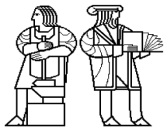

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STOPPING PANDEMIC FLU:

GOVERNMENT AND COMMUNITY INTERVENTIONS IN A MULTI-COMMUNITY MODEL

Karima R. Nigmatulina[1] and Richard C. Larson[2]

[1]Operations Research Center,
Massachusetts Institute of Technology,
Cambridge, MA, 02139, USA

[2]Engineering Systems and Civil and Environmental Engineering,
Engineering Systems Division,
Massachusetts Institute of Technology,
Cambridge, MA, 02139, USA

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Karima R. Nigmatulina [a], Richard C. Larson [b]

[a] Operations Research Center, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA

[b] Engineering Systems and Civil and Environmental Engineering, Engineering Systems Division, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA

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Abstract

Focusing on mitigation strategies for global pandemic influenza, we use elementary mathematical models to evaluate the implementation and timing of intervention strategies such as travel restrictions, vaccination, social distancing and improved hygiene. A spreadsheet model of infection spread between several linked heterogeneous communities is based on analytical calculations and Monte Carlo simulations. Since human behavior will likely change during the course of a pandemic, thereby altering the dynamics of the disease, we incorporate a feedback parameter into our model to reflect altered behavior. Our results indicate that while a flu pandemic could be devastating; there are coping methods that when implemented quickly and correctly can significantly mitigate the severity of a global outbreak.

Keywords

stochastic & simulation modeling, pandemic flu, dynamic feedback, OR in health services, heterogeneity, behavior changes

Introduction

Influenza pandemics have occurred intermittently over centuries killing millions of people worldwide. When a novel influenza virus emerges from the animal or avian reservoir humans do not have immunity to this new strain and so everyone is susceptible. While medical advances over the past century have been significant, it still takes four to six months, sometimes more, to develop and produce sufficient vaccine. Thus, if a new flu virus emerges, it can spread quickly throughout the world causing a pandemic. Such a disaster would not only place extraordinary and sustained demands on the public health and medical care systems, but will also burden the providers of essential services and strain the operations of all businesses. Federal government forecasts estimate that up to 40% of the US population may be absent from their daily routines for extended periods of time as a result of illness or care-giving responsibilities [IPNSPI, (May 2006)]. High rates of worker absenteeism could in turn affect critical infrastructure, including the operations of water treatment facilities and power plants, while efforts to slow the spread of disease could limit the availability of food. A pandemic would impact all sectors of society.

The U.S. National Intelligence Council's 2020 Project "Mapping the Global Future" identified a flu pandemic as the single most important threat to the global economy [Karesh, Cook (2005)]. A report from the Lowy Institute for International Policy concluded that even a very mild pandemic, like the 1968-9 version, would result in a global economic loss of $330 billion and a human loss of 1.4 million [McKibbin (February 2006)]. A catastrophically severe 1918 version is forecasted to wipe out $4.4 trillion of global economic output and kill more than 140 million people [McKibbin (February 2006)]. The potential number of deaths is greater than those forecasted from a nuclear exchange between two warring nations.

The current most discussed pandemic threat is caused by the H5N1 strain of the Influenza A virus which has resulted in an outbreak of avian influenza in Asia, Africa and Europe. The virus has infected birds in over 35 countries and has resulted in the deaths, through illness and culling, of over 200 million birds across Asia. Various control measures have been attempted, but the virus persists and is endemic in Southeast Asia, found in long-range migratory birds, and is unlikely to be eradicated soon. The H5N1 virus is able to infect a wide range of hosts, and as of August 31st 2007 has been reported to have infected 327 people in twelve countries, resulting in 199 deaths [WHO (August 2007)]. While this virus has not shown an

ability to transmit efficiently between humans, there is concern that it will acquire this capability through genetic mutation or exchange of genetic material with a human influenza virus. Even if the currently circulating H5N1 virus does not result in the next human pandemic, evidence suggests that a different influenza strain is likely to emerge and cause the next catastrophic pandemic. For example: H9N2 infected children in China in 1999 and 2003; H7N2 caused infections in New York and Virginia in 2002 and 2003; and H7N3 infected poultry workers in Canada in 2004[CDC (2005)]. In 2003 H7N7 infected more than 1,000 people in the Netherlands, even passing from human to human [Ensernik (2004)]. Overall, the National Academy of Sciences, CDC and chief medical personnel across the world agree that an influenza pandemic is only a matter of time [Gerberding (2005), Car-Brown(2005), Knox(2005)].

The potential magnitude of this disaster requires advance planning, early preparedness and rapid action after detection of efficient transmission of a new and lethal virus. During the past few years policymakers have begun to realize the severity of this threat, and preparedness plans have started to develop across many layers of government. The US Department of Health and Human Services issued guidelines in November 2005, but left it to the states to make specific plans, indicating that states shouldn't rely of the federal government for much help during a pandemic. States have released versions of their pandemic plans, but most states do not include personal contact-avoidance or other more nonpharmacologic containment steps [Holmberg (2006), HHS (2007)]. One authority was even quoted saying that "short of obtaining [antiviral] drugs, there isn't much we can do to prepare" for a pandemic [Weaver (2005)]. To explain this omission, policymakers point to the lack of epidemiologic data proving the effectiveness of nonpharmaceutical community interventions. However, evidence from the SARS outbreak indicate that improved hygiene, masks and other behavioral changes decreased the spread of respiratory disease by 90% [Lo (2005)]! Modeling these disease spread processes helps us understand the potential effect of interventions before the flu hits. The goal is to help provide decision makers with a systematic approach to evaluating and comparing the effectiveness of various government imposed containment strategies and voluntary behavioral changes.

In this paper, we review the implications and then build on Larson's model [Larson (2007)] to consider the spread of infection between several loosely linked communities. After adding this spatial structure, we discuss the effectiveness of more complex and realistic control

strategies and consider the consequences of reactive behavioral changes. The analysis of imposed interventions includes the evaluation of travel restrictions' efficacy in stopping the spread of the virus to neighboring communities. We also consider different distribution strategies of limited vaccine. Since people are likely to alter their daily behavior based on the information they receive regarding the extent of the infection, we propose a unique approach to incorporating human reaction into our model and then analyze its impact. After examining each of these factors individually we compare and consider their combined potential in decreasing the extent of the outbreak. Our results indicate that with proper planning, even without any vaccines or anti-virals, we can make a difference in the course of the next pandemic.

1. Background

1.1 Literature Review

The types of models that have been used to describe the spread of infection range from basic differential equations models to detailed stochastic agent based simulations. One of the most widely used approaches relies on one specific parameter for the description of infection spread – the basic reproductive number R_0: the average number of infections a typical infectious individual will generate in a fully susceptible population [Diekmann (1990)]. An infection can grow in a fully susceptible population if and only if $R_0>1$ [Hethcote (2000)]. As the population of susceptibles is depleted the generation specific reproduction number, $R(t)$ reflects how many secondary infections will result from each newly infected individual on generation t. There are three types of approaches based on the basic reproduction number: models that express R_0 in terms of parameters that describe the virus' virulence and morbidity [MacDonald (1952), Hyman (2000)], models that fit the R_0 parameter to data using branching or martingale models [Becker (1974, 1989)] and models that use endemic equilibrium data to derive R_0 [Dietz (1975, 2002)]. While using $R(t)$ or R_0 provides a computationally intuitive basis for describing disease dynamics, this approach neglects important heterogeneity and stochasticity complexities [Eubank (2004), Larson (2007)] . Unfortunately, while R_0 has some benefits, it has often been a limiting modeling approach that many adhere to without question.

Many recent models have incorporated information about social network structures in order to understand the impact of social mixing patterns. Network models can range from simple lattice and random mixing networks, to small-world graphs, to incredibly detailed social

networks where the nodes represent people, and edges represent specified relationships or interactions. These networks provide a backbone for stochastic Monte Carlo models that simulate how an infection could spread from one source node to the rest of the population. These studies have shown that the degree, betweenness and farness of nodes alter disease dynamics [Christley (2005)].

There are also stylized models of more realistic social networks such as the Glass et al. model. In their work all persons within each household were linked to each other with mean link contact frequencies of 6/day. Every person also belonged to 1 multiage extended family group with a mean link contact frequency of 1/day. Furthermore, mean link contact frequencies for children in a school are 6/day. Teenager classes, adult work, and gatherings of older adults result in 1 mean link contact per day. By incorporating these more realistic nuances the group found the importance of children mixing schools as a key driver of infection. Their dramatic finding was that children and teenagers who compose only 29% of the population are responsible for 59% of infection. This group did not rely on R_0, in fact they point out that the calculation of R_0 from small-community data such as theirs is ambiguous.

A significant portion of current research has taken this even further making use of the advancement of computer capabilities. For example, Los Alamos with the use of their supercomputer, initially created for nuclear weapons' study, models every individual within the US and study flu spread [German (2006)]. Using census data and transportation information they produced a complex program which simulated, at a very detailed level, the interaction of over 240 million "people" over 180 days. The modelers openly acknowledge that "the spontaneous public response to news of an approaching pandemic will affect social behavior in unpredictable ways." To reflect that in their simulation they implement various social distancing behaviors that are expected given an initial pandemic curve. The problem is that human reaction should reflect the updated epidemic, but this dynamic concept is not incorporated. As a result the social intervention strategies are terminated too early to be fully effective. The researchers' conclusions are that vaccines and antiviral drugs will be the salvation to the pandemic disaster; however, limiting contact between people through travel restrictions, quarantine and school closing will only buy time, perhaps enough time for vaccine production, but will not stop the epidemic.

Two other recently developed agent-based models attempt to predict the scenario that could occur in Southeast Asia where the disease is expected to commence. Ferguson et al.

conclude that as long as the virus was less transmissible than the 1918 flu, combining geographically and socially targeted prophylaxis and social distancing could stop a nascent pandemic[Ferguson (2005)]. Similar in intention, the Longini et al. group has similar findings [Longini (2005)]. Both works highlight the importance of early diagnosis and immediate treatment, the significance of proper timing is a shared finding that should sway policy makers' flu containment measures. Yet again these models do not attempt to model reactive human behavior changes because it is too unpredictable.

1. 2 Model Basics

In order to capture the complexities of a heterogeneous population, we follow Larson's approach and divide the population of each community into several groups based on their daily social activity levels. We will assume that face-to-face social contacts within each community will occur as a homogenous Poisson process with rate parameters dependant on the level of social activity. For the rest of the numerical calculations and simulations we split the population of each community into 3 groups: high, medium and low activity persons. Let us define:

λ_H^A = Average number of social contacts of a High activity person in Community A/day
λ_M^A = Average number of social contacts of a Medium activity person in Community A/day
λ_L^A = Average number of social contacts of a Low activity person in Community A/day
n_H^A = Initial total population of High activity persons in Community A
$n_H^{I\,A}(t)$ = Number of High activity infective & asymptomatic persons in Community A on day t
$n_H^{S\,A}(t)$ = Number of High activity susceptible persons in Community A on day t *

Let us clarify that throughout our work we define one day as one generation of the infectious period of the virus. One day in our model is closer to 2-3 actual days.

We initiate the outbreak with one infectious individual who spreads the disease during day 0. By the end of this day the initial seeder self-isolates, recovers or dies, and only the newly infected individuals spread the virus on day one. Evidence of self-isolating behavior has been observed in practice [Zeng (2002)] and reflects peoples' departure from the infectious category. An infected individual never reenters the susceptible population since people gain immunity if they survive the disease. This pattern continues for the rest of the outbreak.

* The remaining variables for each of the activity groups are defined according to the above established pattern.

From Larson's paper we know that for a random person on day *t* in Community A the probability that the next interaction will be with an infected individual is:

$$\beta^{A}(t) \equiv \frac{\lambda_{H}{}^{A} n_{H}^{I\ A}(t) + \lambda_{M}{}^{A} n_{M}^{I\ A}(t) + \lambda_{L}{}^{A} n_{L}^{I\ A}(t)}{\lambda_{H}{}^{A} n_{H}{}^{A} + \lambda_{M}{}^{A} n_{M}{}^{A} + \lambda_{L}{}^{A} n_{L}{}^{A}}$$

Given all the λ's and assuming homogeneous susceptibility:

p = probability that a susceptible person become infected, given contact with an infectious individual.

We know that the probability that a random susceptible High activity person in Community A gets infected on day t is:

$$p_{H}^{S\ A}(t) = 1 - e^{-\lambda_{H}{}^{A}\beta^{A}(t)p}$$

In **Table 1,** we present the base case parameter values that we continue to use throughout this paper to present the results of our modeling analysis based on the above formulations.

Graph 1 is an illustration of average infection spread within a hypothetical community; notice that the virus spreads faster through a population with several activity levels when compared to a homogeneous community with an equivalent overall average activity level. The imprecise, but widely accepted, definition of R_0 is the average number of people infected by the initial seeder in a fully susceptible population. For the heterogeneous and uniform communities, the expected number of daily contact of a randomly selected person from either population will be the same, thus using one interpretation, without knowledge of the intra activity group interactions, R_0 is identical in both instances. **Graph 1** illustrates a fundamental flaw in the usage one averaging parameter such as R_0 (or *R(t)*) as the sole modeling factor.

Diversity of human activity levels is not the only heterogeneity that differentiates individuals; we can also include heterogeneity of people's susceptibility to infection. We can split the population into groups based on their vulnerability to the disease; in this case we define different probabilities of transmission given contact with an infected individual. For the sake of fair comparison we ensure that on average susceptibility - the probability of infection given contact - is identical in the uniform and diverse populations. Scenarios of how different types of disparities within the population affect the proliferation of the disease are summarized in **Graph 2**. Again, the diverse groups have a higher and earlier epidemiological peak, and potentially fewer total infections since the disease can die out faster. Relying singly on R_0 would not have

captured the possibility of these significantly different outcomes. R_0 is meaningless and often misleading without knowledge of the societal structure and immunal propensity to the flu of the underlying population. A central observation from G**raphs 1 & 2** is that the immunally weak and socially active individuals are not only themselves more predisposed to the flu, but are also the key spreaders of infection to the other groups.[†]

2. Spatial Spread: Multi-Community Models

Historical examples show that one infected traveler is enough to infect a whole population. During the 1918-1919 flu many Alaskan villages were completely devastated by influenza because the man who brought the villagers their mail also brought the flu [Underwood (2005)]. In China's remote Shanxi province, the spread of the 1918 pandemic was traced to a single woodcutter, tramping from village to village [Greger (2006)]. In Canada, the virus wore the uniform of a stubborn Canadian Pacific Railways official who flouted quarantine, dropping off infected repatriate soldiers from Quebec all the way west to Vancouver [Greger (2006)]. The only places to escape unscathed during the 1918 pandemic were 3 small islands completely shut off from the outside refusing even mail delivery [Herda (1995)]. On mainland one successful resort town in New Zealand went to the extreme of cutting itself off from the world using a "rotating roster of shortgun-wielding vigilants" [Greger (2006)].

There are more recent examples of one traveler sparking a large outbreak; a pilgrim returning from Mecca was the source of a large smallpox outbreak in Yugoslavia in the early 1970s that resulted in 174 Yugoslav cases and 35 deaths [WHO (1972)]. The pilgrim contracted the infection in Baghdad while visiting a religious site, but because his symptoms were mild, he was never confined to bed and was able to continue his travels, return home and start an outbreak. Finally, in the case of SARS, studies indicate that thermal screening and health declarations of travelers didn't significantly stop the flow of determined travelers or the spread of SARS [Bell (2004)]. These examples indicate the importance of a model that captures geographical dispersion of infection resulting from very few traveling infected people.

[†] These qualitative results are supported by findings of the real-time surveillance system at Boston's Children's Hospital which found children, who, compared to adults, have more contacts and increased vulnerability, to be the drivers of seasonal flu; in particular, preschoolers are considered to be "hotbeds of infection" [Neergaard (2005)].

2. 1 Fully Connected Communities Model

Two Communities Model

The first layer of realism that we added to Larson's model is spatial complexity: we developed a loosely connected multi-community structure using Monte Carlo simulation to model disease spread between cities. In a two community model each community has its own demographic and epidemiological composition. The populations are loosely connected by very few random daily travelers. A certain number of randomly selected people from each activity level *j*, T_{AB}^{j}, travel overnight from A to stay exactly one day in B before returning home the next night. In the base case $T_{AB}^{j} = T_{BA}^{j} = 2$, giving us a total of 12 travelers going back and forth between two communities. During a visitor's one-day stay in the adjacent community his interaction level does not change from what it was within his/her home community.

We initiate the outbreak with an infectious seed in Community A, and the disease propagates to other individuals within this community (**Graphs 1 and 2)**. Since travelers continue their movement between communities, eventually it is likely that one of the travelers becomes infected, thus he becomes the passageway for the transition of the infection from one community to another. Let us emphasize that there are 2 ways that Community B can get the infection:

1. An infected individual residing in A travels from A to B and infects people in Community B which instigates the outbreak in B (even though the traveler returns to A at the end of the day)
2. A susceptible individual residing in B travels from B to A and gets infected while visiting Community A. The newly infected individual returns home to Community B and becomes the initial spreader within his community.

We have two processes competing to bring the pandemic to Community B. After the pandemic is in both populations, we assume that the few individuals traveling back and forth, with or without the infection, will not change the disease dynamics in either of the communities.

This structure allows us to apply large population-based averaging techniques to model the occurrences within the community. At the same time, we use Monte Carlo simulation to model the stochastic person-to-person transmission of infection to reflect the varying intra community spread of infection. Using this structure, we address the question: if the initial case of

the virus occurs on day 0 within Community A, on average how quickly will it spread to an adjacent community?

The probability of the virus spreading to a new community changes on a daily basis. In order to find the probability that on day *i* at least one infectious individual from activity level *j* visits Community B, we can "identify" this random individual and find the probability that this traveler gets infected during day *i-1*. The probability that exactly *k* infected individuals of activity level *j* travel from A to B and bring in the virus on day *i* is:

$$p_j^{AB}(k,t) = \binom{T_{AB}^j}{k}\left(1 - e^{-\lambda_j{}^A \beta^A (t-1)p}\right)^k \left(e^{-\lambda_j{}^A \beta^A (t-1)p}\right)^{T_{AB}^j - k}$$

Thus the probability that none of day *i*'s travelers from A to B are infectious is:

$$\prod_j p_j^{AB}(0,t) = \prod_j \left(e^{-\lambda_j{}^A \beta^A (t-1)p}\right)^{T_{AB}^j}$$

Symmetrically, the probability that a traveler from Community B gets infected and brings back home the infection on day *i* is the same. So $p_j^{AB}(k,t) = p_j^{BA}(k,t)$. Lastly the probability of having the infection enter for the first time on day *i* is:

$$P(i \text{ is the 1st day of infection in B}) = \prod_{t=0}^{i-1}\prod_j p_j^{AB}(0,t)\,p_j^{BA}(0,t) * \left(1 - p_j^{AB}(0,i)\,p_j^{BA}(0,i)\right)$$

Notice that the probability of never infecting a neighboring community is greater than 0, thus the expected time till the next community gets contaminated is infinity. As a result we can't rely on expected value, instead it is helpful to know the probability that day *t* is the first day of infection entering into the neighboring community. From **Graph 3** we see the probability of infection spread is almost certain if the twelve travelers maintain their trips and if the virus is relatively transmissible amongst individuals.

Performing sensitivity analysis on the transmissibility parameter we find that if *p* is low enough, not only will the infection die out quickly within Community A, but the probability of spreading to Community B also decreases significantly. One approach is to use the often referred to fact that infection dies out at $R_0<1$ and apply it to calculate the point at which the virus would not be able to grow into an epidemic. One way to evaluate R_0 is to consider the number of daily contacts multiplied by the probability that one such contact will lead to transmission and then averaged over the whole population. Assuming that the population is large enough and that each

interaction outcome is independent of the others R_0 can be simplified to the population's average number of daily contacts multiplied by the average probability of transmission per contact. Then in the community on average there will be (50+10+2)/3 =20.67 daily contacts, so this implies that a $p<0.0484$ should stop the pandemic. Yet when we use our heterogeneous community model we find different results. **Graph 4** illustrates how the probability of spread to the neighboring communities changes with the transmissibility of the infection. The infection will not spread to its neighboring communities if probability of transmission is decreased to below $p<0.03$, which is significantly different then $p<0.0484$. As long as the virus does not achieve epidemic status within the initial community, it is not likely to transfer to neighboring towns, but heterogeneous communities make the infection more persistent.

We also varied the number of travelers between the cities from our baseline number of 12 daily travelers between two communities of 300,000 each to between 1 to 120 daily travelers. Our results are summarized in **Graph 5**. We find that as the number of travelers increases the infection becomes more likely to reach the adjacent community earlier. The startling finding is that even with only one daily highly-active traveler between the two communities the disease still spreads to the adjacent community with an incredibly high probability.

Travel Restrictions

This result indicates that travel restrictions unless 100% effective will fail to stop infection spread. Yet during SARS some governments forced travel restrictions, and even simple travel advisories decreased the number of voluntary travelers to SARS infected communities [Bell (2004)]. This experience suggests that travel patterns will change in the case of flu, so it is interesting to further consider the potential effect of travel restrictions.

From **Graph 3** we see which days are the most risky for the spread of infection, so we restrict travel during those critical days. The results in **Graph 6** indicate that partial restrictions, such as halving the number of travelers, are practically ineffective. This is because during the outbreak the number of sick grows exponentially, while the restriction only decreases travel by a fixed factor, as a result incomplete travel controls only delay the spread, by one or two days until the exponentially growing number of sick becomes high enough. In order to stop the disease from moving into a neighboring city all travel must be stopped and the intervention must be initiated early on (~Day 5) and sustained beyond the peak of the epidemic (~Day 15) until the

threat of the transition is small. Since travel restrictions need to last during the peak of the epidemic, the more virulent strains of the virus, which flame out faster, will require earlier, but shorter travel restrictions.

The worst case is when travel restrictions are used in combination with other interventions that spread out the burden of the virus over a longer period. If combined with vaccination, antiviral or social distancing measures the travel restrictions duration becomes overly burdensome. Lastly, once a travel restriction fails and an infected individual enters a fully susceptible town, the travel restriction becomes totally useless because it does not change the dynamics of the disease within the newly infected town. Overall, travel restrictions are expensive, almost impossible to implement and are often ineffective.

Three Communities Model

Now let us consider a fully interconnected three community model with one infection source community and two neighboring susceptible communities (Figure 1). Since the number of travelers is miniscule, the addition of another community does not alter the overall dynamics. The infection spreads almost concurrently to all of its adjacent communities, usually within the early half of the pandemic in the original community (**Graph 7**). The severity of the virus is going to be the same in the secondary communities unless the virus changes its epidemiological parameters or the community alters its behavior. Given the highly connected nature of our society, unless preventative measures are put in place, the virus will spread very rapidly attacking many cities in a very short time. In addition, travel restrictions will not be effective and high active individuals will make it difficult to eradicate the infection. This can be catastrophic for the healthcare and other emergency systems which may be able to handle individual disasters, but not the "equivalent of 50 Hurricane Katrinas" hitting the United States all at once.

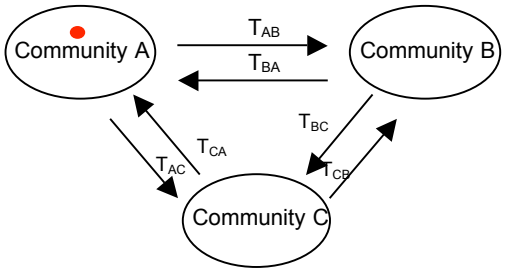

Figure 1.

A three-community model that is loosely connected through daily travelers.

Another possible scenario is one where susceptible cities are connected to multiple sources of infection. The spread to Community C occurs when one of the competing processes: infection spreading from Community A or entering from Community B occurs. The time of infection transfer is likely to be dominated by the Community that is experiencing a more severe epidemic. If the flu is present in both Communities A and B on day 0 the spread to Community C is likely to occur slightly earlier, but still there is a short time lag between the peak of the epidemic in the source and secondary community epidemics (**Graph 8**). In a pandemic the flu will spread to new cities at accelerating speeds; as more cities become infected, the faster other cities will also get the disease.

2.2 Chain Community Model:

Next we address how the infection spreads to an indirectly connected community over a longer period of time. We create a chain model where the population consists of 5 communities labeled A through E and all travel is restricted between "adjacent" communities. (i.e., A residents can only visit B, B residents can only visit A or C, etc). As seen in **Graph 9**, in our base case, once the infection enters a new community the scenario is repeated. This stylized model allows us to study the spatial disease propagation through a set of towns along the river, interstate or trade route. We avoid creating complicated community connection schematics that would be area specific, but detailed geographically tailored models exist [Ford (January 2006), Colizza (2007)].

In addition to insight on infection spread on a larger scale, we consider the effectiveness and timing of interventions impacting several communities over time. As the government and public learn more about the disease, they will apply the lessons learned in the early infected communities to control and alter the course of the epidemic. A model should incorporate these response and control strategies in order to assess the expected damage of the pandemic. This provides a direct segway into the next section of this paper: interventions and behavior changes and their effects in slowing down the spread of infection.

3. Interventions and Behavior Changes:

If the flu becomes easily transmissible, some people have a fatalistic view that nothing short of a vaccine will stop the infection and all other efforts will only slightly postpone and slow down the virus. There is currently a dearth of strong evidence concerning the efficacy of social

containment strategies in decreasing the cumulative burden of infection, which is particularly troublesome given the fact that many of these interventions will carry significant economic, social, ethical, and logistical consequences. At the same time World Health Organization (WHO) recommends nonpharmaceutical public health interventions as a means of containing the infection, delaying its spread and otherwise reducing the impact of the disease [WHO (2004)]. Our results indicate that these behavior altering strategies could be more effective than expected. In this section we describe which nonmedical policies and behavior changes have the potential to stop the epidemic and how they compare to the benefits of the medical interventions. The range of possible disease management strategies can be separated into pharmaceutical interventions: vaccines, antivirals, and non-medical responses: closures, social distancing, self isolation, masks, etc. We also distinguish between the government interventions and community and self-imposed feedback reactions to news of the pandemic.

3.1 Government Interventions:

Antivirals

Antivirals, if supplied early and consistently to the exposed population, should be effective in preventing and treating flu in individuals. Economic costs and logistics are challenges for communities considering the use of antivirals for treatment and prophylaxis. For effective treatment antivirals must be administered within 48 hours of the infectious contact, yet there is little information on a procedure which would allow cities to administer the drugs sufficiently quickly to many people. Additionally, prophylactic use requires repeat doses during the period of exposure. As a result limited stockpiles may force the creation of prioritization schemes focused on maintaining vital systems. Ethical concerns may arise if some individuals or communities can afford to stockpile drugs, while others cannot. Selective stockpiling can deplete supplies and lead to inappropriate use of these limited resources (e.g., for those who do not have influenza). In addition, the drugs have sometimes been associated with serious adverse reactions. Finally, resistance to antiviral drugs could develop rapidly and this intervention could be rendered completely useless.

There is limited information regarding which virus parameters the antivirals will alter – the length or level of infectivity, the mortality or morbidity level or simply the duration of

infection. In general we can deduce that antivirals are likely to help delay and mitigate the peak of the outbreak. However, due to many parameter uncertainties and execution complications, antiviral interventions are not considered quantitatively in this paper.

Vaccines

No country in the world will have sufficient vaccine stockpiles that are ready before the onset of the epidemic and will cover the entire population. Given the current practical considerations for vaccine development – manufacturing capacity, ability of candidate vaccine strains to grow in eggs, and the biological safety containment of parent strains – at least four to six months after the isolation of the virus will be needed to produce the first doses of vaccine [Stohr (2004)]. At the same time many believe that if we are able to slow down or prevent infection spread for those 4 to 6 months, eventually the vaccine will be the ultimate cure for the epidemic [Monto (2005), GlaxoSmithKline(2007)]. New cell based production lines give people hope that the wait for an effective vaccine may be shorter. Since a large portion of experts is relying on vaccine effectiveness, we incorporate vaccination strategies into our model.

In our simple vaccination model we assume that vaccination equally changes the probability of infection given contact with an infected individual for all vaccinated individuals. In this model vaccine efficacy is determined by the parameter v_{eff}. Thus the probability of becoming infected on any given day for a highly active and vaccinated individual from Community A becomes:

$$p_H^{V\,A}(t) = 1 - e^{-\lambda_H{}^A \beta^A(t)\, p v_{eff}}$$

Note, that we acknowledge that there are no vaccines that offer perfect protection, or vaccination strategies that perfectly identify individuals' activity levels. However, since there are no data indicating the value any of these parameters, we consider some extreme value in our analysis.

The goal is to gain insight that can be applied to develop reasonable policy recommendations even without precise parameter data.

Since the amount of vaccine, especially early on, will be limited, vaccination plans require judicious and preplanned distribution of this minimal supply. We consider targeting certain population groups as a possible strategy to more optimal vaccine allocation. Before addressing the tradeoffs between vaccine efficacy, vaccine quantity and the delivery time we confirmed that the most beneficial allocation of limited vaccine is the prioritized distribution of the vaccine to the most socially active individuals as early as possible. It is clear that during a pandemic scenario many members of the community will self isolate. At the same time certain people may not be able to significantly decrease their average daily number of contacts. Doctors, nurses even grocery store cashiers are all likely to still have significantly many contacts and these individuals are the ones that should be the first to receive the limited vaccine. This prioritized distribution will not only ensure the least number of infected individuals, but also provide the most resilient social structure for the duration of the pandemic.

Next we found that given limited vaccine it is best to focus on stopping the infection in specific cities rather than equally dividing the vaccine amongst all potentially susceptible cities. For example, suppose there is sufficient vaccine for either 1) vaccinating 90% of the highly active population in Community A or 2) vaccinating 45% of the highly active individuals in both communities A and B. While the first vaccination strategy may seem unethical or unfair to members of Community B, it is the better strategy in the sense that it will result in fewer cumulative infections. It will also decrease the likelihood of Community B ever getting infected. While this raises moral concerns, we do not address them in this paper.

Another tradeoff that should be considered is between a larger quantity of less effective vaccine versus a smaller quantity of more effective vaccine. The precise antigenic properties of a nascent pandemic strain cannot be predicted ahead of time; however, stockpiles of vaccine for the expected strain are often created ahead of time. This vaccine supply is likely to be poorly antigenically matched to the actual pandemic virus, but it will be available in larger quantities earlier on. First we address the question of quality of effectiveness versus quantity of the vaccine. We compared the pandemic curves between communities where the vaccine effectiveness was the vaccine quantity and vice-versa. For example, we compared a vaccine that is 30% effective and is distributed to 85% of the individuals to a scenario where a vaccine of 85% efficacy is distributed to 30% of the population. The results are practically identical for the two cases. This suggests that stockpiling simply for the sake of quantity may not be the best strategy. Yet the true benefit of stockpiling lies in the ability to have readily available vaccine very early on. It is clear from **Graph 10** that the vaccine will only be effective if it takes effect in less than seven days after the virus enters the population. Mass vaccine production takes several months and several weeks are necessary before an administered vaccine becomes effective. This suggests that unless we can have stockpiled quantities of a viable vaccine we will not be able to rely on vaccination.

Since there is no guarantee that the vaccine will be equally effective in all individuals we consider a possibility where a certain portion of the vaccinated people experiences lesser benefits of the vaccine either as a result of improper administration or biological diversity. This is also similar to administering two types of vaccine: the stockpiled less effective vaccine and the antigenically matched vaccine. We incorporate this by splitting the vaccinated population into further groups of those who experience the full benefits of the vaccine and those who feel a

lesser benefit. Now we define two parameters: v^{H}_{eff} high vaccine efficacy, v^{L}_{eff} low vaccine efficacy. The remaining calculations are identical. We compare scenarios where the average vaccine efficacy is the same regardless of the uniformity of the efficacy. We find that the vaccine that is uniformly effective in all vaccinated individuals is slightly worse than the vaccine that has different benefits for the vaccines. For example, it is preferable to have a vaccine that offers 100% protection in 50% of the vaccinated individuals and 0% protection for the rest then to have a vaccine that provides 50% protection in all of the vaccinated people. It is also clear that the suboptimality gap define between these two scenarios grows if we assume optimal allocation and larger quantities of the vaccine.

3.2 Behavior Changes:

Historical Accounts

It is unlikely that society will implement measures from 1918-1919 making it "unlawful to cough and sneeze" punishing violators with up to a year in jail [Hudson (1999)]. Making it a crime to shake hands and throwing people in jail for not wearing masks is an extreme that would only perpetuate panic and protest [Collier (1974)], but it is clear that even without forceful implementation people will try to decrease their likelihoods of getting ill by improving hygiene related behaviors. Most people will not maintain their daily routines if they discover that there is a deadly disease attacking within their city, state, country or world. Based on the information portrayed in the media, individuals are likely to both limit their daily contacts and decrease the closeness of the remaining contacts. History has provided us with multiple examples of people responding to news of a disease by altering their daily behavior.

Recent statistical studies of the 1918 influenza pandemic in US cities have supported the hypothesis that early implementation of multiple nonpharmaceutical interventions could reduce transmission rates by 30-50% and lower the peak death rates by about 50% [Bootsma (April, 2007), Hatchett (April, 2007)]. The timing and force of these interventions have been attributed as one of the main reasons for the variation of different cities' experiences [Bootsma (April,

2007)]. The array of outcomes ranges from the Philadelphia one hump epidemic curve lasting a month and a half with a peak excess death rate of over 250/100,000 population, to the St. Louis two wave four month experience with a peak excess death rate of less than 75/100,000 population [Hatchett (April, 2007)]. The findings of these studies suggest that these interventions within cities helped save lives during the 1918-1919 pandemic, and may help save future lives.

A much more recent example of the social behavior changes that occurred during SARS supports the importance of incorporating non-pharmaceutical interventions into our model. Surveys indicate that during the SARS outbreak in Hong Kong 78% of the population covered their mouths while sneezing or coughing, 76% of individuals wore masks, 65% washed their hands after contact with a possibly contaminated objects [Lo (2005)]. Economic factor studies in Hong Kong, Singapore and Toronto indicate that there was a sharp drop in interactive social activities as restaurants and entertainment centers suffered sharp drops in clientele [Fan (2003)]. Specifically in Hong Kong, tourism was crippled in March when the WHO issued a rare warning for travelers to avoid Hong Kong and the Guangdong Province. As a result of weakening demand airlines slashed more than a third of flights and hotels reportedly were up to 90% empty [Wiseman (2003)]. In Singapore sales were down about 30% as people avoided stores and malls, some stores suffered up to 75% declines in sales [Wiseman (2003)]. It is clear that voluntary activities like tourism were strongly affected by fear of the disease.

Similarly, in a more Western city of Toronto, during the SARS outbreak there was a reported drop of up to 71.5% in revenue per available hotel room for downtown Toronto. This translates into hotel occupancy rates in the range of 30% to 40%, instead of the seasonal 70% average [Rosszell(2003)]. Additionally, at least five major citywide conventions were called off, contributing a loss of over 20,000 attendees, and this doesn't include the vast amount of individual-hotel convention businesses that were also cancelled [Rosszell(2003)]. Other Toronto SARS casualties include over 800 bus tours, music concerts, corporate travel, and school field trips; the list of voluntary social behavior changes goes on and on [Rosszell(2003)]. All these examples are strong evidence that people will not maintain their daily actions. While we have not found any reports correlating these behavior reactions to media reports on a daily basis, we know that the effect of these "soft" and self-imposed interventions was significant [Tang(2003)]. Thus

while there are significant gaps in our knowledge concerning these behavior changes, overlooking these behavior changes would be indefensible.

Modeling the Human Concern Factor

It is clear that people will react to the news of infection spread and alter their daily routines depending on the severity of the news. There are several social behavior models that predict that people will alter their behavior given knowledge of a deadly infection. Coping responses affect human functions to moderate and decrease the negative impacts and stressors in life's circumstances [Pearlin (1981)]. Protection motivation theory, the transactional model of stress and coping, the health belief model (HBM) and behavior intention model (BIM) all indicate that individuals will attempt to assess their perceived risk or attitude towards the threat based on factors like threat severity and their vulnerability [TCW (2004)]. Combining this threat assessment with the perceived response efficacy and the level of confidence in one's ability to react appropriately, individuals determine their intended and actual behavior [TCW (2004)]. A comparative study of the HBM and BIM in predicting human intentions regarding the swine flu vaccination program undertaken in October 1976 found that while the BIM is a better predictor, practitioners can apply the concepts of either model to the decision making process [Oliver (1979)]. Motivated by various social science risk perception and health behavior models, a survey based study of 5 European and 3 Asian regions revealed that in a hypothetical influenza pandemic the precautionary measures would be taken across all regions, the measures included avoidance of public transportation, entertainment venues and partial isolation within the home [Sadique (September, 2007)]. In the scenario where vaccines and antivirals are unavailable, the concern level will increase throughout the epidemic and individuals' coping options will be to limit their daily contacts and/or decrease the probability of transmission given contact. Before delving into these two cases we first explain our approach to evaluating the overall perceived level of concern in communities.

It is difficult to predict which kind of information people will use to assess their "perceived threat". Logical choices for evaluating susceptibility will be the virus' proximity to home and its virulence, while mortality and morbidity rates are likely to determine perceived severity. Since we do not specify the death rate for the disease the number of infected individuals is the best gauge that reflects both community members' vulnerability to the disease and the

severity of the threat. We apply the concepts of the various behavior models and use this factor to gauge human reaction. Before we proceed, let us point out that while our approach may seem primitive, there has been little progress in the field of quantitative health behavior modeling [Weinstein (2004)]. Our approach suggests one method to incorporating behavior changes into our model and it is supported by the Sadique's questionnaire study results, but further research is required in this area [Sadique (September, 2007)].

In order to incorporate behavior change into our model we use $\pi_X(t)$ as a feedback parameter that indicates the "concern level" within Community X on day t. If $\pi_X(t)$=1 then there is no anxiety or behavior change within the community, for $\pi_X(t)$=0 the community practically shuts down. We describe three possible data sets that the population could use to gauge their risk levels, to define their $\pi_X(t)$ and consequently alter their behavior.

1. The first communities that experience the virus will not be able to use the lessons learned by their neighbors. Early on the only information people will have will be the experience of their own community. People may use the number of yesterday's new infections ignoring everything that happened before yesterday. We quantify this memoryless approach of evaluating the risk factor as $\pi^1_X(t, C_1)$:

$$\pi^1_X(t, C_1) = \left(1 - \frac{\text{Number of infected people in Community X from day } t-1}{\text{The total population in Community X}}\right)^{C_1}$$

C_1 an input that represents the importance of yesterday's information to the people. For C_1 =1 the number of infected individuals is linearly correlated to the risk level. As C_1 grows, the relevance and impact of yesterday's news grows polynomially.‡

2. Individuals are likely to rely on more than yesterday's information. Since the media is likely to present the cumulative number of infections within the community, this is another possible data set that people may use to estimate their risk levels. We quantify the related concern parameter $\pi^2_X(t)$ as:

$$\pi^2_X(t, C_2) = \left(1 - \frac{\text{Number of infecteds in Community X upto and including day } t-1}{\text{The total population in Community X}}\right)^{C_2}$$

‡ Let us point out that the authors have not been able to find the application of the behavior forecasting models to predict general behavior changes in the case of pandemic flu, but we have found numerous examples of HBM used to estimate altered human interactions to reduce their risk for HIV infection. Studies in this area indicate that there may be non-linear relationships between the factors and the dependent variable, thus we allowed for this variability through the addition of the C parameters. [Stiles (2004)]

C_2 is another input which represents the strength of impact of this cumulative information. We acknowledge that C_1 will have a smaller impact than C_2 of the exact same value. [§]

3. It is also clear that if a city's adjacent communities all get infected the level of concern within the city will be heightened to reflect the suffering of its neighbors. This presents us with another factor in evaluating the behavior change feedback parameter, $\pi^3_X(t)$:

$$\pi^3_X(t, C_3) = \left(1 - \frac{\text{Number of infecteds in all Communities up to and including day } t-1}{\text{The total population in all Communities that have been infected}}\right)^{C_3}$$

Again C_3 is an input representing the impact of this information. Notice the denominator is the population of only the infected communities, so this reflects a human informational bias that focuses on only the infected communities.[‡]

In reality each individual is likely to change her behavior using a combination of all three described approaches. In our model we can uniformly alter the actions of people within each group using $\pi_X(t, C_1, C_2, C_3) = \pi^1_X(t, C_1) * \pi^2_X(t, C_2) * \pi^3_X(t, C_3)$ as the feedback parameter for behavior change. The two parameters that will incorporate $\pi_X(t, C_1, C_2, C_3)$ to reflect changing behavior due to awareness and alarm over the infection are λ and p.

Limited Contact

People in all activity levels are likely to decrease the number of contacts that they have on a daily level. It is highly probable that children will be kept at home, public transportation will be avoided, entertainment activities such as shopping or going to the movies will be temporarily suspended, even the number of contacts within the office may decrease as conference calls replace face-to-face contacts [Sadique (September, 2007)]. All these behavior changes were observed during the SARS outbreak [Wiseman]. We model this behavior change by updating the average number of daily contacts, λ^j by multiplying it by, $\pi_X(t, C_1, C_2, C_3)$, the appropriate level of impact. As can be seen from **Graph 11**, relying on yesterday's information as the indicator for the concern level results in a lowered peak of the epidemic but a much slower decline of the disease. While the cumulative number of infections is decreased the virus maintains its presence within the community for a long period of time thus increasing the probability of infecting the neighboring communities and making travel restrictions ineffective.

[§] Studies in this area indicate that there may be non-linear relationships between the factors and the dependent variable, thus we allowed for this variability through the addition of the C parameters.

However, as implied earlier people are likely to use more than just yesterday's information to define their behavior. If the community "remembers" the number of people who were infected before yesterday then the decline of the virus will be much faster. **Graph 12** illustrates the potential success of social distancing in decreasing the cumulative number of infecteds to a small fraction of the total population and in stopping the infection within a community. Refer to **Graph 13** to see how the experiences of prior infected communities can benefit the communities further down the infection chain. Social distancing where the average number of daily contacts is decreased up to 80%, at the height of the danger for each activity group, is extent of limited contact sufficient to stop the outbreak in Community B. It is clear that the most cautious communities that change their behavior prior to the infection entrance are the most successful. This voluntary public action will also decrease the probability of the infection entering the community in the first place.

The average number of interactions is likely to decrease, but it is unlikely that the λ's are going to change the same for each activity level. Highly active people will be able to decrease their number of interactions drastically, but less active people may be unable to sever their few, but vital ties to the community. For example, a politician may decide to cancel his/her campaign rally, stay at home and contact his office through telecommunication. On the other extreme, a retired handicapped grandmother whose only daily contact is with her grandson who brings her daily groceries, is not likely to change her pattern at all.

This leads us to consider the scenario where only the highly active individuals, with many voluntary contacts, limit their daily contacts. The results are presented in **Graph 14**; just changing the behavior of the highly active individuals has a similar level of impact as decreasing the behavior of the whole community. If the highly active individuals decrease their number of daily contacts by a little over 80% during the riskiest time, then the massive communitywide outbreak could be prevented. This has important implications for policies during the pandemic. For instance, this result underlines the importance of closing schools since children have a high number of non-vital daily contacts within a school setting. All individuals who act as social focal points should decrease their average number of contacts especially if this can be done without disrupting the community.

Decreased Probability of Transmission

Reduced closeness of contact and improved hygiene are coping mechanisms that will decrease the probability of transmission given contact between an infected and susceptible individual. In order to reflect this phenomenon we update the probability of transmission given contact on a daily basis by multiplying p^j by the appropriate, $\pi_X(t, C_1, C_2, C_3)$, level of impact. In our model the impact of this decreased susceptibility is the same as the impact of decreased contact. Since our model provides us with the expected number of infecteds, we incorporate decreased probability of transmission by integrating a multiple of the risk factor in the exponent. As before if people start taking precautions based solely on yesterday's information they will lower the peak and extend the length of the epidemic curve (**Graph 11**). If the probability of transmission is dependent on all information up to and including yesterday then the length of the epidemic is shorter (**Graph 12**). Also, we can combine the two protective approaches and decrease the average number of contacts and limit the probability of transmission. For the example shown in **Graph 14**, the extent of social action required of the highly active individuals to stop the outbreak is a decrease to an average of 15 daily contacts and a transmission parameter of about 5.5%.

Implications of Behavior Models

Some of the concepts that are highlighted in the social behavior predicting models strengthen the importance of our findings. One of the important factors in the BIM is the perceived behavioral control – the ability to perform the behavior [TCW (2004)]. If individuals believe that they can easily fulfill the requirements necessary they are much more likely to act accordingly [TCW (2004)]. This implies that the relevant institutions should be prepared to implement appropriate leave of absence laws and help citizens maintain high levels of hygiene during the pandemic. BIM also emphasizes the importance of subjective norms – humans actions reflect what others believe is the right thing to do [TCW (2004)]. In the course of the pandemic public figures from the local and federal governments could influence their constituents if they present the importance of the control measures to the public. The transaction model of stress and coping indicates that in a stressful situation individuals will demonstrate "information seeking behavior", thus it is important that the media portrays information in a constructive manner [TCW (2004)]. One study indicates that educating the public is one way to ensure the cooperation of individuals: when people don't understand the risks they do not act [Hong

(2006)]. The main conclusion that can be drawn from these various behavior feedback models is that the information portrayed in the media: both about the extent of the epidemic and people's ability to manage the situation, will help determine peoples' reactions and therefore directly impact the course of the pandemic.

4. Conclusions and Policy Implications

> "How would a nation so greatly moved and touched by the 3,000 dead of September 11th react to half a million dead? In 1918–1919 the mortality rate was between 2.5% and 5%, which seems merciful in comparison to the 55% mortality rate of the current avian flu. In just 18 months, this avian flu has killed or forced the culling of more than 100 million animals. And now that it has jumped from birds to infect humans in 10 Asian nations, how many human lives will it or another virus like it take? How, then, would a nation greatly moved and touched by 3,000 dead, react to 5 or 50 million dead?"
>
> ~Senator Bill Frist, 2005.

Conclusions

The paradox of a pandemic is that while it is a worldwide catastrophe it is going to be felt at the intensely local level since there is no one who will be "outside" of the pandemic to send help [Greger (2006), Dept.Agr. (2006)]. Communities will have to use their own resources to cope with the pandemic. Therefore it is vital that all levels of society: families, schools, businesses, cities, states, countries, are all prepared for the pandemic. The best plan will require the cooperation of the American people, and in order to gain the trust and understanding of 300 million people it is important to be ready and prepared to educate the public on the important factors of the infection.

While epidemiologists sometimes refer to a lack of parameter knowledge as reason to avoid adding complexity to models, we believe that intuitive understanding of disease dynamics can only be improved by looking at lessons learned from experience, logic, and most importantly well organized models. In the end, mathematical models remain just that – models, not real life. All models use assumptions and simplifying approaches and no approach should be thought of as the only modeling strategy. Even the most established modeling approaches should not be seen as boundaries, but as starting points for future work. By moving beyond the highly used R_0 parameter in our modeling work, we were able to observe the vital importance of highly active individuals in the spread of infection. Avoiding this limiting approach we were able to include a dynamically updating component to describe reactive behavior changes into our model. As a

result our study provides insights regarding the effectiveness of intervention strategies in reducing the illness and death caused by pandemic influenza and its spread in the community.

Policy Implications

The bad news is that a flu pandemic is coming; the good news is that our society has the capacity to mitigate its outcome. To succeed we require careful, deliberate and thorough plans that are prepared and reviewed today, before the outbreak, and are ready to be implemented immediately at the first sign of a dangerous easily transmitting flu strain. Ethical dilemmas of forced restrictions or unequal treatment should be dealt with now, otherwise they will consume crucial time when our society should be taking action. In this research we addressed several disease management strategies; we hope that our insights are used in the creation and updating of pandemic flu containment policy.

Travel restrictions are impossible and useless once the infection is circulating within the country. There is no easy way to regulate the travel patterns of all individuals through all transportation networks including cars, buses, trains, etc, so the restrictions will be imperfect. Imperfect travel restrictions are extremely costly, but even worse, they are also futile. Our recommendation regarding travel restrictions is to avoid government enforced travel restrictions, but possibly create early travel advisories before the virus enters the country to prevent recreational and voluntary travel and potentially delay the pandemic without severe economic losses.

From our research we find while these advisories may slightly delay the spread of the flu, they will not stop it from reaching the US. Virtually every community in the US should be prepared that they will become infected. The focus of these communities' mitigation strategies must be inner-community interventions: social distancing, hygienic steps and if possible partial vaccinations. If communities are able to decrease their maximum number of daily infected individuals they will reduce the probability of intra-community infection transmission as a byproduct of the inner community action.[**] Our findings are encouraging and support the hypothesis that limited interaction will decrease the effect of the pandemic. The deeper insight of this result is that these interventions are effective because they attack the source of the problem

[**] The reverse is not true. Travel restrictions have no impact on inner community infection dynamics.

by decreasing the exponential growth factor. Preventing exponential explosion of the number of infecteds will prevent the pandemic.

Another result of our behavioral study is that the focus must be on the group most culpable for infection spread: the highly susceptible and highly active individuals. These are the people who must be deterred from maintaining their daily actions. In addition, it is critical for all people to remember the effect of the epidemic and maintain their distance beyond the peak of the outbreak. The media should present information regarding the events over the whole history of the epidemic, remind communities about the state of their neighboring and other communities and educates individuals and empowers them to take preventative action. These informative messages will determine human behavior and that will determine the course of the pandemic.

Acknowledgement.

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5. Tables

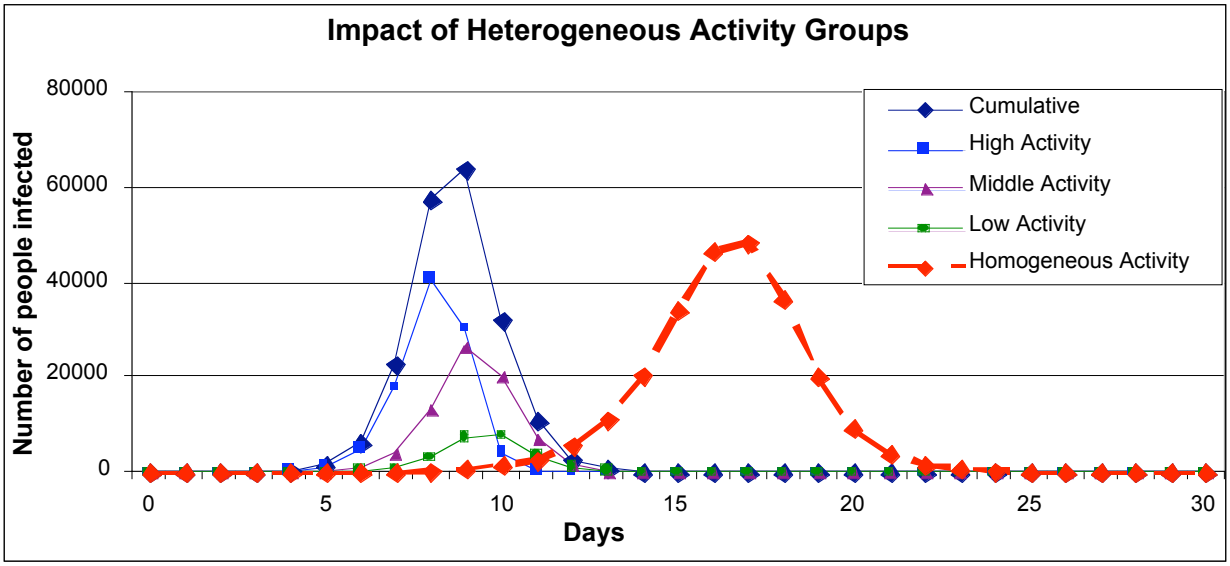
Parameter Name	Parameter Label	Community A
Population of High activity level	n_H^A	100,000
Population of Medium activity level	n_M^A	100,000
Population of Low activity level	n_L^A	100,000
Social contacts of High activity persons	λ_H^A	50
Social contacts of Medium activity persons	λ_M^A	10
Social contacts of Low activity persons	λ_L^A	2
Probability of successful transmission given contact	P	.10
Travelers from A to B of High activity level	T_{AB}^H	2
Travelers from A to B of Medium activity level	T_{AB}^M	2
Travelers from A to B of Low activity level	T_{AB}^L	2
Travelers from B to A of High activity level	T_{BA}^H	2
Travelers from B to A of Medium activity level	T_{BA}^M	2
Travelers from B to A of Low activity level	T_{BA}^L	2

Table 1.

Parameters used as the base case for the research. [††]

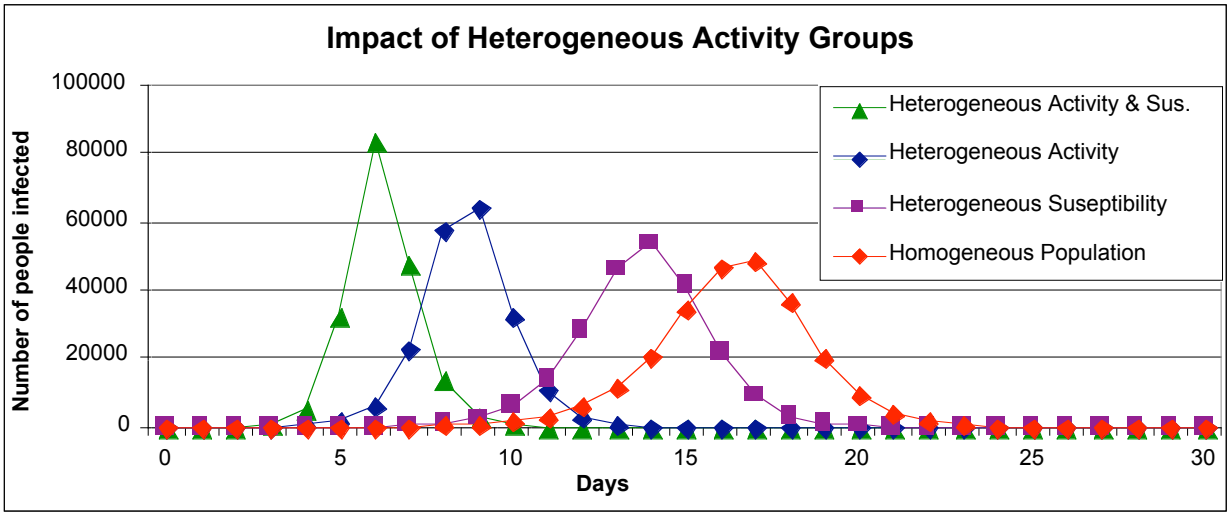
[††] We use the Wallinga paper as a base for our average number of daily contacts [Wallinga (2006)].

6. Graphs/Figures:



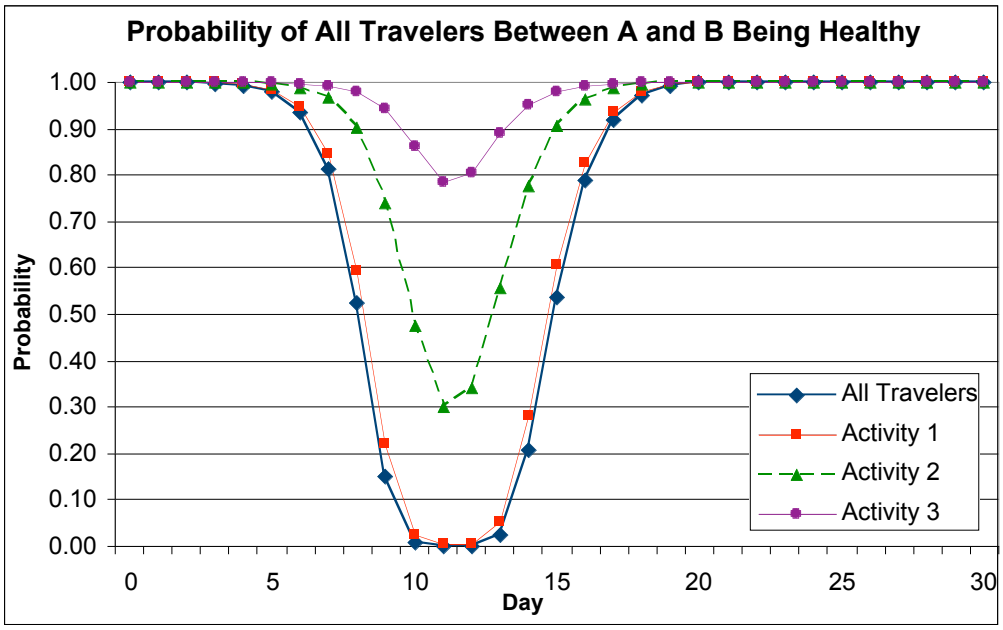
Graph 1: Comparing spread of infection between heterogeneously and uniformly active communities of 300,000 individuals.

In the case of the heterogeneous group, we use the base case parameters (Table 1). Every individual in the homogeneous population has an average of $\lambda = 20.66$ daily contacts. There is no heterogeneity in the susceptibility of either population. $p = 10\%$. The total number of infections is higher in the uniform group, but the peak is decreased and delayed.



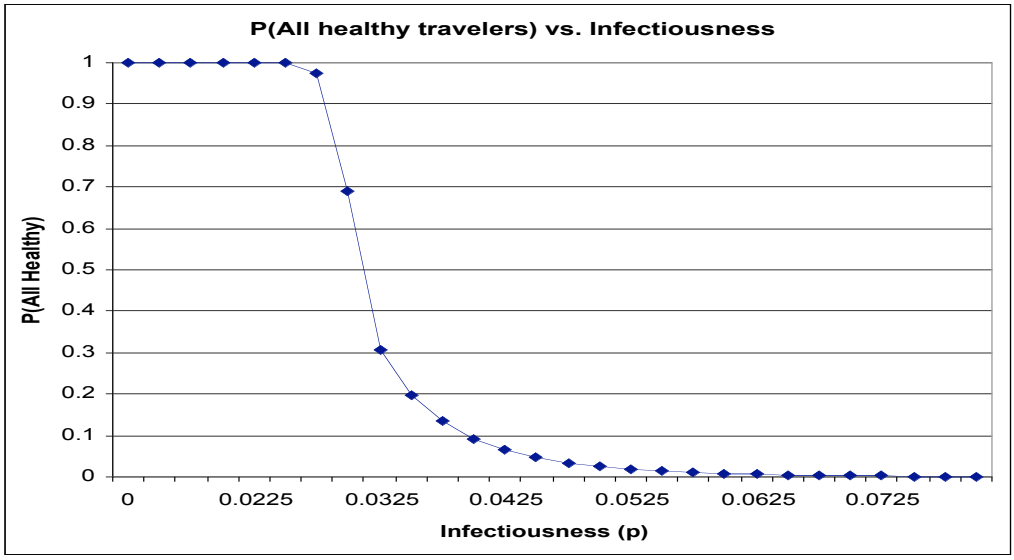
Graph 2: The impact of various heterogeneities on the epidemic curve.

Heterogeneity in contact patterns is presented with the base case parameters. Heterogeneous susceptibility in the most vulnerable group in the population is p_1= 20%. Members of the second group have a stronger resistance, p_2=10%. The most resilient group, has p_3 = 5%. Individuals in the homogeneous population have an average of 20.66 contacts per day and a p = 10% probability of getting infected given contact. The most diverse population spreads the infection most rapidly, but has the fewest cumulative number of infections.



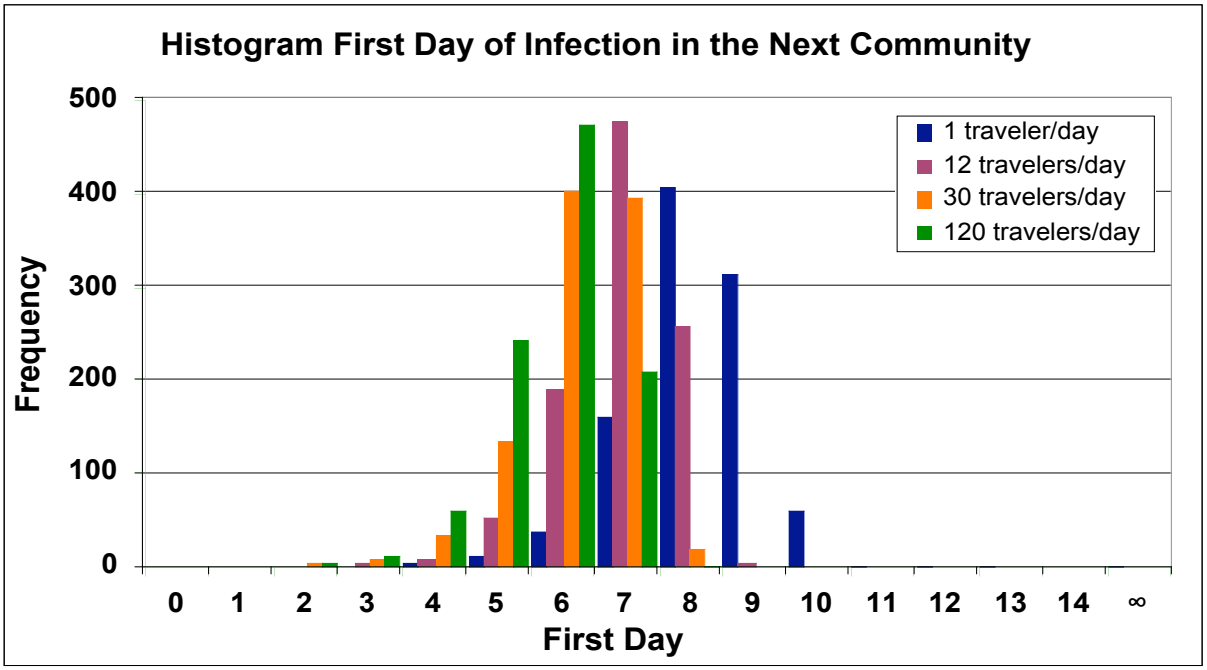
Graph 3. Probability of infection not spreading to a neighboring community on day *i*.

Given that the infection begins in Community A, the probability that all travelers between A and B stay healthy changes on a daily basis. It is most likely that an individual from the highest activity level will be the initial spreader.



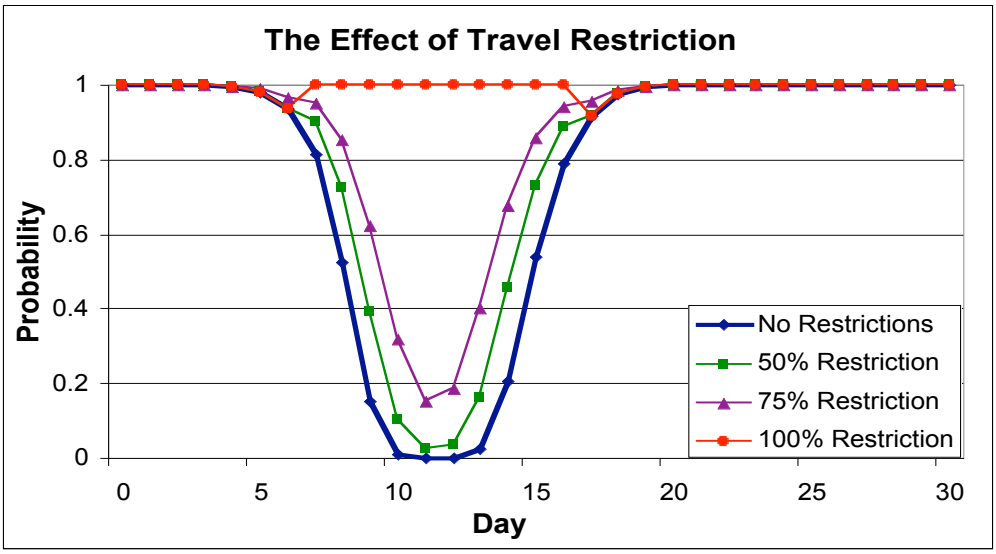
Graph 4. Sensitivity of Infection Transfer on the Susceptibility parameter.

From the above graph we see that if we can decrease the probability of infection given contact to bellow 2.5%, the infection is very unlike to enter Community B. The infection dies out in Community A without achieving epidemic status. Using average community parameter and $R_0 < 1$ as the point at which the virus no longer achieves epidemic status predicts that the infection should not be able to spread at $p<0.0484$.



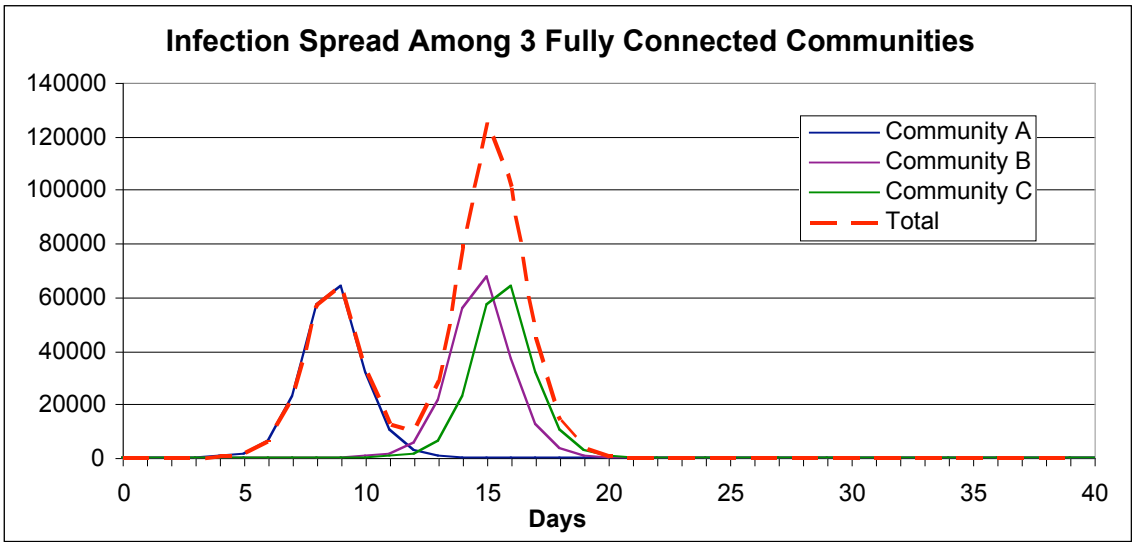
Graph 5: The histogram for the number of days between infection initiations amongst neighboring communities.

The number of days between infection transitions into neighboring communities is not very varied when neither community has intervention strategies. Even when the number of travelers is varied from 120 down to 1 traveler per day, the first day of infection in Community B only changes by 2 days.



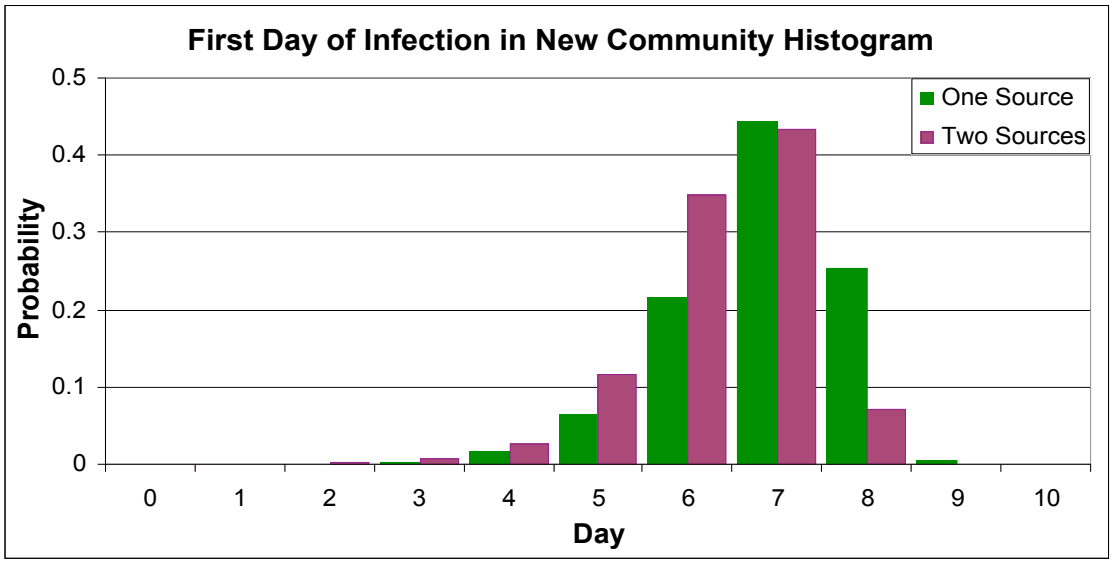
Graph 6. The effectiveness of various levels of travel restrictions.

We had 2 travelers going in each direction from each activity level – thus 12 people traveled on a daily basis in the base case with no restrictions. Simulations of varying levels of travel restrictions indicate that in order to be effective travel restrictions must be started early and maintained for a large portion of the epidemic. In addition partial travel restrictions are not effective in preventing the spread of the disease.



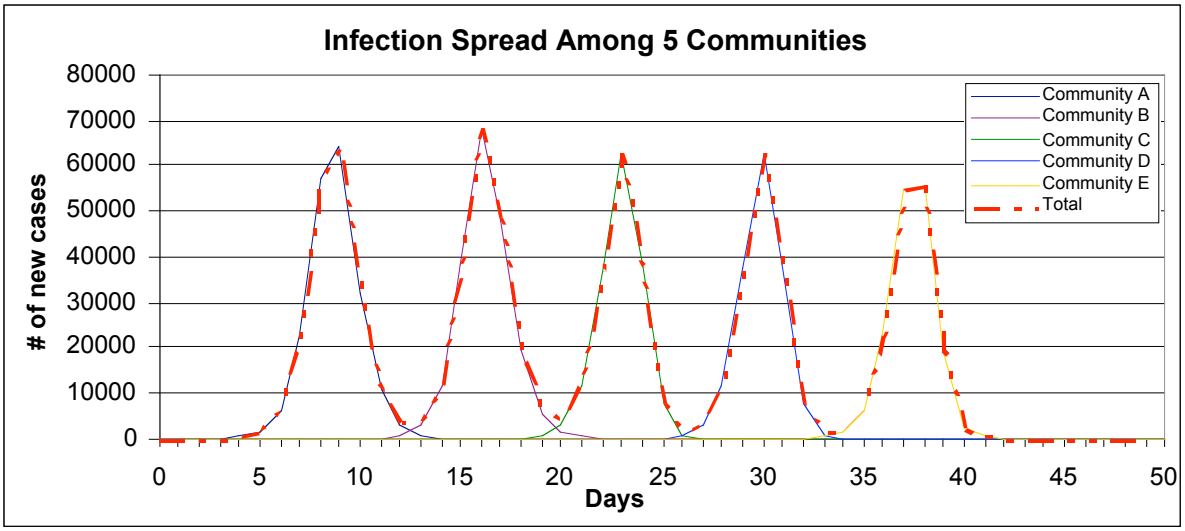
Graph 7. Infection will spread concurrently to all neighboring communities.

The infection begins in Community A and after a small time lag the outbreak reappears in the neighboring communities. The problem is that the neighboring communities are likely to be hit all within the same time period amplifying the burden experienced by the country as a whole.



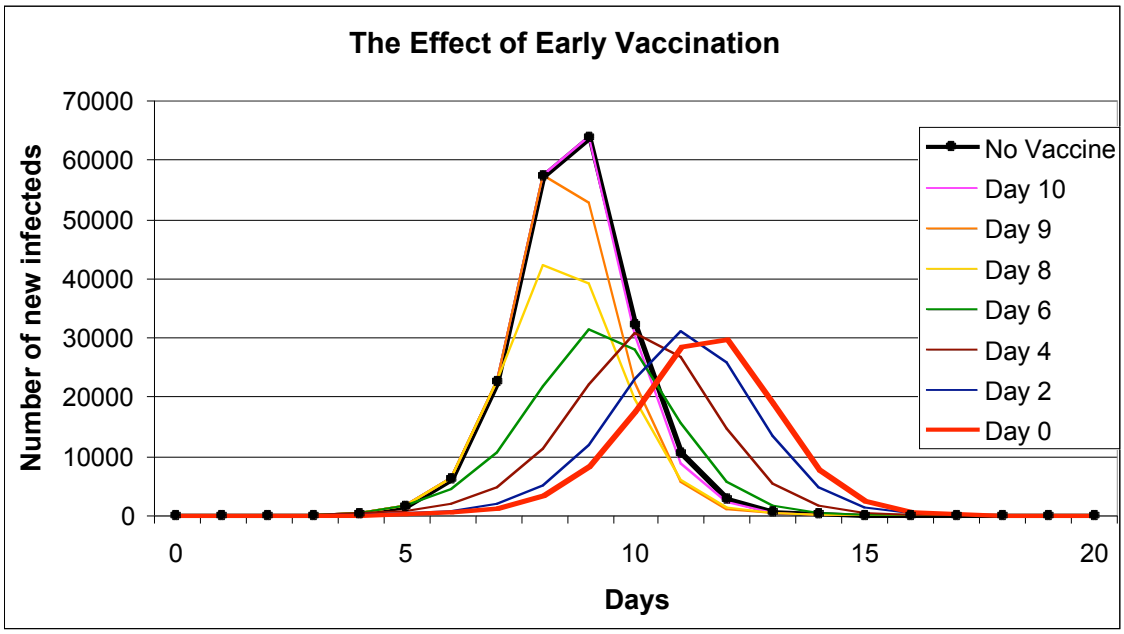
Graph 8: The histogram for the number of days between infection initiations amongst three neighboring communities.

The number of days between infection transitions into neighboring communities is not very varied when neither community has intervention strategies. When a susceptible community neighbors two infected communities the first day of infection is likely to be only slightly earlier. In this case the first day of infection is expected half a day earlier.



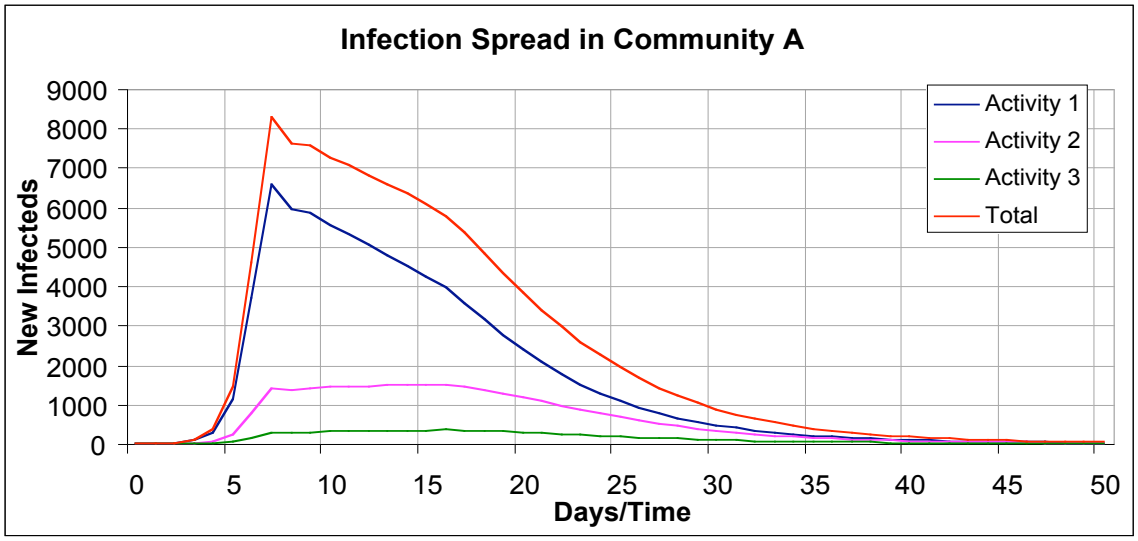
Graph 9. Typical spread of infection over a chain of 5 connected communities with no intervention strategies.

In a chain of 5 connected, identical communities the infection spreads almost identically, if no intervention strategies are put into place. On average it takes about 6 to 7 days for the infection to jump to the next neighboring community.



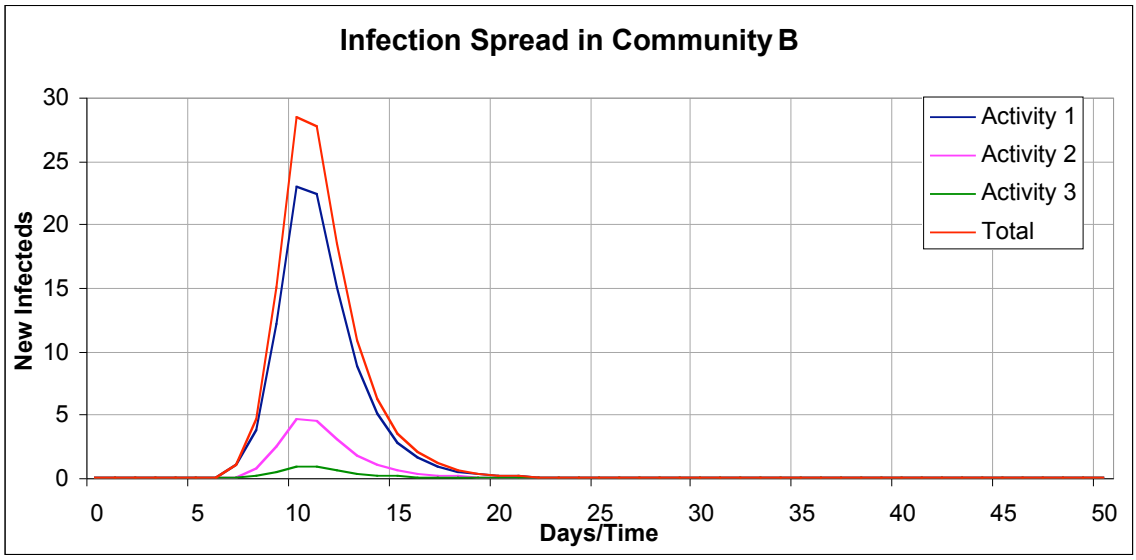
Graph 10. The effect of timely vaccination

In all cases the community vaccinates 50% of the highly active individuals with a vaccine that has 75% effectiveness in all of the vaccinated individuals. The varying factor is the day that the vaccine starts protecting the vaccinated individuals. If the goal is to significantly reduce the total number of infected individuals then the community will only have about 5 to 6 days to vaccinate the highly active people before vaccination become useless.



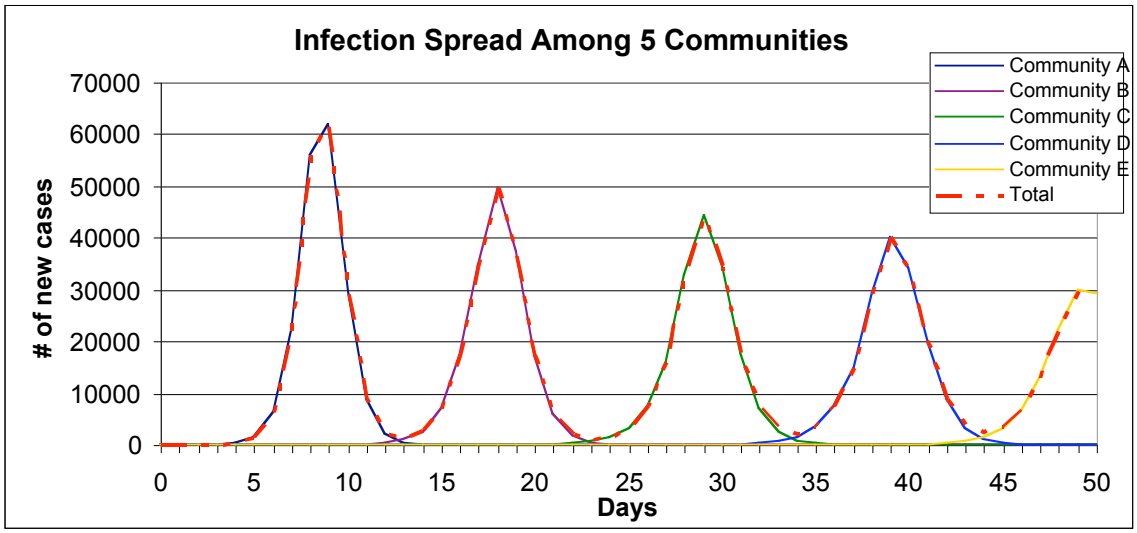
Graph 11: Infection spread within a community that reacts, by proportional scaling back the average number of contacts for all its members, to previous day's news only.

This proportional scaling back of the average number of contacts can be described as social distancing. Notice that the peak of the infection is lower and earlier; in addition the infection duration is drawn out over a longer period of time. This elongation of the disease makes travel restriction less feasible. At the same time the total number of infections is decreased to 117,174. For similar reactionary hygiene improvements we have the same expected results as social distancing.



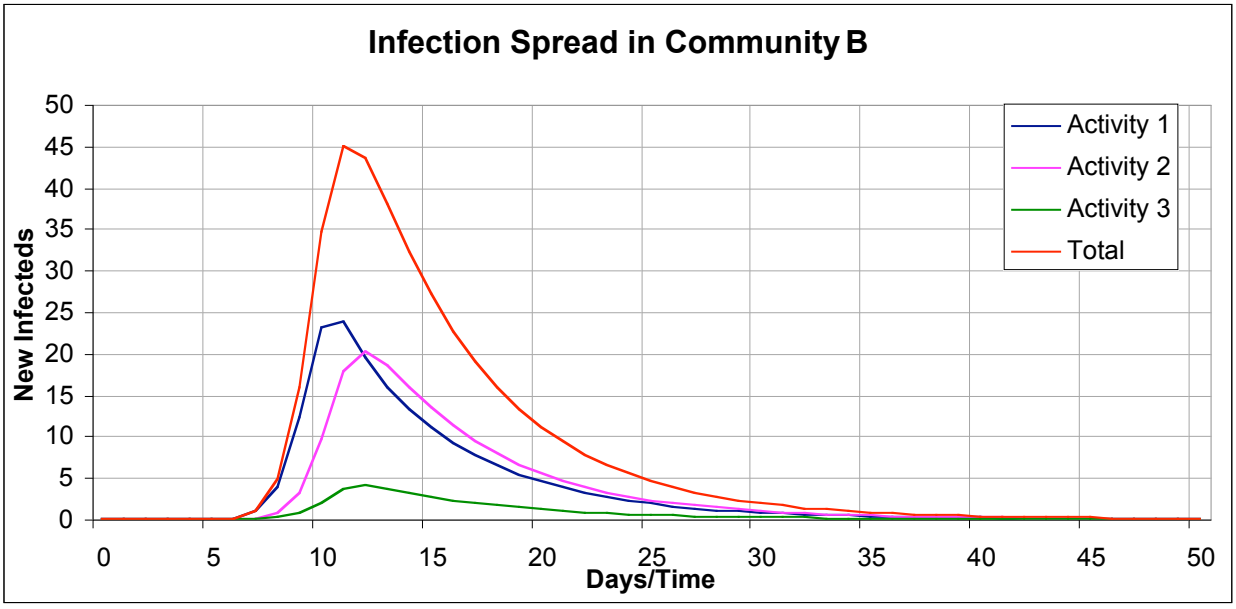
Graph 12: Infection spread within a community that reacts, by social distancing, to news cumulative over all previous days across all communities.

Social distancing that occurs before the infection has a chance to strike a significant portion of the population is very effective. Here Community B reacted to the news of an outbreak in Community A. In this example social distancing successfully decreases the total number of infecteds to 120 people. The extent of social distancing decreases the average number of daily contacts to 14, 3 and 1 for each activity group and the probability of transmission down to 5%.



Graph 13: The spread of infection amongst a linked chain of five communities where each community implements an intermediate level social distancing strategies based on the experiences of the previous communities.

As communities learn more from the experiences of other communities the extent of the infection decreases in communities that get infected later.



Graph 14: Infection spread within a community that reacts by social distancing only in the highly active group, to news over all previous days across all communities.

Social distancing just the highly active group has practically the same result as social distancing the whole community. The main difference is that the tail of the infection is elongated. From this we learn the importance of the highly active group. In this example the total number of infecteds is 380 people. The extent of social action taken by the highly active individuals decreases the average number of their daily contacts to about 15 and the transmission parameter to about 5.5%.

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