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Virtual Epidemic in a Virtual City: Simulating the Spread of Influenza in a United States Metropolitan Area

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Abstract

A wide variety of biological, physiological, social, economic and geographic factors may affect the transmission, spread, and impact of influenza. Recent concerns about an impending influenza epidemic have generated a need for predictive computer simulation models to forecast the spread of influenza and the effectiveness of prevention and control strategies. We designed an agent-based computer simulation of a theoretical influenza epidemic in Norfolk (Virginia) that included extensive city-level details and computer representations of every Norfolk citizen, including their expected behavior and social interactions. The simulation introduced 200 people infected cases on November 27, 2002 (Day 87) and tracked the progress of the epidemic. On average, the prevalence peaked on Day 178 (12.2% of the population). Our model showed a cyclical variation in influenza cases by day of the week with fewer people being exposed on weekends, differences in emergency room and clinic visits by day of the week, an earlier peak in influenza cases and persistent high prevalence among people age 65 or older, and the daily prevalence of infection among health care workers. The level of detail included in our simulation model made these findings possible. Compared to other existing models, our model has a very extensive and detailed social network, which may be important since individuals with more social interactions and extensive social networks may be more likely to spread influenza. Our simulation may serve as a virtual laboratory to better understand the way different factors and interventions affect the spread of influenza.

INTRODUCTION

A wide variety of biological, physiological, social, economic and geographic factors may affect the transmission, spread, and impact of influenza.^{1–5} In particular, social networks and interpersonal interactions can drive the propagation of any transmissible infectious disease.^{6–8} For example, people with extensive social contacts may be more likely to contract and spread influenza than people who are socially isolated.^{9, 10} The nature, degree, and intensity of the social contact also may be very important. Therefore, any predictive model that fails to account for specific social behavior and interactions may not accurately portray an influenza epidemic.

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Recent concerns about an impending influenza epidemic have led to the development of predictive computer simulation models to forecast the spread of influenza and the effectiveness of prevention and control strategies. Many of these models lack the granularity required to represent many of the person-to-person interactions that contribute to epidemics as they do not include any city-level details, such as the specific geographic, economic, and climate characteristics of a city. Few account for important differences in behavior among different members of the population. None to our knowledge fully incorporate city-specific social networks and interactions.

We designed an agent-based computer simulation of a theoretical influenza epidemic in Norfolk (Virginia) that included extensive details about the city and computer representations of every Norfolk citizen, including their expected behavior and social interactions. The simulation tracked the progress of the epidemic throughout one year. This paper describes the construction and execution of the model and presents results generated by the model.

METHODS

Our influenza model is an extension of the BioWar simulation.¹¹ BioWar is an agent-based computer simulation of five different US metropolitan areas: Washington D.C., Norfolk (Virginia), Pittsburgh, San Diego, and San Francisco. Each city is modeled using specific census, geographic, weather, school district, and business/entertainment location data. Each individual in the city is represented by a computer simulated agent. During the course of the simulation, individual agents go about their lives, making decisions based on programmed probabilities, interacting with each other, and participating in a wide range of activities.

The model is programmed in C++. The simulation model runs were executed at the Arctic Region Supercomputing Center (ARSC) at the University of Alaska-Fairbanks on a Cray XD1 supercomputer with AMD Opteron 250 Single Core processors (two cores per node) and AMD Opteron 280 Dual Core processors (four cores per node) with 16 Gigabytes (GB) of shared memory. The software is multithreaded. Four threads were used in both the city construction runs and the virtual experiment runs.

The City

For our influenza simulation, we chose Norfolk, a moderate-sized United States city without significantly unusual or unique geographic or socio-demographic qualities. Based on the 2000 U.S. Census data, our model of Norfolk included 1,569,541 people.¹² The simulated city consisted of a number of specific locations found in Norfolk including homes, workplaces, schools, pharmacies, doctor's offices, emergency rooms, stadiums, theaters, stores, restaurants, universities, and military facilities. Locations could be open or closed, depending on the day, time of day, and weather. For example, inclement weather could lead to school closures. Geographic, location, and weather data came from U.S. Census Bureau reports on cartographic boundaries for schools, Metropolitan Statistics Area (MSA) boundaries and business patterns, and National Oceanic and Atmospheric Administration (NOAA) Climate Data.^{13–20}

Time

Since our data came from 2002, the simulation commenced on a virtual date of September 1, 2002 and ended on a virtual date of August 31, 2003. Time progressed in four-hour "ticks" with decisions, agent movement, and all other actions and changes occurring at each "tick" (i.e., 4 am, 8 am, 12 noon, 4 pm, 8 pm, and midnight)

Agent Characteristics

Each agent has a specific set of socioeconomic and demographic characteristics. The distribution of these characteristics was based on U.S. Census Bureau data.¹² Each agent's constellation of characteristics (e.g., race, socioeconomic status, and gender) affects its social network size, movement, and probability of different behaviors (e.g., health care seeking behavior), based on data from the General Social Survey (GSS).^{21–23}

Agent Movement

Individuals move throughout the city in four-hour time “ticks,” i.e., every four hours the individual either stays in the same location or moves to different location. The probability of an agent moving to a given location depends on the time of day, day of the week, and month of the year. For example, agents are more likely to be at work during the daytime on weekdays and at home during the nighttime and on weekends. Each agent's probability of moving to a specific recreational area also varies from day to day and season to season. Agents cannot move to closed locations (e.g., school on a weekend). The GSS and Environmental Protection Agency Time Use Survey generated data for agent movements.^{19, 21, 24}

Agent's Social Network

Each agent has a social network: a set of specific relationships of varying degrees and intensity to a certain number of other agents. Different agents have different sizes and types of social networks. Potential members of each agent's social network include spouse, parent, sibling, child, other family member, coworker, neighbor, friend, advisor, schoolmate, and fellow group member (e.g., clubs). The social network parameters came from the GSS survey data and additional social network research.^{13, 21, 25–27} The size and composition of each agent's social network depends on the agent's race, location, age, gender, occupation, and socioeconomic status.

Agent Interactions

Agents interact with each other based on the CONSTRUCT multi-agent model of group and organizational behavior.^{28–31} An agent is more likely to interact with other agents who are in close proximity during a given time tick. Also, an agent tends to interact with agents who are in his/her social network. The probability of interaction depends on how closely related the agents are within the social network (e.g., an agent is more likely to interact with a spouse than with friends or co-workers).

Influenza Infection

We introduced 200 cases of influenza into the population on Day 87 of the simulation (Wednesday, November 27, 2002). This was analogous to plane-load of patients with influenza entering and rapidly dispersing throughout Norfolk. For each simulation run, the 200 cases represented a random cross-section of the Norfolk population. For our simulation, influenza had an incubation period of 2 days and duration of illness for 11 days, parameters derived from information from the Centers for Disease Control and Prevention (CDC), the U.S. Army Medical Management of Biological Casualties Handbook (“Blue Book”), and expert opinion.^{32–34} In the initial base case model, an infected agent had a 50% probability transmitting influenza to each non-infected agent with which it interacts. Our model assumed that this transmission rate is the same for all people. This is based on the 50% serologic attack rate used in previous models and derived from the 1957 pandemic.^{35, 36} (The World Health Organization currently advises using a 25% clinical attack rate with half of all cases being clinically evident.)³⁷

Additionally, we performed sensitivity analyses for the transmission rate (varying the rate by 10% increments from 10% to 100%), the incubation period (1,2,3, 5, and 7 days), and the contagious period (2,3,5,7,10,15). The base case scenario assumed 0% immunity, i.e., no vaccination and the epidemic strain would have no similarity to previous years' strains. Additional sensitivity analyses varied the immunity rate from 0% to 100% by 10% increments. The model assumed that immunity was the same across all agents, regardless of demographic characteristics. Agents infected with influenza have probabilities of developing different symptoms. If present, each symptom has a certain evoking strength score based on INTERNIST-1 Quick Medical Reference (QMR) scoring system.^{38–41} The more severe and closely associated a symptom is with influenza, the higher the evoking score is.

Health Care System

The sum of an agent's evoking strength scores determines its health care seeking behavior (Figure 1). An evoking strength score of 0 means that the agent is completely asymptomatic and does not seek any medications or medical attention. An agent with a higher evoking strength sum has more severe symptoms and will go to the pharmacies to purchase over-the-counter medications. More severe symptoms will motivate patients to go to the clinic or emergency room.^{38–41} An agent's race affects its probability of seeking health care for a given set of symptoms.^{21–23}

This paper conforms to the relevant ethical guidelines for human and animal research.

RESULTS

We ran the entire simulation 10 times. Each simulation run took approximately 14 hours to complete. Each simulation run consumed on average 4 GB of the 16 GB available. Storing each simulation run occupied on average 768.1 megabytes. In Figure 2a, the solid line represents the average of these 10 runs, the upper dashed line represents the maximum prevalence and the lower dashed line represents the minimum prevalence for each day of the 10 runs. The number of cases peaks on average day 185. The average peak number of cases is 195,968 (12.8% of the population) with a maximum peak number of cases of 198,720 (13.0% of the population) and a minimum peak number of cases of 192,923 (12.6% of the population). Of the 10 simulation runs, the earliest peak occurs on Day 179; the latest peak occurs on Day 193.

The curve is the same shape as a standard epidemic curve generated by a traditional compartment model with a R_0 (basic reproductive ratio) of 2.0. The biggest difference from a compartment model curve is that we see variations by day of the week. The incidence of influenza cases is cyclical, increasing on weekdays and decreasing on weekends, resulting in a bumpier curve rather than a smoother one.

Figure 2b shows the results of varying the transmission rate by 10% increments. Table 1 identifies the corresponding R_0 for each transmission rate. A transmission rate of 20% or less fails to generate an epidemic curve (corresponding to a R_0 of 1.0 or less).

Figures 2c and 2d demonstrate the effects of varying the incubation period (1,2,3, 5, and 7 days), and the contagious period (2,3,5,7,10,15), respectively. An incubation period of 5 days or greater fails to generate a significant epidemic curve. Figure 2e illustrates how introducing different levels of immunity to the population changes the epidemic curve. A population immunity level of 30% or greater quells the epidemic.

Figure 3 illustrates the emergency room and clinic visits over time. The number of health care visits increases as the number of active influenza cases increase. On average, the number of

emergency room visits peak at 102,344 (maximum peak, 104,245; minimum peak, 100,271) on Day 187 (earliest peak, 179; latest peak, 193). The number of clinic visits peaks at 33,467 (maximum peak, 34,207; minimum peak, 32,712) on Day 183 (earliest peak, 176; latest peak, 190), 2 days earlier than the peak of emergency room visits. At the peak, on average 64,299 (62.8%) emergency room visits are by whites, 32,277 (31.5%), by African Americans 3,183 (3.1%) by Hispanic Americans, and 2,644 (2.6%) by Asian Americans. At the peak, on average 20,826 (62.2%) clinic visits are by whites, 10,642 (31.8%) by African Americans, 1,119 (3.3%) by Hispanic Americans, and 902 (2.7%) by Asian Americans. The number of visits also varies cyclically by day of the week, lagging the incidence of cases by several days. The cycle had a periodicity of 7 days with weekend days (Sunday highest) always seeing the highest number of influenza-related health care visits. In our simulation runs, the initial seed cases were introduced on a Wednesday, the day before Thanksgiving. The variation in emergency room and clinic visits is greater than the variation in influenza incidence. (The model assumes that clinics are open seven days a week during the epidemic.)

Figure 4 shows the breakdown of influenza cases by age. At its peak, the average distribution of cases is as follows: 14,416, ages 12 years or younger; 15,753, ages 12 to 20; 135,059, ages 21 to 64; and 32,983, age 65 years or older. As you can see, the number of influenza cases in people age 65 or older peaks earlier [on average Day 180 (172–186)] than the rest of the population [Day 188 (180–200) for 12 years or younger; Day 186 (179–193) for ages 12–20 years old; Day 185 (179–193) for ages 21–64 years old]. The prevalence of influenza also remains high among those 65 years and older for a longer period of time than among other age groups.

Figure 5 shows the break-down of influenza cases by race. At the peak, on average 123,281 whites (maximum, 124,897; minimum, 121,102), 61,743 African Americans (maximum, 62,851; minimum 60,972), 5,966 Hispanic Americans (maximum, 6076; minimum, 5,859), and 5,023 Asian Americans (maximum, 5,148; minimum, 4,886) are infected. There does not appear to be any significant difference in rates of infection among the different races. On average, the peak in emergency room visits occurs earlier for Whites and African Americans (Day 187; Earliest, 179; Latest, 193) than Asian Americans (Day 191; Earliest, 186; Latest, 200).

At the peak, 143,885 working individuals are afflicted with influenza (maximum, 139,922; minimum, 135,189), of which 6,043 (4.2%) are health care workers (maximum, 6,194; minimum, 5,921). The first health care worker case is infected four days after the 200 infectious cases are introduced into the population.

DISCUSSION

Computer simulation models have aided research and planning in a wide variety of arenas including manufacturing, environmental studies, transportation, the military, and health care.^{42–44} Such models have helped better understand the factors and sequences involved in different processes. They have served as virtual laboratories to conduct virtual experiments that demonstrate the potential effects of different interventions and policies. Simulation models also have helped identify and target further areas of research.

Computer simulation is particularly useful in studying a potential infectious disease epidemic such as influenza. Retrospective data on influenza epidemics is very limited and may not be applicable to different times and settings. Conducting clinical trials that involve the experimental release of highly transmissible and virulent influenza would be impractical and unethical. Moreover, any large-scale public health natural experiment would require considerable planning and resources. There has been considerable recent attention to pandemic

influenza planning. Evidence suggests that another influenza pandemic will occur in the future. When, where, and how it will begin and progress is unknown.^{45, 46} Scientists and policy makers have been very interested in better understanding the potential behavior and impact of influenza in an epidemic setting to better inform research initiatives, influenza vaccine and antiviral development, policy making, and resource allocation. This has motivated the development of different influenza computer simulation models.

Every existing model has its relative strengths and weaknesses. Different models are appropriate for different situations and for answering or informing different questions. Rather than compete, the different types of models complement each other. While compartment models offer relative simplicity and generalizability, agent-based models incorporate individual decision-making and behavior. Compartment models treat the population as homogenous blocks of people who share the same characteristics and decision making.^{3, 47–50} The output from compartment models tends to be gross population disease incidence and prevalence, without details on geospatial location of diseased individuals, disease behavior in specific sociodemographic groups, and health care seeking behavior. Agent-based models consist of more autonomous virtual individuals that make choices and take action just as individuals would.⁵¹ Since most compartment models include very little detail about patients and city characteristics, they do not account for many potentially important social, psychological, geographic, and economic factors and are limited in their ability to test certain specific policies and strategies.

A number of agent-based models of disease spread exist. The Ferguson, et. al., and Germann, et al., models are representations of the entire United States.^{52, 53} By covering much larger geographic areas but not including as much city-level and population-level detail as our model, these models are more useful for national planning but less useful for detailed individual city planning. The Longini, et al., model is a representation of a typical American community, making it more generalizable to different communities but less specific to any single real community.⁵⁴ Perhaps the most similar existing simulation to ours is the EpiSims model, which incorporates more transportation and transportation infrastructure data but less social interaction, social network, and behavior data than our model.^{55, 56}

Our model shows the weekly variation in influenza cases and presentation to the emergency rooms and clinics. The incidence of influenza cases decreases on weekends due to less interaction among people (i.e., fewer people are at work or school). This finding supports the importance of school and workplace closures in mitigating spread of an epidemic.^{57, 58} Compared to the day-to-day variability in influenza incidence, the day-to-day variability in health care visits is accentuated because patients may be less likely to go to the emergency room or clinic on weekends. Understanding this variation can better assist health care system planning, such as predicting the required daily surge capacity.

Our results suggest that influenza may strike earlier and remain at a high prevalence longer among people age 65 years or older. Since our model assumed no difference in the transmission and immunity rates among different age groups, this finding is due solely to the differences in location, movement, and contact rates of the elderly.^{21–23} This is consistent with the fact that many older individuals are located in communal areas such as nursing homes. The elderly may serve as a “reservoir” for influenza during the epidemic, generating new cases over a long period of time. Perhaps targeting the elderly for vaccination campaigns or transmission among the elderly may be essential in stemming an influenza epidemic. Future studies may look at the effects of changing immunity and transmission rates among different age groups.

The model runs show no significant differences in infection rates among the different races and predicted the racial mix of patients presenting to the clinics and emergency rooms. An

agent's race affects its social network size and composition as well as its health-care seeking behavior.^{21–23} The GSS social network data suggests that different races on average have different social networks and that certain races on average may be more or less likely to seek different levels of health care, even when controlling for other socioeconomic characteristics. In our model, different races do not have any biological or clinical differences. So any difference in infection rates and health care use is based solely on differences in the location, social interaction, and behavior of members of each race. The racial mix of patients presenting the emergency room and clinics can help identify the location of the epidemic in the city (e.g., if an unusually high number of African Americans presents to the health care system, one may suspect that the disease is more widespread in neighborhoods with larger African American contingents). This may help direct control measures (e.g., where to deliver vaccines, antivirals, and initiate social distancing measures). It also can inform how to allocate health care resources for treatment (e.g., which hospitals will experience surges and need additional staffing). Anticipating the racial mix of people presenting to the health care system can provide important information about the size and extent of the influenza attack. Racial distributions that are dramatically different from those predicted by the computer simulation model suggest that the disease is less widespread, remaining confined to specific neighborhoods and, in turn, specific races. The slightly later presentation of Asian Americans to the emergency rooms calls for a closer look at the social data (e.g., are Asian Americans less likely to go to the emergency room? Do Asian Americans have less access to emergency rooms?)

Our model also shows the number of workers afflicted with influenza during the epidemic. Infected workers lead to increased absenteeism and decreased productivity. Productivity may decrease to a point where operations break down. This is especially important in essential operations, such as health care. Having a substantial number of health care workers infected seriously impedes the health care system's ability to combat the epidemic. A logical next step would be to compare the numbers from our model with the personnel needs of different industries.

Compared to other existing models, perhaps the most distinguishing feature of our model is its extensive and detailed social network. Most models assume that members of the population randomly mix with each other and that all members of the population have a relatively equal number and extent of social interactions. By contrast, our model's social network attempts to replicate the actual social interactions that each member of the city would have. Our model also includes considerable city-level detail such as weather and geographic information that influence these social interactions.

Accurately portraying a city's true social interactions may be very important. A very socially active individual may be more likely to spread influenza than socially isolated individuals. Depending on who is initially infected, influenza may spread more quickly through certain socio-demographic groups. Certain sociodemographic groups may have less access to health care, making the detection and control of an epidemic more difficult. As a result, spread of influenza can depend on the time of day, day of the week, and time of the year.

Including detailed social networks in influenza epidemic models is becoming more important as investigators and policy makers increasingly focus on the role of non-pharmaceutical interventions (e.g., social distancing), in quelling an influenza epidemic.^{59, 60} Social distancing measures (e.g., closing schools, limiting public gatherings, and quarantining exposed individuals) aim to keep infectious patients away from susceptible patients.^{60–62} These measures may be pivotal for several reasons.⁵⁷ There may not be enough advance warning to identify and administer the appropriate vaccine.^{63–65} Antiviral stockpiles will be limited and mobilization and distribution may take time.⁶⁶ Antiviral resistance is real potential problem.

⁶⁷ Moreover, some models have illustrated the potential benefits of social distancing measures even with vaccination and anti-virals.⁶⁸

Limitations

Simulation computer models are by definition idealized simplifications of natural events and processes. They incorporate numerous assumptions and cannot possibly account for every factor. The objective of simulation modeling is not to provide exact answers but to better understand the phenomena and raise appropriate questions. Simulation modeling can serve as important adjuncts, but should never replace other types of experiments.

No one can accurately predict the specific characteristics of the influenza virus that will create an epidemic.^{69, 70} During the influenza epidemic, the virus will be more transmissible and potentially more virulent than traditional seasonal influenza. However, the exact transmissibility, incubation period, infectious period, morbidity, and mortality remain unclear. To date, avian influenza cases have been too sporadic to make any reliable predictions.^{71–73}

Another limitation of the current model is that immunity and transmission rates do not vary by age or other demographic characteristics (e.g., immunity among elderly is the same as among younger people). Future iterations of the model may incorporate such variation. Moreover, our model does not account for potential influx and efflux of people to and from Norfolk. Essentially, the simulation treats Norfolk as an isolated island. In reality, people will be constantly moving in, out (especially in the setting of an epidemic) and through the city.

Although our model generates a conventional epidemic curve, rigorous validation requires running the model and comparing the results to real world data. However, in general, validating influenza epidemic models is rather challenging. Very little data on influenza epidemics is available beyond the 1918–19, 1957–58, and 1968–69 global epidemics.^{49, 74–76} The available data may not be applicable to different times and populations. We could not use seasonal outbreaks of influenza for validation either. Seasonal influenza is a very different entity with different behavior and characteristics so that it can never reach epidemic proportions. Moreover, even data on seasonal influenza is limited, since a large percentage of patients afflicted with influenza go undiagnosed or do not seek medical attention.

In the current version of our model, uninfected agents do not change their behavior during the epidemic. In actuality, fear and panic likely will alter daily interactions and movement.⁷⁷ Moreover, public health responses and public policy changes should disrupt the daily routines of uninfected agents. An ongoing project is to incorporate such changes into the model.

Our health care model is relatively crude. The health care system is essentially a “black box.” Agents enter the health care system and emerge either alive or dead. Furthermore, the model does not account for any operations changes that may occur during an epidemic.^{78–80}

Finally, our model may have limited generalizability to other cities. The specific characteristics and their populations may be so different that results may not hold across different cities. However, we are in the process of building influenza models for other cities and will be able to compare results and scenarios.

Conclusions

This paper presents a computer simulation of a theoretical influenza epidemic in Norfolk (Virginia). The agent-based simulation model is the first to include such specific city-level details and account for the individual social networks, interactions, and behavior of each citizen in the city population. Although the model has its limitations, the results correspond to those of a conventional simpler compartment model. This provides encouraging validation of our

model and suggests that it can not only generate general results similar to a compartment model but also allow us to study a lot more different factors and scenarios than a simpler model. Ultimately, the goal of any simulation is not to predict exactly what may happen during an epidemic but rather to observe how things may proceed and raise appropriate questions. Our simulation may serve as a virtual laboratory to examine the effects of changing different parameters and introducing different interventions.

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FIGURE 1.
Disease and Health Care System Model

FIGURE 2.

FIGURE 2a. Epidemic Curve from 10 Simulation Runs

FIGURE 2b. Effects of Varying Influenza Transmission Rates

FIGURE 2c. Effects of Varying Length of Incubation Period

FIGURE 2d. Effects of Varying Length of Infectious Period

FIGURE 2e. Effects of Varying Population Levels of Immunity

FIGURE 3.
Health Care System Visits

FIGURE 4.
Influenza Cases by Age Group over Time

FIGURE 5.
Influenza Cases by Race over Time

Table 1Transmission Rates and Corresponding R_0

Transmission	Peak Prevalence	R_0
10%	0.02%	1.0
20%	0.07%	1.1
30%	2.28%	1.3
40%	7.25%	1.7
50%	12.97%	2.0
60%	17.51%	2.5
70%	21.98%	2.9
80%	25.35%	3.2
90%	29.87%	3.8
100%	31.47%	4.0