. Bombardt, Jr., *Primary Pneumonic Plague Transmission and BW Casualty Assessments*, IDA Paper P-3657 (Alexandria, VA: Institute for Defense Analyses, December 2001).

Bombardt's 2003 influenza model⁵ uses a SEIRX model similar to that presented in the plague paper; the primary innovation is the incorporation of structured populations. The sub-populations are modeled using scale-free networks (networks that grow in a predictable manner). Each sub-population is capable of having a unique transmission rate vis-à-vis all other sub-populations. These sub-population transmission rates are derived from and sum to the historical aggregate transmission rate. The paper does not employ structured populations in its analysis of potential future outbreaks.

The final model published in this series is the 2006 Severe Acute Respiratory Syndrome (SARS) model.⁶ The SARS model is similar to the influenza model except that it incorporates more sophisticated method of structuring the population. Like all previous methods, the SARS model is dependent on a disease transmission rate derived from historical outbreak data. The structured population model as presented allows for the incorporation of a number of different non-medical outbreak controls, such as quarantine, contact tracing, and patient isolation; these are accomplished via the removal and reinsertion of individuals in both the susceptible and infectious cohorts. Although not outlined explicitly in the published paper, medical outbreak controls, such as prophylaxis and vaccination, can theoretically be included in a similar fashion.

2. Basic Methodology of Bombardt Contagious Disease Models

All of the published Bombardt models share a common methodological flow, shown in Figure A-2. The methodology begins with the collection and assessment of data from a historical outbreak of a contagious disease and information on the characteristics of that disease. The quality of such data can vary widely for the purposes of this methodology, but ideally would provide documentation of the time of onset, duration of illness, and outcome for every individual who became ill during the course of the outbreak. The methodology uses these data as input to the set of SEIR differential equations and to determine the number of new infections per day during the outbreak.

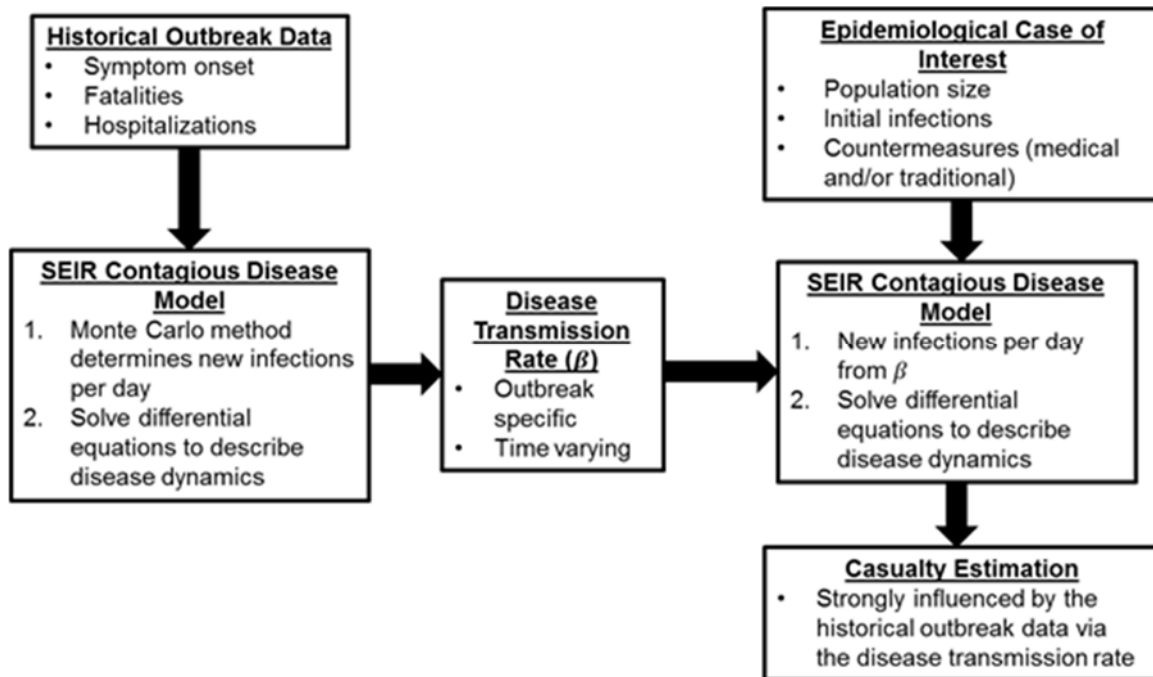
The next step in the methodology involves backtracking from fatality/recovery or symptom onset data to determine the average number of new infections per day. This calculation uses a Monte Carlo algorithm to account for random variation in incubation period and duration of illness; the output is a temporal profile of estimated new infections per day.

The resulting daily number of new infections is then combined with the SEIR model to reproduce the historical outbreak. The daily number of susceptible individuals,

⁵ John N. Bombardt, Jr. and Heidi E. Brown, *Potential Influenza Effects on Military Populations*, IDA Paper P-3786 (Alexandria, VA: Institute for Defense Analyses, December 2003).

⁶ John N. Bombardt, "Congruent Epidemic Models for Unstructured and Structured Populations," *Mathematical Biosciences* 203 (2006): 171–203.

contagious individuals, and the daily number of new infections of the reproduced historical outbreak are used to derive the disease transmission rate β . The β values change over time, reflecting prevailing epidemiological circumstances and changes in population behavior during the course of the outbreak.



Source: Adapted from Bombardt, *Smallpox Transmission and BW Casualty Assessments*, Figure I-2: 8.

Figure A-2. Basic Contagious Disease Model Methodology

Once β has been calculated for the historical outbreak, it can be used analytically to address “what if” questions and to generate estimates of casualties over time for postulated scenarios. In this portion of the methodology, β serves as an input to the SEIR model, where values for other parameters, such as population size, number of initial infections, and control measures of various types, are selected to describe scenarios of interest.

B. Model Revisions

1. Modeling of Medical and Physical Control Measures

Beginning with the 2000 smallpox model, each instantiation of the Bombardt methodology considers some form of medical or physical control measures. In all cases, these controls are represented within the model by removing individuals from one or more of the S, E, and I cohorts and, in some cases, subsequently returning them to the S, E, I, or R cohorts.

The 2006 SARS model, for example, allows for consideration of the effects of hospital isolation of infectious individuals and quarantine of non-symptomatic individuals, which would include members of both the susceptible (S) and exposed (E) cohorts. Figure A-3 shows the manner in which this is implemented. Quarantined individuals who are removed from the susceptible cohort (Q_S) will not become ill during quarantine; once the quarantine period ends, they are returned to the susceptible cohort. Quarantined individuals from the exposed cohort (Q_E), on the other hand, will become ill during quarantine; these individuals immediately enter hospital isolation (H), where they are assumed to be prohibited from transmitting the disease until such time as they are removed from the population because of death (R_F) or recovery (R_R). Members of the exposed cohort who transition to the infectious cohort (I) outside of quarantine also enter hospital isolation, but with some assumed delay after onset of symptoms. Note that both quarantine and isolation can be universally applied to all individuals in the relevant cohorts, or restricted to a subset thereof.

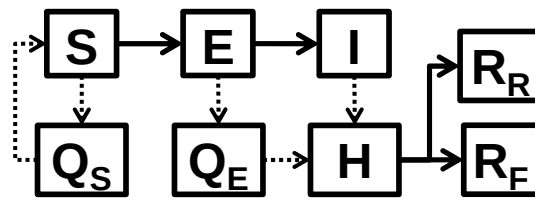


Figure A-3. Implementation of Physical Control Measures

None of the published Bombardt models allows consideration of the effects of medical treatment, which could reduce or eliminate time spent in the infectious cohort and/or change the outcome of illness. Conceptually, however, medical treatment could be represented in the same manner as vaccination and post-exposure prophylaxis, but with manipulation of the infectious cohort. As shown in Figure A-4, successfully vaccinated individuals (V) are simply removed from the S cohort. Post-exposure prophylaxis is assumed to be administered to individuals who are not showing symptoms of illness; this would include individuals in both the S and E cohorts. Once the efficacious period associated with the prophylaxis ends, however, individuals are returned to the S cohort.⁷ As with physical control measures, both types of medical control measures can be applied to some or all individuals in the relevant cohorts.

⁷ The disposition of individuals from the E cohort who receive prophylaxis can vary by disease. In the 2001 plague model, such individuals are assumed to be immune from further infection and are retained in the X cohort indefinitely. For other diseases, effective truncation of the incubation period may restore individuals to their original susceptible state, in which case they would be returned to the S cohort, as shown in the figure.

To represent medical treatment, then, individuals would be removed from the infectious cohort immediately upon symptom onset or at some point in time thereafter, at which point they would enter a new I_m cohort. The behavior of individuals in this cohort—the extent to which they continue to transmit disease, the time between initiation of treatment and removal, etc.—would depend on the specific nature and effects of treatment.

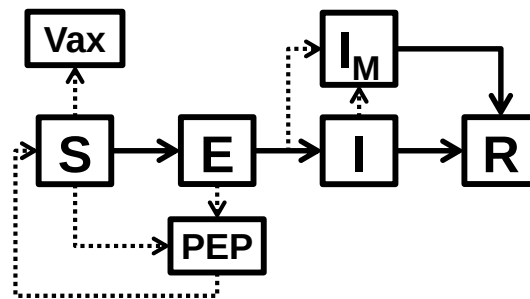


Figure A-4. Implementation of Medical Control Measures

With the addition of medical treatment, represented through the removal of individuals from the infectious cohort, the contagious disease methodology would allow consideration of a comprehensive set of physical and medical control measures. However, none of the published versions of the model allowed these measures to be considered *in toto* for any single disease. Much of the developmental work in IDA's present effort, then, has been devoted to creating a unified version of the model in which individuals can be removed and reinserted into any cohort, and in which users can select from any combination of physical or medical control measures.

2. Enhanced Time-Varying Disease Transmission Rate

As discussed above, Bombardt's published models rely on a disease specific time-varying disease transmission rate (β) that was calculated from a historical outbreak. The manner in which the β functions are calculated, by backtracking from either daily fatalities or daily symptom onsets to determine the number of new infections per day, results in a transmission rate that is strongly linked to the historical outbreak. Due to their close relationship with the historical outbreak, the β values force the modeled outbreak to behave similarly to that of the historical outbreak. While this behavior is ideal for the purpose of recreating a past outbreak, its application towards a wide range of analytic scenarios is limited. In other words, the accuracy of the model is dependent upon the similarities between the epidemiological circumstances of the historical outbreak and those of the scenario being modeled.

To lessen the model's dependencies on the circumstances of historical outbreaks, the current analysis uses a new methodology for calculating a time-varying disease

transmission rate. Both methodologies start with the same step—determining the daily number of new infections during a historical outbreak. As discussed previously, this process involves backtracking each symptom onset or fatality/recovery in time using a Monte Carlo method to capture the inherent variability in the latent period and duration of illness. Given the daily number of new infections for the historical outbreak, the SEIR model can be run to determine the number of people in each cohort (S, E, I, and R) on each day. At this point the two methodologies diverge. The original methodology combines the daily number of new infections with the daily numbers of susceptible and contagious individuals to determine β . The new methodology determines a time-varying disease transmission rate from the daily new infections and the daily number of contagious individuals (members of the I cohort), as well as two additional parameters not used in Bombardt's previous models: the daily number of close contacts per contagious person as well as the conditional probability of transmission.

In the new methodology, a fully stochastic SEIR agent-based model is run subsequent to the point at which the new methodology diverges from the original one.⁸ In the stochastic SEIR model, the number of new infections is determined by the number of potential disease-causing interpersonal contacts each contagious person experiences each day as well as the probability that the disease will be transmitted, given such a contact.

The values for these two new parameters can be derived from the literature on historical outbreaks of disease and from other model parameters. The probability of infection, given a close contact, sometimes referred to as the attack rate, can be found in the literature for certain disease outbreaks. Given the probability of infection, the daily number of potential disease-causing contacts can be determined by dividing the number of new infections per day from the historical outbreak (as calculated from the Monte Carlo backtracking process) by the probability of infection. For example, if on a given day there were four new infections, and the probability of infection is 50 percent, the number of potential disease-causing contacts that occurred on that day is 8 ($4 \div 0.5 = 8$). The daily number of close contacts is then divided by the daily number of contagious individuals, resulting in the number of daily close contacts per contagious person. With the daily number of potential disease-causing contacts per contagious person and the probability of each of the contacts causing disease transmission, the stochastic model can calculate the number of daily new infections, contagious individuals, and susceptible individuals, which in turn are used to calculate β .

Although the β functions calculated from the two aforementioned methodologies have the same interpretation (the daily rate at which each contagious person transmits the disease to members of the susceptible population), the numeric values of the functions

⁸ An agent-based model is one in which each individual is tracked. In comparison, the models published by Bombardt treat populations as a whole and can therefore lead to results with fractions of individuals.

differ depending on which methodology was used and, furthermore, the outbreak dynamics predicted by the SEIR model using these two different β functions will differ dramatically. In other words, if one were to compare two modeled scenarios in which all parameters except for the β values were the same, the results of the SEIR models would be substantially different. The results of the scenario that was modeled using β calculated using Bombardt's original methodology would appear similar to the historical outbreak. In the case that the modeled scenario had an identical number of initial infections as the historical outbreak, the model would reproduce the historical outbreak. However, the results of the scenario that was modeled using the newly developed method of calculating β will be dissimilar to the historical outbreak. Since it is unlikely that any analytic scenario of interest will share similar epidemiological circumstances to those of the historical outbreak, it is preferred to use the newly developed method of calculating β .

3. Consideration of Structure and Movement

All of the published Bombardt models consider a single population at risk (PAR), wherein it is assumed that individuals are mixed uniformly—any susceptible individual has an equal chance of becoming exposed—or that mixing is structured by some assumptions about the distribution of potential disease-causing contacts among individuals. To consider structure and movement within military populations, IDA took an alternative approach. This approach builds on the newly implemented capability, described above, to remove and return individuals to various cohorts.

In lieu of a single PAR, the revised model subdivides the population into multiple sub-PARs, each of which can be thought of as a military unit, organizationally and/or geographically distinct from others. Each of these sub-PARs is assumed to be evenly mixed, and outbreaks of disease are evaluated separately for each sub-PAR. The rate at which the disease spreads within a PAR is determined by a set β values calculated for that specific PAR.⁹ Outputs are then summed over all sub-PARs for the population as a whole. This division of the population into sub-PARs is the way in which the model now represents *structure*.

Movement in the model is now represented by the removal of an integer number of individuals from one cohort in one sub-PAR, and insertion of those individuals into the same cohort in another sub-PAR, a process that is conceptually the same as that used to

⁹ The methodology used to calculate the β values for any population assumes that the infection is introduced into the population at a single point in time (day zero) in the form of a number of initial infections who are all on the first day of their latent period. However, each sub-PAR in the SEIR model will experience the arrival and departure of members of both the E and I cohorts on days following the start of the outbreak. These arrivals and departures are not accounted for in the methodology used to calculate the β values, and it is currently not clear how this inconsistency will affect the results of the model. Additional development of the model, namely the manner in which the β values are calculated, and employed, is necessary in order to fill this knowledge gap.

represent physical and medical control measures. Movement between sub-PARs can be defined in terms of rates or absolute numbers of individuals. These individuals are randomly selected from within a sub-PAR and can be from any cohort; the probability that an individual will be pulled from a given cohort at any given time is determined by the proportional representation of that cohort within the sub-PAR at that time.

The random selection of individuals from specific cohorts represents a significant departure from past contagious disease modeling conducted at IDA. All prior models were entirely deterministic (i.e., for a given set of input parameters the model will always produce the same results). By incorporating a random process, the selection of individuals to move from certain cohorts, the model now contains a stochastic element, and therefore each run of the model for a given set of input parameters will not return the same result. To capture the inherent variability with the random process, the model is run numerous times for a given set of input parameters and the results can be statistically assessed.

Figure A-5 provides a notional representation of population structure and movement as now considered for military populations. Each rectangle represents an evenly mixed sub-PAR, while the arrows represent the specified movement between each sub-PAR. As suggested by Figure A-5, this model allows individuals from any of the four cohorts (S, E, I, or R) to move from one PAR to another, with the exception of those who died due to their infection (i.e., fatalities).

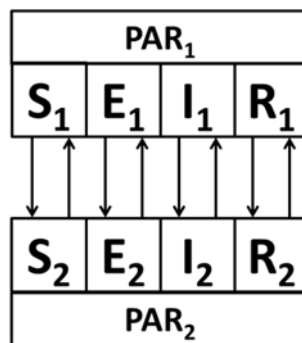


Figure A-5. Notional Depiction of Population Structure and Movement

Representation of structure and movement in this way is conceptually similar to the way military units are typically represented for modeling purposes—as groups of individuals sharing a common geographic location, with interactions between units at different locations. Required input data would therefore be fairly simple to generate from

the types of force laydowns used as inputs to other components of the *AMedP-7.5* methodology, such as calculation of individual CBRN challenges.¹⁰

In addition, this representation allows for consideration of an additional type of physical control measure, restriction of movement (ROM). ROM is defined as the partial or total prohibition of individuals leaving one sub-population for another, and is readily considered in the model by simply reducing or eliminating movement of individuals from one sub-PAR to another.

C. Summary of Enhanced Model Capabilities

The enhanced IDA model of contagious disease dynamics depicts a variety of responses a deployed force could use in an effort to contain the spread of the disease. The countermeasures are:

- Restriction of Movement (ROM): the partial or total prohibition of individuals leaving one sub-population for another
- Pre- and Post-exposure Prophylaxis (PEP): disease-specific medical countermeasure given to either members of the susceptible cohort (pre-exposure) or the exposed but non-symptomatic cohort (post-exposure) that grants them temporary immunity, if susceptible, or aborts the infection prior to them becoming contagious, if already infected
- Immunization: disease-specific medical countermeasure given to the susceptible cohort that grants immunity to the disease for the duration of the outbreak (may or may not be life-long immunity)
- Quarantine and Hospital Isolation: modeled together to represent the efforts of removing the contacts of an infectious person from the general population and prohibiting the spread of disease by individuals who have been diagnosed with the disease and are in the medical system

The conceptual approach to consideration of these control measures also provides a means of representing the spread of a contagious disease through any group of predefined sub-populations, referred to as the *structure* of the population, and for any description of the transfer of individuals from one PAR to another of that structure, referred to as *movement*. This feature of the model is used in the present analysis, to determine the extent to which estimates of casualties from contagious disease would change if structure and movement are considered.

¹⁰ Carl A. Curling and Sean M. Oxford, *NATO Allied Medical Publication 7.5 Study Draft 2 (AMedP-7.5 SD.2): NATO Planning Guide for the Estimation of CBRN Casualties*, IDA Paper NS P-5154 (Alexandria, VA: Institute for Defense Analyses, November 2014): 1-7.

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Appendix D. Abbreviations

ADM	Advanced Development and Manufacturing
AFHSB	Armed Forces Health Surveillance Branch
ALS	Analytical Laboratory System
AMedP	Allied Medical Publication
AO	Area of Operations
ASD/HA	Assistant Secretary of Defense for Health Affairs
ATSD/NCB	Assistant to the Secretary of Defense/ Nuclear, Chemical, and Biological Defense Programs
BSV	Biosurveillance
BW	Biological Warfare
CALS	Common Analytical Laboratory System
CBDP	Chemical and Biological Defense Program
CBRN	Chemical, Biological, Radiological, and Nuclear
CBRND	Chemical, Biological, Radiological, and Nuclear Defense
CDC	Centers for Disease Control and Prevention
CLIA	Clinical Laboratory Improvement Amendments
CLIP	Clinical Laboratory Improvement Program
DNA	Deoxyribonucleic Acid
DNBI	Disease and Non-Battle Injury
DOD	Department of Defense
DODI	Department of Defense Instruction
DRSi	Disease Reporting System Internet
EEEV	Eastern Equine Encephalitis Virus
EID	Emerging Infectious Disease
ESSENCE	Electronic Surveillance System for the Early Notification of Community-based Epidemics
FDA	Food and Drug Administration
GEIS	Global Emerging Infections Surveillance and Response System
GEMS	Global Entity Management System
GHSA	Global Health Security Agenda
HHS	Health and Human Services

HIV	Human Immunodeficiency Virus
HSA	Global Health Security Agenda
ID	Infectious Dose
IDA	Institute for Defense Analyses
IHR	International Health Regulations
JBAIDS	Joint Biological Agent Identification and Detection System
JPEO-CBD	Joint Program Executive Office—Chemical and Biological Defense
JRO-CBRND	Joint Requirements Office- Chemical, Biological, Radiological, and Nuclear Defense
JSTO-CBD	Joint Science and Technology Office—Chemical and Biological Defense
JWICS	Joint Worldwide Intelligence Communications System
MERS-CoV	Middle East Respiratory Syndrome Coronavirus
MSF	Médecins Sans Frontières
MTF	Medical Treatment Facility
NATO	North Atlantic Treaty Organization
NCMI	National Center for Medical Intelligence
NGDS	Next Generation Diagnostic System
NGS	Next-Generation Sequencing
NIPR	Non-Secure Internet Protocol Router
OIF	Operation Iraqi Freedom
PAR	Population at Risk
PCR	Polymerase Chain Reaction
PEP	Pre-Exposure Prophylaxis
ROM	Restriction of Movement
RSOI	Reception, Staging, Onward-movement, and Integration
SARS	Sudden Acute Respiratory Syndrome
SEIR	Susceptible, Exposed, Infected, and Removed
SIPR	Secret Internet Protocol Router
SME	Subject Matter Expert
SPOT-JAMMS	Synchronized Predeployment and Operational Tracker—Joint Asset Movement Management System
TRADOC	US Army Training and Doctrine Command
US	United States
USAMRIID	US Army Medical Research Institute for Infectious Diseases
WHO	World Health Organization

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14. ABSTRACT IDA assessed the potential risk to US military forces and objectives posed by outbreaks of emerging infectious disease and recommended initiatives to improve DOD capabilities to mitigate that risk. IDA developed a qualitative set of producibility, employability, and effectiveness characteristics of concern for evaluating the potential risk of EIDs, and conducted a quantitative assessment of operational impact using an IDA-developed model of contagious disease dynamics. The modeling results indicated that some emerging diseases could indeed threaten US military forces and objectives in a variety of scenarios including natural outbreaks, improvised biological operations, and biological warfare attacks. The IDA team also found that outbreak response capabilities could be easily ranked in terms of effectiveness, with medical countermeasures providing much more effective than procedural controls such as restriction of movement. Moreover, to be effective, response capabilities needed to be implemented rapidly, at a time when there would be few symptomatic cases of illness to serve as triggers. The research team used this latter finding to recommend requirements for biosurveillance initiatives intended to detect disease outbreaks.					
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