INSTITUTE FOR DEFENSE ANALYSES

Assessing Measures to Mitigate the Effects of an Emerging Infectious Disease

27 April 2016
Biological Medical Defense Conference
Munich, GERMANY

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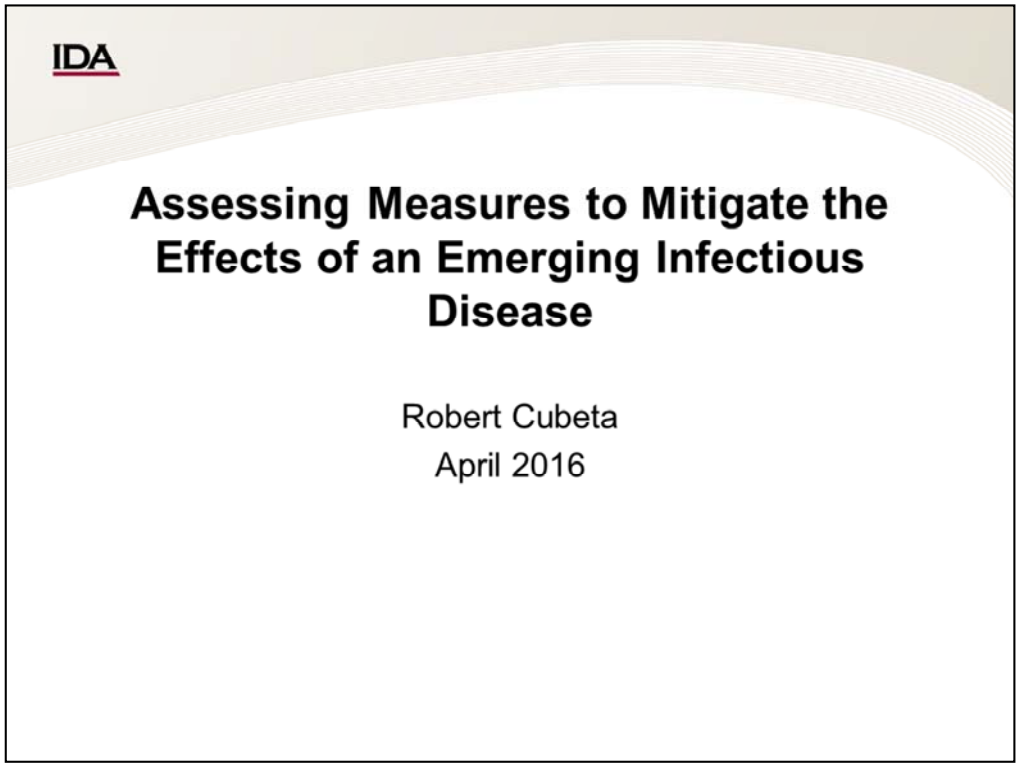
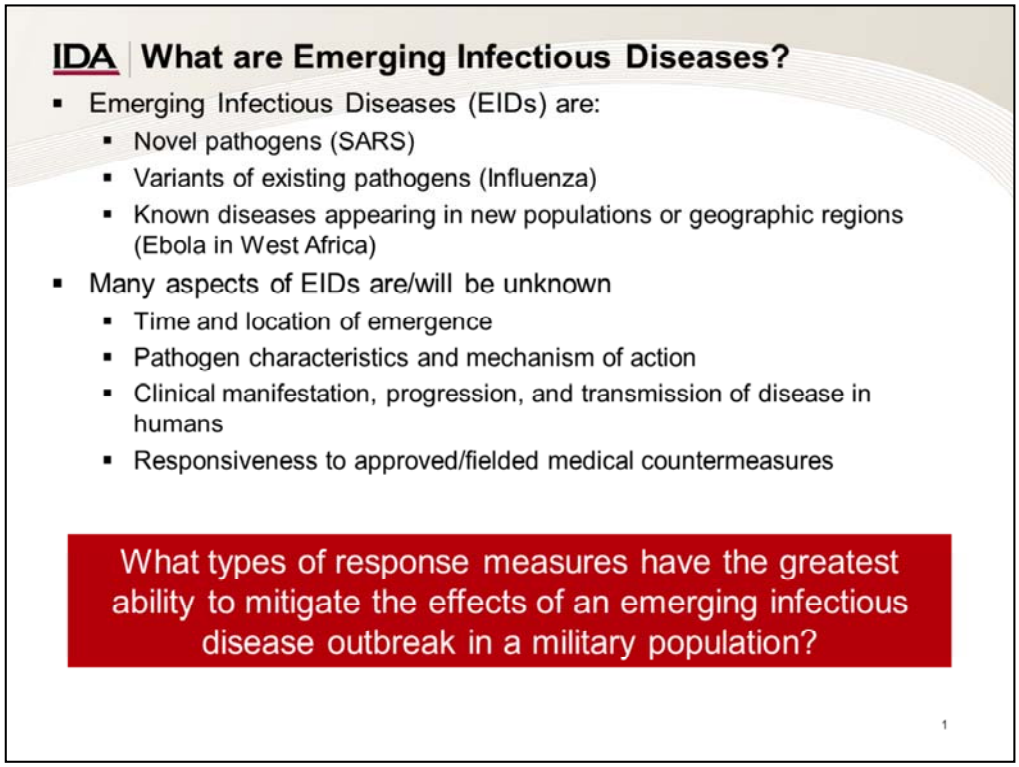


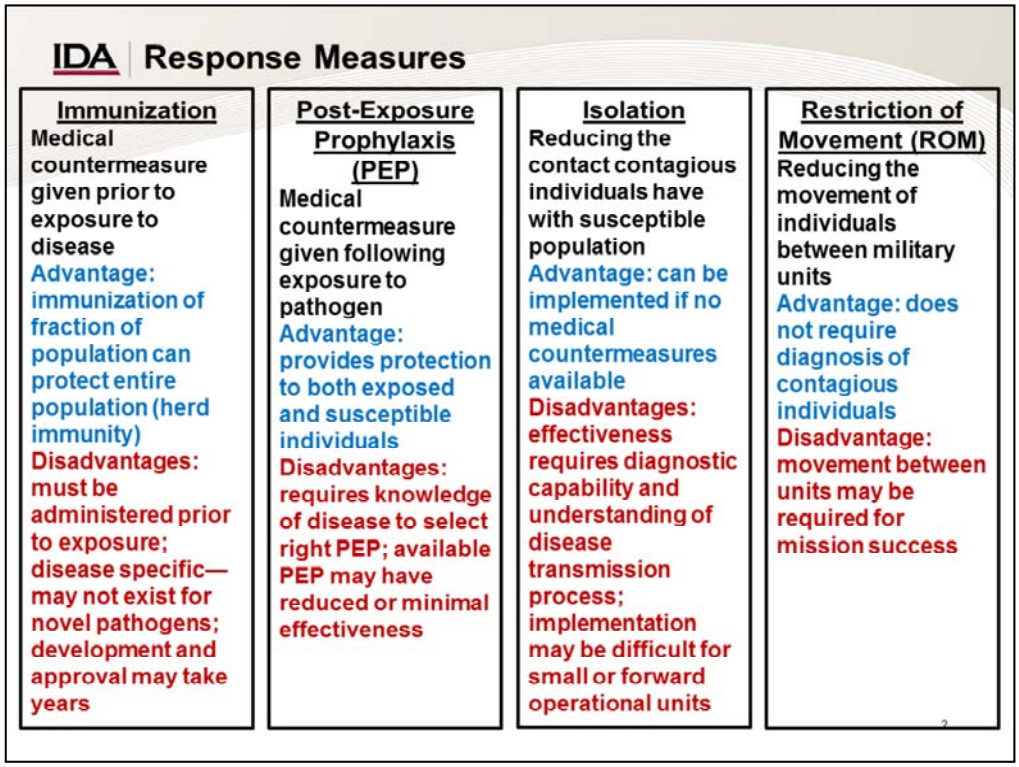
It seems that every day we are reminded of the dangers of newly emerging infectious diseases. Whether it's the Zika virus in South America or the Ebola outbreak in West Africa, Emerging Infectious Diseases are a global humanitarian and economic concern. Additionally, these diseases have the potential to substantially disrupt military operations. This potential is the focus of recent research conducted for the U.S. Department of Defense by the Institute for Defense Analyses in Alexandria, Virginia. The portion of the research I'll discuss today addresses the question: what responses can be taken to mitigate the effects of an Emerging Infectious Disease on a military population? And which response would be most effective?



But before discussing EID response measures, I want to quickly go over what exactly I mean when I say Emerging Infectious Disease. Both the World Health Organization and the U.S. Centers for Disease Control consider a disease “emerging” if it falls into one of three categories: Novel pathogens that have never appeared before, such as SARS. Variants of diseases that already exist, either seasonal variants like influenza or antibiotic resistant strains of diseases. The third and final category are known diseases appearing for the first time in a new population or geographic region (Ebola in West Africa).

Perhaps the greatest challenge in responding to an EID is the lack of knowledge about the disease. When and where will the disease emerge? What is the pathogen, how does it behave, what is its mechanism of action? How does it manifest, progress, and transmit in humans? And finally, how responsive is the disease to approved and fielded medical countermeasures?

The ability to respond to an EID outbreak is substantially reduced by these unknown elements. Which leads us to the questions at hand, given this vacuum of knowledge about the disease, what types of response measures will have the greatest ability to mitigate the effects of an EID outbreak in a military population?



To answer that question, we first must know what potential response measures exist that could be used to mitigate the effects of an EID outbreak.

The first response is immunization, which includes vaccine and pre-exposure prophylaxis. The benefits of immunization are apparent, if a large portion of the population is not susceptible to the disease, then an outbreak will not pose a major risk. Furthermore, due to the benefits of herd immunity, only a fraction of a population must be immunized in order to protect everyone. That said, immunizing a population is a difficult task. The drug must be researched, approved, and administered before exposure occurs, a process that can take years. Often times, vaccines are disease specific, so it's impossible to research a vaccine for a disease that has yet to emerge.

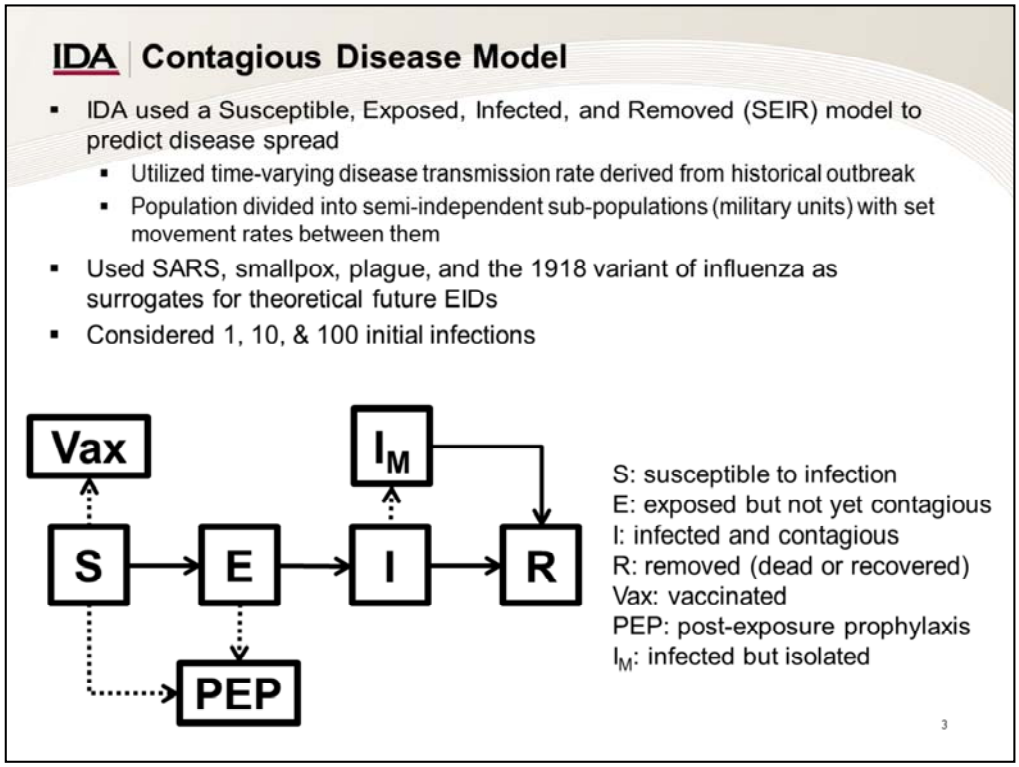
The second response measure is post-exposure prophylaxis (PEP). Unlike immunization, these medical countermeasures are administered following exposure. Not only can they reduce an individual's susceptibility to the disease, they also can protect those who have already been exposed. However, knowing what PEP to administer requires knowledge of the disease—which, as I said earlier, is often limited or non-existent for EID. Moreover, existing PEP may not be effective against emerging diseases. In the case that a disease-specific countermeasure is required, then you are stuck with research and regulatory problems similar to developing a vaccine.

In the context of this work, isolation refers to the isolation of contagious individuals after they have been diagnosed with the disease. The advantage of this procedural control is that it can be implemented in the absence of medical countermeasures. However, it requires a diagnostic capability and an understanding of the disease transmission process—both of which might not be fully developed for a newly emerged disease. Additionally, effectively isolating an individual in certain military environments may not be possible.

The final response measure is restricting the movement of individuals between military units. Like isolation, this procedural control can be implemented in the absence of medical countermeasures. However, unlike isolation, restriction of movement does not require diagnostic capabilities. The problem with restriction of movement, is that it has the potential to disrupt military operations.

While these responses are not a complete list of available response options, they represent the range of possible options.

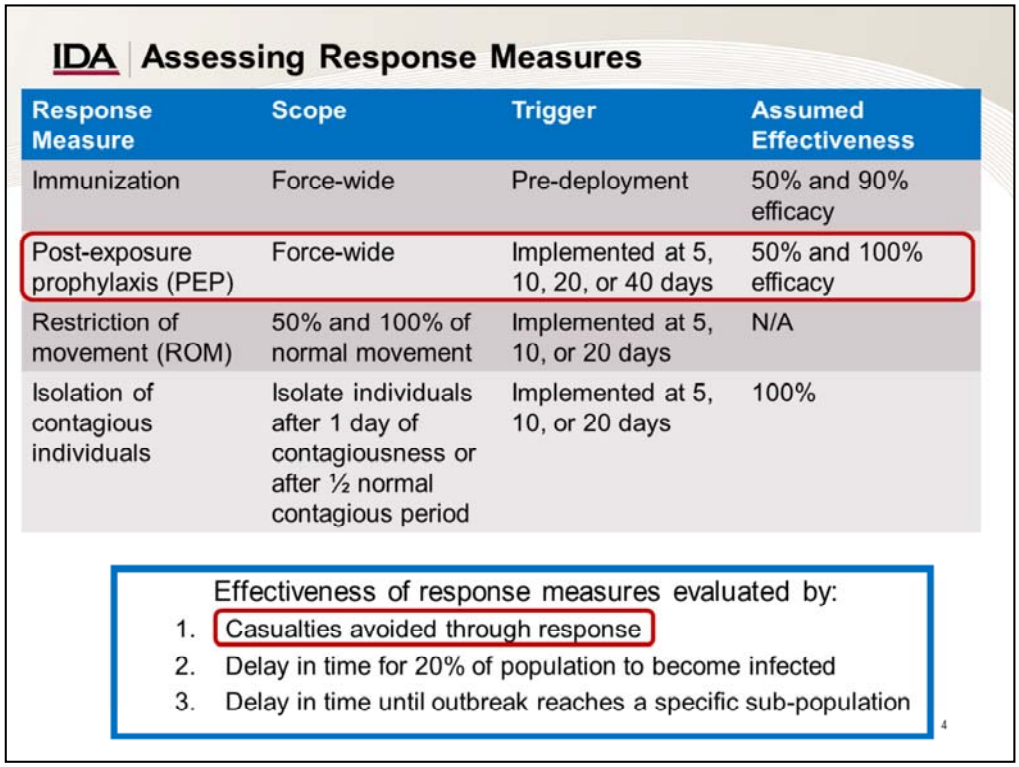
Each response requires a different level of knowledge about the emerging disease in order to implement, and therefore, the challenge is to gain enough knowledge about the disease in time to implement an appropriate response.



To assess how effective each of the 4 response measures is at mitigating the effects of an EID, IDA researchers developed a contagious disease model. We used a Susceptible, Exposed, Infected, and Removed (SEIR) model to predict the spread of disease given the 4 response measures.

The model utilizes a time-varying disease transmission rate that was derived from historical outbreak data for a given disease. The population in which we modeled the disease spread was divided into semi-independent sub-populations with set movement rates between them. The population was considered in this manner—instead of as a single population—to model restrictions of movement.

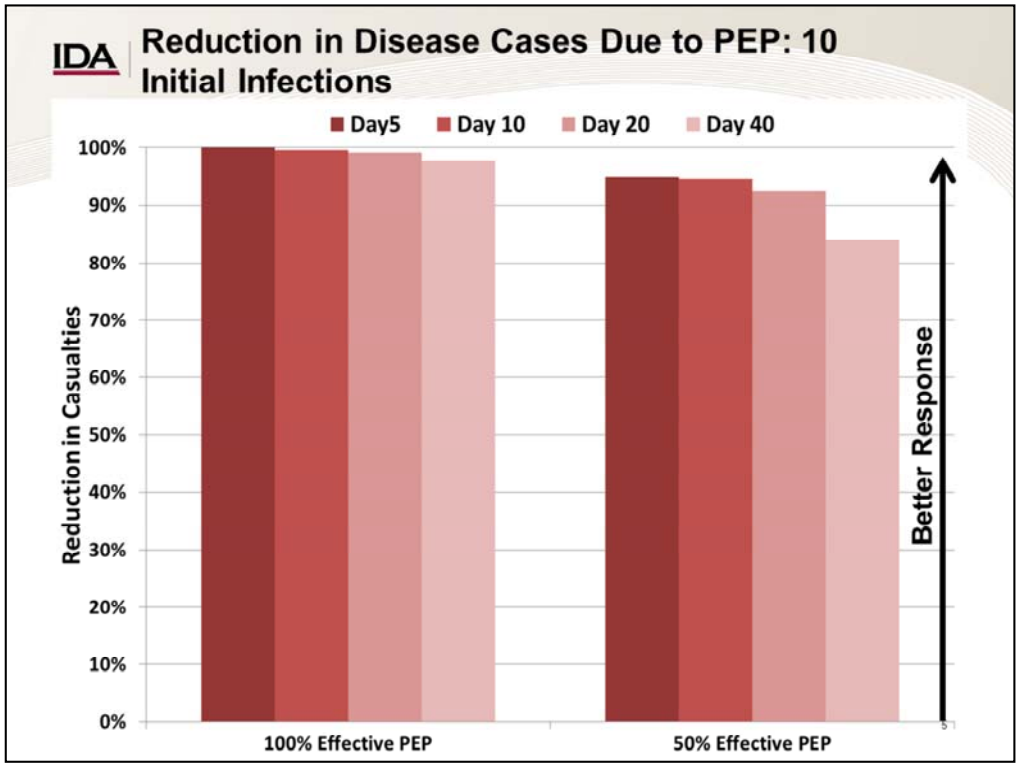
Because the disease transmission rates used in the model are derived from historical outbreak data, it is not possible to model a “made up” yet-to-have-emerged disease. Therefore, we used SARS, smallpox, plague, and the 1918 variant of influenza as surrogates for theoretical future EIDs. While fielded vaccines or post-exposure prophylaxis may not currently be available for all 4 of these diseases, we will postulate their existence to allow us to investigate how effective the response measures could be.



To assess the effect of the 4 response measures, we modeled each parametrically.

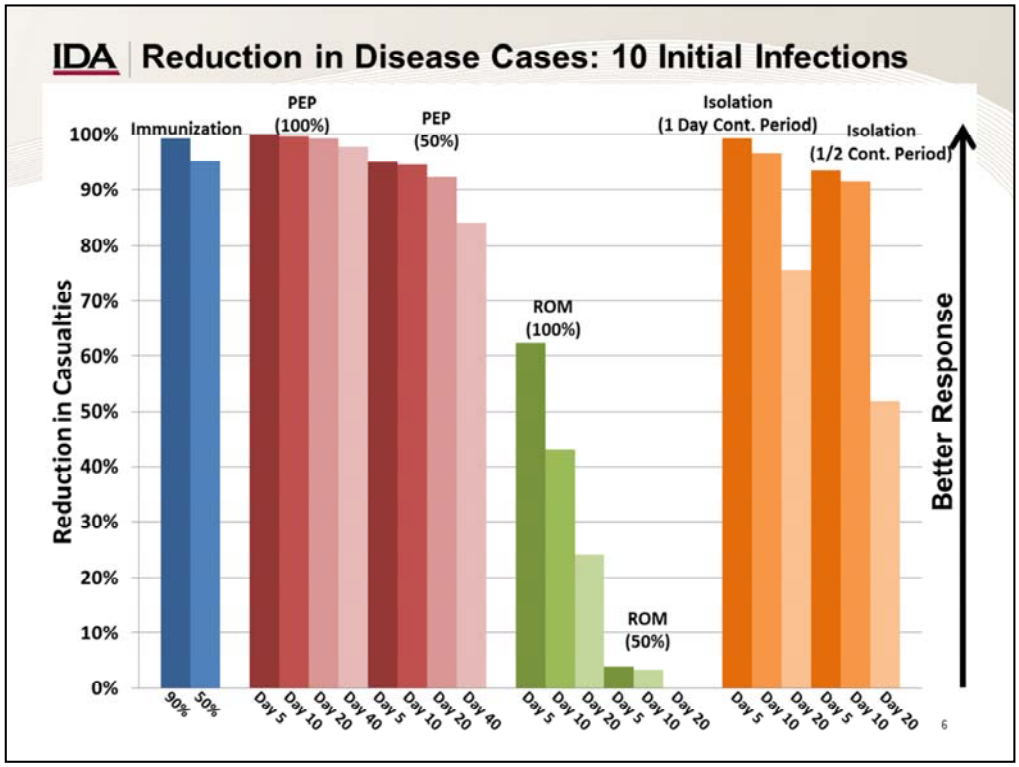
To quantify the efficacy of the 4 response measures, we looked at three measures of effectiveness. First, how many casualties were avoided by executing the response. Second, how long did the response measure delay the time required for 20% of the population to become infected. Third and finally, how long did the response measure delay the time it took for the outbreak to reach a specific sub-population or military unit.

For this presentation, I am going to show only a subset of the results of the analysis, and we will start by looking at casualties avoided through the administration of PEP.



As you may recall, we modeled PEP as being either 100% effective or 50% effective. Additionally, we looked at PEP being administered 5, 10, 20, and 40 days following the start of the outbreak. Note that this figure is showing the reduction in casualties, so a 100% reduction means the response measure reduced the total number of casualties to zero, while a 0% reduction is casualties means the response measure had no effect on the number of casualties. As we see here, PEP is highly effective at reducing casualties. Even when delayed by multiple weeks, the response greatly reduces the number of casualties caused by the EID. Another note is how well a PEP with reduced effectivity works at preventing casualties. We can see that reducing the effectiveness of the PEP by 50% does not result in half a reduction in casualties. This is a promising indication for EIDs that are resistant but not completely immune to existing medical countermeasures.

We see that PEP is an effective response measure, so let's look at how it compares to the other three response measures we investigated.



This figure is nearly identical to the previous figure, but in addition to PEP, it shows immunization, restriction of movement, and isolation.

Starting with immunization—similar to trends we saw in PEP—it's highly effective at reducing casualties even when the immunization itself is only partially effective. This illustrates the idea of herd immunity, that immunizing part of a population can protect the entire population.

Jumping to isolation, we see that it too is relatively effective, but only if administered early. The longer you wait before implementing, the less effective it is.

On the other hand, restriction of movement is the worst response measure at reducing casualties. Even in the best-case scenario we modeled—total movement restriction 5 days after the start of the outbreak—it only reduces the total casualties to a half. Furthermore, partial restriction of movement was almost entirely ineffective at reducing casualties.

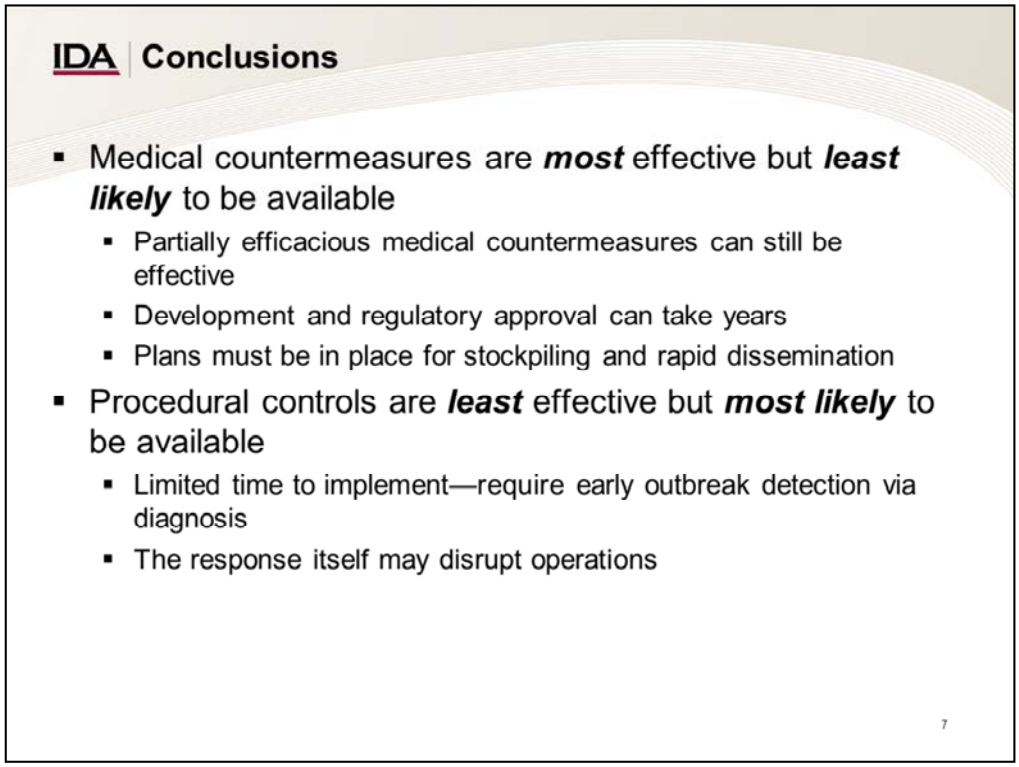
As a reference point, the average latent period of SARS is 8 days. So in order to implement a countermeasure on day 5, you must recognize that an outbreak is occurring before the majority of the initial infections have developed symptoms.

So it's clear that not all of our 4 response measures are equally effective at mitigating the effects of the outbreak.

In fact, you can rank the 4 measures based on their ability to mitigate the effects of an EID. It's clear that the medical countermeasures (immunization and PEP) were the most effective response at preventing casualties. That said, medical countermeasures also require the greatest amount of effort to develop and implement.

In addition to having the greatest effectiveness, the two medical countermeasures also had the lowest cost of delay. This refers to how quickly the response becomes ineffective when delayed.

Finally, the procedural controls—isolation and restriction of movement—are more operationally disruptive. Yes, there will likely be some disruptive medical side effects to the administration of the medical countermeasures, but they are not nearly as disruptive as isolating large portions of your force, or restricting the movement between units, both of which would pose significant challenges for the conduct of operations.



To conclude, medical countermeasures are the most effective at mitigating the effects of an EID outbreak. Even a countermeasure with a substantially reduced efficacy can still greatly reduce the number of casualties. That said, these countermeasures are the least likely to be available. Development of a disease-specific vaccine or treatment can take years. So there is a strong incentive to identify EIDs that could have an operational impact as soon as possible after the point of emergence and begin investment in disease characterization and development of countermeasures.

If medical countermeasures are not available, a very responsive disease surveillance system must be in place to detect an outbreak rapidly enough to enable an effective procedural control. As we saw on the previous slide, ROM and isolation must be implemented within a few days of the start of the outbreak. This means that you would have to detect the outbreak based on only a couple of symptomatic individuals in a population of hundreds or thousands. Compound that with the issue that many EIDs of concern will likely exhibit non-specific early symptoms and the problem becomes a true challenge. Furthermore, even if you can implement these procedural controls in time, the response itself will likely be highly disruptive to the operation. In another part of the research, we found that a deployed military population may have 20-25% of the population move between locations every day. So the response that reduces that movement to zero is certain to be disruptive.

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QUESTIONS?

Additional portions of this study are presented in poster IP 08:
"The Impact of Emerging Infectious Diseases on Military Operations"

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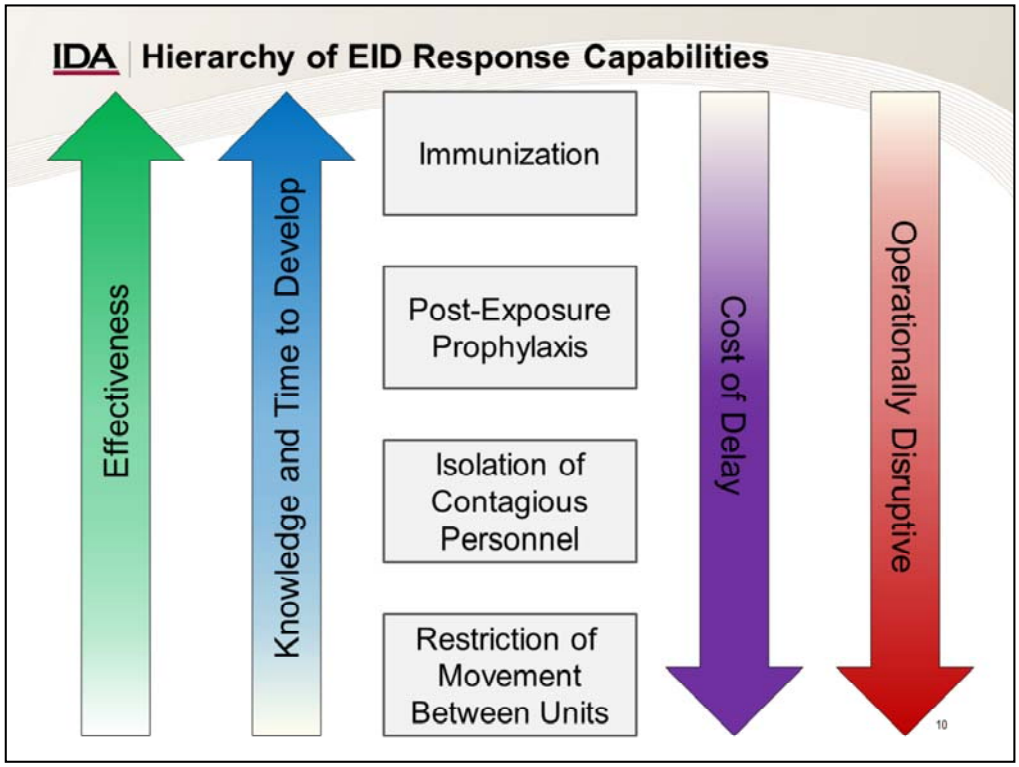
Parameter*	SARS	1918 Influenza	Smallpox	Plague
Incubation Period (days)	Triangular distribution (μ=8.5,σ=3.1)	Lognormal distribution (μ=1, σ=1)	Normal distribution (μ=15, σ=2.0)	Normal distribution (μ=3, σ=0.66)
Contagious Period (days)	Triangular distribution (μ=9.3,σ=2.3)	Lognormal distribution (μ=5, σ=1)	Normal distribution (μ=11,σ=2.23)	Normal distribution (μ=3, σ=0.83)
Case Fatality Rate	0.18	0.06	0.35	0.92

*Disease parameter value derived from historical outbreak data; documentation available upon request from the authors



In fact, you can rank the 4 measures based on their ability to mitigate the effects of an EID. The previous figure indicates that the medical countermeasures (immunization and PEP) were the most effective response at preventing casualties. That said, they also require the greatest amount of effort to develop and implement. Compare the time it takes to research and develop a new vaccine to the time it takes to restrict movement between military units. It's years vs. nearly instantaneous.

In addition to having the greatest effectiveness, the two medical countermeasures also had the lowest cost of delay. This refers to how quickly the response becomes ineffective when it is delayed.

Finally, the procedural controls—isolation and restriction of movement—are more operationally disruptive. Yes, there likely will be some disruptive medical side effects to the administration of the medical countermeasures, but they are nowhere near as disruptive as isolating large portions of your force, or restricting the movement between units. These responses will pose significant challenges for the conduct of operations.

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