

A PANDEMIC INFLUENZA SIMULATION MODEL FOR PREPAREDNESS PLANNING

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ABSTRACT

Pandemic influenza continues to be a national and international public health concern that has received significant attention recently with the recent swine flu outbreak worldwide. Many countries have developed and updated their preparedness plans for pandemic influenza. School closure has been recommended as one of the best ways to protect children and indeed all susceptible individuals in a community during a possible disease outbreak. In this paper, we present a geospatial and temporal disease spread model for pandemic influenza affecting multiple communities. School closure, one of the social distancing policies, is investigated in this paper with several questions such as: at what level should schools be closed, for how long should they be kept closed, and how should be the re-opening decisions made. These questions are considered in terms of minimizing: the total infection cases, total mortalities, and the impact on educational services to school children.

1 INTRODUCTION

The World Health Organization (WHO) has reported that the avian influenza (H5N1) virus is threatening human life worldwide, as it may soon have the ability to efficiently transmit from person to person which would likely cause a pandemic (WHO 2005). Preparedness plans for pandemic influenza generally focus on establishing efficient mitigation strategies for inter-related communities and providing adequate medical services. Several decisions need to be made before, during, and after the pandemic outbreak to manage the impacts of the disease successfully, minimize loss of life, and minimize the effect on daily business operations. However, because the population that will be potentially affected by pandemic influenza is very large and diverse, different strategies, including non-pharmaceutical and pharmaceutical interventions, will inevitably need to be employed in different communities.

In this paper, we develop an age structured geospatial disease spread model to estimate the spread pattern of the disease geographically in Arizona, U.S. over time. The simulation model divides the state into multiple communities, which are the counties of the state.

Our objective in this paper is to study one of the non-pharmaceutical mitigation policies, school closure, during an outbreak of pandemic influenza. The presented simulation model of this paper allows decision makers to test various school closure strategies in terms of limiting activities in schools in each county separately at different times or in all schools in the state at once, closing schools at each county separately at different times or closing all schools at once by a state-wide declaration. We also quantify the effects of the reopening decision for school closures without using any pharmaceutical interventions.

In the rest of the paper, we first present a literature review and then state the major contribution of this paper to pandemic flu modeling. Next we give the mathematical details of the simulation model with its structure. After presenting the analysis for different scenarios we present our conclusions in the last section.

2 LITERATURE REVIEW

Increasing concerns on the possibility of an influenza pandemic caused by the avian flu virus (H5N1), have led many researchers to study this possible catastrophic event from different viewpoints and with different methodologies. Research on pandemic influenza has mostly focused on: 1) modeling the disease spread and building geospatial and temporal simulation models to estimate the global path of the pandemic spread 2) evaluating possible non-pharmaceutical and pharmaceutical interventions at the global and local levels and recently 3) the logistical issues related the community response and preparedness activities with exercising the preparedness plans (Grais et al. 2004; Ferguson et al. 2005; Germann et al. 2006; Wu et al. 2006; Cauchemez et al. 2008; Davey et al. 2008; Ekici, Keskinocak and Swann 2008). Ekici, Keskinocak and Swann (2008), classified the common ways of modeling infectious disease spread into four groups: using differential equations, simulation modeling (Ferguson et al. 2006; Germann et al. 2006; Wu et al. 2006), random graphs and lastly difference equations (Rvachev and Longini 1985; Grais, Ellis and Glass 2003).

Community preparedness and policy making to mitigate the effects of the disease to social life is of great interest to governments at local, state and federal levels. It is also of interest to profit making companies and non-governmental organizations in order to sustain continuity of their regular activities. In this paper, we use a differential equation based disease model to simulate the spread of disease in communities to answer several questions about the timing and methods of school closure.

As it was the case in the 1918 flu pandemic, it is very likely that there will be multiple waves of pandemic hitting people in the next pandemic influenza caused by avian flu virus H5N1 (Castillo-Chavez et al. 1989; Chowell et al. 2006; Ferguson et al. 2005). The intervals between the waves of previous pandemics were several months apart in some instances (Merler et al. 2008). Estimating the time differences between the peaks of multiple waves of pandemic infections is also of great interest to policy makers, in terms of allocating critical resources to mitigate community impacts. Merler et al. (2008), indicate that natural and political barriers can change the structure of the contact network, possibly reducing the interactions among the individuals who are infected and susceptible and as a result delay the course of epidemics. They also indicate that social distancing policies (such as school) closure affecting the contact rate of individuals are some of the important strategies that affect the timing of the multiple waves of pandemic. Thus, policy makers should consider this fact when making closure decisions. In addition to this, the genetic drift (i.e. mutation) of the influenza virus is another important factor affecting the time period of the waves, since the appearance of new strains can reduce the immunity of the population. Bootsma and Ferguson (2007) also indicated that the timing of the containment and mitigation policies will determine the time between the peaks of pandemic waves. Thus, while the time period between the waves does not have a completely predictable pattern, it is at least partially controllable with social distancing policies. In this paper, our model generates multiple waves of epidemic based on the timing of social distancing interventions and application of non-pharmaceutical mitigation measures. As a result, the immunity of the population to the virus strain that causes the pandemic is one important factor determining the characteristics of the waves of pandemic. Because we do not consider any pharmaceutical intervention and any immunity given to people through vaccination, policies related to implementation of social distancing strategies can determine the time period between the waves. Seasonality in transmission, changes in the contact rates and antigenic evolution of the virus are possible reasons for multiple wave patterns of epidemic and may not have predictable patterns. The change in the transmission rate with the ability of the virus to increase its transmissibility through several mutations is one of the characteristics of the virus that helps predict the timing and size of the second and third waves of pandemic.

Because there exists a lot of uncertainty on the characteristics of the virus that will cause the pandemic, during the early stages non-pharmaceutical interventions such as social distancing and preventive sequestration will play a significant role. Our simulations and earlier studies (Lofgren et al. 2008; Germann et al. 2006; Ferguson et al. 2005; Ciofi degli Atti et al. 2008) showed that without using any pharmaceutical intervention to mitigate disease spread such as antiviral distribution or vaccination the population will still remain vulnerable to the disease and when social restrictions are removed, individuals who did not initially catch the virus will have high probability to get infected in a later wave. The primary gain from social distancing is the time between the waves which presents good opportunities to implement pharmaceutical based policies during the time between pandemic waves. School closure, a community mitigation policy is controversial regarding how effective it is in terms of reducing the impacts of a pandemic. For example Lofgren et al. (2008) claimed that is not an effective strategy itself unless accompanied by other mitigation strategies. On the other hand, Ekici, Keskinocak and Swann (2008) indicate that the transmission of the disease can also be reduced by institutional and household quarantine. By using the time that is gained with social distancing interventions, it is likely that appropriate vaccines can be developed to vaccinate unimmunized individuals and distribute antiviral prophylaxis for possible exposures.

In the literature there are two performance measures commonly used to evaluate the effectiveness of intervention policies: peak infectivity and infection attack rate (IAR) (Ekici, Keskinocak and Swann 2008). Peak infectivity is the percentage of the population infected at the peak and IAR is the cumulative percentage of people who have been infected

(can be symptomatic or asymptomatic) during the course of a pandemic. School or workplace closure and social distancing measures such as travel restrictions and quarantine during the peak can reduce the peak infectivity but may not significantly reduce IAR (Ferguson et al. 2005; Germann et al. 2006). Social distancing measures delayed the spread in the 1918 and 1957 pandemics (WHO, 2005) but had little impact on IAR. However, delaying the spread and the peak is desirable for planning purposes, since it provides more time to get prepared and can lead to a smaller peak. In this paper, we also evaluate different strategies of implementing school closures based on these performance measures. In the next section we present the details of the simulation model that we used to evaluate different school closure strategies.

3 SIMULATION MODEL

The primary purpose of our model was to simulate multiple communities with individuals traveling from one county to another county on a daily basis. These travels are the main reason for the spread of the disease in the state. The populations of the counties are divided into five age groups: Pre-School children, Elementary School age, Middle School age, High School age students and Adults. The daily travel data that we used in the model is from US Census Data (2000) on the daily numbers of people commuting from one county to another in the state. The population structure and the travel network of the model is presented in Figure 1. This type of network is called a “fully connected community” in Nigmatulina and Larson (2009), since it allows travels from one location to any other location without considering only immediate neighboring locations. We also assume that only the individuals who are in the Adults age group are traveling on a daily basis, since the school age children will be in their schools during the day.

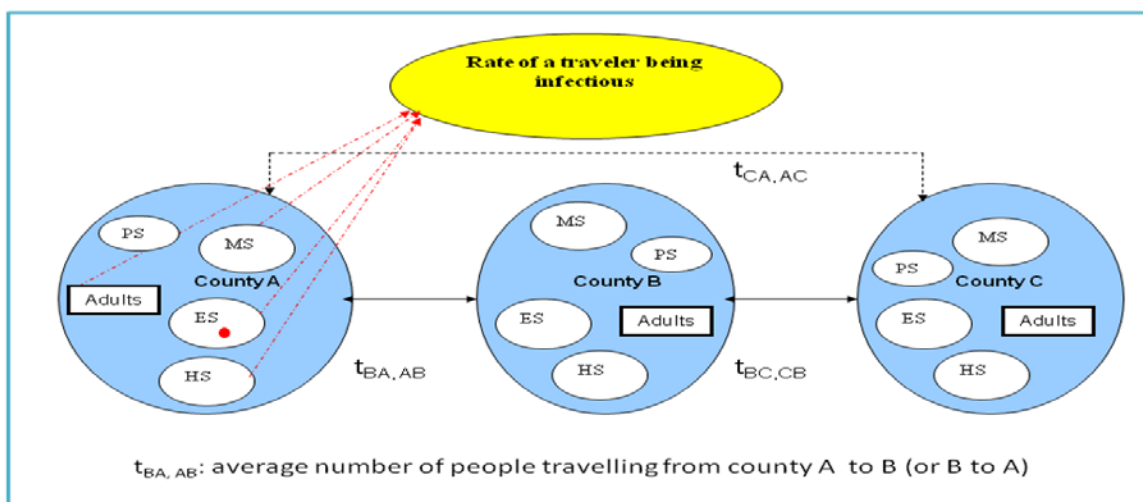


Figure 1: Structure of the multiple community models with age groups

However, we also assume there is a mixing of each age group with lower proportions with their households at home with the average household size of five people. The mixing structure of the model is presented with Figure 3.

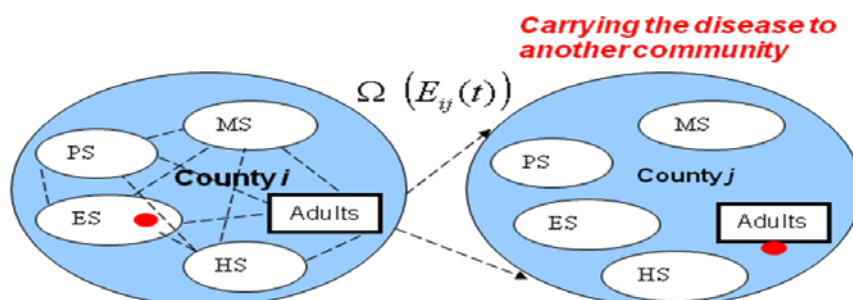


Figure 2: Mixing structure of age groups in a county and transfer of the disease to other counties

The age structure of the model captures different susceptibility of individuals to the disease at different ages with their activity levels and activity level of individuals are determined based on average number of their contacts. The transmission

rates for the individuals at different age groups are presented in Table 1 (Longini et al. 2004) which shows that the susceptibility of individuals decreases slightly with an increase in their age. Thus, the model captures the age immunity and age related differences with average contacts and infection transmission rates.

Table 1: Transmission rates at each age group

Transmission Rates	Elementary Schools	Middle Schools	High Schools
Elementary Schools	0.0145		
Middle Schools		0.0125	
High Schools			0.0105

The disease spread dynamics is formulated as a compartmental flu model with the transport operator that was first introduced by Rvachev and Longini (1989). The natural history of the disease in individuals is shown in Figure 3 (Castillo-Chevaz et al. 1989; Ekici, Keskinocak and Swann 2008).

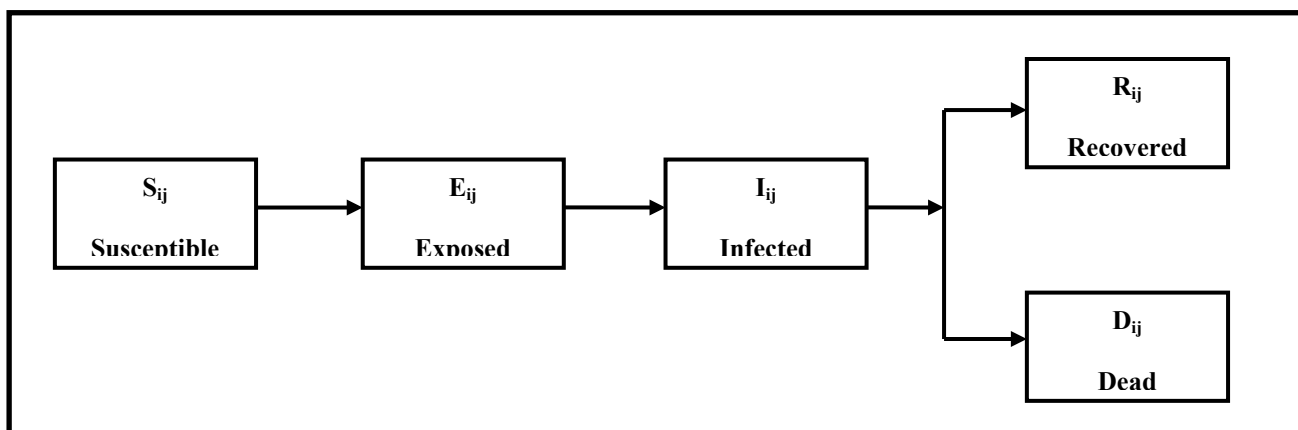


Figure 3: Natural history of influenza

3.1 Mathematical Model

We formulate a compartmental disease spread model in which the whole population in each age group of a county is divided into compartments of susceptible, exposed, infected, recovered and dead. In addition, we also assume the entire population is susceptible to the disease at the beginning and transmission dynamics start with an introduction of an infectious individual to one of the age groups in a community.

Let I be the set of counties in the state and let K be the set of links in the transportation network connecting the counties with daily commuting as the flow in the network. That is $(i, l) \in K$ if and only if county i is connected through direct travel and $i, l \in I$. Let $T = (t_{i,l})$ be an arbitrary symmetric transport matrix where $t_{i,l}$ equals to total number of individuals in county i having contacts with individuals from county l ($t_{i,l}$ is equal to zero for all age groups other than adults). Let $\Omega : R^I \rightarrow R^I$ be the transport operator defined on the susceptible and exposed compartments as given in (1) and (2):

$$[\Omega(S_i(t))] = S_i(t) + \sum_{\{(l,i) \in K\}} \left(t_{l,i} \frac{S_l(t)}{N_l} \right) - \sum_{\{(i,l) \in K\}} \left(t_{i,l} \frac{S_i(t)}{N_i} \right) \tag{1}$$

$$[\Omega(E_i(t))] = E_i(t) + \sum_{\{(l,i) \in K\}} \left(t_{l,i} \frac{E_l(t)}{N_l} \right) - \sum_{\{(i,l) \in K\}} \left(t_{i,l} \frac{E_i(t)}{N_i} \right) \tag{2}$$

Because $\Omega : R^I \rightarrow R^I$ is a linear operator we can use it in our differential equation based SEIR model given with equations (3)-(7). Each county, i has the model variables for susceptible, $S_i(t)$, exposed, $E_i(t)$, infected, $I_i(t)$ and recovered, $R_i(t)$; we

also define the variable $D_i(t)$ which represents those who do not recover (i.e. die). The model dynamics can be written as the following system of equations with the defined parameters:

α : Infection rate

β_{ij} : Contact rate of age group j in county i .

μ : Infectious mortality rate.

σ : Rate of progression from exposed to infected (σ^{-1} is latent period)

γ : Recovery rate for infected people

N_{ij} : Total number of people in county i age group j .

$$\frac{dS_{ij}(t)}{dt} = -\alpha_j \Omega(S_{ij}(t)) \left[\sum_{k \in J} \beta_{ik} \left(\frac{(\Omega(E_{ik}(t)) + I_{ik}(t))}{N_{ik}} \right) \right] \tag{1}$$

$$\frac{dE_{ij}(t)}{dt} = \alpha_j \Omega(S_{ij}(t)) \left[\sum_{k \in J} \beta_{ik} \left(\frac{(\Omega(E_{ik}(t)) + I_{ik}(t))}{N_{ik}} \right) \right] - \sigma \Omega(E_{ij}(t)) \tag{2}$$

$$\frac{dI_{ij}(t)}{dt} = \sigma \Omega(E_{ij}(t)) - \mu I_{ij}(t) - \gamma I_{ij}(t) \tag{3}$$

$$\frac{dR_{ij}(t)}{dt} = \gamma I_{ij}(t) \tag{4}$$

$$\frac{dD_{ij}(t)}{dt} = \mu I_{ij}(t) \tag{5}$$

We also assumed that only the exposed individuals are travelling to neighboring communities and causing the spread of the disease, since symptomatic infectious individuals are more likely to either be hospitalized or prefer to stay at home (self quarantined). Because the transport matrix that we used is symmetric, we do not allow any migration from one location to another in the dynamics of the model.

3.2 Other Model Parameters

The simulation model is also functionalized with the changes in the average contact rates of individuals in each school age groups with an associated policy. The model allows decision makers to limit the school activities in each county separately, limit the activities in the all state schools at the same time and close schools separately at different times or close them all once. Without considering any pharmaceutical interventions in the community mitigation strategies, the decisions for schools to mitigate the effects of the pandemic are listed as limitation of general activities such as sport gatherings and group workings and also the closure of the schools. Thus, the average number of contacts of school aged each individual changes with the implementation of these policies. The average numbers of contacts of individuals within each school age group under normal conditions is presented in Table 2. We assume that each school age children will have a higher mixing rate within his/her age group and individuals will have fewer contacts with the individuals from other age groups.

Table 2: Mixing Rates of Age Groups with Different Policies

Contacts (People/day)	Elementary School	Middle School	High School
Elementary School	20	5	5
Middle School	5	30	5
High School	5	5	40

The school closure policy is implemented in the model as a factor changing the number of daily contacts of individuals. For example when the schools are closed we assume school children will have contacts only with their households and when the activities are limited at schools their contact rate will be significantly decreased. The changes in mixing rates with policy implementation are presented in Table 3. Note that elements in row one in this table are the diagonal elements of Table 2. The off diagonal elements when activities are limited or schools are closed are equal to zero.

Table 3: Changes in Mixing Rates with School Closure Policies

Policy Implemented	Elementary School	Middle School	High School
Normal	20	30	40
Activities Limited	10	15	20
Schools Closed	5	5	5

For simulating disease transmission, several parameters should be also estimated *a priori* because of the existing uncertainty about the biological characteristics of avian flu virus after mutation to be able to transmit from human to human. These parameters are estimated in the literature based on the previous pandemic influenza outbreaks in history (Keeling and Rohani 2008; Chowell and Nishiura 2008). We used 2% infected mortality rate in our model and it is an expected rate of mortality for individuals who get infected in the next pandemic (Mnieszewski et al. 2008). Other disease parameters that we used in our model from the literature are incubation period as 2 days and the infectious period as 4 days (Mnieszewski et al. 2008; Chowell et al. 2006).

4 DECISION ANALYSIS AND RESULTS

The presented simulation model in this paper was used by the Arizona Department of Health and Human Services with the Arizona Department of Education to test their pandemic preparedness activities. The exercise took place at the Decision Theater of Arizona State University with two different sessions, one on February 12th, 2009 and the other on Feb 18th, 2009. Officials from different counties in the state attended the sessions. In this section we present results to compare several school closure and reopening strategies applied during these exercises by using the presented simulation model. We first run the simulation model without any interventions as the base run, with having an index case (first infectious individual) in an elementary school in Yuma County. Figure 4 shows the infections of Maricopa County and Pinal County (which are the first two highly populated counties in the state), Yuma County (has the index case) and the total student infections in the state without any intervention policy applied.

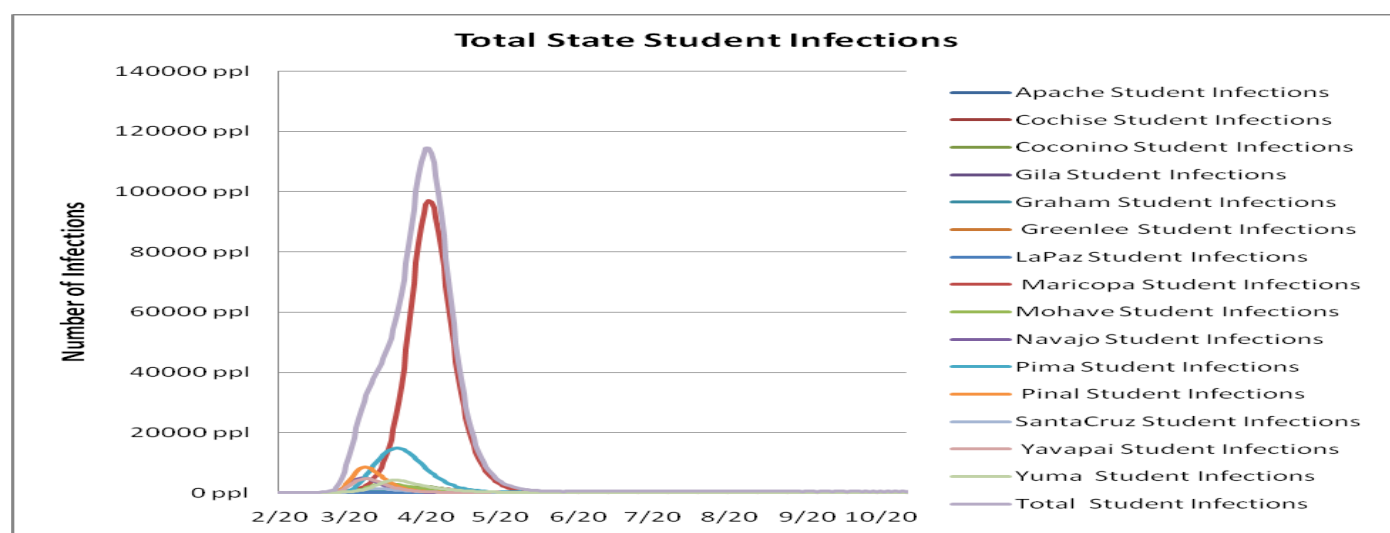


Figure 4: Estimated Total Number of Infections by County and Month without Interventions

We also present results for two additional scenarios which actually display results of the actions that were taken during the actual school closure exercise for Arizona. In the next section we compare these different strategies with the base run in terms of IAR, peak infectivity and peak time of infections.

4.1. Results for Two Additional Scenarios

We present the results from the two school closure exercises described above. These exercises resulted in two different decisions. Based on the results of key decisions made during the first exercise, the simulation results of infections in the state are shown below. The actions in this exercise include closing schools in Yuma early with the first case in the state at the end of February, and all state school closure with the first mortality case confirmation in early March. After 8 weeks of school closure all schools in the state were reopened with limitation on the activities such as sport gatherings and group workings. These decisions resulted in an overall statewide infection rate of 45.12%, student infection rate of 20.5% and a total of 0.59 % of student deaths. Figure 5 presents the infections of students in the state.

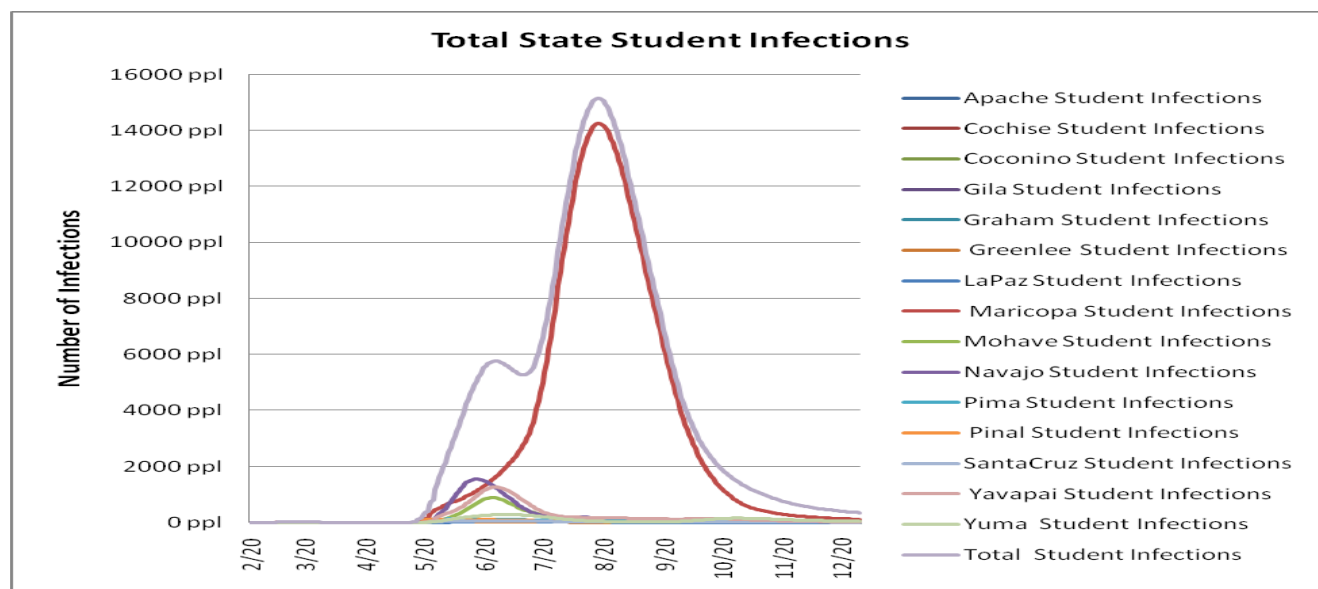


Figure 5: Exercise 1- Estimated Infections by County and Month

As shown in Figures 5, the majority of these infections and the resulting mortalities were concentrated in Maricopa due to the large population in this county. Also of note is that, the decision to reopen schools resulted in an increment in student infections and deaths during the second wave of the pandemic which began in late July. That is because the school reopening decision increased the contact rate of students which resulted into a high number of infections.

The second exercise has the actions of closing schools in the whole state after the first death in Yuma in early March (as opposed to the first case as in first exercise) and not reopening again until the end of December. These decisions resulted in an overall statewide infection rate of 42.08%, student infection rate of 3.35% and a total of 0.10% student deaths. Similar to the first exercise, the majority of these infections and deaths were concentrated in Maricopa County. From an epidemiologic perspective, an interesting result from this exercise was the apparent elimination of a second pandemic wave. As shown in Figure 6, the pandemic peaked in March; however, prolonged school closure decreased contact rates and resulted in a much shorter pandemic duration. We note that that, schools had to be closed for more than 8 months which may not actually be an acceptable decision.

4.2. Comparison of Results from Scenarios

In Table 4, we demonstrate a comparative analysis of several different hypothetical decisions as compared to the results based on the actual group decisions in the first and the second exercises. In a no intervention scenario we assumed that the pandemic would run its course with no school closure or restricted activity. For the first exercise, the results from the group decisions fell somewhere between these two hypothetical scenarios. Delaying statewide school closure until the first death in Arizona (or approximately three weeks following the first case) resulted in a higher number of student deaths during the pandemic. Delaying school closure did not appear to substantially increase the percentage of the total population that became infected. For the second exercise, the group results were significantly better than no intervention scenario. The decision not to reopen schools significantly reduced total infection rates and total mortality rates.

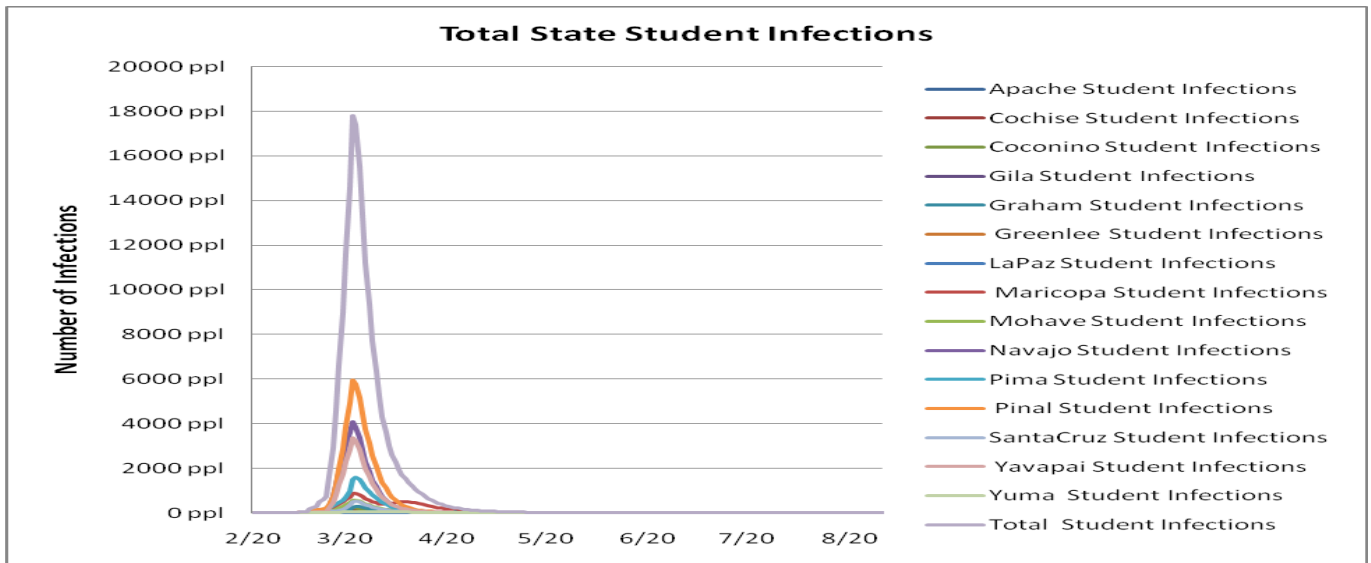


Figure 6: Exercise 2- Estimated Infections by County and Month

The Arizona Pandemic Influenza School Closure Exercises provided a valuable forum for schools and health officials to collaborate on a comprehensive strategy for closing schools in the event of an influenza pandemic. As with any sector, the education system will be severely strained during such an outbreak. A comprehensive response from the federal level all the way down to individual schools is required to meet the challenges. Additionally, roles and responsibilities for all responders and stakeholders must be clearly delineated in response plans, and coordinated exercises must be conducted to prepare our communities, schools, and children for a prolonged school closure.

The findings in this paper can be useful to guide schools, community partners, local and state governments, and other stakeholders in developing a comprehensive strategy for school closure integrated this strategy into state-wide response plans.

Table 4: Comparison of Different Scenarios

<i>Comparison Metrics</i>	<i>No Intervention Case</i>	<i>Exercise Result 1</i>	<i>Exercise Result 2</i>
<i>Total Infected Population</i>	3,073,305	2,681,579	2,501,459
<i>Infected Population (%)</i>	51.70	45.12	42.08
<i>Total Students Infected</i>	653,752	232,087	37,917
<i>Students Infected</i>	55.03	20.50	3.35
<i>Total Deaths in Population</i>	81,017	68,969	63,427
<i>Deaths in Population (%)</i>	1.36	1.16	1.07
<i>Total Student Deaths</i>	18,672	6,623	1,083
<i>Student Deaths (%)</i>	1.65	0.59	0.10
<i>Peak Student Infections (%)</i>	10.00	1.33	1.57
<i>Peak Day</i>	57	174	27

5 CONCLUSIONS

This paper presented a geospatial-temporal disease model which can be used to simulate several school closure and reopening policies in the course of an influenza pandemic. The simulation model has the capability of testing policies such as limiting activities in each county separately and in the whole state simultaneously; and closing the schools in each county separately and in the whole state simultaneously. This capability gives the opportunity for decision makers to test several school closure policies to identify the best strategy in terms of minimizing the number of infections in schools with minimum discontinuity in education. The results show that school closures can reduce the number of infections at the early stages of pandemic but because it does not change anything about the immunity of the community and most of the population will still remain susceptible to pandemic influenza; it is very likely to have multiple waves of infections. However, the delays give an opportunity for medical authorities to deliver vaccines if an appropriate one becomes available. In addition, it also reduces the peak of infections significantly during the pandemic and this avoids hospitals and other medical agencies becoming overwhelmed with a tremendous amount of demand for treatment and gives time for them to get better prepared.

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