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February 2020
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IDA Paper P-10877
Log: H 19-000498

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**About This Publication**
**This work was conducted by the Institute for Defense Analyses (IDA) under contract HQ0034-14-D-0001, project CA-6-4259, "Medical CBRN Defense Planning and Response Project," for the Joint Staff, Joint Requirements Office (JRO) for Chemical, Biological, Radiological and Nuclear (CBRN) Defense (J-8/ JRO) and the U.S. Army Office of The Surgeon General (OTSG). The views, opinions, and findings should not be construed as representing the official position of either the Department of Defense or the sponsoring organization.**

**Acknowledgments**
**The authors are grateful to Mr. Douglas P. Schultz and Dr. Emily D. Heuring for reviewing, John C. Everett for editing, and Mrs. Amberlee Mabe-Stanberry for producing this document.**

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# Executive Summary

Operationally significant outbreaks of contagious disease in a military theater pose significant challenges to commanders, who need to balance the immediate need to maintain operational tempo and achieve military objectives with the need to protect the health of the force and maintain long-term combat effectiveness. The purpose of this paper is to provide a set of broad, analytically supported guidelines for implementing disease outbreak response measures in an operational environment. Candidate measures evaluated by IDA were medical countermeasures (MedCMs), isolation, quarantine, and operational- and strategic-level restriction of movement. This paper is intended to inform decisions by commanders, medical advisors, and medical staffs by identifying the conditions under which various control measures could be used to greatest effect. Depending on the operating environment and the nature of the disease, specific control measures may be easier or more difficult to implement and more or less effective.

The guidelines provided in this paper are derived from a quantitative analysis of the conditions needed for effective implementation of outbreak response measures, combined with a qualitative discussion of the constraints on those conditions imposed by diseases and various types of military operations. The analysis is, at heart, based on a simple concept: disease outbreaks grow when each contagious individual, on average, infects more than one other individual and wane when each contagious individual, on average, infects less than one other individual. In evaluating candidate outbreak response measures, the IDA team asked the basic question: *Will a given response measure decrease the number of infections caused, on average, by each contagious individual to less than one?*

The IDA team used data on four diseases—smallpox, plague, Sudden Acute Respiratory Syndrome (SARS), and the 1918 variant of influenza—to demonstrate the relationships between disease characteristics and the conditions for effective outbreak response. These relationships were then used to develop guidelines for the implementation of various response measures under different operational environments.

This paper focuses on measures to prevent contagious individuals from infecting others within a population at risk (PAR). However, decision makers must also remain cognizant that those individuals are patients in need of complex and sophisticated medical care. In many cases, the manifestation of disease will be such that the patients cannot be readily moved out of theater and that care must be provided with locally available assets. Providing sufficient care for these individuals will be a significant and separate challenge but one that can be mitigated if outbreak response measures are effective.

## MedCMs

MedCMs are medical interventions—generally pharmaceuticals—that diminish the susceptibility of personnel exposed to pathogens, or that treat illnesses resulting from such exposure. The effectiveness of MedCMs as an outbreak response option depends on three factors: availability, efficacy, and time window for administration. For the four diseases that the IDA team considered, Figure ES 1 shows the calculated minimum efficacy needed for MedCMs to cause an outbreak to wane.

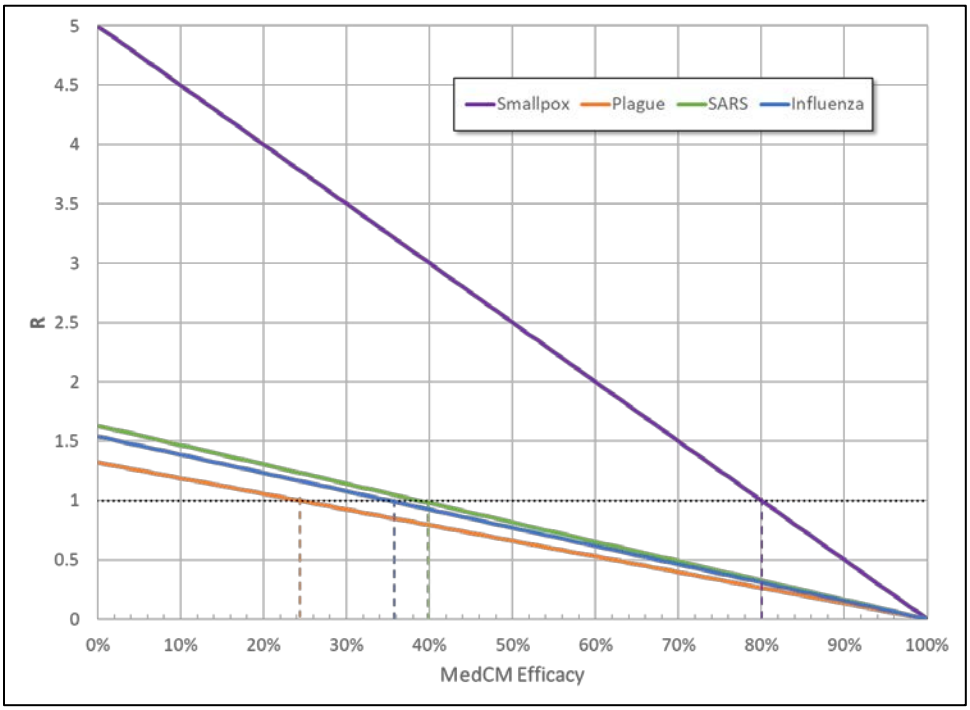


**Figure ES 1. Calculated Minimum Vaccine Efficacy Requirements**

The availability of MedCMs is perhaps the single most important factor in planning and executing an effective outbreak response. When MedCMs are available, they provide decision makers with a highly effective response option that can be administered at generally low operational cost. It is important for decision makers to understand that MedCM efficacy does not necessarily have to be very high to be effective. As shown in Figure ES 1, the minimum MedCM efficacy requirements for plague, influenza, and SARS are 24%, 35%, and 39%, respectively. These efficacy requirements imply that for at least some diseases, MedCMs can be an important outbreak response even when facing resistant strains of disease or diseases against which they are only partly effective.

## Isolation

Isolation is the separation of infectious individuals from a healthy population. Depending on the ease of transmission and the severity of disease, procedures for isolation

in a military setting could range from confinement to quarters, to retention in a hospital isolation ward, to treatment within a high-level containment care facility such as those used in 2014 to treat Ebola patients. The IDA team analyzed the effectiveness of isolation based on its ability to cause an outbreak to wane, considering who must be isolated (contagious individuals) and when they must be isolated (before they have the opportunity to infect others).

Figure ES 2 illustrates the maximum time that isolation can be delayed and still be an effective response measure for four diseases: smallpox, plague, SARS, and influenza.

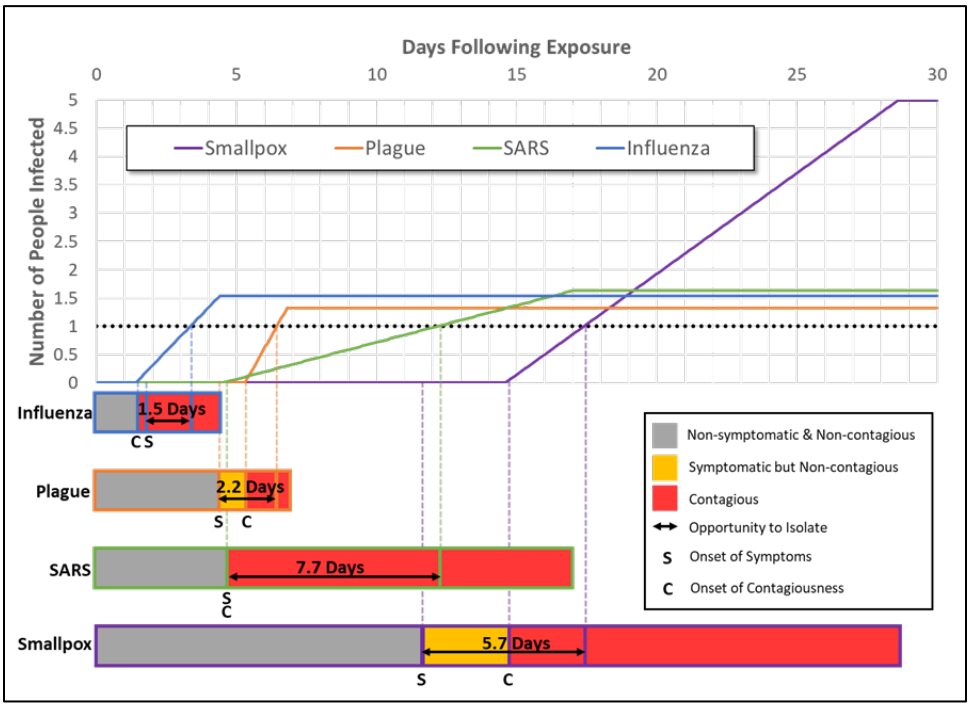


**Figure ES 2. Time Window for Isolation**

Some types of operations will inhibit the ability of individuals to be isolated in accordance with the required timelines. Operational challenges include poor or degraded transportation networks within the area of operations, non-permissive environments, and large-scale operations where forces are widely dispersed over a large geographic area. Options for overcoming these challenges include the augmentation or conversion of deployed Role 2 facilities to isolate contagious individuals until they can be moved out of the area, siting isolation facilities close to affected units to minimize the delays in reaching isolation, and requesting the deployment of additional hospitals to the theater to increase isolation capacity.

## Quarantine

Quarantine is the segregation of healthy but potentially exposed individuals from the remainder of the healthy population, until it can be determined that the segregated individuals are free of infection. The purpose of quarantine is to eliminate the possibility that contagious individuals will spread disease, from the onset of their contagious period to the time at which they are isolated. The necessary duration of quarantine is related to the incubation period of the disease, and individuals in quarantine would typically be subject to active, continued health monitoring by medical personnel.

Quarantine can be implemented in any number of ways. This paper assesses three different quarantine strategies that could potentially be used in an operational setting:

- Quarantine in place,
- Confinement within a dedicated quarantine facility, and
- Quarantine of an entire unit in rear or permissive areas.

These three options differ significantly in terms of operational cost of implementation. Selection of any one will depend on the imperatives of the disease in question and the tolerance that operational commanders will have for absorbing the costs of quarantine in any given operation.

In general, quarantine in place is the most desirable option for managing an outbreak with minimal disruption to operations. However, for diseases like influenza (with very short windows of opportunity for isolation) or for diseases like plague (with severe consequences for delayed medical treatment), quarantine in place may not be feasible. In these cases, individuals at risk of developing disease should be removed from their units and placed in dedicated quarantine facilities at locations proximate to isolation facilities. Finally, in some cases, units will experience sufficiently high disease casualty rates to prevent that they are no longer mission capable. In these cases, units should be moved offline and quarantined in rear or permissive areas.

## Operational and Strategic Restriction of Movement (ROM)

Operational ROM is the restriction of contact between units or personnel that have not yet been affected by an outbreak and those that may have been affected within a theater of operations. Strategic ROM is the prevention of movement of units or personnel into and out of the theater. The objective of this outbreak response measure differs from others. Whereas MedCMs, isolation, and quarantine are aimed at ensuring that the outbreak wanes with each successive generation of disease cases, the goal of ROM is to prevent or delay the spread of disease to a particular population or unit to preserve immediate mission capability, prevent international spread of disease, and protect home nations. In ROMs most restrictive form, healthy personnel are prohibited from moving into or out of the unit

for the duration of ROM and contact with other units is suspended. More relaxed forms of ROM may allow some level of personnel movement. However, the more individuals move between units, the less likely that those individuals who become ill will be within the controlled unit at the onset of illness.

The IDA team used a simple model of population structure and movement to determine the maximum number of individuals that can move each day before the probability that an incubating case of disease moves into a disease-free unit within a defined period of time is greater than 50%. The team found that this number varies greatly by disease. For example, during an outbreak of SARS where 2% of the population overall is symptomatic, no more than 24 people can move into a unit per day to ensure at least a 50% chance that the unit will remain disease free for the next 3 days. Results for influenza were similar. On the other hand, keeping a unit disease free from plague or smallpox is possible only if movement of personnel into that unit is almost completely prohibited.

## Additional Considerations

In addition to guidelines for specific response measures, medical planners and decision makers should take a number of actions when planning or implementing outbreak response in any operational environment in order to maximize the speed and effectiveness with which an outbreak is controlled:

- **Provide medical treatment facilities (MTFs) with additional personnel protective equipment (PPE) and infection control capability as needed.** Standard precautions used for infection control in deployed MTFs may provide insufficient protection against highly contagious infectious disease. Depending on the mode of transmission and transmissibility of the disease, standard precautions may need to be augmented with enhanced PPE and the adoption of additional infection control procedures to protect medical personnel and other patients and to restrict contamination to controlled areas.
- **Promulgate public health guidance.** Medical advisors, with the assistance of their staffs, should promulgate public health guidance throughout the area of operations to enhance public hygiene and limit exposures, manage contagious patients, and facilitate implementation of outbreak response measures. This guidance should be regularly revisited and updated as warranted as the outbreak progresses.
- **Establish and maintain situational awareness**. During disease outbreaks of operational concern, operational staffs must maintain a robust common operating picture, with primary support from medical staff. The importance of situational awareness as an enabler of successful outbreak response cannot be overemphasized. Decision makers at all levels must emphasize the need for regular,

consistent, and complete case reporting. Routine disease reporting mechanisms, timelines, and information may be insufficient for this purpose. Staffs may need to direct alternative procedures and reporting mechanisms. Staffs should ensure that clinical and diagnostic laboratory facilities are included in the reporting chain and that they have access to all relevant laboratory reports and findings.

# Contents

# 1. Introduction

For several years, the Institute for Defense Analyses (IDA) has supported the U.S. Army Office of the Surgeon General (OTSG) in its roles as the U.S. head of delegation to the North Atlantic Treaty Organization (NATO) Chemical, Biological, Radiological, and Nuclear (CBRN) Medical Working Group and as custodian of multiple standardization agreements included in the NATO CBRN Medical Working Group's program of work. IDA's support in this area has included concept development and analysis for OTSG's development of command guidance for Allied medical operations in a CBRN environment, recently promulgated as *Allied Medical Publication 7.6 (AMedP-7.6): Commander's Guide on Medical Support to CBRN Defensive Operations*.[1]

Operationally significant outbreaks of contagious disease in a military theater pose significant challenges to commanders, who need to balance the immediate need to maintain operational tempo and achieve military objectives with the need to protect the health of the force and maintain long-term combat effectiveness. *AMedP-7.6* provides information for commanders and their medical advisors on actions that can be taken to control the spread of disease and requirements for the implementation of those actions. *AMedP-7.6* further states that any medical advice on disease control measures should have an analytical basis:

> In the event of an operationally significant outbreak of contagious disease in theatre, Medical Advisors should be prepared … [to provide] disease-specific measures to control the spread of disease, *with an assessment of both effectiveness and potential for operational degradation* (italics added).[2]

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1 North Atlantic Treaty Organization, *Allied Medical Publication 7.6 (AMedP-7.6): Commander's Guide on Medical Support to Chemical, Biological, Radiological, and Nuclear (CBRN) Defensive Operations*, NATO STANAG 2873, Edition A, Version 1 (Brussels, Belgium: NATO Standardization Organization, February 2018), https://www.coemed.org/files/stanags/03_AMEDP/AMedP-7.6_EDA_V1_E_2873.pdf.

2 North Atlantic Treaty Organization, *Allied Medical Publication 7.6 (AMedP-7.6)*, 7-5. As part of NATO's ongoing effort to consolidate and integrate medical doctrine, *AMedP-7.6* incorporates the operational level guidance provided in an older standardization agreement (STANAG), now superseded: Military Committee Joint Standardization Board, *Medical Advice on Restriction of Movement*, NATO STANAG 2278 NBC/MED, Edition 1, Ratification Draft 1 (Brussels Belgium: NATO Standardization Agency, October 2004). The portions of *AMedP-7.6* related to disease outbreak response measures are taken from this document.

Although *AMedP-7.6* lists some of the issues that Medical Advisors might consider in this assessment, it does not provide specific guidance on how that assessment should be conducted or the criteria that should be used. This lack of specific guidance is, in part, because the effectiveness and the operational costs of disease control measures are situationally dependent on the causative agent and the nature of the operation. Moreover, previous work at IDA[3] has shown that evaluation of the costs and benefits of disease control measures can be quite complex and the results can be counterintuitive. This paper augments the guidance provided in *AMedP-7.6* by providing analysis to support medical staff planning and command decisions on measures to control outbreaks of contagious disease in theater, whether occurring naturally or caused intentionally. Although the information provided herein is intended primarily to support decision making for Allied operations, it would also be relevant to U.S. military operations more broadly.

The purpose of this paper is to provide a set of broad, analytically supported guidelines for implementing disease outbreak response measures in an operational environment. Candidate measures include medical countermeasures (MedCMs), isolation, quarantine, and operational- and strategic-level restriction of movement. As described in subsequent sections, the guidelines—or "rules of thumb"—provided here are derived from analysis of requirements for effective implementation of various measures and account for the challenges posed by different diseases and by missions of different types. These guidelines are intended to inform command decisions by identifying the conditions under which various control measures should be used. Depending on the operating environment and the nature of the disease, specific control measures may be easier or more difficult to implement and may be more or less effective.

This paper focusses on operationally significant outbreaks of contagious disease: those that threaten the accomplishment of mission objectives or generate intolerable health risks to the fighting force and therefore warrant the attention of commanders at the operational or strategic level. During normal operations, military medical units at all levels should be trained and equipped to manage small numbers of patients who are ill with common and relatively benign contagious diseases.[4] The guidelines provided here would only

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[3] See, for example, Julia K. Burr et al., *Emerging Infectious Diseases Study*, IDA Paper P-5302 (Alexandria, VA: Institute for Defense Analyses, August 2016).

[4] See Chairman of the Joint Chiefs of Staff, *Joint Health Services*, Joint Publication 4-02 (Washington, DC: Chairman of the Joint Chiefs of Staff, 11 December 2017, Incorporating Change 1, 28 September 2018), https://www.jcs.mil/Portals/36/Documents/Doctrine/pubs/jp4_02ch1.pdf. A routine sick call is managed at the first responder/Role 1 level (II-2), while control of communicable diseases is generally the responsibility of preventive medicine units assigned at the forward resuscitative care (Role 2) and theater hospitalization (Role 3) level (III-1). The ability to isolate contagious disease patients in theater is typically provided at Role 3 (I-6). In NATO doctrine, standard preventive medicine capabilities and infection control within medical treatment facilities are described in North Atlantic Treaty Organization, *Allied Joint Medical Publication 4: Allied Joint Medical Force Health Protection Doctrine*,

be relevant when (1) this baseline capability is inadequate because of the severity of the disease, the number of casualties, or the insufficiency of standard precautions in preventing the spread of disease and (2) when operationally significant outbreaks occur as a result.

Standard disease control measures might break down for any number of reasons:

- Some diseases, like influenza, can be contagious before the onset of symptoms.
- Mechanisms of disease transmission—and the requirements for controlling them—may not be fully understood for newly emerged diseases such as severe acute respiratory syndrome (SARS).
- Operational circumstances, including high operational tempo and large geographic distances between combat units and isolation facilities, can increase the time that it takes to isolate contagious personnel.
- Limitations in deployed laboratory capability may delay the diagnosis of the causative agent of disease and the associated awareness of the type of outbreak responses needed to contain it.
- Biological warfare attacks could generate large numbers of near-simultaneous primary infections, overwhelming available isolation capabilities from the outset.
- In any contagious disease outbreak, deployed military personnel are unlikely to be the only source of contagion. Host nation civilians and animal or insect vectors may also contribute to the spread of disease.

In the context of contagious disease outbreaks, consequences can be measured in terms of casualties incurred, and personnel losses are often considered an indicator of operational degradation.[5] Thus, operationally significant outbreaks by this measure would be those that exceed some defined casualty threshold, expressed as total numbers or percent of population within the overall force or within specific units. The threshold itself may vary since tolerance for casualties can differ by operation, as does the impact of casualties within specific units or among specific types of personnel. The IDA team, in its assessment of outbreak response measures, used personnel losses as the primary measure of outcome.

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NATO STANAG 2561, Edition A, Version 1 (Brussels, Belgium: NATO Standardization Organization, July 2018), https://www.coemed.org/files/stanags/02_AJMEDP/AJMedP-4_EDA_V1_E_2561.pdf.

5 For an assessment of various measures of operational degradation in a CBRN environment and the pros and cons of using personnel losses for this purpose, see Robert A. Zirkle et al., *Operational Effectiveness Analyses (OEA)*, IDA Document D-4666 (Alexandria, VA: Institute for Defense Analyses, August 2012).

Commanders should be aware that not all cases of highly contagious disease will lead to outbreaks of sufficient magnitude as to be operationally significant. Even when baseline medical capabilities are inadequate for managing these cases, for reasons discussed previously, the propagation of disease through the military population may still be limited. Epidemiological research has shown significant variation in the propensity of individuals to spread disease.[6] In general, the large majority of secondary infections are caused by a small percentage of contagious disease cases, and a significant percentage of contagious individuals do not infect any other individuals. Consequently, the manifestation of a few cases of highly contagious disease is not automatically cause for serious alarm. Because of the potential severity of the consequences, however, medical advisors and medical staff should closely monitor any such cases of disease and be prepared to recommend and implement outbreak response measures if indicators show that the disease is spreading.

This paper focuses on measures to prevent contagious individuals from infecting others and spreading disease throughout a population at risk (PAR). However, decision makers must also remain cognizant of the fact that those individuals are patients who need complex and sophisticated medical care. In many cases, the manifestation of disease will be such that the patients cannot be readily moved out of theater and that the needed care must be provided with locally available assets. Providing sufficient care for these individuals will be a significant and separate challenge but one that can be mitigated if outbreak response measures are effective.

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6 J. O. Lloyd-Smith et al., "Superspreading and the Effect of Individual Variation on Disease Emergence," *Nature* 438, no. 7066 (November 17, 2005): 355–359, https://www.nature.com/articles/nature04153. This study provides estimates of individual variability in spreading disease. Combining these estimates with a traditional Susceptible, Exposed, Infected, Removed (SEIR) epidemiological model, the IDA team estimated the total number of secondary cases that would occur in an outbreak generated by a single primary case of pneumonic plague in a population of 1,000. In 37% of the 2000 trials conducted, there was no secondary transmission at all, and, in over 70% of trials, the total number of expected cases was 40 or fewer. However, approximately 18% of the time, significant secondary transmission did occur, and the number of expected cases exceeded 400. As this simple calculation demonstrates, a few highly contagious casualties—even those with severe illnesses, such as pneumonic plague—are unlikely to generate operationally significant outbreaks. Nonetheless, the risk of such outbreaks is significant, and, if they should occur, they are likely to have substantial impact.

# 2. Analytical Approach

The guidelines provided in this paper are derived from a quantitative analysis of the conditions needed for effective implementation of outbreak response measures, combined with a qualitative discussion of the constraints on those conditions imposed by diseases and various types of military operations. The analysis begins with a theoretical approach to evaluating outbreak response measures, based on their contribution to reducing the mean number of secondary infections generated per contagious individual. This theoretical approach is discussed in this chapter, together with additional measures of the effectiveness of outbreak responses and the potential operational costs associated with implementing them.

## A. $R_0$ and the Effectiveness of Outbreak Response Measures

The quantitative analysis described in this paper is, at heart, based on the relationship between two variables: (1) the basic reproductive number of a disease, $R_0$, defined as the mean number of infections that would be caused by an infected individual in an entirely susceptible population[7] and (2) $R$, the mean number of infections caused by an infected individual in a population where susceptibility is constrained for various reasons. Values for $R_0$ are disease specific and are influenced by factors such as mode of transmission and infectivity.[8]

At a basic level, outbreaks grow when each contagious individual, on average, infects more than one other individual and wane when each contagious individual, on average, infects less than one other individual. To illustrate this concept, consider an outbreak of a disease with a given $R_0$ within a well-mixed population of $N$ individuals, of which some subset $S$ is susceptible to infection. On average, in the absence of any response, each contagious individual is expected to cause $R_{no\ response}$ new infections during their infectious period:

$$R_{no\ response} = R_0 \frac{S}{N}. \quad (1)$$

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7 Lloyd-Smith, et al., "Superspreading and the Effect," 355.

8 Estimated $R_0$ values for most contagious diseases are widely available in the literature. While estimates may vary for a given disease, depending on the data used to derive it, there is generally broad agreement on the relative magnitude of $R_0$ between different diseases.

If the population is entirely susceptible, then $\frac{S}{N} = 1$, and, on average, each contagious individual will cause $R_0$ infections. However, as the number of susceptible individuals in the population decreases, so does the number of new infections that are expected to be caused by each contagious individual. Equation 1 can be used to illustrate the point at which the outbreak will begin to wane, by considering the case when each contagious individual infects, on average, fewer than one other individual (i.e., $R_{no\ response} < 1$):

$$R_0 \frac{S}{N} < 1 \tag{2}$$

$$\frac{S}{N} < \frac{1}{R_0}. \tag{3}$$

In other words, an outbreak will wane when the fraction of the population that is susceptible to disease drops below $\frac{1}{R_0}$. The higher the value of $R_0$, the more the susceptible population needs to be reduced, which is one reason why outbreaks of some diseases may be more difficult and take longer to control than others.[9]

Eventually, outbreaks of contagious disease will end naturally as susceptible individuals fall ill and the residual susceptible population falls. This certainty suggests two possible, related approaches for outbreak response: limiting the opportunities for contagious individuals to infect others and limiting the inherent susceptibility of the population.

The first approach focuses response efforts on contagious individuals, and the second approach focuses on the population with which they interact. In evaluating either approach, the basic question is as follows: *Will a given response measure decrease the number of infections caused, on average, by each contagious individual to less than one?* More formally, suppose that some function $f_{response}$ exists that characterizes the reduction in an individual's transmission due to a given response measure. The function $f_{response}$ depends on the parameter(s) that describe that response $(x_1, x_2, \dots x_n)$ for a particular disease. As will be shown in Chapter 3, the functional form of $f_{response}$ and the parameters $(x_1, x_2, \dots x_n)$ that describe it will depend on the specifics of what response(s) are being considered. By incorporating $f_{response}$ into Equation 1, Equation 4 expresses the expected number of infections an individual will cause given some response, $R_{response}$:

$$R_{response} = f_{response}(x_1, x_2, \dots x_n) R_0 \frac{S}{N}. \tag{4}$$

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[9] Since the focus of this paper is on evaluating measures to control ongoing outbreaks, the analysis is primarily interested in determining when outbreaks stop. Even so, the same concept applies to outbreak prevention. Outbreaks will not begin if each of the first cases of disease causes less than one additional case of disease, or if the fraction of susceptible individuals is below $\frac{1}{R_0}$ when the first cases of disease occur.

When $f_{response}(x_1, x_2, \ldots x_n) = 1$, the response measure is **completely ineffective**. Each contagious individual will generate, on average, $R_0 \frac{S}{N}$ cases (i.e., $R_{response} = R_{no\ response}$). On the other hand, when $f_{response}(x_1, x_2, \ldots x_n) = 0$, the response measure is **completely effective** (i.e., $R_{response} = 0$). No individual who is infectious will cause any new cases, and therefore no further disease transmission will occur. That being said, a given response does not need to be completely effective to cause an outbreak to wane and eventually stop. For this analysis, a given response will be considered effective if it is capable of causing an outbreak to wane:

$$R_{response} = f_{response}(x_1, x_2, \ldots x_n) R_0 \frac{S}{N} < 1. \quad (5)$$

The inequality in Equation 5 can then be used to identify values for the set of response parameters $x_1, x_2, \ldots x_n$ that are needed for a given response to be effective. The process of identifying the set of parameter values for a specified response that will cause an outbreak of a given disease to wane is the principle objective of Chapter 3.

At the beginning of an outbreak in a disease-naive population, the entirety of the population is likely to be susceptible to infection, $S = N$, or, equivalently, $\frac{S}{N} = 1$. Therefore, at the beginning of such an outbreak the inequality in Equation 5 can be rewritten as

$$R_{response} = f_{response}(x_1, x_2, \ldots x_n) R_0 < 1. \quad (6)$$

Because $\frac{S}{N} \leq 1$ for the entirety of any outbreak, the left-hand side of inequality in Equation 5 is always less than that of the inequality in Equation 6. Given that, the values of the response parameters $x_1, x_2, \ldots x_n$ that satisfy the inequality in Equation 6 will also satisfy the inequality in Equation 5. In other words, satisfying the requirements for a response to be effective at the beginning of an outbreak will also ensure that the response is effective at later stages of the outbreak. Therefore, the IDA team used the inequality in Equation 6 as the point of departure for analyzing each of the responses under consideration in the present analysis.

As can be seen in Equation 5 and Equation 6, as the value of $R_0$ changes, the parameter values associated with an effective outbreak response may also change. Since $R_0$ will vary with disease, a response that would be effective in controlling one disease may not be effective against another. This concept reinforces the need to provide commanders with guidelines that consider the challenges posed by diseases of various types.

When evaluating candidate outbreak responses, reducing $R$ to less than 1 is necessary but may not be sufficient to minimize operational impact. After all, as shown in the beginning of this section, $R$ can eventually be reduced to less than 1 in the absence of any outbreak response measure as a larger percentage of the population falls ill. To be fully effective, response measures should reduce the number of infected individuals and the duration

of the outbreak, both of which can be accomplished by reducing $R$ as much and quickly as possible. The sooner $R < 1$, and the closer $R$ gets to zero, the shorter the outbreak and the fewer total cases.

The objective of reducing $R$ as quickly as possible provides a means of comparatively assessing outbreak responses. If several candidate responses can effectively reduce the average number of infections caused per contagious individual, the one that does so most, and most rapidly, would be best. In addition, during military operations, unit combat effectiveness is closely related to casualty rates. The effectiveness of response measures can also be evaluated on their ability to prevent the number or percent of personnel infected from exceeding a defined threshold or to limit the spread of an outbreak to a defined number of units.

The implementation of outbreak response measures will likely prove disruptive to military operations. When comparing measures, the potential operational impact—or cost of implementation—is a key consideration. As with the benefits of implementation, operational impact can be measured in terms of personnel losses. For example, the number of people quarantined unnecessarily is a good way of considering the potential impact of quarantine since it reflects personnel lost to a unit, albeit partially or temporarily, and can be directly weighed against casualties expected in the absence of quarantine. At the same time, other operational costs and risks may be associated with outbreak response that are more difficult to quantify or depend on the type of operation. For example, the impact of restricting movement of personnel between units will depend on the degree of movement during normal operations. To provide a consistent means of comparison, the evaluation of response measures described in this paper considered the cost of implementation in terms of personnel losses whenever possible.

Military force health protection doctrine[10] mandates the use of disease prevention and control measures by military personnel in garrison, training, and field environments, facilitated by preventive medicine units and personnel at all levels of command. Deployed military forces routinely use measures such as vector control, waste handling and disposal, and personal hygiene to prevent disease and minimize its spread.

During contagious disease outbreaks, additional public health measures can be used to augment existing disease prevention measures and support early detection of cases. These measures include handwashing mandated at regular intervals or upon entry/exit from designated locations, limitations on gatherings of personnel, maintenance of physical distance in social situations, and so forth. The effectiveness of such measures depends on

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[10] See, for example, Department of the Army, *Force Health Protection*, Army Techniques Publication No. 4-02.8 (Washington, DC: Headquarters, Department of the Army, 9 March 2016), https://armypubs.army.mil/epubs/DR_pubs/DR_a/pdf/web/atp4_02x8.pdf and North Atlantic Treaty Organization, *Allied Joint Medical Publication 4*.

route of transmission and infectivity of the specific disease. These factors heavily influence $R_0$ and are generally considered in the literature when values for $R_0$ are derived. The IDA team assumed that measures of this type would be implemented throughout the deployed force as appropriate.

The IDA team used four different contagious diseases to illustrate the concepts and analysis provided in this paper: smallpox, pneumonic plague, SARS, and influenza. Table 1 shows the specific characteristics and associated values used.

**Table 1. Selected Contagious Disease Characteristics and Values**

| Characteristics | Plague | Smallpox | SARS | Influenza |
|---|---|---|---|---|
| $R_0$ | 1.32[a] | 5[b] | 1.63[a] | 1.54[c] |
| Incubation Period (Days) | 4.3[d] | 11.6[d] | 4.49[e] | 1.4[c] |
| Early Symptoms (Days) | 1[d] | 3[d] | N/A | 0.23[c] |
| Later Symptoms (Days) | 1.5[d] | 14[d] | 12.5[e] | 2.76[c] |

[a] J. O. Lloyd-Smith et al., "Superspreading and the Effect of Individual Variation on Disease Emergence," *Nature* 438, no. 7066 (November 17, 2005): 355–359, https://www.nature.com/articles/nature04153.

[b] Raymond Gani and Steve Leach, "Transmission Potential of Smallpox in Contemporary Populations," *Nature* 414, no. 6865 (December 13, 2001): 748–751, https://www.nature.com/articles/414748a.

[c] Corey M. Peak et al., "Comparing Nonphamaceutical Interventions for Containing Emerging Epidemics," *Proceedings of the National Academy of Sciences of the United States of America* 114, no. 15 (April 11, 2017): 4023–4028, https://doi.org/10.1073/pnas.1616438114.

[d] Sean M. Oxford et al., *Technical Reference Manual to Allied Medical Publication 7.5 (AMedP-7.5) NATO Planning Guide for the Estimation of CBRN Casualties*, IDA Document D-8122 (Alexandria, VA: Institute for Defense Analyses, October 2016).

[e] John N. Bombardt, "Congruent Epidemic Models for Unstructured and Structured Populations: Analytical Reconstruction of a 2003 SARS Outbreak," *Mathematical Biosciences* 203, no. 2 (October 2006): 171–203, https://doi.org/10.1016/j.mbs.2006.05.004.

## B. Development of Guidelines

To begin the development of operational guidelines, the IDA team reviewed various outbreak response measures available to commanders and established key parameters that could be used to describe and evaluate each measure. Examples of such parameters are the efficacy of MedCMs, and the delay between symptom onset and isolation. With the objective of reducing the mean number of infections caused by a contagious individual to less than one ($R < 1$) and for the four diseases listed in Table 1, the IDA team then established the range of parameter values over which a given response measure would be effective. Chapter 3 describes the requirements for effective outbreak response measures and the assessment used to develop them.

Next, the IDA team identified potential challenges to implementing outbreak responses in different operational environments. Operational challenges can influence key response parameters and may reduce the effectiveness of some responses or increase their costs. In essence, the operational environment will determine whether it is possible to implement outbreak responses in an effective manner. Because not all challenges will be present in all types of operations or in all disease outbreaks, this step is critical in the assessment of the utility of response measures and, ultimately, in generating guidance for commanders who must respond to outbreaks during a specific operation. The output of this step is a matrix that describes, in general terms, the magnitude of the challenge to specific responses in different operational circumstances or from different types of diseases and allows a prioritization of responses by type of operation. Chapter 4 discusses response implementation challenges and their implications.

Chapter 5 summarizes the disease and operational factors that determine the requirements for and feasibility of implementing outbreak responses and provides guidelines for selecting and implementing outbreak response measures that account for those factors. These guidelines also incorporate a number of additional insights developed during the assessment described in Chapter 3 on questions such as the likely availability of information at various points in time or the penalty for delaying a response to avoid its operational impact.

# 3. Evaluation of Outbreak Response Measures

The IDA team assessed the effectiveness of two broad categories of response measures: MedCMs and restriction of movement (ROM). In the context of a contagious disease outbreak, ROM is broadly used in reference to physical control measures intended to limit the spread of disease by preventing contact between healthy personnel and those personnel who are or could be infectious.[11] Modern military operations are characterized by a high degree of movement of personnel between units and locations.[12] Any outbreak response measures that limit movement will have at least some—and possibly quite significant—impact on operations. This paper assesses the benefits of three different types of ROM: isolation, quarantine, and operational/strategic ROM.

Collectively, these measures are intended to limit the opportunities for contagious individuals to spread disease and/or to limit the vulnerability of healthy individuals if they are exposed. All the measures discussed in this chapter have the potential to foster the desired end state for outbreak response, where $R_{response} < 1$. Sections 3.A–3.D provide a general discussion of each type of response measure and describe, analytically, the circumstances in which that potential can be realized for each response measure, defined formally as

$$R_{response} = f_{response}(x_1, x_2, \ldots x_n)R_0 < 1. \quad (7)$$

Of course, efforts to stop a militarily significant outbreak of contagious disease should consider all potential response measures and incorporate all those that can effectively contribute. Figure 1 illustrates the concept for combining response measures. The response begins when $R = R_0$[13] and collectively pushes the value of $R$ downward so that the mean number of new infections caused per contagious individual is somewhere between 1 and 0.

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11 North Atlantic Treaty Organization. *Allied Medical Publication 7.6 (AMedP-7.6)*, 7-4.

12 For example, available data on U.S. military personnel movements in Afghanistan in 2012 showed that for the median unit, 20%–25% of personnel changed locations each day, and that no unit had fewer than 5% of personnel moving each day. See Burr et al., *Emerging Infectious Diseases Study*, 68.

13 As previously discussed in Section 2.A, $R = R_0$ when the entire population is susceptible to infection—as would likely be the case at the beginning of an outbreak. If a significant portion of the population was not susceptible to infection, then $R < R_0$, in which case $R$ would be closer to one than had the entire population been susceptible.

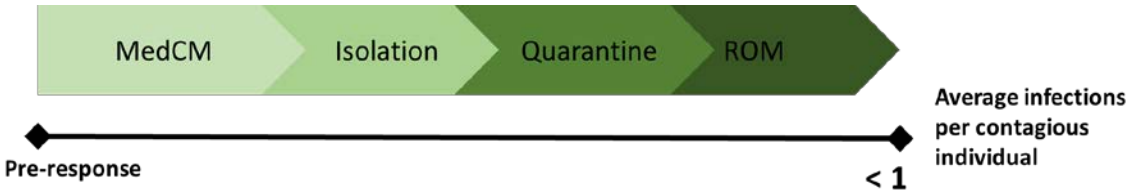


**Figure 1. Outbreak Responses in Combination**

Each response pushes *R* some distance further along the line. All responses do not have to be implemented for the overall objective to be accomplished. If any single response, or combination of responses, results in the value of *R* falling below one, the remaining responses do not have be used.

The order in which responses are shown is the same as that in which they are discussed in Sections 3.A–3.D and is deliberate. MedCMs are the only truly binary response option (i.e., they either exist or they do not exist for a given disease), and, hence, their availability has perhaps the single greatest influence on outbreak response of any single parameter. Isolation, as noted, is a standard practice for controlling the spread of disease, but the discussion that follows can shed significant light on specific, disease-dependent requirements for implementation. Quarantine and operational/strategic ROM are generally considered responses of last resort because of the large numbers of personnel affected and the associated operational costs. Here, consideration is given to both of the requirements for these measures and potential ways to limit the costs while maintaining effectiveness.

## A. MedCMs

MedCMs[14] are medical interventions—generally pharmaceuticals—that diminish the susceptibility of personnel exposed to pathogens or that treat illnesses resulting from such exposure. As outbreak response measures, MedCMs can serve two functions: (1) they can limit the vulnerability of individuals to a given disease, thus reducing the size of the susceptible population, *S*, and (2) they can shorten the duration and severity of disease, hence limiting the opportunities for sick individuals to expose others. MedCMs can be administered as pre-exposure prophylaxis, as post-exposure prophylaxis, and as therapy for those who are ill.

Pre-exposure prophylaxis is the administration of MedCMs, such as vaccination, to military personnel before any possible exposure, to reduce or eliminate an individual's vulnerability to a given pathogen. In general, immune response to vaccination will take

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[14] The definitions, acronyms, and concepts for use of MedCMs provided in this section are derived from North Atlantic Treaty Organization, *Allied Medical Publication 7.1 (AMedP-7.1): Medical Management of CBRN Casualties*, NATO STANAG 2461, Edition A, Version 1 (Brussels, Belgium: NATO Standardization Organization, June 2018), 3-1–3-4.

days or weeks to develop and may require multiple doses to reach maximum effectiveness. Consequently, vaccines are most effective if administered well before the start of any outbreak of disease. At the same time, if conducted before deployment, vaccination would have no impact on operations ongoing at the time of the outbreak. Antibiotics and antiviral drugs can also serve this function but are, to a degree, dependent on the pathogen involved. Their effects are typically more transitory, however, and, hence, they are most appropriate when an urgent risk of exposure is possible, probably post-deployment.

Post-exposure prophylaxis is administered after possible exposure to a given pathogen to prevent illness or reduce its severity. Vaccination can be provided to a PAR after the start of an outbreak. Historically, providing vaccinations has proven to be a successful strategy for limiting the spread of disease and ultimately stopping outbreaks.[15] Implementing a vaccination program during an ongoing military operation would be challenging for any number of reasons, particularly in a non-permissive environment and even more so in an Allied operation involving multiple nations with multiple health regulations. In addition, the delay between vaccination and conferred immunity may be too long to prevent an outbreak from spreading enough to pose an operational risk. This time delay would typically be much shorter for antibiotics and antiviral drugs, which would also be easier to administer in an operational setting. Even so, use of these drugs as post-exposure prophylaxis would cause the same level of operational disruption as using them for pre-exposure prophylaxis.

As a component of medical treatment, therapy drugs can facilitate the control of disease outbreaks by limiting the duration and severity of illness and the associated opportunities for infection to spread. This paper assumes that therapy drugs would be used as appropriate in the treatment of contagious disease casualties and would not be a subject for command decisions on outbreak response measures.

The use of MedCMs as an outbreak response measure, in any form, is not without potential cost. If a decision to use antibiotic/antiviral pre-exposure prophylaxis is made, implementation would need logistics, medical, and administrative support to disseminate, administer, and track these drugs. Moreover, some personnel may suffer side effects, including potentially severe allergic reactions. All these costs could result in at least some disruption to operations.

The IDA team analyzed the effectiveness of all types of MedCMs discussed in this paper by considering three factors: availability, efficacy, and time of administration.

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

## 1. Availability

Is a MedCM against the pathogen in question available? Has it been licensed by the Food and Drug Administration? Has it been procured in sufficient quantities? Is a readily available source of the countermeasure accessible in the event that more is needed? The answers to these questions are, of course, highly disease dependent. This paper does not consider the availability of specific MedCMs as part of the assessment of response measures. Rather, availability is a condition that must be met before other parameters can be evaluated. If MedCMs are available, then they must meet certain requirements for efficacy and time to administration.

## 2. Efficacy of MedCMs

In this paper, efficacy is defined as the probability that a MedCM will have its desired effect within the population of interest. If a vaccine against influenza, for example, has an efficacy of 90%, then 90% of the population to which it has been administered[16] will be immune to influenza and any given individual within that population will have a 90% chance of being immune.

The IDA team analyzed MedCM efficacy based on its ability to cause an outbreak to wane. To do this analysis, the IDA team defined the function $f_{MedCM}(\epsilon_{MedCM})$, which describes the reduction in an infectious individual's transmission due to the PAR being administered some MedCM with efficacy $\epsilon_{MedCM}$. To cause an outbreak to wane, the MedCM response must reduce the susceptibility of the contacts of infectious individuals such that, on average, less than one of the infectious individual's contacts becomes infected. Therefore, the values for $\epsilon_{MedCM}$ that will result in an effective MedCM response are those that satisfy the following inequality (based on the inequality in Equation 6):

$$R_{MedCM} = f_{MedCM}(\epsilon_{MedCM})R_0 < 1. \quad (8)$$

Once the form of the function $f_{MedCM}(\epsilon_{MedCM})$ is expressed, then specific efficacy values for an effective MedCM response can be determined. Pre- and post-exposure prophylaxis alter disease transmission by reducing individual susceptibility to infection. Assuming universal administration of MedCMs within a population, the portion of individuals whom an infectious individual can potentially infect is reduced by

[16] Efficacy, as defined here, refers to the probability of individual response given the administration of a MedCM. As discussed here, efficacy is an intrinsic characteristic of the MedCM and the pathogen that it targets. The overall effectiveness of any MedCM is clearly influenced by the rate of MedCM administration within a population and the rate of compliance among those designated to receive it. However, these factors are specifically excluded here because they can be influenced positively (through command direction and emphasis) and negatively (ease of distribution) in an operational environment. The challenges of ensuring that MedCMs are taken by those who need them are discussed in Chapter 4.

$(1 - \epsilon_{MedCM})$.[17] As a result, $f_{MedCM}(\epsilon_{MedCM}) = 1 - \epsilon_{MedCM}$, and, therefore, the values of $\epsilon_{MedCM}$ that will cause an outbreak to wane are those that satisfy

$$R_{MedCM} = (1 - \epsilon_{MedCM})R_0 < 1. \quad (9)$$

Given the $R_0$ value for the disease of interest, determining the value of $\epsilon_{MedCM}$ needed to ensure $R < 1$ is straightforward:

$$\epsilon_{MedCM} > 1 - \frac{1}{R_0}. \quad (10)$$

To illustrate the use of the inequality in Equation 10, the IDA team calculated the vaccine efficacy requirements for four known contagious diseases: smallpox, pneumonic plague, influenza, and SARS. Table 2 summarizes these minimum required efficacies for the $R_0$ values specified in Table 1. For example, for the reported smallpox $R_0$ value of 5,[18] the resulting efficacy of a vaccine needed to cause a smallpox outbreak to wane is as follows:

$$\epsilon_{MedCM} > 1 - \frac{1}{5} \quad (11)$$

$$\epsilon_{MedCM} > 80\%. \quad (12)$$

**Table 2. Minimum Required MedCM Efficacy**

| Disease | Minimum Required MedCM Efficacy |
|---|---|
| Plague | 0.24 |
| Smallpox | 0.8 |
| SARS | 0.39 |
| Influenza | 0.35 |

This same concept can be expressed graphically by plotting $R_{MedCM}$, as in Figure 2. The values of interest are the $\epsilon_{MCM}$ values that correspond to $R_{MedCM} < 1$, shown as a dotted horizontal line that intersects the vertical axis at 1. Dashed vertical lines intersect the horizontal axis at the minimum value of $\epsilon_{MedCM}$ for each of the four diseases.

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[17] This formulation of $f_{MedCM}$ is limited to describing the effect reducing population-wide susceptibility due to administration of a MedCM. The other potential benefits of MedCMs (e.g., aborting the infection of those incubating the disease or reducing the severity of disease progression) are not captured by this formulation.

[18] Raymond Gani and Steve Leach, "Transmission Potential of Smallpox in Contemporary Populations," *Nature* 414, no. 6865 (December 13, 2001): 748–751, https://www.nature.com/articles/414748a.

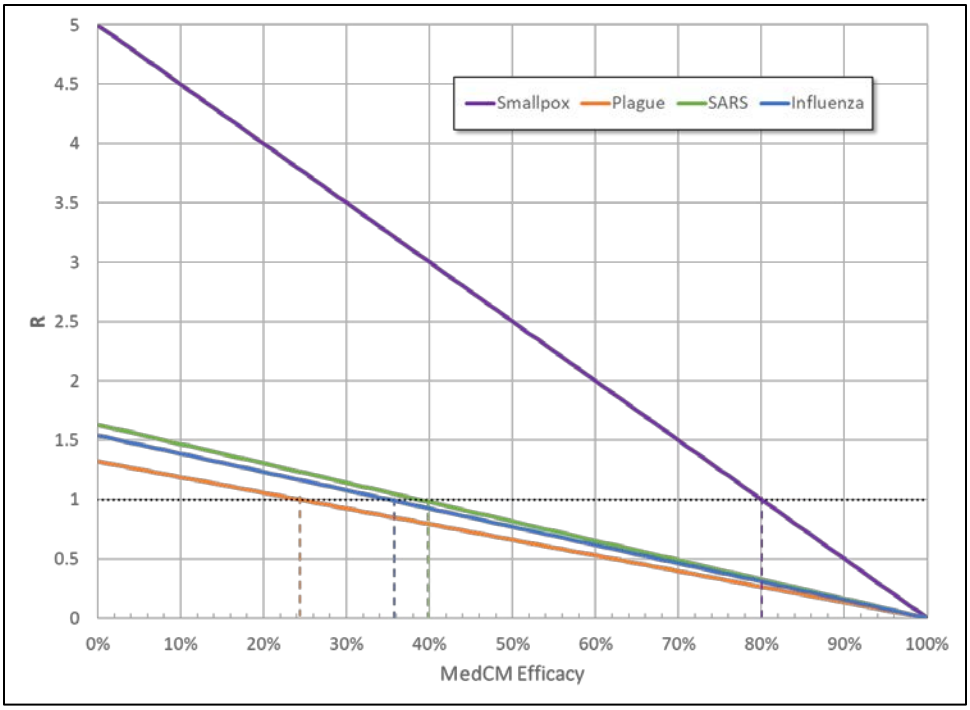


**Figure 2. Calculated Minimum Vaccine Efficacy Requirements**

## 3. Time to Administration

Assuming that MedCMs are available and that a decision has been made to use them, some delay will occur before they can be effectively administered. MedCMs still need to be delivered to the target population. The time to do so depends on how the countermeasure is stockpiled and distributed, the mechanism of administration and whether it must be done by medical personnel, the number of doses required, and the time needed to generate the desired physiological response after administration.

Because the analytic approach used to evaluate efficacy requirements for MedCMs does not consider the temporal progression of the outbreak, the IDA team used a simple "generational" model to consider the relationship between the efficacy of MedCMs and the time at which they are administered.[19] A generation of a disease is sometimes referred to as the serial interval, the duration of which is defined as the "time interval between successive infections in a chain of transmission."[20] As with other aspects of the IDA analysis, the generational model begins with *R*, the number of new infections caused per contagious

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[19] The IDA team chose to use a simple generational model rather than a more sophisticated SEIR contagious disease model. This simple model minimized the computational burden of the analysis and allowed the team to more efficiently examine the entire parameter space of interest.

[20] Emilia Vynnycky and Richard G. White, *An Introduction to Infectious Disease Modelling* (Oxford, UK: Oxford University Press, 2010), XXV.

individual. Assuming that each contagious individual causes the same number of infections, the total number of new infections in a generation is simply $R$ multiplied by the number of contagious individuals in the previous generation:

$$c_t = c_{t-1}R_{t-1} = c_{t-1}R_0\,\frac{S_{t-1}}{N}, \tag{13}$$

where $c_t$ is the number of new cases in generation $t$ of the outbreak, and $S_{t-1}$ is the number of susceptible individuals in the population during the previous generation.

The cumulative number of cases that have occurred up to a given generation, $C_t$, is the sum of the number of cases in each previous generation. With the variable $i$ used to represent the individual generations being summed over, $C_t$ can be formally represented as follows:

$$C_t = \sum_{i=1}^{t} c_i = \sum_{i=1}^{t} c_{i-1}R_0\,\frac{S_{i-1}}{N}, \tag{14}$$

where $c_0$ and $S_0$ are the number of infected and susceptible individuals, respectively, at the start of the outbreak.

Given that the number of susceptible individuals in any given generation is the total population minus the cumulative number of cases of disease,

$$S_t = N - C_t. \tag{15}$$

Substituting the expression in Equation 15 for $C_t$ generates a function that describes the cumulative number of cases over each generation of the outbreak, for known values of $R_0$, $N$, and $c_0$:

$$C_t = \sum_{i=1}^{t} c_{i-1}R_0\left(1 - \frac{C_{t-1}}{N}\right). \tag{16}$$

Figure 3 provides an example of cumulative smallpox casualties, calculated using the generational model of outbreak progression defined in Equation 16. In the figure, the outbreak started with one initial smallpox infection in a population of 3,000 individuals. As can be seen, this notional outbreak remains relatively small for the first four generations but expands rapidly from the fifth generation onwards.

The simple generational model can be readily updated to consider the impact of MedCMs on the progression of an outbreak. In this model, the number of susceptible individuals at a given point in time is calculated by subtracting the cumulative number infections from the total size of the population:

$$S_t = N - C_t. \tag{17}$$

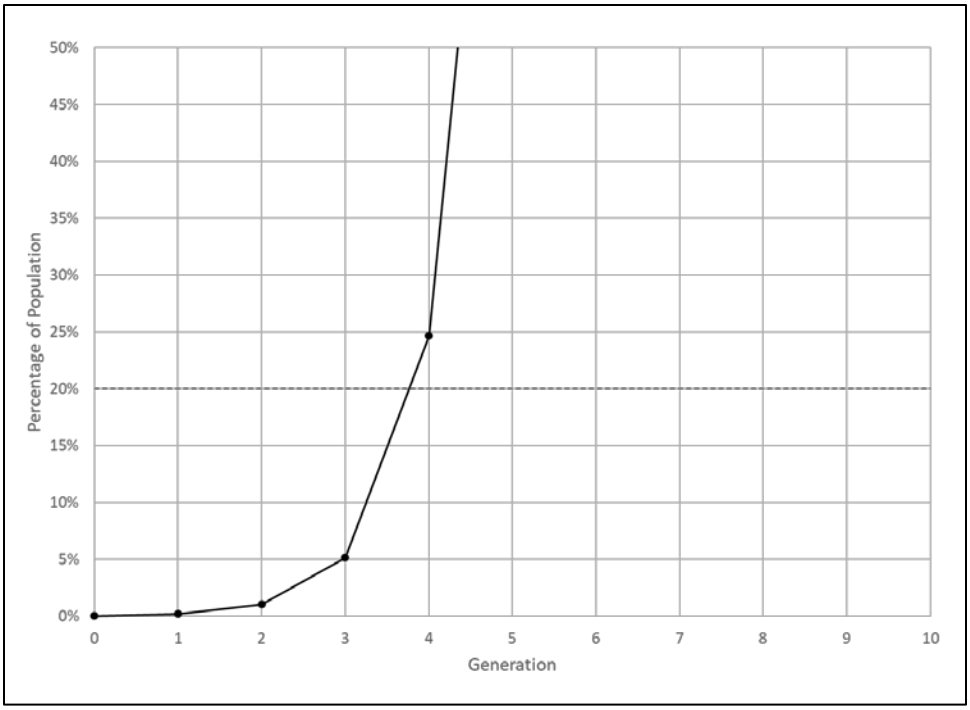


**Figure 3. Notional Cumulative Number of Infections Calculated Using Generational Model of Outbreak Progression**

However, if MedCMs are implemented during an outbreak, then the susceptible population needs to be reduced to account for the individuals protected against infection. Given the efficacy of the MedCM, $\epsilon_{MedCM}$, and the generation during which it was administered, $t_{MCM}$, the number of individuals at a given generation who are protected against infection due to receiving the MedCM, $M_t$, is as follows:

$$M_t = \begin{cases} 0 & t < t_{MedCM} \\ \epsilon_{MedCM} S_{t_{MedCM}} & t \geq t_{MedCM} \end{cases}. \tag{18}$$

The new number of susceptible individuals would then become

$$S_t = N - C_t - M_t. \tag{19}$$

The generational model of outbreak progression, updated to include consideration of MedCMs, is as follows:

$$C_t = \sum_{i=1}^{t} c_{i-1} R_0 \left(1 - \frac{C_{t-1}}{N} - \frac{M_{t-1}}{N}\right). \tag{20}$$

This model can now be used to investigate the utility of MedCMs from multiple perspectives, such as determining the efficacy of MedCMs required given the time of administration, the impact of delays in administration of a MedCM of known efficacy, or the combinations of efficacy and the time of administration that will prevent cases from

exceeding a defined threshold. Figure 4 illustrates one application of the model, which describes the dependence of the cumulative number of cases, $C_t$, on the value of $\epsilon_{MedCM}$ for a given time of administration. The black "No Response" line shows the same cumulative number of cases estimated for the parameter values used in Figure 3 ($N = 3000, c_0 = 1,$ and $R_0 = 5$). The colored lines show the administration of MedCMs with various efficacies during the third generation of the outbreak ($t_{MedCM} = 3$).

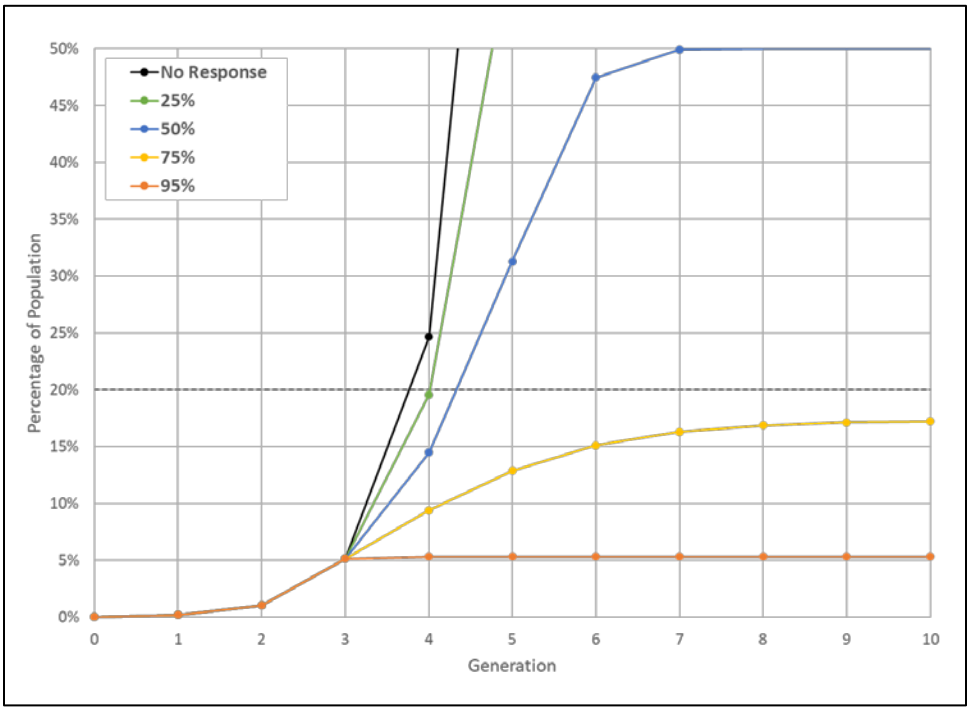


**Figure 4. Notional Consideration of MedCMs in a Generational Model of Outbreak Progression**

In this notional example, MedCMs with efficacies of 95% (orange line) and 70% (yellow line) cause the outbreak to begin to wane within one or two generations following administration and prevent the total number of infected individuals from exceeding 20% of the population. At 50% efficacy (blue line), MedCMs also cause the outbreak to wane but at much higher rates of infection. Finally, although the vertical axis is not shown in its entirety, MedCMs of 30% efficacy (green line) will delay progression of the outbreak but will neither stop it nor prevent the infection of the entire population. Yet, even at efficacies that are too low to stop an outbreak on their own, MedCMs can make marginal contributions that, in combination with other response measures, will result in an effective response (see Figure 1).

The generational model, in its simplicity, has the benefit of requiring very few inputs, depending only on the $R_0$ of the disease and the size of the population, $N$. The model is inherently agnostic to the temporal characteristics of the disease, such as the duration of

the incubation and contagious periods. The downside of this simplified approach is that the model does not explicitly track the outbreak over time (i.e., in terms of the number of days following the introduction of the disease into the population) but rather will only track the outbreak in terms of its generations. Therefore, to translate the generations into explicit points in time, additional assumptions regarding the duration of each generation must be made.

As defined previously, the duration of a generation is the "time interval between successive infections in a chain of transmission." [21] Because symptom onset is the most apparent way to mark this time interval, this paper considers the duration of a generation to be the time between the point at which a contagious individual first developed symptoms and the point at which the infected individual developed symptoms. The problem with this definition, in a simple model like that used here, is that the timing between two successive cases will not always be the same. A contagious individual can infect someone else at the start of their contagious period, at the end of his or her contagious period, or at any time in between:

- If a contagious individual causes an infection at the start of his or her contagious period, the generation time will be equal to the duration of the latent period of the disease (exposure to onset of the contagious period). This generation time is the minimum possible.
- If a contagious individual causes an infection at the end of his or her contagious period, the generation time will be equal to the duration of the latent period plus the duration of the contagious period. This generation time is the maximum possible.
- If a contagious individual is equally infectious over the duration of his or her contagious period, as assumed here, then the average generation time will be equal to transmission halfway through the contagious period. In this case, the average generation time is equal to the latent period plus half of the contagious period.

By assuming that the time between each successive generation of an outbreak is equal to the mean latent period of the disease plus half of the contagious period, the timing of each generation can be *estimated*. As the outbreak progresses, the number of cases in each generation increases, and the variability in their timing also increases. At some point, generations will begin to overlap. Individuals infected early in one generation will develop symptoms before individuals infected late in the prior generation. Therefore, the accuracy

[21] Ibid.

of the estimated time between generations decreases as the outbreak progresses. The generation times for the four diseases shown in Figure 2 are shown below in Table 3, along with their corresponding values for $R_0$.

**Table 3. Generation Times and $R_0$ for Various Diseases of Interest**

| Disease | Generation Time (Days) | $R_0$ |
|---|---|---|
| Smallpox | 21.6 | 5 |
| Plague | 6.1 | 1.32 |
| SARS | 10.7 | 1.63 |
| Influenza | 2.9 | 1.54 |

To characterize the tradeoff between the efficacy of MedCMs and how quickly they are administered, the IDA team ran the generational model over a range of values of $\epsilon_{MedCM}$ and $t_{MedCM}$ for each of the four diseases of interest. All runs of the model used a single initial infection in a population of 3,000 individuals. The results of the modeling were then analyzed to determine the combinations of the two parameters that ensure that no more than 20% of the population will become infected. The curves shown in Figure 5 represent the combinations of parameters that resulted in infection of 20% of the population, and, therefore, the areas under the curve represent the values of the parameters that will ensure no more than 20% of the population will be infected. To facilitate comparison across the four diseases, the vertical axis, which represents the generation in which MedCMs were administered (i.e., $t_{MedCM}$), has been scaled based on the assumed generation times shown in Table 3. As discussed previously, as outbreaks progress, subsequent generations can overlap. Therefore, the vertical axis in Figure 5 should be considered an approximation.

As seen in Figure 2 and in Figure 5, a direct relationship exists between the $R_0$ value for a specific disease and the corresponding required MedCM efficacy. On Day 0, which can be used to represent pre-exposure prophylaxis, smallpox, with its $R_0$ of 5, has a much higher efficacy requirement than does plague, with its $R_0$ of 1.32.

Once the curves in Figure 5 reach the knee, they quickly become asymptotic. The shape of these curves suggests that once the measure of effectiveness for MedCM efficacy is selected (e.g., that needed to reduce *R* below 1 or prevent 20% of the PAR from becoming ill), increases in efficacy beyond the minimum value calculated to meet that requirement will not significantly improve the outcome. For example, in the case discussed here, the objective is to cause *R* to fall below one before 20% of the population has become ill. The efficacy needed for an influenza MedCM to do so is approximately 25% if administered on Day 0. It climbs to 30% by Day 25. After that, however, increasing efficacy to 100% will not increase the amount of time available for effective administration.

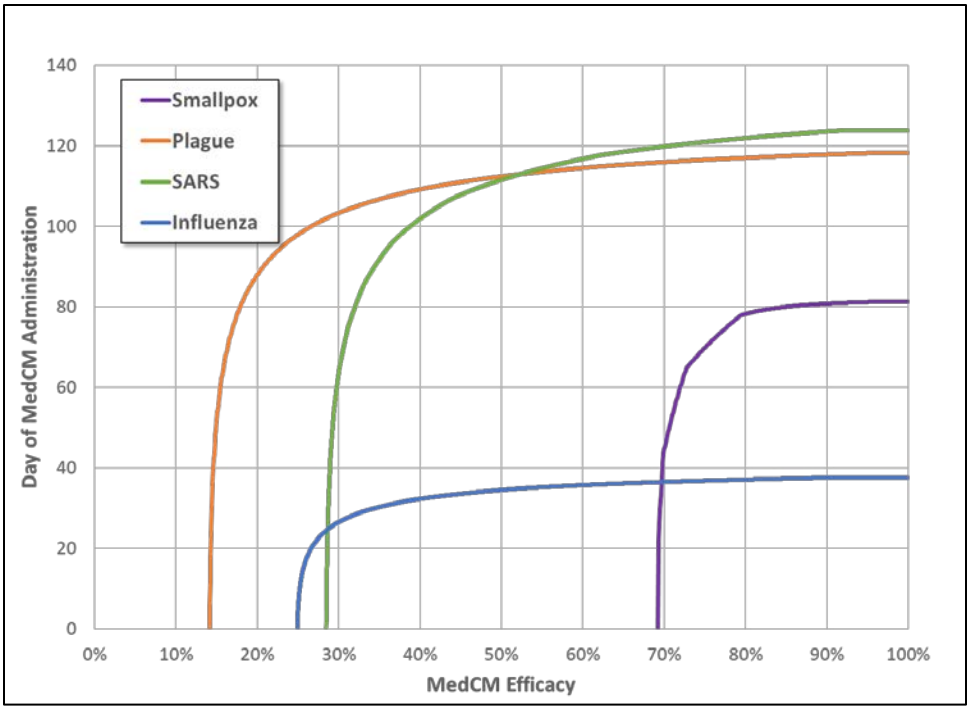


**Figure 5. MedCM Parameter Values That Prevent 20% of a Population from Being Infected**

Perhaps more importantly, the shape of the curves shows that a definable window of time exists in which MedCMs can be administered effectively. The point within that time window at which MedCMs are administered makes little difference; however, once that window has been exceeded, MedCMs become largely ineffective.

## B. Isolation

Isolation is the separation of infectious individuals from a healthy population. Depending on the ease of transmission and the severity of disease, procedures for isolation in a military setting could range from confinement to quarters, to retention in a hospital isolation ward, to treatment within a high-level containment care facility such as those used in 2014 to treat Ebola patients.

Isolation of contagious patients is a routine medical practice, in combination with a set of infection control practices—collectively referred to as Standard Precautions—that include "hand hygiene; use of gloves, gown, mask, eye protection, or face shield, depending on the anticipated exposure; and safe injection practices."[22] For most infectious diseases, these practices are sufficient to limit the spread of disease and avoid outbreaks.

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[22] Jane D. Siegel et al., *2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings* (Atlanta, GA: U.S. Centers for Disease Control and Prevention, October 2017), 66, https://www.cdc.gov/niosh/docket/archive/pdfs/NIOSH-219/0219-010107-siegel.pdf.

The guidelines developed in this paper are relevant only when standard infection control practices, including routine isolation, would be insufficient. Even in such circumstances, however, enhancement of standard infection control practices should be one of the first response measures considered since isolation will continue to contribute substantially to outbreak response efforts. Such enhancement would include ensuring that medical treatment facilities (MTFs) have equipment and personnel capable of providing a higher-than-standard level of infection control and protection for medical personnel, facilities, and other patients.[23]

At the same time, the capacity for isolation within an operational theater could be limited, and it may be difficult to move casualties into isolation in timely fashion. Options for increasing isolation capacity in theater include establishment of isolation rooms or wards within an existing MTF, conversion of an existing MTF to an isolation facility, and establishment of dedicated isolation facilities. The feasibility of any of these options depends on the nature of the operation and the type of disease.

The IDA team assumed that once a contagious patient had been isolated, isolation was appropriate and effective in preventing further transmission of disease—either to medical personnel or to the larger PAR. Preventing nosocomial transmission of disease is often challenging, and outbreaks of disease do occur in health care settings.[24] Such outbreaks are largely outside the scope of this analysis; however, the PAR in such outbreaks is small and specific and is contained within the medical treatment system. Any mixing between this population and the larger military population is limited at best. Although nosocomial outbreaks will not directly contribute, to any large extent, to the progression of the outbreak within the larger military force, these outbreaks can result in a reduction in medical capacity that will make it more difficult to implement response measures. Commanders should be aware of the potential need to replace any medical capabilities lost to nosocomial outbreaks, and, as discussed later in this paper, they should ensure that MTFs designated to receive contagious patients are appropriately equipped and trained.

The IDA team analyzed the effectiveness of isolation based on its ability to cause an outbreak to wane, considering who must be isolated (contagious individuals) and when they must be isolated (before they have the opportunity to infect others). To parameterize these factors, the IDA team defined the reduction in a contagious individual's transmission due to some isolation response capability, $f_{Iso}(\epsilon_{Iso}, D_{Iso})$, as a function of two parameters:

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23 North Atlantic Treaty Organization. *Allied Medical Publication 7.6 (AMedP-7.6)*, 6-11.

24 In particular, the SARS outbreak of 2003 was characterized by a high level of nosocomial transmission. Health care workers constituted the largest single group of infected individuals, with an estimated 19%–57% of all probable SARS cases. See Nelson Lee and Joseph J. Y. Sung, "Nosocomial Transmission of SARS," *Current Infectious Disease Reports* 5, no. 6 (December 2003): 473–476, https://link.springer.com/article/10.1007/s11908-003-0089-4.

- $\epsilon_{Iso}$: the fraction of the contagious population that will be isolated and
- $D_{Iso}$: the delay from the appearance of symptoms in an individual to the isolation of that individual.

To cause an outbreak to wane, isolation must prevent contagious individuals from, on average, infecting one or more susceptible individuals. Therefore, the range of values for $\epsilon_{Iso}$ and $D_{Iso}$ that constitute an effective response are those that satisfy the following inequality (based on the inequality in Equation 6).

$$R_{Iso} = f_{Iso}(\epsilon_{Iso}, D_{Iso})R_0 < 1. \quad (21)$$

The remainder of this section is devoted to deriving the function $f_{Iso}(\epsilon_{Iso}, D_{Iso})$, which expresses the relationship between $\epsilon_{Iso}$ and $D_{Iso}$ and specifies the space in which isolation is effective at causing the outbreak to wane.

The IDA team derived $f_{Iso}(\epsilon_{Iso}, D_{Iso})$ by considering one parameter at a time, first analyzing the case in which all contagious individuals are isolated ($\epsilon_{Iso} = 1$). In this case, the effectiveness of the response is solely dependent on how quickly contagious individuals are isolated following the onset of their symptoms ($D_{Iso}$). Figure 6 illustrates the maximum time that isolation can be delayed and still be an effective response measure for four diseases: smallpox, plague, SARS, and influenza.[25]

In Figure 6, **Days Following Exposure** on the horizontal axis refers to the time after which an individual has been infected with disease. On the vertical axis, **Number of People Infected** shows the average cumulative number of infections per individual during the illness, assuming that infectiousness is constant through the duration of the contagious period.[26] For each disease, the shape of the corresponding curve is determined by the mean values of the durations of each stage of illness as well as $R_0$.[27] For example, the smallpox curve shows that individuals are not contagious for a lengthy period following exposure. Smallpox has a mean incubation period of 11.6 days and is not contagious until an average

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[25] Values and associated references for mean incubation period and duration of illness for these diseases can be found in Table 1.

[26] If infectiousness is not constant throughout the contagious period, the cumulative number of infections caused per individual would be represented by a curve instead of the straight line shown in Figure 6. From a practical standpoint, if infectivity is greater earlier in the period, the time window for isolation will be shorter. If infectivity is more contagious later in the period, the time window will be longer.

[27] Although the durations of each stage of illness and $R_0$vary among individuals, the average values of these distributions adequately characterize the effectiveness of isolation. Recall that a given response measure is considered to be effective if it can reduce the *average* number of new infections caused per contagious individual to less than one. Therefore, even if some individuals still generate more than one new infection, as long as the population average is below one, the response is still considered effective.

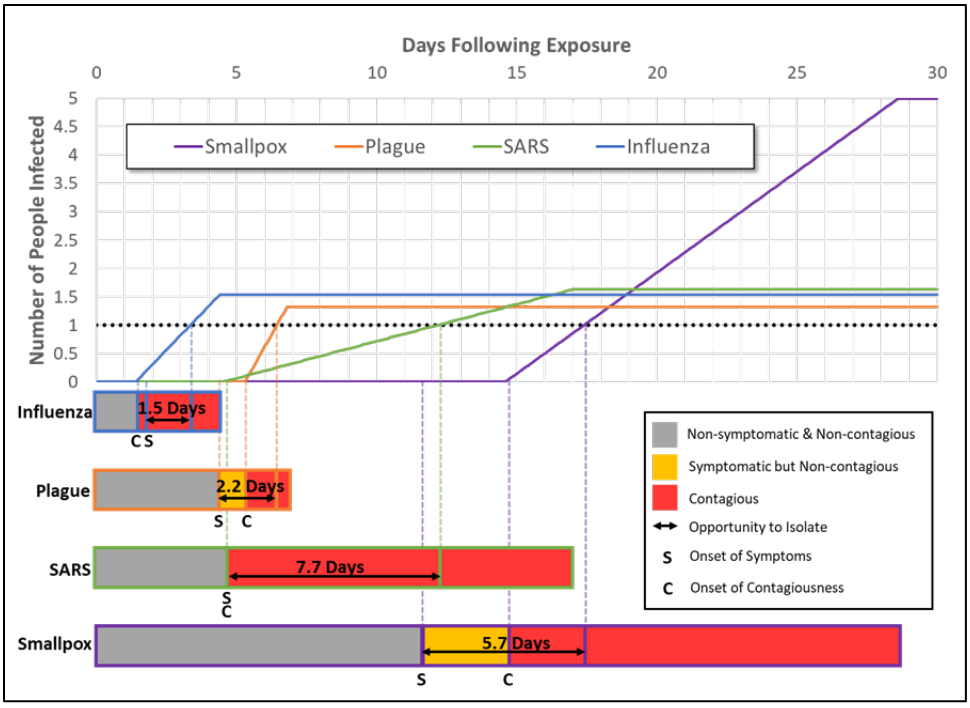


**Figure 6. Time Window for Isolation**

of 3 days after the onset of symptoms. Once smallpox cases become contagious, these cases, on average, infect 5 additional individuals over the next 14 days, at which point they cease being contagious and cause no further infections.

A set of horizontal bars is shown in the lower half of Figure 6. The segments within the bars represent the mean duration of different stages of illness. The gray segment shows the mean duration of time before the onset of either symptoms or the period of contagion, whichever comes first. The yellow segment shows the mean duration of a symptomatic but noncontagious period, if such a period exists for that disease. The red segment shows the mean duration of the contagious period. Below each bar, the letters *S* and *C* show the mean time at which individuals become symptomatic and contagious.

The time window in which isolation must be implemented is shown as the black arrow within each bar, with the duration provided above the arrow. In other words, the black arrows show the range of $D_{iso}$ values that will result in an effective isolation response for each disease—assuming that all contagious individuals are isolated (i.e., $\epsilon_{Iso} = 1$). The start of that time window is the point at which individuals develop symptoms of disease, designated as time *S* in Figure 6.[28] The end of that time window is the point at which individuals infect one other individual (i.e., where each disease's curve intersects the dotted

[28] Before symptom onset (or, perhaps, detection of some form of biomarker that would be indicative of infection), it is not possible to differentiate individuals who will become ill from those who will not

black line). The duration of the time window, which varies from just under 2 days for influenza to nearly 8 days for SARS, is determined by various characteristics of the disease: the duration of the incubation period, the duration of the contagious period, the time of symptom onset relative to contagiousness, and $R_0$.

For example, the rate of disease transmission depends on $R_0$ and the duration of the contagious period, which, in combination, determine the slope of the line from zero to $R_0$ in Figure 6. The lower the rate of disease transmission, the longer the window in which isolation can be an effective response measure. Even though smallpox has the highest $R_0$ of the four diseases shown, it has a long contagious period. The rate of transmission is therefore low, and it takes a long time for a contagious individual to cause one additional infection. By contrast, plague has the lowest $R_0$, but its short contagious period means that an individual will cause another infection shortly after becoming contagious.

When the symptoms appear relative to the onset of the contagious period also impacts the time window for isolation. The order of these two events may vary by disease. Influenza is contagious before it is symptomatic, plague and smallpox are symptomatic before they are contagious, and SARS is simultaneously symptomatic and contagious.[29] If symptoms appear before the contagious period, then the time window is extended. If the contagious period begins before the onset of symptoms, then the window is shortened.

From this discussion, the time window for effective isolation can be calculated as follows:

$$\frac{T_C}{R_0} + (T_L - T_I), \tag{22}$$

where $T_C$ is the mean duration of the contagious period, $T_L$ is the mean time between exposure and the start of the contagious period, and $T_I$ is the mean duration of the incubation period. Therefore, in the event that all contagious individuals are isolated (i.e., $\epsilon_{Iso} = 1$), the following inequality must be satisfied for an isolation response to be effective:

$$D_{Iso} < \frac{T_C}{R_0} + (T_L - T_I). \tag{23}$$

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become ill. Segregation of people from the general population before they are known to be infectious would be considered quarantine, not isolation.

[29] Corey M. Peak et al., "Comparing Nonphamaceutical Interventions for Containing Emerging Epidemics," *Proceedings of the National Academy of Sciences of the United States of America* 114, no. 15 (April 11, 2017): 4023–4028, https://doi.org/10.1073/pnas.1616438114; Sean M. Oxford et al., *Technical Reference Manual to Allied Medical Publication 7.5 (AMedP-7.5) NATO Planning Guide for the Estimation of CBRN Casualties*, IDA Document D-8122 (Alexandria, VA: Institute for Defense Analyses, October 2016); John N. Bombardt, "Congruent Epidemic Models for Unstructured and Structured Populations: Analytical Reconstruction of a 2003 SARS Outbreak," *Mathematical Biosciences* 203, no. 2 (October 2006): 171–203, https://doi.org/10.1016/j.mbs.2006.05.004.

The first term in the right hand side of the inequality in Equation 23 defines the mean time it takes for a contagious individual to infect another individual, while the second term either extends or shortens the time window depending on when symptoms appear relative to the start of the contagious period:

- If symptoms appear before a person is contagious (i.e., $T_I < T_L$), then $(T_L - T_I) > 0$ and, therefore, the time window for which isolation can be effective is longer than $\frac{T_C}{R_0}$.
- If symptoms appear after a person becomes contagious (i.e., $T_I > T_L$), then $(T_L - T_I) < 0$ and, therefore, the time window for which isolation can be effective is shorter than $\frac{T_C}{R_0}$.[30]
- If symptoms appear at the same time as infectiousness (i.e., $T_I = T_L$), then $(T_L - T_I) = 0$ and, therefore, the time window for which isolation can be effective is equal to $\frac{T_C}{R_0}$.

Although isolation of contagious individuals is standard medical practice, it is possible that some of those individuals will be missed (e.g., the disease may be challenging to diagnose or an individual clinical presentation may be unusual). In large-scale disease outbreaks, deployed medical units may have insufficient isolation space, thus limiting the number of people who can be promptly or effectively isolated. In these circumstances, isolation must occur more quickly than the times defined to offset individuals who are not isolated and who consequently infect others without constraint.

To quantify the impact of failing to isolate some portion of contagious individuals ($0 \leq \epsilon_{Iso} \leq 1$), the IDA team defined two boundary cases for the time at which isolation could occur:

- Case 1: Isolation occurs no later than the onset of the contagious period ($D_{iso} \leq T_L - T_I$). In this case, those individuals who were isolated (the portion $\epsilon_{Iso}$ of all contagious individuals) were isolated quickly enough to prevent their expected disease transmission in its entirety. Therefore, the only secondary cases are caused by those who were not isolated, so $f_{Iso}(\epsilon_{Iso}, D_{Iso}) = (1 - \epsilon_{Iso})$, and correspondingly,

[30] Notice that there is no mathematical constraint on the relative absolute values of the two terms in Equation 22. It is theoretically possible for $|T_L - T_I| > \frac{T_C}{R_0}$ and $T_L - T_I < 0$, which would result in $\frac{T_C}{R_0} + (T_L - T_I) < 0$. In this case, the window of opportunity in which individuals need to be isolated will be negative. In other words, on average, an individual will infect at least one other person before he or she has developed symptoms. Because symptom onset is considered to be the earliest trigger to isolate an individual, it would not be possible to implement an effective isolation response for such a disease.

$$R_{Iso} = (1 - \epsilon_{Iso})R_0. \quad (24)$$

- Case 2: Isolation occurs after the end of the contagious period ($D_{iso} > (T_L - T_I) + T_C$). In this case, isolation was delayed to the point such that it had no effect on mitigating disease transmission, so $f_{Iso}(\epsilon_{Iso}, D_{Iso}) = 1$, and correspondingly,

$$R_{Iso} = R_0. \quad (25)$$

These two boundary conditions provide the limits on the time at which isolation would occur—sometime during the contagious period. In these cases, the number of new infections caused per individual will be bound by boundary Case 1 and boundary Case 2. Assuming a constant rate of disease transmission, the value of $R_{Iso}$ can be represented as shown in Figure 7.[31]

As shown in Figure 7, the relationship between $R_{Iso}$ and $\epsilon_{Iso}$ and $D_{iso}$ is represented by three line segments, whose functional form can readily be defined. The two horizontal line segments represent boundary Case 1 and boundary Case 2 and therefore can be represented by their corresponding equations—Equation 24 and Equation 25—for $R_{Iso}$. Connecting the two horizontal line segments is a line representing individuals who are isolated at some point during their contagious period. The functional form of this line can be found by determining its slope and Y-intercept:

$$R_{Iso} = \frac{\epsilon_{Iso}R_0}{T_C} D_{Iso} + \left[(1 - \epsilon_{Iso}) - \epsilon_{Iso}\frac{T_L - T_I}{T_C}\right]R_0. \quad (26)$$

With the equations for all three of the line segments in Figure 7 defined, the overall equation describing the efficacy of isolation can be written as the following piece-wise defined function:

$$f_{Iso}(\epsilon_{Iso}, D_{Iso}) = \begin{cases} 1 - \epsilon_{Iso} & \text{, if } D_{iso} \le T_L - T_I \\ \frac{\epsilon_{Iso}D_{Iso}}{T_C} + \left[(1 - \epsilon_{Iso}) - \epsilon_{Iso}\frac{T_L - T_I}{T_C}\right] & \text{, if } T_L - T_I < D_{iso} < T_L - T_I + T_C. \\ 1 & \text{, if } D_{iso} \ge T_L - T_I + T_C \end{cases} \quad (27)$$

[31] In the event that $T_L - T_I < 0$, Figure 7 will not have the first horizontal section; instead, the positively sloped line will intercept the $R_{Iso}$ axis at some positive value that is dependent on the value of $T_L - T_I$. As previously described, in this situation, it may be possible for a contagious individual to cause more than one new infection before developing symptoms. In this case, the line will intersect the $R_{Iso}$ axis at a value greater than one, and no value of $D_{iso}$ will be able to result in an effective isolation response.

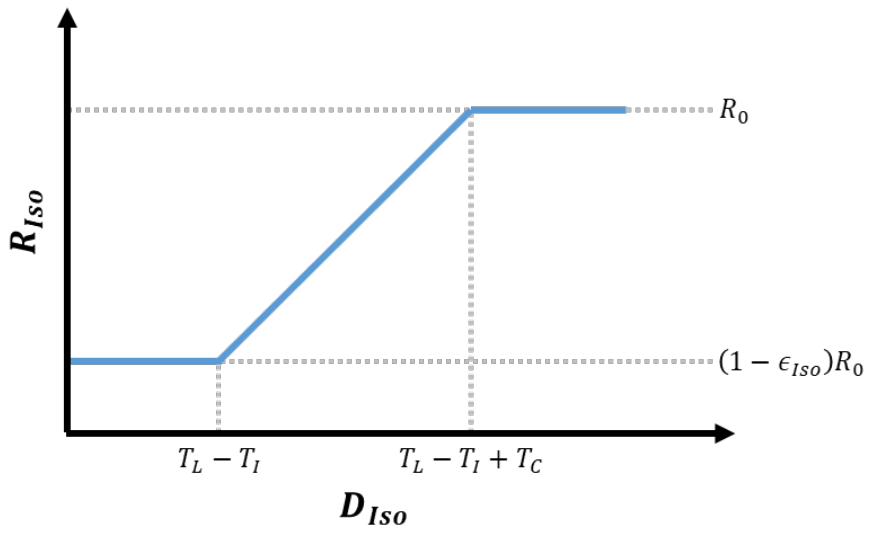


**Figure 7. The Impact of Isolation Parameters on the Spread of Disease**

Equation 27 can then be used to determine the values of the parameters $\epsilon_{Iso}$ and $D_{Iso}$ that will result in an isolation response being effective for a given disease:

$$R_{Iso} = f_{Iso}(\epsilon_{Iso}, D_{Iso})R_0 < 1. \quad (28)$$

The equation for $f_{Iso}(\epsilon_{Iso}, D_{Iso})$ (and therefore also for $R_{Iso}$) depends on the same disease factors described earlier: the mean duration of the contagious period ($T_C$), the mean time between exposure and the start of the contagious period ($T_L$), the mean duration of the incubation period ($T_I$), and $R_0$.

Figure 8 shows how the inequality and equation (see Equation 28) can be used to determine the range of values that $\epsilon_{Iso}$ and $D_{Iso}$ must fall within for isolation to be effective against a SARS outbreak. The horizontal and vertical axes of Figure 8 represent the efficacy of isolation ($\epsilon_{Iso}$) and the delay in isolation ($D_{Iso}$), respectively. The average number of new infections caused per contagious individual ($R_{Iso}$) is measured using the color bar shown to the right of the figure. The single black contour line bounds the region of benefit: the combinations of isolation efficacy and the delay in isolation where $R_{Iso} < 1$, and, therefore, isolation is an effective response measure.

Several interesting observations can be made from Figure 8. If $D_{Iso} > 12.5$ days, then $R_{Iso} = R_0 = 1.63$ for all values of $\epsilon_{Iso}$. Because $R_{Iso} = R_0$, isolating contagious individuals after the end of their contagious period does not do anything to reduce disease transmission, and every disease case will cause $R_0$ additional cases. At the other end of the isolation-delay spectrum, if $D_{Iso} = 0$, then $\epsilon_{Iso}$ can drop to about 0.4 before isolation stops being effective. If individuals can be isolated at the onset of their symptomatic period, the outbreak will be stopped even if only 40% of contagious individuals are isolated in this

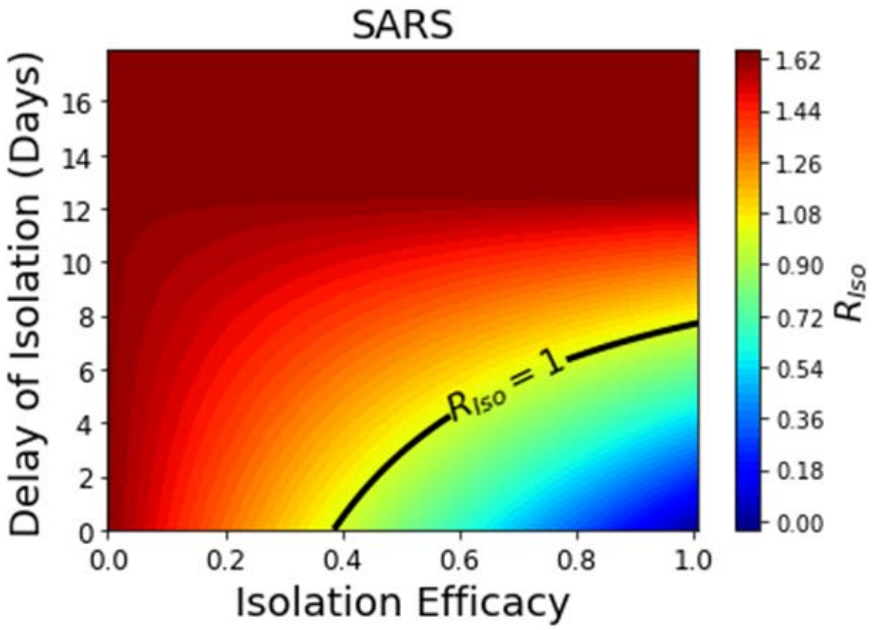


**Figure 8. Isolation Parameter Values that Result in an Effective Response against SARS**

fashion. On the other hand, if $\epsilon_{Iso}$ falls below 0.4, isolation will be ineffective no matter how quickly it is implemented. Yet as $\epsilon_{Iso}$ increases, the window of time for isolation also increases: when $\epsilon_{Iso} = 1$, then $D_{Iso} = 7.7$—the same time window shown in Figure 6.

The overall size and shape of the region of benefit shown in Figure 8—and the observations derived from it—are dependent upon the specific characteristics of SARS. The regions of benefit for isolation calculated by the IDA team for smallpox, plague, and influenza are shown below in Figure 9. The lines represent the combinations of $\epsilon_{Iso}$ and $D_{Iso}$ where $R_{Iso} = 1$, and the regions of benefit are the areas under the curves.

As can be seen, the points where lines intersect with the horizontal and vertical axes in Figure 9 and the overall area under the curves differ greatly by disease. These points of intersection represent the limits of either of the parameters that influence the effectiveness of isolation. These limits can determine the minimum percent of contagious individuals that must be isolated, no matter how quickly isolation can be implemented, or vice versa, the maximum time window within which isolation must occur, even if 100% of those who are contagious can be isolated.

In general, diseases with short latent and contagious periods, such as influenza and plague, have smaller regions of benefit. Consequently, the requirements for isolation will be more rigorous for these diseases: isolation must be accomplished more quickly and must encompass a higher percentage of the contagious population. It also suggests that in outbreaks of these diseases, isolation alone is more likely to be insufficient and require augmentation with additional responses such as quarantine. One the other hand, diseases

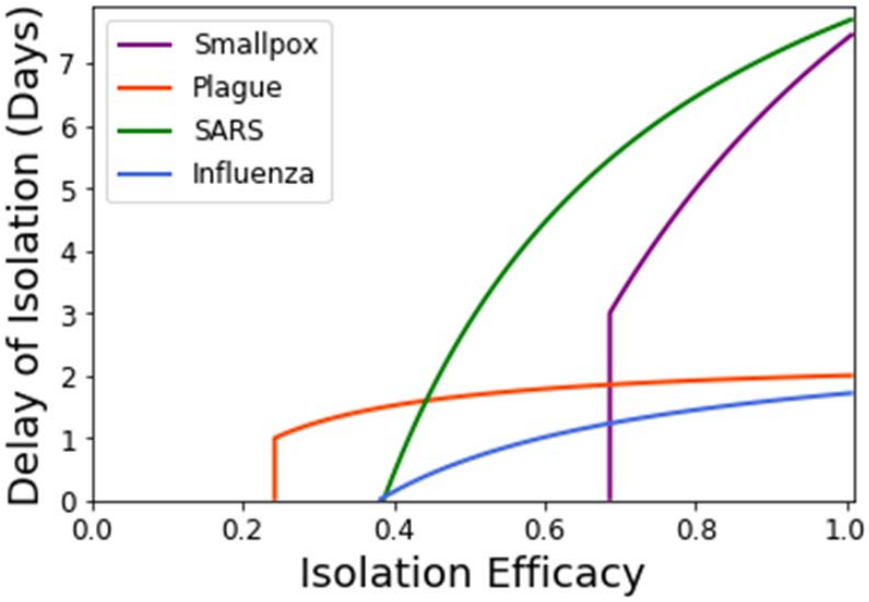


**Figure 9. Isolation Parameter Values That Result in an Effective Response against SARS, Plague, Smallpox, and Influenza**

with longer latent and contagious periods, such as smallpox and SARS, have larger regions of benefit, and outbreaks of these diseases will likely be easier to contain with isolation alone.

The plague and smallpox curves include a vertical section, where the value of $\epsilon_{Iso}$ is constant across a range of values of $D_{Iso}$. This portion of the curves represents the time period where individuals exhibit symptoms of those diseases but are not yet contagious. As discussed, this period extends the window in which isolation must occur and makes it easier to implement isolation effectively. Without this additional time, the curves for these two diseases would shift downward such that the curved portion of the line would intersect the horizontal axis and the region of benefit for isolation would be reduced substantially. On the other hand, diseases that are contagious before the onset of symptoms, such as influenza, have their windows for the implementation of isolation constrained. As can be seen in Figure 9, the region of benefit for influenza is indeed the smallest of the four diseases considered.

Different operational environments may constrain one or both of these parameters (i.e., $D_{Iso}$ and $\epsilon_{Iso}$), increasing the time required to isolate individuals or reducing the probability that every contagious individual will be placed in isolation. Operational commanders and medical advisors can use the relationships between these two parameters, defined by Equations 26 through 28 and illustrated in Figure 9, to understand the requirements for isolation and the extent that they must compensate for operational constraints on implementation. Moreover, this information can be used to identify circumstances in which

isolation cannot be sufficient and that warrant a more comprehensive, layered approach involving responses of other types.

## C. Quarantine

Quarantine is the segregation of healthy but potentially exposed individuals from the remainder of the healthy population until it can be determined that the segregated individuals are free of infection. The purpose of quarantine is to eliminate the possibility that contagious individuals will spread disease from the onset of their contagious period to the time at which they are isolated. The necessary duration of quarantine is related to the incubation period of the disease, and individuals in quarantine would typically be subject to active, continued health monitoring by medical personnel.[32]

Quarantine can be implemented in any number of ways. This paper assesses three different quarantine strategies that could potentially be used in an operational setting:

- **Quarantine in place.** Individuals who may have been exposed to contagious disease remain within their unit but are segregated from other unit personnel. They can monitor their own health or be observed by available unit medical personnel to detect any onset of symptoms indicating illness. Individuals who become ill are removed from the unit and placed in isolation.
- **Confinement within a dedicated quarantine facility.** Confinement in a dedicated facility is the traditional form of quarantine. Individuals who may have been exposed to contagious disease are removed from their unit and placed in a quarantine facility, overseen by medical personnel who would monitor the health of quarantined individuals, provide initial treatment to those who develop symptoms, and facilitate their isolation. In an operational setting, this form of quarantine might be used when an individual is known to be at particularly high risk of disease, when an individual's tasks cannot be performed without extensive contact with others, when movement of sick individuals into isolation is hampered by the operational environment, or for diseases that are contagious before the onset of symptoms.
- **Quarantine of an entire unit.** Units suspend their mission and move as necessary to rear or permissive areas. The health of unit personnel is monitored, and any individuals who become ill are removed from quarantine and placed in isolation. This strategy can be employed if a unit's operational capability has already been compromised by the number of contagious casualties experienced and in anticipation of additional casualties among remaining personnel.

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[32] North Atlantic Treaty Organization. *Allied Medical Publication 7.1 (AMedP-7.1)*, 6-13; North Atlantic Treaty Organization. *Allied Medical Publication 7.6 (AMedP-7.6)*, 7-4.

For all three strategies, the IDA team assumed that individuals placed into quarantine before the start of their contagious period and subsequently isolated upon symptom onset would not have any opportunity to spread the disease to others. For diseases that are contagious before symptom onset (e.g., influenza), this assumption holds only if individuals are also assumed not to have contact with each other during quarantine, which could limit the quarantine strategies that are available for such diseases.

The IDA team analyzed the effectiveness of quarantine based on its ability to cause an outbreak to wane. To perform this analysis, the IDA team defined the function $f_Q(\epsilon_Q)$ that describes the reduction in disease transmission due to some fraction of the infected individuals, $\epsilon_Q$, being quarantined and subsequently isolated upon symptom onset, thus eliminating their opportunity to spread disease. To cause an outbreak to wane, enough infected individuals must be quarantined such that contagious individuals (those in quarantine and those not in quarantine) infect, on average, less than one susceptible individual. Therefore, a quarantine response will be considered effective for the range of $\epsilon_Q$ values that satisfy the following inequality (based on the inequality in Equation 6):

$$R_Q = f_Q(\epsilon_Q)R_0 < 1. \tag{29}$$

To determine the form of the function $f_Q(\epsilon_Q)$, consider the example shown in Figure 10. Assume that a given contagious individual (in this case, the blue individual on the far left) transmits disease to six individuals (represented by the gray arrows leading to the six newly infected individuals). Assume further that a quarantine response is implemented in such a way as to quarantine two of the six newly infected individuals (i.e., $\epsilon_Q = 1/3$). This approach is shown in Figure 10 as the two yellow individuals in the blue box labeled "Quarantined." As described previously, the IDA team assumed that quarantine is capable of completely preventing these two individuals from transmitting the disease (shown by the red X's). Therefore, of the six individuals who were infected by the first individual, only four (shown in orange) would go on to continue to spread the disease (shown in the figure as gray arrows originating from the four secondary cases). From this example, we can see that the number of new infections who will further propagate the outbreak, $R_Q$, is simply the number of individuals who were not quarantined (four in this example). Therefore, $f_Q(\epsilon_Q) = 1 - \epsilon_Q$, and $R_Q = (1 - \epsilon_Q)R_0$.

The following inequality, incorporating the full expression for $f_Q(\epsilon_Q)$, distinguishes those quarantine responses that are effective at causing the outbreak to wane from those that are not.

$$R_Q = (1 - \epsilon_Q)R_0 < 1. \tag{30}$$

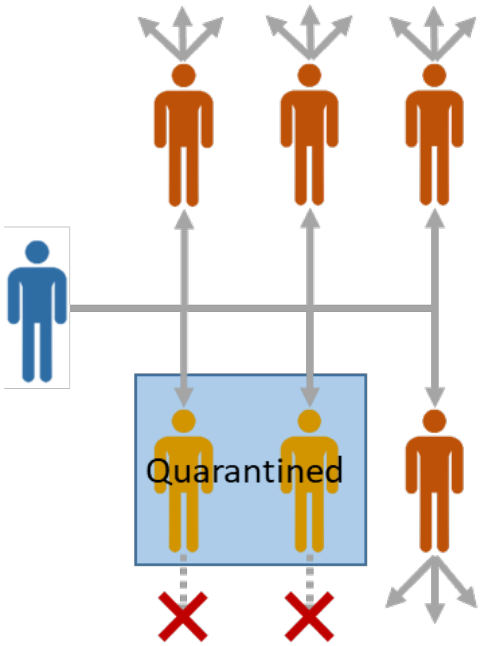


**Figure 10. Diagram of Quarantine Efficacy**

Solving for $\epsilon_Q$ yields the minimum fraction of infected individuals that must be quarantined and subsequently isolated before contacting any susceptible individuals for quarantine to be an effective response on its own:

$$\epsilon_Q > 1 - \frac{1}{R_0}. \tag{31}$$

### 1. Using Quarantine with Isolation

Quarantine augments and complements isolation. It facilitates the isolation of contagious individuals and limits the impact that delays in isolation may have on further spread of disease. Figure 8 provided an example of $R_{Iso}$ as a function of the isolation parameters $D_{Iso}$ and $\epsilon_{Iso}$ for SARS and showed which combinations of parameter values resulted in an effective isolation regime. For the combinations of parameter values that were outside the defined region of benefit for isolation, the addition of quarantine may result in an effective response.

To analyze how quarantine can be used to augment an isolation response, the IDA team derived the function $f_{Q,Iso}(\epsilon_Q, \epsilon_{Iso}, D_{Iso})$ that describes the combined effect of quarantine in combination with isolation on disease transmission. The function $f_{Q,Iso}(\epsilon_Q, \epsilon_{Iso}, D_{Iso})$ was then used to determine the range of values for its parameters ($\epsilon_Q$, $\epsilon_{Iso}$, and $D_{Iso}$) that result in an effective response (in terms of causing an outbreak to wane):

$$R_{Q,Iso} = f_{Q,Iso}(\epsilon_Q, \epsilon_{Iso}, D_{Iso})R_0 < 1. \tag{32}$$

To derive the function $f_{Q,Iso}(\epsilon_Q, \epsilon_{Iso}, D_{Iso})$, recall the example used to derive the function $f_Q(\epsilon_Q) = 1 - \epsilon_Q$, which was illustrated in Figure 10. In this example, an infectious individual transmitted the disease to six individuals, two of whom were successfully quarantined (i.e., $\epsilon_Q = 1/3$) and four of whom were not quarantined and therefore would go on to further spread the disease and propagate the outbreak. Now consider the case in which the first individual was isolated (illustrated in Figure 11). Suppose that the individual was isolated in such a way as to prevent half of the new infections that he or she otherwise would have caused (i.e., the individual transmitted the disease to three individuals instead of six). The dashed gray lines in Figure 11 represent the transmission that would have occurred to the gray individuals if the contagious individual had not been isolated. In this example, the isolation response would be considered ineffective for this individual because he or she infected more than one additional individual (i.e., $R_{Iso} = 3 > 1$). However, if the same quarantine response as that described previously was also implemented, then one-third of the new infections caused by the individual would be quarantined. In this case, one of the three newly infected individuals would be quarantined (the yellow individual in Figure 11), and the remaining two new infected individuals (shown in orange in Figure 11) would go on to spread the disease. To summarize, the number of new infections—those caused by a contagious individual—that have the potential to transmit the disease when responding with quarantine and isolation, $R_{Q,Iso}$, is equal to the portion of the new infections—those caused before the contagious individual entered isolation—that were not quarantined. The example above (the discussion of which begins in the second to last paragraph on page 33) can be generalized as follows: $f_{Q,Iso}(\epsilon_Q, \epsilon_{Iso}, D_{Iso}) = f_Q(\epsilon_Q) f_{Iso}(\epsilon_{Iso}, D_{Iso})$ and accordingly, $R_{Q,Iso} = f_Q(\epsilon_Q) f_{Iso}(\epsilon_{Iso}, D_{Iso}) R_0$, where $f_{Iso}(\epsilon_{Iso}, D_{Iso})$ is defined in Equation 27.

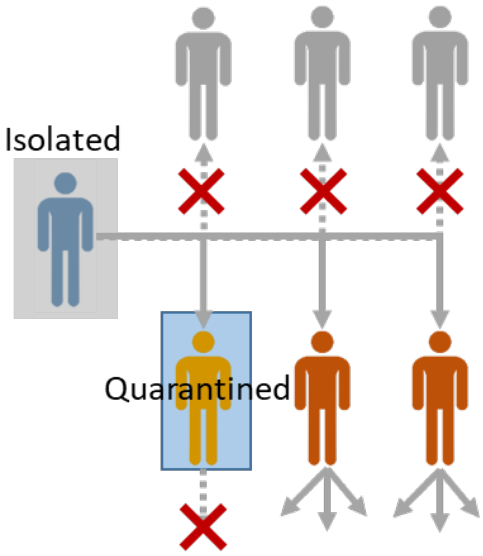


**Figure 11. Diagram of Efficacy of Quarantine when Combined with Isolation**

Since the combined isolation and quarantine response measures will be effective when $R_{Q,Iso} < 1$, this equation can be converted into an inequality to find the set of parameter values needed to cause the outbreak to wane:

$$R_{Q,Iso} = f_Q(\epsilon_Q) f_{Iso}(\epsilon_{Iso}, D_{Iso}) \; R_0 < 1. \tag{33}$$

When values for $D_{Iso}$ and $\epsilon_{Iso}$ are known, solving for $\epsilon_Q$ is straightforward. Figure 12 provides a set of contour plots that shows the fraction of new infections per contagious individual that must be quarantined for a response to be effective, given specific values for $D_{Iso}$ and $\epsilon_{Iso}$. These contour plots are an extension of the region of benefit curves for isolation parameter values, provided in Figure 8 and Figure 9. The x and y axes in Figure 12 are the same as those in the earlier figures; however, the color bar is now showing $\epsilon_Q$ instead of $R_{Iso}$.

The dark blue areas where $\epsilon_Q = 0$ correspond to the region of benefit for isolation alone for each of the four diseases considered, where the combination of $D_{Iso}$ and $\epsilon_{Iso}$ are sufficient to cause the outbreak to wane and quarantine would not be required for an effective response (although it could still cause the outbreak to wane more quickly). The regions outside the blue area show the level of quarantine needed to cause an outbreak to wane when isolation alone is insufficient. For example, consider the point (0.3, 5) in the SARS contour plot. In Figure 8 this point is well outside the region of benefit: having an isolation efficacy of 30% and a delay of 5 days will not be effective in causing a SARS outbreak to wane. In Figure 12, this point falls in the yellow area, where $\epsilon_Q = 0.24$. Therefore given this specific isolation regime, if at least 24% of new infections are quarantined before they become contagious, the outbreak will wane. Quarantine reaches its maximum benefit at the boundary of the dark red areas, where isolation would have no effect on outbreak progression.[33]

## 2. The Cost of Quarantine

The implementation of quarantine presents numerous challenges that may generate significant operational costs. Unlike isolation, which only encompasses symptomatic individuals, quarantine affects healthy individuals who have some identified chance of becoming symptomatic. Determining the subset of the PAR who have been exposed is inherently difficult, particularly in military populations with very high movement rates. In addition, those who *will* become ill are a subset of those who *might* become ill, and that differentiation is impossible to determine a priori with current technology. Therefore, to be effective, quarantine must encompass a number of individuals who will never become ill.

[33] When isolation is ineffective, it is typically due to $D_{Iso}$ exceeding the contagious period of the disease.

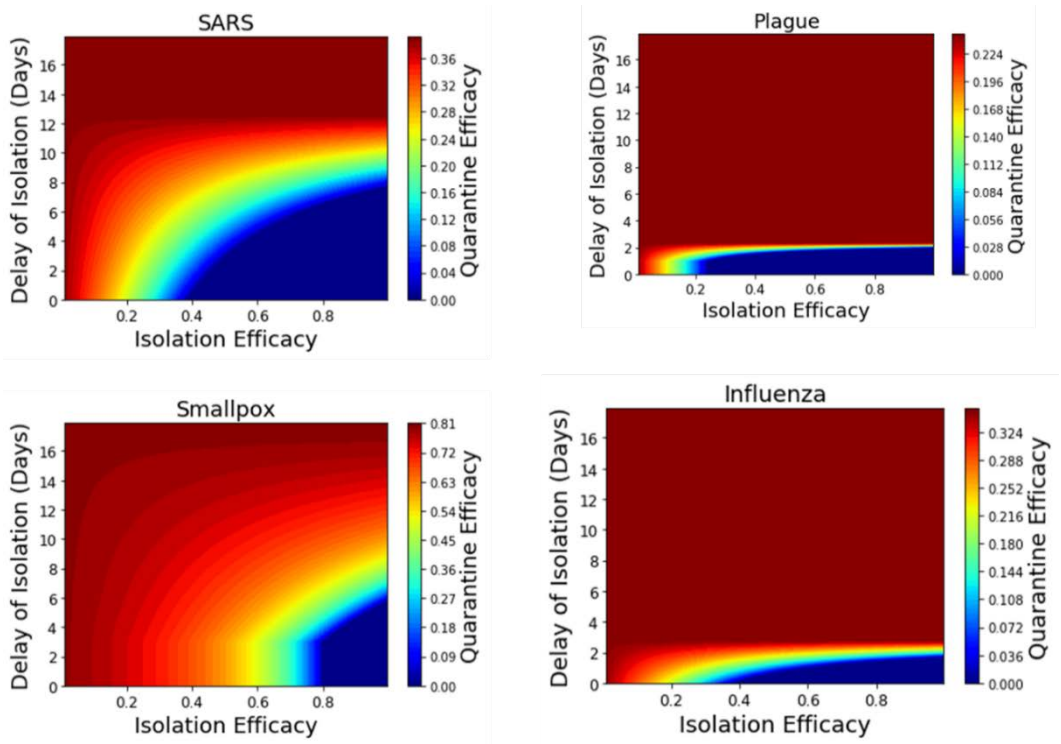


**Figure 12. Fraction of New Infections That Must Be Quarantined to Ensure R < 1, Given Isolation Capability**

While this fact is also true of the prophylactic use of MedCMs, the operational cost of quarantine is likely to be much higher since it involves the physical segregation of those quarantined from the rest of the population. Any decision to implement quarantine should be based on an understanding of potential benefits and potential costs.

The contour plots in Figure 12 showed the value of $\epsilon_Q$—the percent of those who *will* become ill who become quarantined—required to ensure that, on average, $R = 1$ for a given set of $D_{Iso}$ and $\epsilon_{Iso}$ for a given disease. Given the level of quarantine required to stop an outbreak, the question then becomes the following: What is the cost of implementing that level of quarantine? Quarantine has many potential costs, such as the cost of determining the PAR, the cost of establishing and maintaining quarantine facilities, or the cost of monitoring the health of individuals in quarantine. These costs are discussed in the next chapter when considering the relative ease or difficulty of implementing response measures in an operational environment.

In the discussion that follows, the cost of quarantine is measured in terms of the number of healthy, susceptible individuals who are quarantined but who *will not* become ill—the "unnecessarily quarantined"—for every individual who is quarantined and *will* become ill. Here, this cost is defined as $Q_S$.

To this point, $Q_S$ assumes that the operational cost of the loss of an unnecessarily quarantined individual is the same as the loss of a contagious individual. Obviously, this

assumption is not always true because healthy individuals can continue to contribute to their mission while sick individuals cannot. Moreover, quarantine is transient, and those individuals who are unnecessarily quarantined can return to their mission when quarantine ends. To account for this difference in operational value, the variable, $\alpha$, can be added to the $Q_S$ expression so that cost is now represented as $\alpha Q_S$. The value of $\alpha$ represents the relative impact on operations due to the loss of an unnecessarily quarantined individual and the loss of a contagious individual and can range from zero to one. If $\alpha = 1$, then the loss of a quarantined individual is equal to that of a contagious individual. Alternately, if $\alpha = 0$, then the loss of quarantined individuals has no impact on the operation.

The tolerance that operational commanders will have for absorbing the costs of quarantine in any given operation is a function of many factors, including the prospects for stopping the outbreak through other means. This assessment is intended to provide a framework for medical planners and decision makers to understand the factors that influence the potential magnitude of quarantine costs and opportunities for mitigating them.

If a very high percentage of individuals in the incubating stage of disease must be quarantined to stop an outbreak (i.e., the required value of $\epsilon_Q$, as shown in Figure 12), the prospective cost of missing even small numbers of such individuals is also very high. To ensure that quarantine captures sufficient numbers of individuals who will become ill, it would have to be broadly implemented and encompass nearly everyone within the exposed population. The number of unnecessarily quarantined individuals per incubating individual ($Q_S$) would be commensurately large. The inverse is true when the required value of $\epsilon_Q$ is low.

Disease characteristics, particularly mode of transmission and infectivity, drive the required value of $\epsilon_Q$ and the likely value of $Q_S$. Highly infectious respiratory diseases, such as measles, that spread through airborne droplets and particulates and are persistent in the environment can potentially expose very large numbers of people. Other diseases, such as Ebola, spread through direct physical contact with skin or bodily fluids and generally cause much smaller numbers of potential exposures. Similarly, these characteristics influence the ease with which potentially exposed individuals can be identified. Disease characteristics also determine the duration of quarantine, which is generally a function of the upper bound of the incubation period of the disease. Quarantine in outbreaks of diseases with very short incubation times will, therefore, be shorter and less costly than those outbreaks during which incubation is quite long.

Specific disease characteristics may drive the value of $Q_S$ to levels that may be prohibitively high. However, options exist for implementation of quarantine in a manner that will reduce the value of $\alpha$, thus making quarantine more feasible. The value of $\alpha$ might be less than one, or even approach zero, in two of the three quarantine strategies considered in this paper. If units are experiencing high rates of illness or are perceived as being particularly at risk, they may be taken offline, quarantined in a rear area, and/or held in reserve

for the duration of quarantine. In this case, the contribution of healthy individuals to the mission may already be limited by overall unit degradation. Here, the operational cost depends less on the loss of unnecessarily quarantined individuals and more on the availability of replacement units and the length of time before the quarantined unit can resume operations. Alternatively, quarantined individuals who are segregated within their unit may be able to continue to perform their tasks with minimal operational impact.

Implementation of a traditional concept of quarantine, where individuals who may have been exposed to contagious disease are removed from their unit to a dedicated quarantine facility, is the most costly by the measure described previously. Because these individuals would otherwise be executing their tasks within their units and are completely lost for the duration of the quarantine period, the value of $\alpha$ in this strategy is equal to one.

## D. Operational and Strategic ROM

Operational ROM is the restriction of contact between units or personnel who have not yet been affected by an outbreak and those that may have been affected within a theater of operations. Strategic ROM is the prevention of movement of units or personnel into and out of the theater. The objective of this outbreak response measure differs from others. Whereas MedCMs, isolation, and quarantine are aimed at ensuring that the outbreak wanes with each successive generation of disease cases, the goal of ROM is to prevent or delay the spread of disease to a particular population or unit, to preserve immediate mission capability, prevent international spread of disease, and protect home nations.[34]

Operational and strategic ROM will disrupt a force's ability to execute several aspects of modern military operations, such as tactical maneuver and just-in-time resupply. The extent of disruption depends on the ROM strategy adopted. For example, cessation of all movement between units, whether in whole or in part, would have a greater impact than cessation of movement between units with contagious individuals and the unaffected units with which they have regular contact. Yet, despite the broad potential for operational degradation, operational commanders may choose to restrict movement between units in circumstances where the immediate gains offset the costs. For example, ROM may be a viable option when critical military objectives must be accomplished in the immediate future by specific units, when other control measures are unavailable or ineffective, or when a stopgap measure is needed until other control measures can be brought to bear.

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[34] North Atlantic Treaty Organization. *Allied Medical Publication 7.1 (AMedP-7.1)*, 6-15; North Atlantic Treaty Organization. *Allied Medical Publication 7.6 (AMedP-7.6)*, 7-4.

Units subject to operational or strategic ROM continue to operate in place. Individuals may or may not be subject to health monitoring, depending on the early signs and symptoms of the disease in question. Units are assumed to be self-sustaining for as long as possible. Any needed resupply, maintenance, and so forth are conducted by means that prevent person-to-person contact. Any individuals who do become ill are removed from the unit and placed in isolation.

In ROM's most restrictive form, healthy personnel are prohibited from moving into or out of the unit for the duration of ROM, and contact with other units is suspended. More relaxed forms of ROM may allow some level of personnel movement. However, the more individuals move between units, the less likely that those individuals who become ill will be within the controlled unit at the onset of illness.

The IDA team assessed the risk of disease spreading through the movement of infected but asymptomatic individuals into a previously disease-free population for various rates of movement into the population. This assessment will help medical advisors and operational commanders understand the relationship between the movements of individuals and the spread of disease and lead to more informed decisions on whether and how best to restrict movement to reduce the likelihood of disease spreading to a disease-free population by a certain time.

The IDA team made a number of assumptions in this assessment:

- Although military populations are made up of multiple units with potentially complex movement patterns, IDA considered a simplified population, with individuals moving between only two groups: (1) the unit or population that must be kept disease free and (2) all individuals outside that unit, some of whom have become ill.
- Movement between the two subpopulations is represented as a daily exchange of individuals, and the total number of individuals in each subpopulation is constant.
- Ill individuals are not permitted to move into the disease-free population, but all asymptomatic individuals in the subpopulation with disease—whether incubating or not—are equally likely to move into the disease-free population.
- As an outbreak grows larger with time, the number of cases of symptomatic and asymptomatic infected individuals likewise increases, but these numbers were held constant in the assessment, meaning the results are valid only for short forecasts into the future during which time the assumption of constant numbers of infected individuals is not far from reality.

The likelihood that a unit can remain disease free for some time period of interest (perhaps the day it is needed to lead an operation) is a function of the number of individuals who move into that population and the likelihood that those individuals will be incubating disease. Specifically, the probability of a unit remaining free of disease ($P_{No\ Disease}$) can be described as

$$P_{No\ Disease}(N, n, E, t) = (1 - E)^{nt}, \tag{34}$$

where *t* is the time period of interest (measured in days), *n* is the number of individuals who move each day, *N* is the total number of individuals in the population in which disease is occurring, and *E* is the portion of the population in which disease is occurring that is incubating the disease but is currently asymptomatic.

See Appendix A for the mathematical derivation of Equation 34.

This relationship can be used to determine the maximum daily movement of individuals that can be allowed before the probability of an infected but asymptomatic individual entering the disease-free population exceeds some threshold risk level.

For example, Figure 13 shows the maximum number of individuals who can move daily from a population with some percentage of SARS cases[35] before a greater than 50% probability exists that an incubating case of disease moves into the disease-free unit within the time period of interest. In this figure, the curves represent time periods for keeping the unit disease free for 3 days (red line), 5 days (blue line), or 7 days (green line).

In this example, if a commander wanted to ensure at least a 50% chance of a particular unit remaining SARS-free for the next 3 days, then he or she may decide to implement a policy restricting the movement of individuals from a population with 2% of the population symptomatic with SARS to no more than 24 individuals per day.

The IDA team generated the same set of curves for the other diseases discussed in this paper (see Figure 14). While the shape of these curves is similar across all four diseases, the values shown on the y-axis are very different. As shown in the figure, the likelihood that even very small numbers of moving individuals will spread plague reaches 50% at extremely low rates of disease. For this disease, keeping a unit disease free may be possible only if movement of personnel into that unit is almost completely prohibited. Results for smallpox are very similar. For influenza and SARs, on the other hand, greater numbers of moving individuals can be allowed.

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[35] The value of *e* is unknowable during an outbreak. To approximate this value, the IDA team used a simple SEIR contagious disease model that relates the number of infected but asymptomatic individuals to the number of symptomatic individuals at a given time, which is something decision makers could know. Early in an outbreak of SARS, the instantaneous number of infected but asymptomatic individuals is approximately 2.2 times the number of symptomatic individuals.

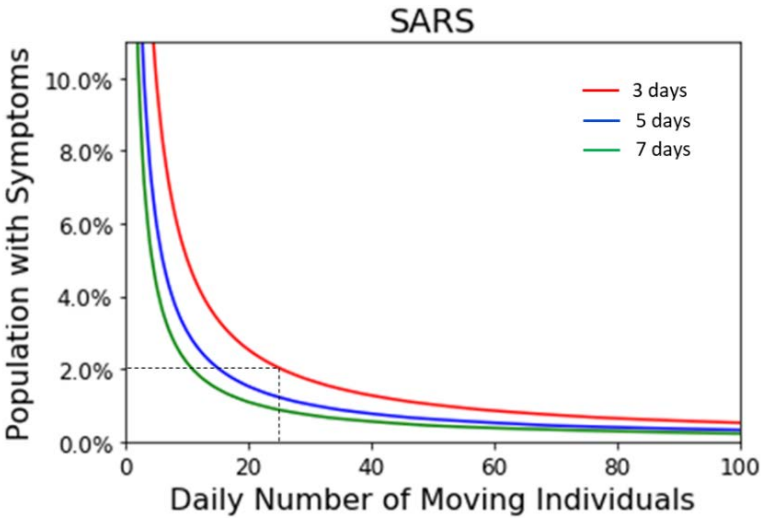


**Figure 13. Maximum Movement of Personnel Allowed to Keep a Unit SARS-Free for a Period of Interest**

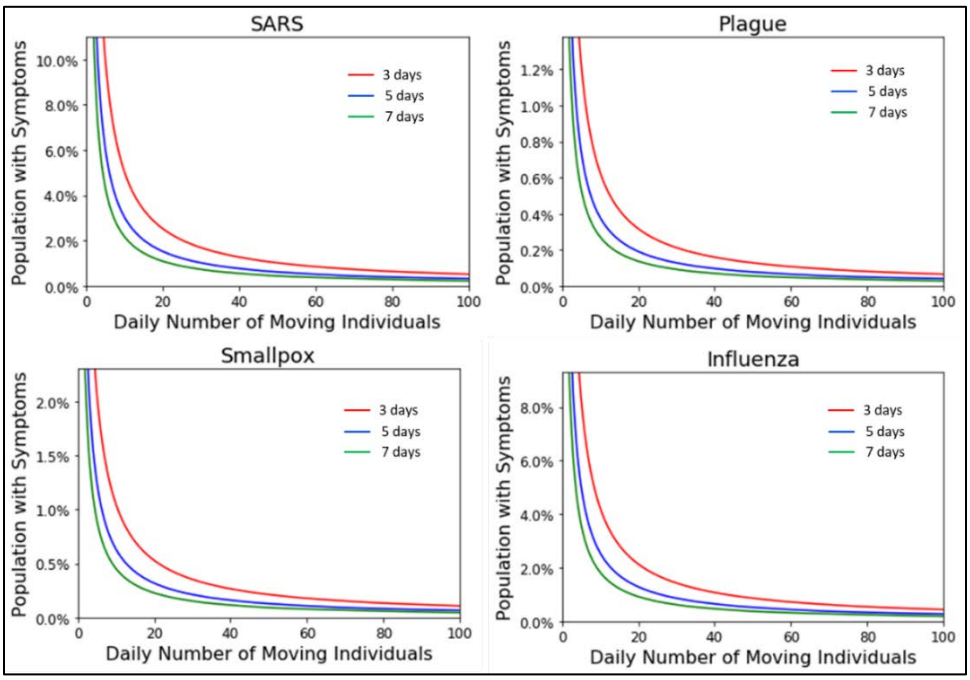


**Figure 14. Maximum Movement of Personnel Allowed to Keep a Unit Disease Free for a Period of Interest**

The key disease parameters that influence the results shown in Figure 14 are $R_0$ and the duration of the contagious period. These parameters, in turn, determine the relationship between the number of current cases of disease within a population and the number of individuals who are currently incubating disease. In the early stages of SARS and influenza outbreaks, the number of incubating cases would typically be fewer than current disease cases at any point in time, while the opposite is true for plague and smallpox outbreaks.

## E. Cessation of Response Measures

After implementing a response measure to mitigate an outbreak of disease in the force, commanders continually need to weigh the benefits of ending the response measure against the risk of additional individuals developing symptoms. Commanders can use knowledge about the duration of the disease's incubation period and the time between infection and the onset of symptoms to inform the duration of response measures (i.e., quarantine or the restriction of movements between units) as well as how far back in time contacts should be traced to identify other cases.

For a well-characterized incubation period distribution, a calculable probability exists that an individual exposed and infected at a given time will develop symptoms by some future point. If an individual was exposed to a disease at some time $t_1$, then the cumulative distribution function of the disease's incubation period evaluated at time $t_2 - t_1$, $F(t_2 - t_1)$, represents the probability that the individual will have developed symptoms by time $t_2$. The quantity $1 - F(t_2 - t_1)$ represents the probability that the individual will develop symptoms at some point after time $t_2$. If time $t_1$ is defined as the time the last known case of disease was isolated (assumed to be the last time at which someone could have become infected by a known case) and $t_2$ is the proposed end of the response measure, then $1 - F(t_2 - t_1)$ represents the risk that an individual could present with symptoms after the response measure ends.

This risk of an individual presenting symptoms after a fixed time varies by the shape of each disease's incubation period distribution. Diseases with wider incubation period distributions (i.e., a greater level of variation in their incubation periods) will present a greater risk than those with narrower distributions.

Figure 15 shows the probability that an infected individual will develop symptoms after some time (measured relative to the mean duration of the mean incubation period). For example, after 1.5 times the mean incubation period, nearly zero individuals infected with smallpox would have developed symptoms, whereas nearly 20% of those infected with SARS would still be incubating the disease. In other words, ending a response measure after 1.5 times the mean incubation period since the last known case would present negligible risk for smallpox but would present a risk for SARS.

To generate Figure 15, parameter values to describe the incubation period distribution for each disease of interest were obtained from various journal articles and reports. The incubation period for influenza was characterized by a lognormal distribution with a mean

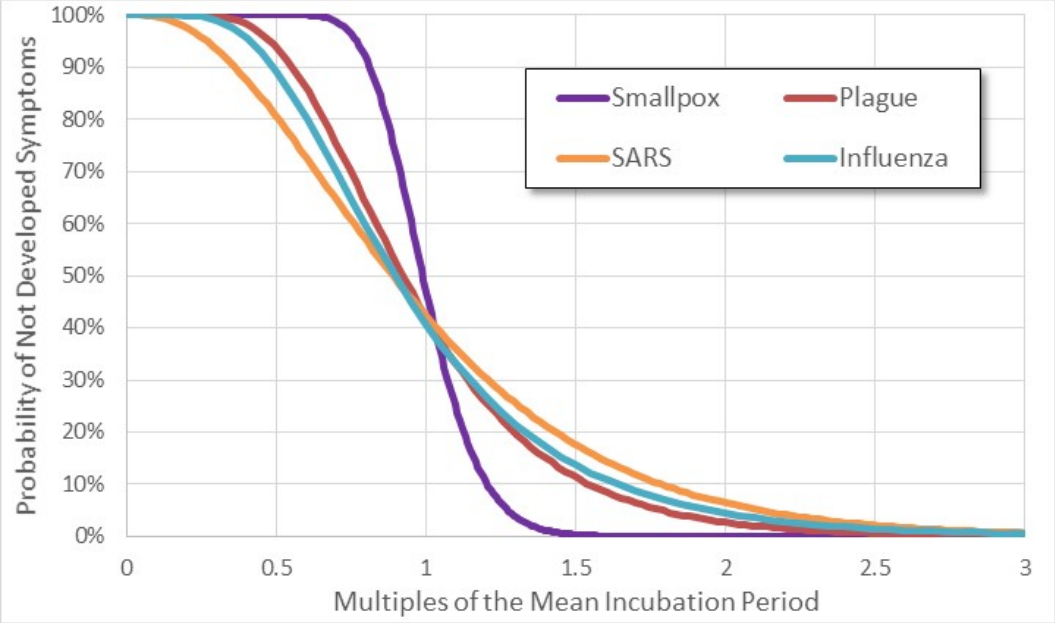


**Figure 15. Probability of Not Developing Symptoms by a Given Time (Measured in Multiples of the Mean Incubation Period)**

value of 2 days and a standard deviation of 1 day.[36] The plague incubation period was characterized by a lognormal distribution with a mean value of 4.3 days and a standard deviation of 1.8 days.[37] The SARS incubation period was characterized by a gamma distribution with a mean value of 4.49 days and a standard deviation of 2.63 days.[38] The smallpox incubation period was characterized by a lognormal distribution with a mean value of 11.6 days and a standard deviation of 1.8 days.[39]

## F. Summary

This chapter defined scaling functions describing the effectiveness of three different outbreak response measures: MedCMs, isolation, and quarantine. These functions can be used to determine the range of parameter values that would drive the value of *R* below one and stop the progression of a disease outbreak.

In addition, this chapter describes the circumstances in which operational and strategic ROM could be used to keep a specific unit of population disease free for a limited period of time and for the specific purpose of supporting immediate operational objectives.

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[36] 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.

[37] Oxford et al., *Technical Reference Manual to Allied Medical Publication 7.5 (AMedP-7.5)*, 23-12.

[38] Bombardt, "Congruent Epidemic Models for Unstructured and Structured Populations," 177.

[39] Oxford et al., *Technical Reference Manual to Allied Medical Publication 7.5 (AMedP-7.5)*, 26-19.

ROM of this type may contribute to the objective of stopping a disease outbreak by reducing the susceptible population for a short period of time, but this contribution would be transient and was not overtly considered here.

The scaling functions used to describe response effectiveness are as follows:

- MedCMs

$$f_{MedCM}(\epsilon_{MCM}) = 1 - \epsilon_{MedCM}. \tag{35}$$

- Isolation

$$f_{Iso}(\epsilon_{Iso}, D_{Iso}) = \begin{cases} 1 - \epsilon_{Iso} & , \text{if } D_{iso} \le T_L - T_I \\ \frac{\epsilon_{Iso} D_{Iso}}{T_C} + \left[(1 - \epsilon_{Iso}) - \epsilon_{Iso}\frac{T_L - T_I}{T_C}\right] & , \text{if } T_L - T_I < D_{iso} < T_L - T_I + T_C. \\ 1 & , \text{if } D_{iso} \ge T_L - T_I + T_C \end{cases} \tag{36}$$

- Quarantine

$$f_Q(\epsilon_Q) = 1 - \epsilon_Q. \tag{37}$$

- Isolation and quarantine used in combination

$$f_{Q,Iso} = f_Q(\epsilon_Q) f_{Iso}(\epsilon_{Iso}, D_{Iso}). \tag{38}$$

Embedded within each of these functions are parameters that influence the effectiveness of outbreak response measures:

- The availability of MedCMs for a given disease,
- The efficacy of MedCMs,
- The time it takes to administer MedCMs within a PAR,
- The time delay from onset of symptoms to isolation,
- The probability that a contagious individual will be isolated,
- The probability that infected individuals will be quarantined before they become symptomatic, and
- The number of people who are unnecessarily quarantined.

Whether outbreak response measures can be implemented in a manner that meets these requirements will be heavily influenced by the operational environment. The next chapter discusses the challenges to effectively responding to outbreaks of diseases of various types in different operating environments.

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# 4. Challenges to Effective Outbreak Response

Operationally significant outbreaks of contagious disease in a military theater pose significant challenges to commanders and present risks to military operations. Controlling these outbreaks is very complex, and success depends on the implementation of response measures in a way that is often driven by the specific characteristics of the disease and in an operational context in which freedom of maneuver, availability of resources, and competing operational objectives are significant constraints. The discussion that follows revisits the key parameters that determine the effectiveness of response and the influence of disease characteristics on the required values for those parameters. It then assesses qualitatively the relative ease of meeting those requirements during operations of various types and, by extension, on the prospects for successful implementation. In short, disease characteristics determine the combined effectiveness of response measures that are required to cause an outbreak to wane. Operational environment determines what is possible and drives the specific selection and combination of response measures that should be used.

## A. Disease Characteristics and Outbreak Response Parameter Values

The derivation of response measure parameters provided in Chapter 3 showed how the requirements for effectiveness varied by disease. For example, in the absence of MedCMs or isolation, 81% of new smallpox infections would need to be quarantined to drive $R$ below one, while only 22% of new plague infections would need to be quarantined. These values result from combinations of disease characteristics that decision makers need to consider when implementing response measures. For the most part, these characteristics are static inputs and cannot be readily changed or manipulated. They provide the backdrop against which response measures are implemented and define the space within which decisions and risk calculations can be made.

### 1. Route of Transmission and Transmissibility

Route of transmission is the mechanism by which a disease spreads from one person to another. Transmissibility is the ease with which a pathogen causes infection in the susceptible population. In combination, these two characteristics determine the value of $R_0$. The higher the value of $R_0$, the greater the challenge of forcing $R$ below one, and the more demanding it will be to plan and execute an effective outbreak response. Among the

diseases considered in this paper, smallpox has by far the highest $R_0$ value and, correspondingly, the most stringent requirements for vaccine efficacy, minimum isolation efficacy (i.e., with no delay), and quarantine.

These disease characteristics also influence the window of opportunity for isolation. To cause an outbreak to wane, individuals need to be isolated as soon as possible but no later than the point in time at which they, on average, infect one additional person. The mean rate at which contagious individuals infect others is determined by $R_0$ and the duration of the contagious period. Diseases with high $R_0$ values and short contagious periods will have shorter windows of opportunity for isolation than those with lower $R_0$ values and longer contagious periods.

In addition, route of transmission and transmissibility determine the biological safety measures—personnel protective equipment (PPE), procedures for limiting staff/patient interactions, sanitation, waste management, and so forth—needed to successfully isolate contagious individuals. These factors also determine the disease-specific public health measures, such as social distancing, that might contribute to outbreak containment.

## 2. Incubation Period and Latent Period

The incubation period is the time between exposure and onset of symptoms. The latent period is the time between exposure and contagiousness. These two time periods are not always the same. For influenza, for example, the contagious period begins before the onset of symptoms. For plague and smallpox, the contagious period begins after the onset of symptoms.

Before the onset of symptoms, individuals who are incubating disease cannot be differentiated from others who may have been exposed but are not incubating disease. Thus, incubation period determines the earliest point at which an individual can be placed in isolation. As shown in Figure 6, the window of opportunity for isolation is shortened when the latent period is shorter than the incubation period and is extended when the latent period is longer than the incubation period—in both cases by an amount of time equal to the difference between these two time periods.

These two periods, in combination, also influence the window of opportunity for quarantine. Whatever strategy for quarantine is implemented, it must be executed before exposed individuals become contagious to be effective. As with isolation, that window is shortened when the latent period is shorter than the incubation period and is extended when the latent period is longer. In the latter case, if individuals are not contagious until they have been symptomatic for some period of time and if they can, with confidence, be isolated within that period of time, quarantine would be unnecessary.

The incubation period of a disease further determines how long those who are suspected of exposure must remain in quarantine before they either become ill or are confirmed to be disease free. To the extent that individuals in quarantine cannot continue to perform their military tasks, the longer the incubation period of a disease, the greater the operational cost of quarantine.

Finally, incubation and latent period also heavily influence the window of opportunity for the use of MedCMs. Influenza has the shortest incubation time of any of the diseases considered and, as seen in Figure 5, by far the shortest period of time for the administration of MedCMs. This relationship generally holds true among diseases with comparable $R_0$ values—in this case, influenza, plague, and SARS. However, diseases with long incubation periods can also have narrow windows of opportunity for MedCMs if they have a sufficiently high $R_0$ value. As shown in Figure 5, smallpox also has a demanding time for the administration of MedCMs despite its much longer incubation period (and even longer latent period).

### 3. Specificity of Symptoms

Many contagious diseases are non-specific in their early stages. They may initially present with flu-like symptoms, such as fever, headache, myalgia, and general malaise, and be difficult to differentiate in a clinical setting from common viral infections until the disease progresses to more severe and more identifiable symptoms. Such diseases can inhibit effective outbreak response by confounding the development of situational awareness and sowing confusion and delay, particularly in the early stages of an outbreak. Clinicians may not suspect that a highly contagious infectious disease is the causative agent of an illness until several cases have occurred and progressed to more clinically recognizable stages. When contagious individuals cannot be readily identified, delays in getting them to isolation will occur, and a substantial fraction of individuals may not be isolated within the required window of time if they are isolated at all. Moreover, the longer it takes to identify contagious individuals, the more contacts they can have within the susceptible population, complicating efforts to determine who should be quarantined.

Emerging diseases are similarly challenging since insufficient information may be available from current or prior outbreaks to determine response requirements, and supporting tools, such as laboratory diagnostic capabilities, may not be available. Decision makers will need to use available information to gauge the prospective requirements for outbreak response. When information gaps occur, they will have to determine whether a more conservative or less conservative approaches to response is warranted. The assessment of response measures provided in this paper can support identification of critical information requirements and prioritization of technical and scientific support in the event of such an outbreak.

Table 4 summarizes the previous discussion. When a disease characteristic determines the values a given parameter must take for an effective response (as determined by the assessment in Chapter 3 and the considerations discussed previously), it is represented by a plus mark. In terms of the number of response-measure parameters affected, the $R_0$ value of a disease has the greatest influence over response requirements. The time between exposure and onset of symptomatic and contagious periods is also key. When responding to outbreaks of diseases with non-specific symptoms or diseases about which little is known, the key challenge is managing uncertainty and delays in outbreak recognition, clinical diagnosis, and case reporting so that contagious individuals can be identified and isolated appropriately.

**Table 4. Disease Characteristics that Determine Required Response Parameter Values**

| Response Measure | Key Parameters | $R_0$ | Incubation/ Latent Periods | Specificity of Symptoms |
|---|---|---|---|---|
| MedCMs | Time to implement | | + | |
| | Efficacy | + | | |
| Isolation | Delay in reaching isolation | + | + | |
| | Percent of ill who are isolated | + | | + |
| Quarantine | Probability of Incubating Individual Being Quarantined | + | + | + |
| | Number of unnecessarily quarantined | + | + | + |
| | Operational value of unnecessarily quarantined | | + | |
| Operational/ Strategic ROM | Probability that a unit will remain free of disease | + | + | |

## B. Operational Challenges to Effective Outbreak Response

The spread of disease within a deployed military population and the ease with which measures can be implemented to effectively stop that spread are influenced by a number of factors. These factors can be present to a greater or lesser extent in operations of various types, and, hence, the feasibility of implementing specific response measures in a manner that meets disease-specific requirements will also vary by type of operation.

### 1. General Operational Challenges

#### a. Rate and homogeneity of mixing

In modern operations, military personnel are highly mobile. One recent IDA study found that in an average deployed unit, 20%–25% of U.S. military personnel changed

locations each day, with a range of 5%–45%.[40] The more that individuals move between units or locations, the faster and further a contagious disease can spread. As disease spreads and the PAR grows, the scope of outbreak response measures must also expand, encompassing an ever larger portion of the force.

Within a deployed force, some personnel and units may move with significantly more frequency than others. Personnel from maintenance and supply units, for example, may move throughout an operating area and mix with other units more frequently than, say, those from a command element. Restricting the movement of such personnel or limiting direct person-to-person contact during necessary movement may be an effective component of outbreak response.

In other types of operations, personnel movements may be more uniform. When mixing is truly homogeneous, each susceptible member of the population is equally likely to have contact with someone who is contagious. In these circumstances, no identifiable set of individuals is more likely to spread disease than others, making it more difficult to use operational or strategic ROM as an effective response. Moreover, when contact rates among individuals are not obviously stratified, it will be more difficult to identify those individuals who are likely to have contacted someone who is contagious. If quarantine must encompass a large percentage of incubating individuals to be effective ($\epsilon_Q$), implementation within a homogeneously mixed population will, by necessity, lead to a relatively high number of unnecessarily quarantined individuals ($Q_S$), thus increasing the cost. By extension, the higher the potential cost of quarantine, the more incentive for quarantine to be implemented in a manner that allows individuals to conduct their military tasks as fully as possible ($\alpha = 0$).

In addition, disease outbreaks in homogeneously mixed populations are likely to be larger and spread more quickly.[41] This situation means that the requirements for outbreak response may be greater and more urgent.

A final consideration is the extent to which the military PAR engages with outside populations, such as host nation civilians, Allied military personnel, or out-of-theater reinforcements. These other populations may serve as ongoing sources of contagion, thus limiting the effectiveness of any response measures as long as contact with these populations continues. However, in an ongoing outbreak of highly contagious disease, these populations would likely be subject to their own outbreak response measures. Decision makers

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[40] Burr et al., *Emerging Infectious Diseases Study*, 68. These movement rates were observed among a subset of the U.S. military deployed to Afghanistan in 2012. Here, units are defined by the discrete locations to which troops were assigned.

[41] Julia K. Burr, Robert L. Cubeta, and Lucas A. LaViolet, *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), 25.

need to understand the nature and adequacy of such measures when determining whether contact between these populations and the deployed military population should be restricted.

### b. Infrastructure within the area of operations

All the response options discussed in this paper involve some level of personnel movement and logistical support. In the modern Western world, national infrastructure promotes rapid movement of personnel and resources. In other parts of the world, transportation and communications networks may be less developed or may be degraded by ongoing conflict or natural disasters.

The effectiveness of MedCMs and isolation depends to a great degree on time—the time it takes to disseminate MedCMs throughout the deployed force and the time it takes to deliver a symptomatic individual to isolation. Decision makers must account for any limitations in infrastructure that may impede the implementation of these measures within the required timelines. As shown in Figure 5, the shortest required timeline for the administration of MedCMs among the diseases considered is around 30 days for influenza. Timelines for other diseases may be even longer. While this amount of time would seem to be sufficient to implement MedCMs in even the most onerous conditions, delivery is only one of the tasks that must be accomplished within the available window. Recall that the timeline begins with the start of the outbreak and must account for the time to recognize the outbreak and to make the decision to use MedCMs.[42]

The time window for isolation, by contrast, is very short for some diseases For example, based on incubation and latent periods, it is 1.5 days for influenza and 2.2 days for plague. Given that not all MTFs may have the ability to effectively isolate highly contagious disease cases, a limited number of destination facilities, such as Role 3 hospitals, may be located at some distance from the outbreak. Getting contagious individuals to these facilities in a timely manner may be challenging, particularly in areas where the transportation network is degraded.

Damaged or undeveloped infrastructure may limit overall movement among the military population and constrain contact between contagious individuals and the susceptible population. These constraints can have a dampening effect on the progression of the outbreak and make outbreak response somewhat less demanding. Ordinarily, constraints on movement would make identification of potentially exposed individuals easier, which, in turn, would promote the effectiveness of quarantine and reduce its cost. However, the

[42] This timeline is that required to avoid a 20% casualty rate within the PAR. The timeline would change if a different measure of effectiveness were used.

inverse is also true when those constraints are driven by poor infrastructure since it inhibits outbreak investigation and the epidemiological work done to support contact tracing.

### c. Permissiveness of the environment

The permissiveness of the military environment determines freedom of maneuver within the area of operations. For outbreak response, an environment unconstrained by adversary action will make responses easier to implement. In operations where military forces are engaged in active combat or are acting as a barrier between other forces in conflict, the operational constraints on movement may be similar to the physical constraints associated with degraded infrastructure. The impact on the dissemination of MedCMs and movement of individuals to isolation will also be similar. In active combat operations, medical resources will need to be allocated for the care of conventional trauma casualties, limiting the resources available for the management of highly contagious disease casualties. Isolation and treatment of complex contagious disease casualties may prove challenging if deployed MTFs are at or near capacity due to trauma casualties. In addition, those isolation and quarantine facilities that do exist will likely be sited far from front lines for reasons of safety and security, thus increasing the distance that individuals must travel to reach those facilities. As noted, combat itself can degrade infrastructure and exacerbate the challenges to effective response posed by the difficulty of moving personnel and materiel.

In some operational environments, forward units may be isolated and self-sustaining, limiting the possibility that an outbreak of contagious disease will reach them. At the same time, organic medical capabilities in those units may be limited. Clinical diagnosis of disease cases may be unlikely, particularly in the early stages of an outbreak when situational awareness is low and/or when the early stages of disease are non-specific. Such circumstances could lead to fewer people being sent to isolation within the required time ($\epsilon_{iso}$).

Quarantine will be much more difficult and potentially costly in a non-permissive environment. Contact tracing or other strategies to differentiate likely exposures from possible exposures may not be possible if the targeted individuals are in units that are forward deployed. Forces engaged in active combat may not be able to self-monitor their health to support forward quarantine strategies. Yet, at the same time, the removal of potentially exposed individuals to quarantine facilities in rear areas could have the same operational cost as if they had become ill ($\alpha = 1$), at least for the duration of the quarantine period.

### d. Sophistication of the adversary

For operations against peer and near-peer adversaries, the challenges associated with non-permissive environments would be exacerbated. The movements required for effective implementation of medical response may be even more difficult, particularly in forward areas where tactical air superiority cannot be guaranteed. This situation may force reliance

on ground transportation to move individuals into isolation or quarantine or to supply forward units with MedCMs.

More sophisticated adversaries will also have greater capability to mount complex biological attacks and create outbreaks of contagious disease that are more difficult to stop. These attacks could generate larger numbers of casualties, begin in multiple locations, or involve pathogens that have been engineered to be resistant to MedCMs. Health risk assessments and medical intelligence in the area of operations support medical planners in anticipating such attacks, preparing for their consequences, and identifying them quickly should they occur.

While all operationally significant contagious disease outbreaks will stress the isolation capacity normally available within a standard medical footprint, those that result from biological agent attacks will certainly do so. Whenever a risk of contagious disease has been identified, medical planners should prepare to expand isolation capacity within the area of operations through the conversion of existing medical facilities or the establishment of dedicated contagious disease facilities, as feasible.

#### e. Scale of the operation

The scale of military operations determines the size of the PAR, the geographic size of the area of operations, the duration of the mission and associated reliance on resupply and rotation of personnel, and the strategic value of mission objectives.

Large-scale operations are more likely to have large and complex unit structures and involve multiple deployment locations and ports of entry. In general, the larger and more complex the structure of the PAR and movements between individual units and locations, the longer it takes for outbreaks to spread throughout the area of operations. This situation provides opportunities for ROM to be used as a short-term measure to protect specific units or locations in support of near-term operational objectives. At the same time, large ports of entry and centralized staging areas may promote the spread of disease if contagious individuals are present in those locations and infect large numbers of people who subsequently move to other areas.

In larger operations, the distances across which individuals and material must be moved may be substantially increased, affecting the time it takes for MedCMs to reach the susceptible population and for contagious individuals to reach isolation. Identification of individuals who should be quarantined may also be more challenging since personnel may transit long distances and multiple locations during deployment.

On the positive side, large-scale operations may deploy with a larger and more sophisticated medical footprint, including multiple hospitals and laboratory facilities. Such a capability will provide in-theater diagnostics and laboratory support for situational awareness and greater organic capacity for isolation and care of contagious patients.

Table 5 summarizes the operational factors that can challenge implementation of outbreak response, or make achievement of response requirements more difficult. Based on the previous discussion, when an operational factor has the potential to make achievement of response parameters more difficult, it is represented by a plus mark. Occasionally, as discussed, operational factors may have a positive influence on the effectiveness of response. These cases are represented by circles.

**Table 5. General Operational Challenges to Key Outbreak Response Parameters**

| Response Measure | Key Parameters | High Rates of Mixing | Poor Infrastructure in Area of Operations | Non-permissive Environment | Sophisticated Adversary | Large-scale Operation |
|---|---|---|---|---|---|---|
| MedCMs | Time to implement | | + | + | + | + |
| | Efficacy | | | | + | |
| Isolation | Delay in reaching isolation | | + | + | + | + |
| | Percent of ill who are isolated | | | + | + | ○ |
| Quarantine | Probability of incubating individual being quarantined | + | + | + | | + |
| | Number of unnecessarily quarantined | + | + | + | | + |
| | Operational value of unnecessarily quarantined | | | + | | |
| Operational/ Strategic ROM | Probability that a unit will remain free of disease | + | | ○ | | ○ |

## 2. Challenges within Different Types of Operations

Military operations vary widely in purpose, scope, and scale. Not all of the operational challenges discussed previously will be present in every operation. Matching challenges to type of operation is a critical step in developing guidelines for commanders, medical advisors, and medical staff charged with planning and implementing outbreak response measures in their specific operation. The remainder of this chapter discusses the extent to which the challenges to effective outbreak response listed above would be present within operations of various types.

Joint Publication 3-0 describes three broad categories of operations in which U.S. military forces may be engaged: (1) military engagement, security cooperation, and deterrence; (2) crisis response and limited contingency operations; and (3) large-scale combat operations.[43] These categories encompass a range of operation types across a continuum of conflict from peace to war. Collectively, they provide good set of exemplar operational types for which outbreak response guidelines should be generated.

### a. Military engagement, security cooperation, and deterrence

Joint Publication 3-0 describes military engagement, security cooperation, and deterrence operations as follows:

> Missions, tasks, and actions [that] encompass a wide range of actions where the military instrument of national power is tasked to support other instruments of national power as represented by interagency partners, as well as cooperate with international organizations (e.g., UN [United Nations], NATO) and other countries to protect and enhance national security interests, deter conflict, and set conditions for future contingency operations.[44]

Such operations are wide-ranging, ongoing, and generally routine efforts within all U.S. Combatant Command areas of responsibility to collaborate with allies, provide situational awareness, and support deterrence. Examples include military engagement activities, emergency preparedness, support for host nation efforts to combat terrorism, freedom of navigation and overflight, protection of shipping, and humanitarian assistance such as the provision of medical care in underserved regions and the construction of basic sanitation facilities.

The IDA team considered forces engaged in such operations to be based in fixed-site installations—on airbases or in garrison or onboard ships. As such, they would be small groups of forces with high rates of homogenous mixing, actively engaged with host nation civilians and allied military forces, and operating in peacetime, permissive environments.

Outbreaks of disease could spread very rapidly in these types of operations, and response measures would need to be undertaken quickly. Of the response options available, these operations would not impede the implementation of MedCMs or isolation not would they pose a challenge to isolating everyone who becomes ill since they are assumed to be small and not involve a dispersal of forces throughout a theater. Quarantine would be more challenging since the degree of mixing would make it difficult to stratify the PAR based

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[43] Chairman of the Joint Chiefs of Staff, *Joint Operations*, Joint Publication 3-0 (Washington, DC: Chairman of the Joint Chiefs of Staff, 17 January 2018, Incorporating Change 1, 22 October 2018), V-4, https://www.jcs.mil/Portals/36/Documents/Doctrine/pubs/jp3_0ch1.pdf?ver=2018-11-27-160457-910.

[44] Ibid., VI-1.

on probability of exposure to contagious individuals. It may also be more costly since the number of unnecessarily quarantined individuals could be quite high for diseases where the required value for the percent of incubating cases who must be quarantined ($\epsilon_Q$) is also high. At the same time, if quarantine encompasses an entire airbase, garrison, or ship, quarantined individuals should be able to continue their peacetime military tasks. Any tasks that cannot be performed can likely be deferred at relatively low cost.

### b. Crisis response and limited contingency operations

Crisis response and limited contingency operations are defined as follows:

> … typically focused in scope and scale and conducted to achieve a very specific strategic or operational-level objective in an operating area. They may be conducted as a stand-alone response to a crisis (e.g., NEO [noncombatant evacuation operation]) or executed as an element of a larger, more complex operation. Joint forces conduct crisis response and limited contingency operations to achieve operational and, sometimes, strategic objectives.[45]

The IDA team considered foreign humanitarian assistance and peace operations as prototypes for operations in this category.

Foreign humanitarian assistance operations are military missions to provide aid and comfort to foreign civilian populations in the aftermath of natural or man-made disasters or conflict. As a condition of mission success, these operations involve contact with local civilian populations, national and foreign aid workers, or military and civilian personnel from other nations contributing to relief efforts. These contacts, while necessary, also represent ongoing potential sources of infection that may not be as amenable to control as those within the military PAR. Local infrastructure, including roads and runways, is likely to be heavily degraded, particularly following natural disasters. The environment is considered permissive although degradation of power, water, and communications may require forces to be more self-sustaining than they might otherwise be in a permissive environment.

In this type of operation, degradation of infrastructure is the primary challenge to outbreak response. The impact is greatest on those response options that must be implemented within a window of time to be effective, specifically the administration of MedCMs and movement of contagious individuals to isolation. Quarantine would be difficult to implement since populations outside the military force could serve as continuing sources of infection and complicate efforts to differentiate the potentially exposed from the broader PAR. This situation may lead to the quarantine of fewer incubating individuals than needed as well as large numbers of unnecessarily quarantined individuals. Moreover, the loss to

[45] Ibid., VII-1.

the operation of individuals in quarantine will be quite high since completion of their military tasks requires ongoing engagement with individuals from outside populations.

Peace operations involve the use of military forces to establish barriers and prevent conflict between combatants in an effort to establish the conditions for peace and recovery of populations, economic activity, and infrastructure. By comparison with humanitarian relief operations, contact with locals during peace operations may be less urgent and less necessary. Infrastructure is likely to be heavily degraded by conflict. The environment will be generally semi-permissive.

In these operations, degraded infrastructure will negatively affect the delivery of MedCMs and the opportunity to move individuals to isolation. Operational restrictions on transportation within the area of operations due to the semi-permissive environment will compound these problems. Military personnel may have less contact with individuals from other populations, allowing greater opportunities for outbreak investigation and contact tracing in support of quarantine effort. However, those opportunities may be constrained if those tasks cannot be done in a safe and secure manner.

### c. Large-scale Combat Operations

Large-scale combat operations are defined as follows:

> [Execution of campaigns] to prevail against the enemy as quickly as possible; conclude hostilities; and establish conditions favorable to the HN [host nation], the US [United States], and its multinational partners. In the context of large-scale combat, campaigns are a series of related major operations aimed at achieving strategic and operational objectives within a given time and space. A major operation is a series of tactical actions, such as battles, engagements, and strikes, and is the primary building block of a campaign. Major operations and campaigns typically include multiple phases ….[46]

The IDA team considered two types of large-scale combat operations: (1) U.S.-led coalitions engaged in expeditionary operations, such as Operation Enduring Freedom in Afghanistan, and (2) NATO Article V operations defending against incursions into Allied territory. These operations are large-scale, sophisticated deployments of military capability, conducted in a non-permissive, active combat environment. They may endure for months or years in pursuit of their strategic objectives and therefore will be supported by a transportation and logistic support network capable of moving large amounts of military capability from the United States forward. While both types of operations will present tactical challenges involving damaged infrastructure and restricted terrain, NATO Article V operations could be conducted in regions with a very sophisticated infrastructure in areas

[46] Ibid., VIII-1.

outside conflict boundaries. Forces engaged in NATO Article V operations will likely face a peer adversary, creating a significant additional challenge for outbreak response.

As discussed previously and shown in Table 5, virtually every component of outbreak response would be significantly more difficult in a non-permissive environment. It may be difficult to meet required timelines for the administration of MedCMs and for moving contagious individuals to isolation. The percent of contagious individuals who can be moved to isolation may be reduced. Opportunities for assessing individual risk of exposure in support of quarantine efforts may be limited, as would be the opportunity to extend quarantine to units engaged in combat. In such circumstances, quarantine would have to be implemented broadly to ensure that it captures a sufficient fraction of incubating individuals, particularly for diseases with high $R_0$ values. A large number of individuals would be unnecessarily quarantined as a result.

Large-scale operations do provide some opportunities and advantages for outbreak response planning. The in-theater medical footprint may be large relative to other types of operations, given a higher expectation of trauma casualties, thus increasing available capability and capacity for isolation and management of contagious casualties. The presence of inter-theater supply networks can further support the augmentation of existing capabilities for isolation. The large geographic areas involved will tend to delay the spread of disease, providing operational commanders with the option to use ROM to protect units for a brief period of time in pursuit of immediate, critical military objectives. The opportunities for doing so may be greater in expeditionary operations, where units may be operating in remote areas.

In NATO Article V operations, allied forces could face a sophisticated adversary with the capability and possible will to cause or exploit outbreaks of contagious disease for military and political gain. As noted previously, man-made outbreaks of contagious disease could generate larger numbers of casualties, begin in multiple locations, or involve pathogens that have been engineered to be resistant to MedCMs. The major additional challenge for outbreak response in this scenario is the magnitude of the response required, and the need to consider multiple measures in the event that available MedCMs have reduced efficacy.

Table 6 maps general operational challenges to the implementation of outbreak response to operations of various types. When an operational challenge exists in a given type of operation, it is represented by a plus mark. As noted previously, not all challenges are present in all types of operations. In general, larger and more complex operations present more challenges and more difficulties in effectively controlling the spread of contagious disease.

**Table 6. Challenges to Effective Response Present in Operations of Various Types**

| Challenge | High Rates of Mixing | Poor Infrastructure in Area of Operations | Non-permissive Environment | Sophisticated Adversary | Large-scale Operation |
|---|---|---|---|---|---|
| Military engagement, cooperation, and deterrence | + | | | | |
| Foreign humanitarian assistance | + | + | | | |
| Peace operations | | + | + | | |
| NATO Article V | + | | + | + | + |
| U.S.-led coalition | + | + | + | | + |

# 5. Summary and Proposed Guidelines

The purpose of this paper is to provide a set of broad, analytically supported guidelines for selecting and implementing disease outbreak response measures in an operational environment. The IDA team began the analysis by postulating that the primary objective of outbreak response is to reduce the average number of infections caused by a contagious individual, *R*, below one. The faster outbreak response can accomplish this objective the better, and one mechanism for doing so is to push *R* close to zero.

The IDA team then established the conditions in which three different response measures—MedCMs, isolation, and quarantine—could be used to meet this objective, either alone or in combination. In that part of the analysis, the IDA team defined the parameters that determined the effectiveness of each type of response and calculated the required values for those parameters for four different contagious diseases. The team also assessed a fourth measure, operational or strategic restriction of movement, as a potential means of protecting high-value military assets in pursuit of immediate, short-term objectives.

As the analysis progressed, it became clear to the IDA team that the required values for response parameters were driven by the characteristics of the diseases considered. The team then identified which specific disease characteristics had the greatest impact on response effectiveness to determine how the requirements for effective response would vary between outbreaks of different diseases.

Finally, the IDA team proposed a number of potential challenges to the implementation of response options in an operational environment. These challenges are described with reference to specific response parameters and the feasibility of achieving required values for those parameters, as determined by the characteristics of disease. As a last step, the IDA team reviewed the range of military operations in which U.S. forces may be engaged to determine which challenges are most relevant in specific types of operations.

The conclusions of the IDA team's analysis are presented in Sections 5.A–5.C in the form of guidelines that operational commanders, medical advisors, and medical staff can use when planning and executing responses to outbreaks of contagious disease in an operational setting. These guidelines are not intended to provide detailed response plans since these plans will be heavily influenced by the host of factors that influence operational planning more broadly, such as the organization and layouts of forces in the area of operation, the concept of operations, the locations and units initially infected, geography, climatology,

and host nation support. Rather, these guidelines are intended to identify those key factors that should be considered by commanders, medical advisors, and medical staffs when selecting and implementing response measures.

These guidelines are divided into three categories:

- General guidelines that should be followed when planning or implementing outbreak response in any operational environment,
- Guidelines related to specific diseases and disease characteristics, and
- Guidelines that account for the challenges to effective response in operations of different types.

## A. General Outbreak Response Guidelines

### 1. Determine the Availability and Efficacy of MedCMs

The availability of MedCMs is perhaps the single most important factor in planning and executing an effective outbreak response. When MedCMs are available, they provide decision makers with a highly effective response option that can be administered at generally low operational cost.

Vaccines are perhaps the canonical form of MedCMs. An operationally significant outbreak of disease has virtually no possibility of occurring in a military population that has been uniformly vaccinated against that disease in advance of deployment. However, vaccines are costly to develop and are not available for all diseases of concern. Even when vaccines exist, they may not be administered because the risk of adverse reactions can outweigh the immediate threat, which is the case, for example, with the current smallpox vaccine. Once a disease outbreak is underway, operational commanders and medical advisors must balance the benefits of the vaccine and the prospects for stopping the outbreak with the risk of adverse reactions. Decisions to implement a vaccine program should consider whether individual risk factors can be identified in advance and whether the required level of immunity within the general population can be established even if those at highest risk of adverse reaction remain unvaccinated.

Even when no vaccine is available against a given disease, antibiotics and antiviral drugs can be effective MedCMs. The vulnerability of a pathogen or a specific strain of a pathogen to various drugs may be unknown at the start of the outbreak. When this vulnerability is not known, establishing the most effective antibiotic or antiviral regimen should be among the first tasks undertaken by medical advisors and medical staffs. Initial attempts to accomplish this effort will likely be done in clinical laboratories that support the MTFs where cases are being treated Operational level medical staff should ensure that the results

of any laboratory analysis are collected, evaluated by subject matter experts or in reach-back laboratories if needed, and disseminated throughout the deployed medical force.

MedCM efficacy is often very high for known, well-characterized diseases. For example, antibiotics are generally assumed to have 95% efficacy when used as a pre-exposure prophylaxis for plague.[47] Similarly, in modern military populations, the smallpox vaccine can be expected to have an efficacy of 95% when administered before exposure.[48] Given that the calculated minimum MedCM efficacy for smallpox is 80% to reduce *R* below 1, this efficacy rate is more than sufficient. Moreover, MedCMs with high efficacy rates can effectively drive *R* much lower than 1 and hasten the end of the outbreak. For example, for MedCMs to push *R* to 0.5 for plague, antibiotics would need an efficacy rate of 60%, much lower than they are estimated to have.

It is important for decision makers to understand that MedCM efficacy does not necessarily have to be very high to drive the value of *R* below 1. Because the $R_0$ values for plague, influenza, and SARS are fairly close to 1 to begin with, the minimum MedCM efficacy for these diseases, as seen in Table 7, is 24%, 35%, and 39% respectively. These minimum efficacy rates imply that for at least some diseases, MedCMs can be an important outbreak response even when facing resistant strains of disease, or diseases against which they are only partly effective.

### 2. Acquire, Disseminate, and Administer MedCMs

When health risk assessments identify endemic or man-made disease threats within an area of operations, medical staff should determine the availability of MedCMs for those diseases and, when MedCMs are available, develop contingency plans for the acquisition, stockpiling, dissemination, and administration of these countermeasures to forces in the theater.

As shown in Table 7, the window of time for successful administration of MedCMs to the force will often be fairly long. Therefore, decision makers can be deliberate in the administration of MedCMs and do so in a way that protects the force as quickly as possible while limiting operational impact. Planning for the use of MedCMs as an outbreak control measure should account for the method of administration, dosing regimen, and any medical support requirements (e.g., if a drug must be administered via the intravenous route).

The more transmissible a disease, the more rapidly it can spread in a population. Therefore, the higher the $R_0$ of a disease, the greater the imperative to make MedCMs universally available to all military personnel within the area of operations.

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[47] Oxford et al., *Technical Reference Manual to Allied Medical Publication 7.5 (AMedP-7.5)*, 23-10.

[48] Ibid., 26-13.

If MedCMs are in limited supply, the medical staff must develop a prioritization scheme for administration that accounts for operational objectives. As a default, they should plan to administer MedCMs first to units and locations affected directly by the outbreak and then to front-line units or other critical capabilities that cannot be replaced or whose loss would significantly affect the accomplishment of military objectives.

### 3. Provide MTFs with Additional PPE and Infection Control Capability as Needed

The IDA team assumed that once a contagious patient has been isolated, isolation was appropriate and effective in preventing further transmission of disease either to medical personnel or to the larger PAR. Ensuring that this is the case is a key task for medical planners and staffs.

Standard precautions used for infection control in deployed MTFs may provide insufficient protection against highly contagious infectious disease. Depending on the mode of transmission and transmissibility of the disease, standard precautions may need to be augmented with enhanced PPE and the adoption of additional infection control procedures to protect medical personnel and other patients and to restrict contamination to controlled areas.

MTFs are unlikely to deploy with augmented infection control capabilities and PPE unless warranted by threats identified during pre-deployment planning. Once an outbreak of disease has been detected, operational medical staff should promptly ascertain the need for augmentation throughout the deployed medical force and push required materiel to MTFs as quickly as possible. Infection control materiel and PPE must be replenished at regular intervals during the outbreak.

### 4. Promulgate Public Health Guidance

Medical advisors, with the assistance of their staffs, should promulgate public health guidance throughout the area of operations to enhance public hygiene and limit exposures, manage contagious patients, and facilitate implementation of outbreak response measures. This guidance should include the following:[49]

- A case definition to support triage and clinical diagnosis,
- Reporting guidance for MTFs and clinical laboratories,
- Recommendations for personal hygiene measures across the force,

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[49] See Mark Bohannon et al., *Report of the Project Team for Smart Defence Project 1.1045, Volume 2: Concept of Operations for Bio-Response, Appendix E: Template for Force Health Protection Guidance*, IDA Document NS D-10974 (Alexandria, VA: Institute for Defense Analyses, January 2020).

- Requirements for isolation and infection control, and
- Recommendations on the use of MedCMs as prophylaxis and therapy.

This guidance should be regularly revisited and updated as warranted as the outbreak progresses.

### 5. Establish and Maintain Situational Awareness

During disease outbreaks of operational concern, operational staffs must maintain a robust common operating picture, with primary support from medical staff. The importance of situational awareness as an enabler of successful outbreak response cannot be over-emphasized. Medical information and medical intelligence reporting should be collected, evaluated, and routinely updated. Medical staffs should establish reach-back mechanisms for accessing subject matter expertise on the disease in question and for conducting sophisticated laboratory analysis of clinical and environmental samples as indicated. Medical advisors should also consider augmentation of staff with epidemiologists and infectious disease specialist medical personnel if they are not already present.[50]

Medical advisors should coordinate with host nation health officials and those associated with other populations at risk within the area of operations and adjacent locations. The purpose of this coordination effort is to monitor the spread of the outbreak outside the military force and to observe the effectiveness of response measures implemented within those populations.

Decision makers at all levels must emphasize the need for regular, consistent, and complete case reporting. Routine disease reporting mechanisms, timelines, and information may be insufficient for this purpose. Staffs may need to direct alternative procedures and reporting mechanisms. Staffs should ensure that clinical and diagnostic laboratory facilities are included in the reporting chain and that they have access to all relevant laboratory reports and findings.

## B. Disease-Related Guidelines

In assessing various response measures, the IDA team used information on four different diseases to illustrate the relationships between disease characteristics and response requirements. The parameter values derived in Chapter 3 for each of these diseases are shown in Table 7.[51] These values can be used as the basis for broad guidelines for responding to outbreaks of these diseases.

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[50] For more information on operational staff activities in support of outbreak response, see Bohannon et al., *Report of the Project Team.*

[51] As discussed in Chapter 3 with regard to isolation and quarantine, requirements for any single measure are less stringent when implemented in combination with others.

**Table 7. Disease-specific Response Parameter Values**

| Smallpox | Plague | SARS | Influenza |
|---|---|---|---|
| **Availability of MedCMs:** | | | |
| Yes | Yes | No | Maybe |
| **Minimum required MedCM efficacy to drive R <1 (R <0.5):** | | | |
| 0.8 (0.9) | 0.24 (0.6) | 0.39 (0.7) | 0.35 (0.7) |
| **Time window for effective administration of MedCMs:[a]** | | | |
| ~70 days | ~100 days | ~100 days | ~30 days |
| **Maximum time window for isolation (probability of isolation = 1):** | | | |
| 5.7 days | 2.2 days | 7.7 days | 1.5 days |
| **Minimum allowed probability of isolation, if isolation occurs one day after symptoms start:[b]** | | | |
| 0.70 | 0.25 | 0.40 | 0.70 |
| **Minimum allowed probability that infected individuals are quarantined before symptom onset if isolation is ineffective (moderately effective):[c]** | | | |
| 0.81 (0.54) | 0.22 (0.17) | 0.36 (0.24) | 0.32 (0.22) |
| **Maximum number of people allowed to move each day to keep a unit disease free for 5 days if 1% of PAR has symptoms:** | | | |
| 8 | 5 | 60 | 1 |

[a] The defined objective of MedCMs in Chapter 3 was to ensure R < 1 before 20% of the population at risk became ill. The time window begins with the exposure of the first case of disease and ends when those to whom MedCMs are administered develop immunity.

[b] The IDA team assumed that the fastest that sick individuals could reach isolation was 1 day after onset of symptoms. The minimum values for the parameter $\epsilon_{Iso}$ provided in this table are based on this assumption.

[c] Figure 10 shows the fraction of new infections that must be quarantined, given isolation capability, for all four diseases. Isolation capability is portrayed here as the combination of isolation delay and effectiveness, with bounding cases where isolation is completely ineffective or completely effective. The former case provides the maximum requirement for quarantine. In the latter case, quarantine would have no value added. In Figure 10, the yellow regions can be considered a "moderately effective" isolation capability. The additional requirement for quarantine to ensure R < 1 is provided in Table 7, primarily to support discussion of guidelines in the sections that follow.

All four of these diseases can be transmitted via the aerosol route and have non-specific symptoms in their early stages. In deployed military populations, with high rates of mixing and significant movement, contact tracing and other methods of stratifying the population based on risk (e.g., anyone who was at a given location in a given window of time) are unlikely to be effective. Consequently, it will difficult to implement quarantine in a manner that minimizes the number of unnecessarily quarantined individuals. If decision makers deem quarantine to be a necessary response to outbreaks of these diseases, it should be implemented in place whenever possible.

## 1. Smallpox Response Issues

Vaccines against smallpox are available and highly effective and should be provided to all personnel not previously immunized. The smallpox vaccine is known to have side

effects in an identifiable subset of the PAR. Individuals who are at risk of side effects may be able to forego vaccination but should be segregated (or removed) from the remainder of the population and held in quarantine until the outbreak ends. Medical advisors and medical staffs should coordinate vaccination programs with the host nation, allied nations, and others involved in the operation to ensure that all PAR can be immunized and the outbreak can be controlled effectively. Additional preventive medicine units may need to be deployed to the area of operations to administer the vaccine.

Compared with other diseases, the maximum isolation window of opportunity for smallpox is relatively long (5.7 days). Moreover, those who become ill with smallpox are not typically contagious for the first day or two, allowing those who become ill to be identified before they are contagious. However, smallpox symptoms are non-specific in the early stages of disease and may be similar to symptoms of common infections like seasonal influenza. As part of the public health guidance for isolation of smallpox cases, the medical staff may wish to recommend a two-phased isolation process, where ill individuals who have yet to meet the case definition of smallpox (e.g., laboratory confirmation or presence of rash) are held separately from those who have not.

Commanders should consider quarantine in place of all personnel in units affected by the outbreak, particularly if vaccination cannot be implemented in a timely manner for some reason. Because personnel who become ill do not pose an immediate risk to others in their unit, incubating personnel should be able to freely perform their military tasks until such time as they develop symptoms.

Operational ROM is a reasonable option for protecting high-value units from smallpox for several days with minimal disruption. The IDA team estimated that eight people could move daily for 5 days before a previously uninfected unit had a higher than 50% chance of developing cases.

### 2. Plague Response Issues

Rapid dissemination of antibiotics to the PAR should cause an outbreak to wane quickly. If a resistant strain of plague is involved, MedCMs should still be a major component of response. Medical advisors and medical staffs should coordinate dissemination of antibiotics with the host nation, allied nations, and others involved in the operation to ensure that all PAR can be immunized and the outbreak can be controlled effectively.

Because of the high fatality rate, commanders should prioritize all efforts to prevent plague casualties from occurring. If MedCMs are disseminated rapidly enough, the outbreak should end with a limited number of cases. However, if any delays occur in implementing MedCMs, any cases that do occur must be isolated immediately. The maximum window of time for isolation of plague casualties is only 2.2 days. Meeting this response timeline may be challenging in operations where casualties occur in forward units engaged

in active combat operations or where significant infrastructure degradation occurs in the area of operations.

Quarantine of units and personnel in place may be less effective for plague than for other diseases. Beyond the short window of time in which isolation can be an effective outbreak response, pneumonic plague is a rapidly progressing disease that must be medically managed in its early stages if death is to be prevented. Once plague patients reach the second, fulminant stage of the disease, the probability of fatality is near 100%, and the patients generate large amounts of contaminated waste that must be managed. Because of the urgency with which sick individuals must be moved to isolation, commanders should plan to establish dedicated quarantine facilities proximate to isolation facilities whenever possible.

Operational ROM is a reasonable option for protecting high-value units from plague for several days with minimal disruption. The IDA team estimated that five people could move daily for 5 days before a previously uninfected unit had a higher than 50% chance of developing cases. Because management of plague casualties is so urgent (with its requirement for rapid isolation and treatment), commanders may choose to completely prohibit all movement into a targeted unit and accept the associated operational disruption.

### 3. SARS Response Issues

Because no approved MedCM exists for SARS, response efforts should focus primarily on isolation. Of the four diseases considered, the window of opportunity for isolation is longest for SARS (7.7 days). In most operating environments, SARS patients should routinely be able to reach isolation within that window.

Commanders should consider quarantine in place of all personnel in units affected by the outbreak. Personnel with an identified risk of exposure to SARS can be segregated from other personnel but should be able to otherwise perform their military tasks.

Of the diseases considered here, SARS is most amenable to the use of operational ROM to protect high-value units from infection, with minimal disruption. The IDA team estimated that some 60 people could move daily for 5 days before a previously uninfected unit had a higher than 50% chance of developing cases.

### 4. Influenza Response Issues

The availability and effectiveness of MedCMs for influenza will depend greatly on the strain involved in the outbreak. If MedCMs are available, they must be administered within 30 days of the start of the outbreak to avoid large numbers of casualties before the outbreak starts to wane. Medical advisors and medical staffs should coordinate vaccination programs with the host nation, allied nations, and others involved in the operation to ensure that all PAR can be immunized and the outbreak can be controlled effectively. Additional

preventive medicine units may need to be deployed to the area of operations to administer the vaccine.

If MedCMs are not available, influenza outbreaks can be difficult to control. Influenza has the shortest time window for isolation (1.5 days) if 100% of cases are isolated. If patients are isolated as quickly as possible (i.e., within a day of developing symptoms), the percent of cases that must be isolated is still over 70%. Forward deployment of isolation capability to expedite movement of patients to isolation is a critically important component of effective response.

Some operational environments may not allow a sufficient percentage of influenza cases to be isolated within the prescribed time period. Decision makers must therefore consider quarantine of personnel in all units affected by the outbreak. The strain of influenza involved and the associated severity of illness are important determinants of the form that quarantine should take. In general, the speed with which cases must be isolated argues for quarantine in its traditional form, where at-risk individuals are held in dedicated facilities proximate to isolation facilities.

Influenza was the disease least amenable to operational ROM. The IDA team found that only when movement between units was completely prohibited would units have any chance of remaining disease free for any period of time.

## C. Operation-Related Guidelines

### 1. Military Engagement, Cooperation, and Deterrence

Military engagement, cooperation, and deterrence missions are assumed to have uniform mixing among personnel within the participating unit(s) and high rates of mixing with host nation civilians and foreign military personnel. These high rates of mixing pose the most significant operational challenges to outbreak response in these missions. Table 8 shows the outbreak response challenges in military engagement, cooperation, and deterrence. As summarized in Table 8, the response parameters most affected are those related to quarantine and ROM.

**Table 8. Outbreak Response Challenges in Military Engagement, Cooperation, and Deterrence**

| Operational Challenge | Response Parameter Affected |
|---|---|
| High rates of mixing | Probability of incubating individual being quarantined |
| | Number of unnecessarily quarantined |
| | Probability that a unit will remain free of disease |

In these missions, no identified operational challenges exist for meeting requirements for MedCMs and isolation. Decision makers should follow the general guidance provided previously for the use of MedCMs, if available, and for ensuring that medical personnel and facilities have the enhanced PPE and infection control capabilities that they need. Standard processes for moving contagious patients for isolation should be followed.

Quarantine could be more challenging. With high rates of mixing, it will be difficult to stratify the population on the basis of contact with contagious individuals and the associated risk of exposure. Consequently, a large fraction of the PAR may need to be quarantined to ensure that this approach is effective. At the same time, these missions occur in peacetime, without the urgency of combat or the operational cost of failure to accomplish mission objectives. Thus, the operational cost of putting individuals in quarantine (the $\alpha$ parameter defined in Chapter 3) will be close to zero regardless of the form that quarantine takes. Moreover, it may be more feasible for individuals to continue to perform peacetime tasks in quarantine, reducing the operational cost even further.

### 2. Foreign Humanitarian Assistance

Foreign humanitarian assistance operations are assumed to require high rates of mixing between military forces and host nation civilians. Consequently, these operations will experience similar challenges to those faced in military engagement, cooperation, and deterrence missions, specifically with regard to quarantine and ROM. Table 9 shows the outbreak response challenges to foreign humanitarian assistance.

**Table 9. Outbreak Response Challenges to Foreign Humanitarian Assistance**

| Operational Challenge | Response Parameter Affected |
|---|---|
| High rates of mixing | Probability of incubating individual being quarantined |
| | Number of unnecessarily quarantined |
| | Probability that a unit will remain free of disease |
| Poor infrastructure in area of operations | Time needed to implement MedCM |
| | Delay in reaching isolation |
| | Probability of incubating individual being quarantined |
| | Number of unnecessarily quarantined |

In addition, as seen in Table 9, poor infrastructure in the area of operations will challenge those aspects of response that depend on the movement of personnel and materiel within a window of time—the time to implement MedCMs and the delay in reaching isolation. Outbreak investigations focused on identifying personnel at risk of exposure may also be impeded by difficulties in traveling throughout the area of operations. If the necessary information cannot be gathered, the population cannot be stratified based on risk of exposure and quarantine cannot be implemented efficiently.

In these missions, decision makers should follow the general guidance provided for the use of MedCMs, if available. Early response planning efforts should be closely coordinated with logistics support staff to ensure that MedCMs can be distributed to the PAR within the timelines determined by the incubation and latent periods of the disease.

Because these missions occur in a permissive environment, the only casualties expected would be those from disease/non-battle injuries. Consequently, unless the provision of medical care is a component of the operation, Role 3 medical care may not be available within the area of operations. The capacity for isolation would therefore be limited. At the same time, military personnel may be dispersed among a number of locations that have been isolated or cut off from others because of flooding or infrastructure damage. Decision makers should consider the augmentation or conversion of deployed Role 2 facilities to isolate contagious individuals until they can be moved out of the area. These facilities should be sited close to locations affected by the outbreak to minimize the delay in reaching isolation. This approach is especially needed for diseases that have short time windows for isolation (e.g., plague and influenza).

Quarantine would be challenging to implement. In addition to the difficulties of conducting investigations to determine risk of exposure, foreign humanitarian assistance operations, by definition, require military personnel to engage with host-nation civilians and/or international aid workers in the accomplishment of their tasks, which are focused on alleviating human suffering. Quarantine would necessarily inhibit such operations, and the operational cost of quarantine would, by definition, be high.

When outbreaks are caused by very severe, highly contagious infectious disease, commanders may wish to consider the implementation of strategic ROM—limiting movement of personnel into and out of the area of operations to prevent the spread of disease to other areas and to home nations. Any healthy personnel who leave the area should be quarantined until the risk of disease has passed.

### 3. Peace Operations

Peace operations are similar to foreign humanitarian assistance operations in the challenges posed by poor infrastructure in the area of operations, particularly with respect to those aspects of response that must be accomplished within a defined window of time. The key difference is the lack of permissiveness in the environment, which compounds the challenge of meeting response timelines and makes many aspects of outbreak response much more difficult. Table 10 shows the outbreak response challenges to peace operations.

Isolation will be particularly challenging. In foreign humanitarian assistance operations, the IDA team recommended that isolation facilities be sited in forward locations that can be reached quickly. In peace operations, it may be difficult to safely move and sustain

**Table 10. Outbreak Response Challenges to Peace Operations**

| Operational Challenge | Response Parameter Affected |
|---|---|
| Poor infrastructure in area of operations | Time needed to implement MedCM |
| | Delay in reaching isolation |
| | Probability of incubating individual being quarantined |
| | Number of unnecessarily quarantined |
| Non-permissive environment | Time needed to implement MedCM |
| | Delay in reaching isolation |
| | Percent of ill who are isolated |
| | Probability of incubating individual being quarantined |
| | Number of unnecessarily quarantined |
| | Operational value of unnecessarily quarantined |

isolation facilities in forward locations. At the same time, if military forces are providing a buffer zone between hostile forces, casualties may not be able to safely transit via ground ambulance to isolation facilities.

As characterized in Chapter 4, peace operations may involve less routine mixing between military personnel and other populations than that found in other types of operations. In addition, military personnel are more likely to be concentrated in a small geographic area. These operational circumstances pose challenges and opportunities for quarantine. They would promote more homogenous mixing among the military population but would also facilitate outbreak investigations and contact tracing.

In these missions, decision makers should follow the general guidance provided for the use of MedCMs, if available. Although it may be difficult to deliver MedCMs to the area where the target population is located, administration to a geographically contained population should be straightforward.

Decision makers should consider the augmentation or conversion of deployed Role 2 facilities to isolate contagious individuals until they can be moved out of the area. These facilities should be sited close to the affected units to minimize the delay in reaching isolation and to provide an appropriate level of security. This approach is especially needed for diseases that have short time windows for isolation (e.g., plague and influenza).

Military forces should also be quarantined in place if it can be accomplished without compromising the mission and, by association, the security of the force. If circumstances are such that personnel cannot be quarantined in place and continue to operate, commanders should consider whole-unit replacement, with removal of units affected by the outbreak to permissive areas where they can be held in quarantine until the risk of disease has passed. The movement of personnel replacement units should be heavily restricted to minimize the risk of those units being infected.

## 4. U.S.-Led Coalition Operations

Coalition operations face the same challenges as other types of expeditionary operations described previously: high rates of mixing, poor infrastructure, and a non-permissive environment. The scope and scale of such operations dramatically increases their complexity, adding even more challenges but also, potentially, offering some opportunities that can be exploited for outbreak response. Table 11 shows the outbreak response challenges in U.S.-led coalition operations.

**Table 11. Outbreak Response Challenges in U.S.-Led Coalition Operations**

| Operational Challenge | Response Parameter Affected |
|---|---|
| High rates of mixing | Probability of incubating individual being quarantined |
| | Number of unnecessarily quarantined |
| | Probability that a unit will remain free of disease |
| Poor infrastructure in area of operations | Time needed to implement MedCM |
| | Delay in reaching isolation |
| | Probability of incubating individual being quarantined |
| | Number of unnecessarily quarantined |
| Non-permissive environment[a] | Time needed to implement MedCM |
| | Delay in reaching isolation |
| | Percent of ill who are isolated |
| | Probability of incubating individual being quarantined |
| | Number of unnecessarily quarantined |
| | Operational value of unnecessarily quarantined |
| Large-scale operations[b] | Time needed to implement MedCM |
| | Delay in reaching isolation |
| | Probability of incubating individual being quarantined |
| | Number of unnecessarily quarantined |

[a] The probability that a unit can remain disease free may be enhanced in a certain non-permissive environments.

[b] The percent of ill who are isolated and the probability that a unit can remain disease free may be enhanced in a large-scale operation.

In large-scale operations, military forces are widely dispersed over a large area. If roads, bridges, ports, and airfields are already limited or degraded by combat, larger distances and longer transit times can make it difficult to meet required response timelines. Although personnel deployed in modern large-scale military operations regularly move between locations, the same mobility restrictions that challenge response may also help to contain the spread of disease.

At the same time, large-scale operations are likely to be supported by a larger and more sophisticated deployed medical force, including hospitals, laboratories, specialized

public health response teams, and extensive evacuation capability. Not only does this added support provide an increased capacity for isolation and management of contagious disease patients, it gives decision makers greater flexibility in the allocation of medical capability to meet the immediate needs of the force.

In addition, transportation networks for logistics and sustainment are generally well-established and routinely used in such operations. Dissemination of MedCMs and enhanced infection control materiel can take advantage of these networks to facilitate response. Commanders typically have strategic control of rear areas where the environment is permissive and where it supports movement of personnel and equipment into and out of the theater of operations, providing greater opportunities for augmentation and resupply of medical units.

Finally, units that are engaged in active combat in these operations plan to be self-sustaining for some period of time. Such units are amenable to the use of ROM as a mechanism for minimizing the risk of disease for an operationally relevant period of time.

In these missions, decision makers should follow the general guidance provided for the use of MedCMs, if available.

Decision makers should consider the augmentation or conversion of deployed Role 2 facilities to isolate contagious individuals in forward locations until they can be moved to hospitals in rear areas. When identifying facilities for this role, medical advisors and staff must consider the need to meet clinical timelines for trauma care as well as the window of opportunity for isolation and the need to limit contact between contagious casualties and trauma casualties at forward medical units and at the point of wounding. Decision makers may also wish to dedicate evacuation assets to the mission of moving contagious disease casualties.

Personnel in forward units that have experienced disease casualties should be quarantined in place and subject to routine health monitoring, following disease-specific procedures established as a component of command-issued public health guidance. Personnel located in or transiting through rear areas should also be subject to routine health monitoring; however, if the window of opportunity for isolation can be readily met, such personnel would not have to be quarantined unless they had been determined to have a high risk of prior exposure.

Commanders should consider the use of operational ROM for forward units that have not experienced any cases of disease. Medical staffs must work closely with logistics personnel to ensure that units subject to quarantine and ROM are appropriately sustained.

Because logistics units typically have high rates of movement and routine contact with deployed personnel throughout the theater, the manifestation of disease in these units is of particular concern. Procedures that do not require any interpersonal contact that could

create a risk of exposure should be established for resupply and maintenance throughout the theater.

## 5. NATO Article V Operations

NATO Article V operations, as conceived here, are assumed to occur within the European theater and are focused on the defense of allied nations against a peer adversary. Peer adversaries are assumed to have the capability and possible will to cause or exploit outbreaks of contagious disease for military and political gain. Man-made outbreaks of contagious disease could generate larger number of casualties more quickly than in naturally occurring outbreaks. These outbreaks may begin in multiple locations, facilitating the spread of disease before the outbreak is recognized and before response measures can be implemented. They may also involve pathogens that have been engineered to be resistant to MedCMs. Overall, the major additional challenge for outbreak response in these operations is the magnitude of the response required and the need to use multiple response measures to compensate for any reduction in the efficacy of available MedCMs.

Unlike most of the operations discussed in this paper, NATO Article V operations are supported by sophisticated transportation, communications, power, and water infrastructure. Throughout much of the area of operations, outbreak response timelines should not be challenged by degraded infrastructure and associated constraints on the movement of personnel and equipment. As noted in Chapter 4, however, personnel deployed in modern large-scale military operations regularly move between locations, facilitating the expansion of disease outbreaks and making assessment of individual risk very difficult. Moreover, peer adversaries have greater capability to challenge local air superiority, limiting the use of air evacuation assets (including rotary wing) and forcing the use of ground transportation. Table 12 shows the outbreak response challenges in NATO Article V operations.

In these missions, decision makers should follow the general guidance provided for the use of MedCMs, if available.

As in coalition operations, decision makers should consider the augmentation or conversion of deployed Role 2 facilities to isolate contagious individuals in forward locations, while considering the need to meet clinical timelines for trauma care and the window of opportunity for isolation. Similarly, decision makers may also wish to dedicate evacuation assets to the mission of moving contagious disease casualties.

In NATO Article V operations, outbreaks of disease may progress more rapidly or lead to more casualties than expected because of adversary actions, and Role 2 facilities may not have sufficient capacity to isolate and manage large numbers of contagious disease

**Table 12. Outbreak Response Challenges in NATO Article V Operations**

| Operational Challenge | Response Parameter Affected |
|---|---|
| High rates of mixing | Probability of incubating individual being quarantined |
| | Number of unnecessarily quarantined |
| | Probability that a unit will remain free of disease |
| Non-permissive environment[a] | Time needed to implement MedCM |
| | Delay in reaching isolation |
| | Percent of ill who are isolated |
| | Probability of incubating individual being quarantined |
| | Number of unnecessarily quarantined |
| | Operational value of unnecessarily quarantined |
| Sophisticated adversary | Time needed to implement MedCM |
| | Efficacy of MedCM |
| Large-scale operations[b] | Time needed to implement MedCM |
| | Delay in reaching isolation |
| | Probability of incubating individual being quarantined |
| | Number of unnecessarily quarantined |

[a] The probability that a unit can remain disease free may be enhanced in a non-permissive environment.

[b] The percent of ill who are isolated and the probability that a unit can remain disease free may be enhanced in a large-scale operation.

casualties. Operational commanders can request deployment of additional hospitals from contributing nations for this purpose. These facilities should be sited in locations that can be readily accessed by ground evacuation assets transporting casualties from affected units.

Personnel in forward units that have experienced disease casualties should be quarantined in place and subject to routine health monitoring, following disease-specific procedures established as a component of command-issued public health guidance. Personnel located in or transiting through rear areas should also be subject to routine health monitoring; however, if the window of opportunity for isolation can be readily met, such personnel would not have to be quarantined unless they had been determined to have a high risk of prior exposure.

Commanders should consider the use of operational ROM for forward units that have not experienced any cases of disease. Medical staffs must work closely with logistics personnel to ensure that units subject to quarantine and ROM are appropriately sustained.

Because logistics units typically have high rates of movement and routine contact with deployed personnel throughout the theater, the manifestation of disease in these units is of particular concern. Procedures should be established for resupply and maintenance throughout the theater that do not require any inter-personal contact that could create a risk of exposure.

# Appendix A.
# Derivation of Equation 34

The following derivation was used to generate Equation 34 in Section 3.D. Let $n$ be the number of individuals that move between two populations every day. As described in Section 3.D, $n$ is assumed to be constant over time and describes the number of people leaving the disease-free population for the population that is experiencing the outbreak within which the outbreak is occurring. Furthermore, in accordance with the assumption that the population sizes remain constant, $n$ also represents the number of people leaving the population that is experiencing the outbreak for the disease-free population. Let $N$ be the total number of individuals in the population experiencing the outbreak, and let $E$ be the portion of that population that is incubating the disease but is currently asymptomatic. For this derivation, $E$ is assumed to be constant over time, which limits the use of the results to short forecasts into the future during which time the assumption is more likely to be valid.

The process of individuals moving into the disease-free population can be simulated as a series of random samples. On each day, $n$ individuals are randomly sampled without replacement from the $N$ individuals in the population experiencing the outbreak. The selection of at least one of the incubating but asymptomatic individuals in a sample would represent the importation of the disease into the disease-free population on that day. Let $X_i$ be the number of incubating but asymptomatic individuals who are selected for movement on day $i$ (i.e., the number who are included in random sample $i$). Accordingly, $X_i$ is a hypergeometric random variable, $X_i \sim H(N, n, E)$. Because the total number of individuals and the number of incubating but asymptomatic individuals in the population remain constant, the collection of $X_i$s are independent and identically distributed random variables. The probability of the disease being introduced into the disease-free population on day $i$ is the same as the probability that at least one incubating but non-symptomatic individual will be selected for movement on day $i$, $P(X_i \geq 1)$.

Although the choice of using a hypergeometric random variable for $X_i$ is the most mathematically justifiable, it depends on the size of the population experiencing the outbreak ($N$). This dependence would limit the applicability of analysis to populations of specified sizes. Furthermore, for large $N$, the calculations involving hypergeometric distributions can become computationally difficult. Therefore, the process of randomly sampling *without replacement* to simulate the movement of individuals into the disease-free population was approximated by sampling *with replacement*. Therefore, the probability of at least

one incubating but non-symptomatic individual being selected for movement on day $i$ can be approximated as $(X_i \geq 1) \approx P(Y_i \geq 1)$, where $Y_i \sim B(n, E)$ is a binomial distributed random variable that approximates $X_i$. The use of the binomial approximation to the hypergeometric distribution is typically justifiable when $\frac{n}{N} < 5\%$.[1]

As was the case for the $X_i$s, the $Y_i$s are independent and identically distributed random variables. Because the $Y_i$s are independent and identically distributed random variables, the probability of at least one incubating but non-symptomatic individual entering the disease-free population is the same for all days. Let $p$ be this probability:

$$p = P(Y_i \geq 1). \tag{A-1}$$

The probability of at least one incubating but non-symptomatic individual entering the disease-free population is equivalent to the probability of not having zero incubating but non-symptomatic individuals being selected for movement,

$$p = 1 - P(Y_i = 0). \tag{A-2}$$

The probability $P(Y_i = 0)$ can be readily calculated from the probability mass function of a binomial random variable, $p_{Y_i}(y) = \binom{n}{y} E^y (1 - E)^{n-y}$. Therefore,

$$p = 1 - p_{Y_i}(0) = 1 - (1 - E)^n. \tag{A-3}$$

Given the probability of at least one infected but non-symptomatic individual moving into the disease-free population on a given day ($p$), we can now consider the process of selecting individuals for movement over a multi-day period. Because $p$ is the same for each day and the process of selecting individuals for movement on each day is independent of the other days, we can consider the process as Bernoulli trials, with a success defined as at least one incubating but non-symptomatic individual being selected for movement (i.e., the success probability is $p$). Let $Z$ be the number of days that elapse before and including the first day on which at least one infected but non-symptomatic individual is selected for movement. For example, if 3 days pass with only non-infected people moving and then on the fourth day at least one incubating but non-symptomatic individual moves, then $Z = 4$. The random variable $Z$, therefore, has a geometric distribution with success probability $p$, $Z \sim G(p)$.

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[1] Neil A. Weiss, Paul T. Holmes, and Michael Hardy, *A Course in Probability* (Boston, MA: Pearson Addison Wesley, 2006).

The probability of at least one incubating but non-symptomatic individual moving into the disease-free population for the first time after some elapsed number of days $t$ is $P(Z > t)$. This probability can readily be calculated using the tail probability formula for geometric random variables:

$$P(Z > t) = (1 - p)^t. \quad \text{(A-4)}$$

Substituting the equation for $p$ into Equation A-4 and simplifying provides the following:

$$P(Z > t) = (1 - E)^{nt}. \quad \text{(A-5)}$$

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# Appendix B.
# Illustrations

## Figures



## Tables

# Appendix C.
# References


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# Appendix D.
# Abbreviations

| | |
|---|---|
| AMedP | Allied Medical Publication |
| CBRN | Chemical, Biological, Radiological, and Nuclear |
| HN | host nation |
| IDA | Institute for Defense Analyses |
| MED | medical |
| MedCM | medical countermeasures |
| MTF | medical treatment facility |
| NATO | North Atlantic Treaty Organization |
| NBC | nuclear, biological, chemical |
| NEO | noncombatant evacuation operation |
| OEA | Operational Effectiveness Analyses |
| OTSG | Office of the Surgeon General (U.S. Army) |
| PAR | population at risk |
| PPE | personnel protective equipment |
| ROM | Restriction of Movement |
| SARS | sudden acute respiratory syndrome |
| SEIR | Susceptible, Exposed, Infected, Removed |
| STANAG | standardization agreement |
| U.S. | United States |
| UN | United Nations |

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| REPORT DOCUMENTATION PAGE | Form Approved OMB No. 0704-0188 |
|---|---|



| 1. REPORT DATE (DD-MM-YY) | 2. REPORT TYPE | 3. DATES COVERED (From – To) |
|---|---|---|
| XX-02-2020 | Final | |

**4. TITLE AND SUBTITLE**

Controlling the Spread of Contagious Disease in an Operational Environment

**5a. CONTRACT NO.**

HQ0034-14-D-0001

**5b. GRANT NO.**

**5c. PROGRAM ELEMENT NO(S).**

**6. AUTHOR(S)**

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**5d. PROJECT NO.**

**5e. TASK NO.**

CA-6-4259

**5f. WORK UNIT NO.**

**7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)**

Institute for Defense Analyses
4850 Mark Center Drive
Alexandria, VA 22311-1882

**8. PERFORMING ORGANIZATION REPORT NO.**

IDA Paper P-10877
IDA Log H 19-000498

**9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)**

Army Office of The Surgeon General DHHQ
7700 Arlington Blvd.
Falls Church, VA 22042-5143

**10. SPONSOR'S / MONITOR'S ACRONYM(S)**

OTSG

**11. SPONSOR'S / MONITOR'S REPORT NO(S).**

**12. DISTRIBUTION / AVAILABILITY STATEMENT**

Approved for public release; distribution is unlimited.

**13. SUPPLEMENTARY NOTES**

**14. ABSTRACT**

Should an operationally significant outbreak of infectious disease occur during an ongoing military operation, US and Joint Force Commanders may consider a variety of measures to limit the spread of the outbreak and minimize its impact on operations and on the health of the force. The selection of any measure or set of measures will depend on a variety of factors, including the type of operation, the availability and effectiveness of outbreak control measures, and the potential operational degradation due to outbreak controls. This paper assesses the potential costs and benefits of a variety of outbreak control measures, including medical countermeasures and restrictions of movement, and considers the influence of several operational challenges and disease characteristics on the outcome. From this assessment, the paper derives a set of generalized rules of thumb to support commanders in selecting outbreak controls.

**15. SUBJECT TERMS** contagious, disease, restriction of movement, isolation quarantine, biological outbreak, outbreak response

| 16. SECURITY CLASSIFICATION OF: | | | 17. LIMITATION OF ABSTRACT | 18. NO. OF PAGES | 19a. NAME OF RESPONSIBLE PERSON |
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