An Integrated Simulation of Pandemic Influenza Evolution, Mitigation and Infrastructure Response

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Abstract–

Decision makers, faced with highly complex alternatives for protecting our nation's critical infrastructures must understand the consequences of policy options before they enact solutions to prevent and mitigate disasters. An effective way to examine these tradeoffs is to use a computer simulation that integrates high level representations of each infrastructure, their interdependencies and reactions to a variety of potential disruptions.

To address this need, the Critical Infrastructure Protection Decision Support System (CIPDSS) project, funded by the Department of Homeland Security Science and Technology Directorate (DHS S&T), has developed a decision support tool that provides insights to help decision makers make risk-informed decisions. With the addition of a disease progression simulation, the CIPDSS tool has a unique ability to provide a high-level, integrated analysis of a pandemic influenza outbreak while representing the impact on critical infrastructures. This simulation models the time-dependent evolution of the disease and can be calibrated to prior data or to other higher fidelity models as appropriate. Mitigation options such as the use of antivirals and vaccines as prophylaxis, treatment or some combination as well as quarantine options can be assessed. Special attention is given to impacts to the population through sickness, targeted quarantine, or fear-based self-isolation and the resulting impacts on critical infrastructure operations.

INTRODUCTION

In the 20th century, three influenza pandemics occurred in the United States with varying degrees of impact depending on the virulence of the influenza. Each pandemic resulted in considerable death, approximately 500,000 in 1918, 70,000 in 1958 and 34,000 in 1968. Currently there is significant concern regarding the impacts of pandemic influenza on the United States population and economy. A key factor in the extent of the economic losses could be disruptions in infrastructure services. To analyze the implications of an influenza pandemic on human health, infrastructure services, and the economy, the Department of Homeland Security directed the Critical Infrastructure Protection Decision Support System (CIPDSS) project [1] to study this important issue.

CIPDSS is a collaborative effort between Argonne National Laboratory, Los Alamos National Laboratory, and Sandia National Laboratories funded by the Infrastructure/ Geophysical Division of the DHS Science and Technology Directorate. CIPDSS has developed and uses a set of interdependent infrastructure models, integrated disruption models and a decision-analytic framework for assessing the trade-offs between alternative protection strategies.

The approach for performing the analyses in this phase of the study is shown in Figure 1. First, an epidemiological model was used to characterize the human health impacts of a postulated 1918-like pandemic influenza, including a representative set of alternative scenarios of societal response to the disease and intervention strategies. The epidemiological results were used to predict workplace absenteeism figures and to analyze impacts on infrastructure operations. Finally, macroeconomic impacts were estimated combining absenteeism, mortality, infrastructure service impacts.

CIPDSS includes consequence models for all critical infrastructures, which are linked via their strongest interdependencies and can be coupled between national and metropolitan geographic scales. The models can be driven by a variety of different scenario modules, which can trigger disruptions in one or more infrastructures that may then cascade through the interdependent infrastructure system, depending on the magnitude of the disruption, choice of mitigation or intervention strategies, and the robustness of the impacted infrastructures. The consequence models are coupled to a configurable decision model that assists decision makers with evaluating complex trade-offs between alternative mitigation and intervention strategies.

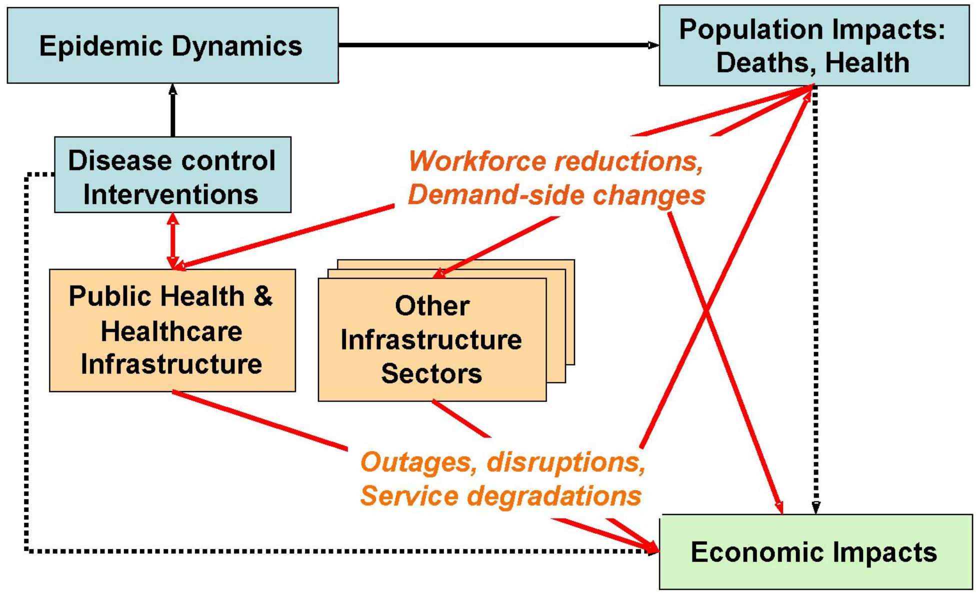

Figure 1: Pandemic Influenza Impacts on Population, Infrastructures and the Economy

PANDEMIC INFLUENZA

Influenza is caused by RNA orthomyxoviruses. Only the types "A" and "B" influenza viruses are known to cause epidemic human disease, with pandemic disease limited to influenza type A viruses [2]. Occasionally, a new strain of influenza emerges that is easily transmissible between humans and for which the global human population has little or no underlying immunity. The result is a pandemic – that is, the worldwide spread of influenza. In 1997, an H5N1 influenza virus circulating in avian populations became highly pathogenic to domestic poultry. Additionally, humans in close contact with the infected birds become infected and suffered a high case fatality rate of over 50% [3]. There is concern that this strain could lead to a new pandemic if it becomes highly transmissible between humans.

The threat of a contagious-disease pandemic to business and critical infrastructure continuity deserves careful consideration. It is different from most other threats for the following reasons:

1. Worldwide impact — unlike many threats that are localized, a pandemic has the potential to impact operations simultaneously across North America and around the world.
2. Duration — an influenza pandemic could severely disrupt operations for six to eight weeks or even longer. Some level of fear would spread through the population prior to the actual outbreak and the actual "sickness" period would range from a day to a week for most individuals.
3. Mortality — the assumed mortality rate in this analysis is 2 percent of symptomatic cases worldwide. Even a low-end mortality rate would cause severe disruption for employees who lose family.

This analysis uses a modified Susceptible-Exposed-Infectious-Recovered (SEIR) epidemiology model (e.g., Hethcote [4]) to represent the spread of an influenza virus with characteristics similar to that responsible for the 1918 pandemic. In conjunction with NISAC, the National Infrastructure Simulation and Analysis Center, seven disease scenarios were modeled for Phase 1, representing a variety of potential population response and intervention strategies. Aggregate human health impacts were calibrated to higher resolution epidemiology results from the NISAC-sponsored analysis. The calibration enables the use of the integrated CIPDSS SEIR model to drive the coupled infrastructure models to assess the cascading effects of the spread of the disease on each infrastructure sector.

For this analysis we sought to use the most current data and resources on past pandemics, National policy plans and guidelines, current vaccine and antiviral breakthroughs, and the biology of the current H5N1 influenza strain with respect to humans.

PREVENTION AND MITIGATION

Disease spread is a dynamic process that is controlled by the number of contacts between susceptible and infected populations and the transmissibility of the disease. The primary strategies for slowing and/or stopping the spread of infectious viral diseases are to stimulate immunity (vaccination), reduce the severity and transmissibility (prophylaxis), and reduction in contact rates (e.g., social distancing). Each of these approaches is discussed in turn.

The primary defense against acquiring influenza is vaccination. Vaccination for seasonal influenza has been shown to prevent disease, reduce the rates of complications such as pneumonia, and reduce the rates of hospitalizations and deaths. Children are significant players in the transmission of influenza, and vaccination reduces the spread to their contacts, thereby reducing the spread of the disease in the household and the community [5]. For healthy working adults, an important burden of influenza is the number of days of restricted activity or bed rest, lost workdays, and number of healthcare visits.

However, because of the time required under current vaccine production techniques, vaccines may not be available at the onset. Currently, the time between identification of the candidate vaccine strain and production of the vaccine for distribution to the population is estimated to be approximately 6 months [6, 7]. As a result, considerable effort is underway to develop better methods to produce vaccines, such as the development of cell-based or generic vaccines. In addition, candidate vaccines for the H5N1 strain are under development. The goal of these vaccines is to provide a sufficient immune response using the smallest amount of antigen in a single dose [6].

Antiviral drugs are potentially useful in the prophylaxis and treatment of seasonal influenza. In the event of an influenza pandemic, antiviral drugs will play an important role in controlling the pandemic. It is likely that a strain-specific vaccine will not be available at the start of a pandemic; therefore, antiviral drugs may serve as the first line of defense against a pandemic [6].

The U.S. stores a limited supply of influenza antiviral medications in the Strategic National Stockpile (SNS) for emergency situations. By the end of fiscal year (FY)06, the federal government planned to have 20 million courses of antivirals stockpiled, with an additional 24 million courses purchased by the end of FY07 and 80 million total doses purchased by the end of FY08. In addition to the federal purchases, the federal government is subsidizing state antiviral purchases, which may have added up to 31 million additional courses of antivirals by the end of FY06.

High infectiousness and the number of contacts people have on a daily basis are the two most important influences on the transmission of an infectious disease. Zones of high infectious contact are often centered on children and teenagers within a community's social network [8]. Targeting this zone can protect the community at large.

DISEASE SCENARIOS

A set of seven scenarios was developed to represent existing mitigation plans as well as provide a broad characterization of possible intervention strategies using different implementations of government and population scale mitigation strategies.

Table 1: Epidemiologic Scenarios

Scenario	Description
Baseline	Constructed based on the National Strategy for Pandemic Influenza. Represents a limited response worst case scenario.
Fear-Based Self Isolation	No government intervention but individuals self isolate out of fear.
NIH's Targeted Layered Containment (TLC)	A multi-tiered intervention strategy. A best case scenario. Therapeutic antiviral treatment administered to symptomatic cases with social distancing.
NIH's TLC Lite	Same as TLC but with no school closure or liberal leave.
Antivirals	The antiviral scenario specifies a stockpile of antiviral courses for persons diagnosed their household contacts.
Partially Effective Vaccine	Vaccination with an unmatched vaccine. The vaccine is half as effective as one formulated specifically to the circulating strain.
Nominal Intervention Strategy	Strain-specific vaccine comes five months after the first cases; antivirals are given to diagnosed cases and their household contacts; a reduction in transmission and contacts from behavior modifications.

MODELS

The technical approach used to analyze the effectiveness of alternative scenarios of pandemic influenza progression and intervention and to assess the impacts of these scenarios on infrastructure operations and the economy was to couple a set of submodels that represent infectious disease spread and intervention, population travel, labor, and infrastructure operations as shown in Figure 2. The population, population travel between regions, and infectious disease models interact to introduce the pandemic flu strain into the population and spread the disease across the nation. The population developing symptoms and needing treatment present a demand on the public health sector. Absenteeism and mortality also affect the functioning of the economy, although this is not shown here.

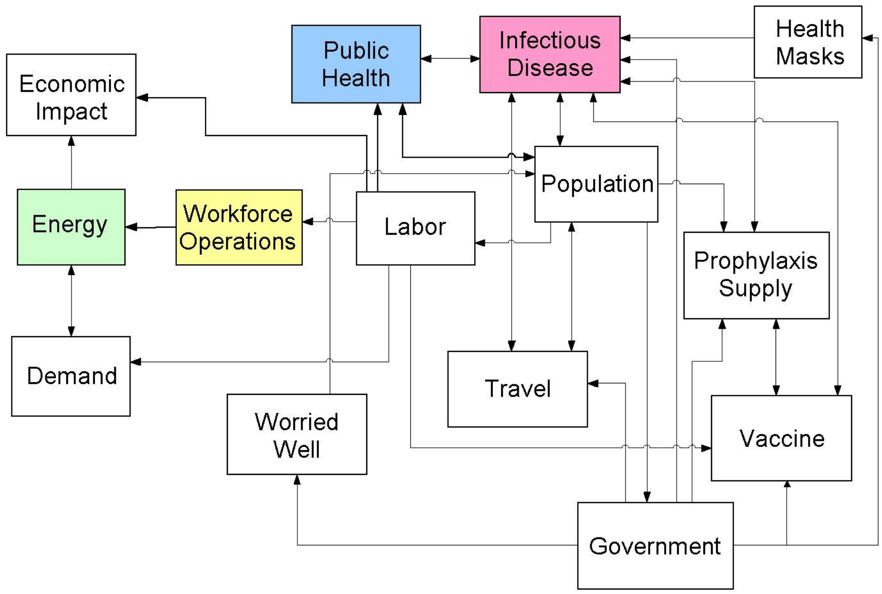

Figure 2: Major elements of the CIPDSS models used in the pandemic influenza impacts analysis

CALIBRATION PROCESS AND RESULTS

For this pandemic influenza analysis CIPDSS calibrated the infectious disease model to both the selected model inputs such as disease characteristics and the results of the NISAC analyses. Calibration of a priori model inputs included transmission characteristics, disease stage residence times, and a 2% overall case mortality rate. Calibration a posteriori then sought to match not only endpoint variables of EpiSimS such as total number of symptomatic cases, but also the entire epidemiological curve for most output variables of interest.

EPIDEMIOLOGY RESULTS

Cumulative illnesses from influenza varied from 1.5 million to 75 million among the seven scenarios (see Figure 3).

The most effective mitigation strategy was the TLC scenario. This scenario assumed that unlimited antivirals are available for therapeutic treatment of symptomatic cases, and prophylactic treatment of household members of diagnosed cases.

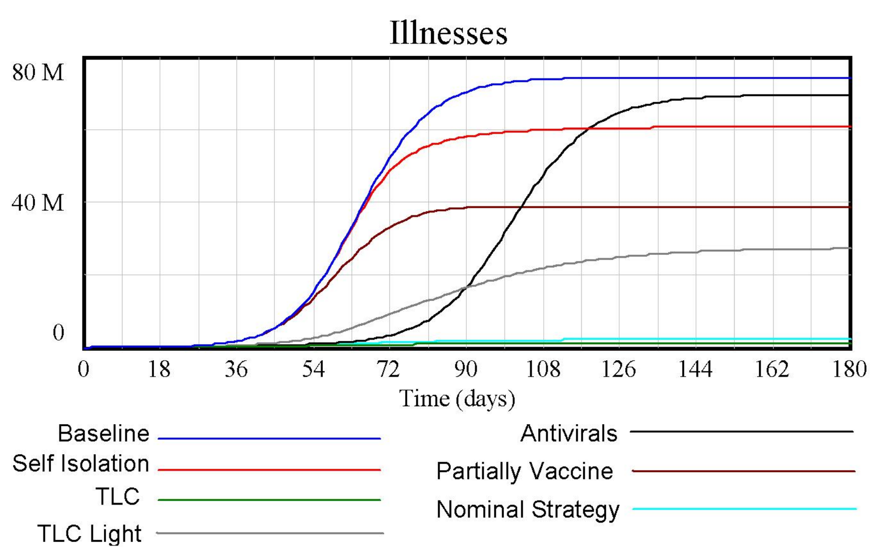

Figure 3: Cumulative influenza illnesses for each scenario

Likewise, the TLC strategy lowered the attack rate (the fraction of the population that becomes symptomatic) significantly below the estimated 20-30% attack rates for a pandemic outbreak.

PUBLIC HEALTH RESULTS

In the baseline scenario and some of the other scenarios, the public health sector is heavily overloaded due to huge demand for care as large numbers of people fall ill from the pandemic and many additional people think they might have the pandemic flu because of having other diseases with flu-like symptoms or simply because of fear (worried well). Furthermore, the ability of the healthcare system to provide care can decline significantly at the same time as the demand for care is increasing, because healthcare providers can also contract the disease or avoid work out of fear of contracting the disease. In the baseline scenario for this study, the peak absentee fraction due to pandemic flu is approximately 8.8% for healthcare providers, compared to 6.5% for the rest of the workforce.

Overloading of the healthcare system is expected to occur at all levels, from physicians' offices to emergency services to hospital care. According to planning assumptions for the severe scenario in the *HHS Pandemic Influenza Plan* (U.S. Department of Health and Human Service, http://pandemicflu.gov/state/antivirals.html), half of the people who become ill with the pandemic flu would be expected to seek outpatient medical care and 11% would need to be hospitalized. The high demand for hospital services is illustrated in Figure 4, which shows the simulated overall national hospital occupancy rate (ratio of hospital inpatients to available staffed beds) for the seven study scenarios. In the baseline scenario, the fear-based self-isolation scenario, the antiviral scenario, and the partially effective vaccine scenario, hospitals become fully occupied, and stay full for a much longer time than the pandemic itself lasts, as hospitals catch up with normal care that was delayed during the pandemic.

Hospital crowding is relieved somewhat sooner in the fear-based self-isolation scenario than in the baseline scenario, and even earlier in the partially effective vaccine scenario, because slightly fewer people get sick. The antiviral scenario is similar to the baseline scenario except that the use of antivirals delays the pandemic for about a month. In contrast, the anticipated intervention and idealized TLC strategies are effective in limiting the spread of the disease and so the healthcare system does not get overwhelmed in those scenarios. The TLC Lite scenario is in-between, with the hospitals being much more crowded than usual, but not completely full.

In the four scenarios with extreme healthcare overloading, there is not enough hospital capacity to accommodate all the people who get seriously ill. As a result, it is expected that many patients will be transferred to large temporary facilities for palliative care. The model simulations indicate that hospitals would handle about 4–5 million pandemic patients in those scenarios, and there would be a need for temporary facilities for an additional 1–3 million patients.

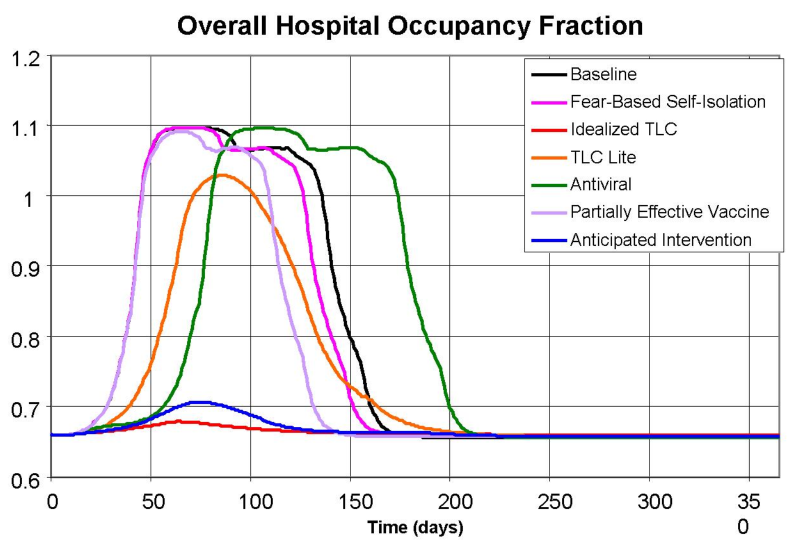

Figure 4: Simulated national hospital occupancy fraction

ABSENTEEISM

The primary mechanism for a pandemic to impact the supply of infrastructure services is through absenteeism and mortality and the resulting potential shortages in labor. Representative results for the total fraction of workers unavailable nationally are given in Figure 5. Results have a similar shape for the larger sub-regions (e.g., FEMA regions, NERC regions, NG regions, etc) that characterize the spatial resolution of this model. Note that the fear-based self-isolation scenario has the largest peak absenteeism rate. The anticipated strategy has a peak about half the size of the Fear-40 scenario, but is wider so that absenteeism is sustained over a longer time.

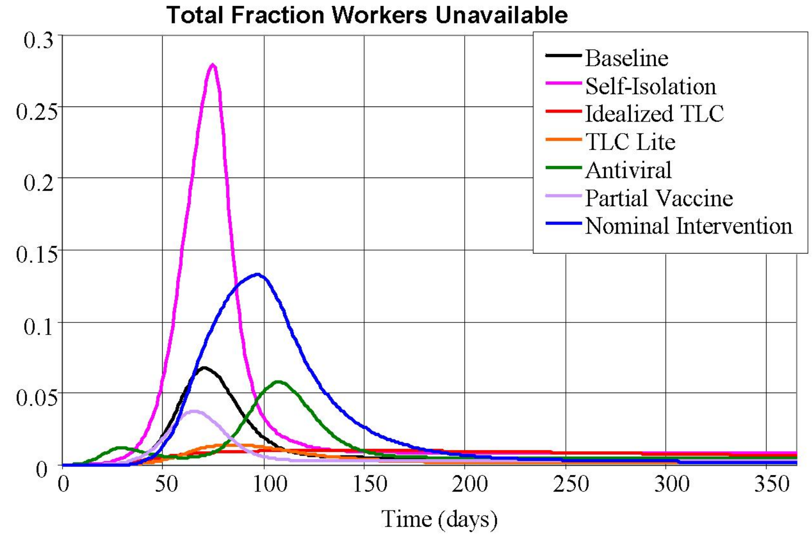

Figure 5: Total fraction of workers unavailable for each scenario

CONCLUSIONS

Seven disease scenarios were modeled representing a variety of potential population response and intervention strategies. Aggregate human health impacts were calibrated to higher resolution epidemiology results from the NISAC-sponsored analysis.

The public health and population response impacts of the pandemic result in labor-supply shocks and, additionally, provide a demand shock for the national healthcare system. Existing models were modified to represent the impacts of the labor-supply and healthcare shocks, and the combined models were used to estimate human health impacts of an unmitigated pandemic, costs and benefits of selected population responses and intervention strategies, impacts on infrastructure operations, and economic costs.

From the perspective of human health impacts, the most effective mitigation strategy was the TLC scenario. The TLC scenario assumed that unlimited antivirals are available for therapeutic treatment of those that are symptomatic, and prophylactic treatment of household members of diagnosed cases. Likewise, the TLC strategy lowered the attack rate significantly below the estimated 20-30% attack rates for a pandemic outbreak. In a number of scenarios, the public health sector is heavily overloaded due to huge demand for care as large numbers of people fall ill from the pandemic and many additional people think they might have the pandemic flu. Furthermore, the ability of the healthcare system to provide care can decline significantly at the same time as the demand for care is increasing, because healthcare providers can also contract the disease or avoid work out of fear of contracting the disease.

This work lays the foundation for the use of CIPDSS models in uncertainty/sensitivity analyses in follow-on work already underway.

[1] Bush, B., Dauelsberg, L., LeClaire, R., Powell, D., DeLand, S., and Samsa, M., "Critical Infrastructure Protection Decision Support System Project Overview," Los Alamos National Laboratory, LA-UR-05-1870, Los Alamos, New Mexico, July 2005.

[2] U.S. Department of Health and Human Services website, "Antivirals-State Allocations," accessed October 16, 2006, http://pandemicflu.gov/state/antivirals.html.

[3] World Health Organization. "Epidemiology of WHO-confirmed human cases of avian A (H5N1) infection," Weekly Epidemiological Record 81, 249–260 (2006).

[4] Hethcote, H. W., "The Mathematics of Infectious Diseases," SIAM Review 42 (4), 599–653 (2000).

[5] Meltzer, M. I., Neuzil, K. M., Griffin, M. R., and Fukuda, K., "An Economic Analysis of Annual influenza Vaccination of Children," Vaccine 23, 1004–1014 (2005).

[6] Monto, A. S., "Vaccines and Antiviral Drugs in Pandemic Preparedness," Emerging Infectious Diseases 12, 55–60 (2006).

[7] Schwartz, B. and Gellin, B., "Vaccination Strategies for an Influenza Pandemic," Journal of Infectious Diseases 191, 1207–9 (2005).

[8] Glass, R.J., Glass, L., Beyeler, W.E. and Min, H.J., "Targeted Social Distancing Design for Pandemic Influenza," Emerging Infectious Diseases 12, 1671–81 (2006).