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Mei, S.; van de Vijver, D.; Xuan, L.; Zhu, Y.; Sloot, P.M.A.

DOI

[10.1016/j.procs.2010.04.187](https://doi.org/10.1016/j.procs.2010.04.187)

Publication date

2010

Document Version

Final published version

Published in

Procedia Computer Science

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[Link to publication](#)

Citation for published version (APA):

Mei, S., van de Vijver, D., Xuan, L., Zhu, Y., & Sloot, P. M. A. (2010). Quantitatively evaluating interventions in the influenza A (H1N1) epidemic on China campus grounded on individual-based simulations. *Procedia Computer Science*, 1(1), 1675-1682. <https://doi.org/10.1016/j.procs.2010.04.187>

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International Conference on Computational Science, ICCS 2010

Quantitatively Evaluating Interventions in the Influenza A (H1N1) Epidemic on China Campus Grounded on Individual-based Simulations

Shan Mei^{a,1}, David van de Vijver^c, Lei Xuan^b, Yifan Zhu^a, P.M.A. Sloot^d

^aCollege of Information System and Management, National University of Defense Technology, China, 410073

^bSchool of Computer Science, National University of Defense Technology, China, 410073

^cDept. of Virology, Erasmus MC, University Medical Centre Rotterdam, Netherlands

^dComputational Science, Informatics Institute, University of Amsterdam, Amsterdam, the Netherlands, 1098 SJ

Abstract

The novel Influenza A (H1N1) virus is attacking the world in 2009. Among others, campuses in China, particularly most university/college campuses for bachelor students, are at-risk areas where many susceptible youngsters live. They most likely interact with each other quite often in dormitories, classrooms and refectories. We model the pandemic influenza A (H1N1) transmission through campus contacts and then forecast the effectiveness of interventions, based on a previously presented Complex Agent Network model for simulating infectious diseases [1]. Our results suggest that pandemic influenza A (H1N1) on campus will die out even with no intervention taken; the most effective intervention is still quarantining confirmed cases as early as possible and, in addition, vaccinating susceptible people can further decrease the maximum daily number of the infected. This study can support quantitative experimentation and prediction of infectious diseases within predefined areas, and assessment of intervention strategies.

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Keywords:

Influenza A (H1N1), Human Swine Influenza, Swine Flu, Infectious Diseases, Complex Agent Networks, Host Agents, Complex Networks, Social Networks

1. Introduction

The novel Influenza A (H1N1), or called Human Swine Influenza/Swine Flu, spreading internationally from Mexico in 2009, has caused a serious epidemic in China. China is highly susceptible to pandemic influenza A (H1N1) due to its big population and high residential density, besides the infectious disease's high infectiousness. According to Ministry of Health of China, until 30th Sep 2009, the provinces in China mainland had reported 19589 confirmed cases, 14348 cured cases, 10 sever cases and very few death cases [2]. However, experts believe that the epidemic will show an uptrend in the subsequent months in China.

Email address: Meishan.ann@gmail.com (Shan Mei)

¹Corresponding author

Pandemic influenza A (H1N1) is thus far a relatively mild illness seen predominantly in those who are healthy and under 24 years of age, perhaps reflecting protection from previous human influenza exposure in older people [3]. Thus the outbreak of pandemic influenza A (H1N1) at school has obtained considerable concerns [e.g. 4, 5, 6, 7]. Initially, most cases were clustered in households and schools, with over 50% of the reported cases in schoolchildren in the 5- to 18-year-old age range [6]. J. Medlock and A. P. Galvani concluded that officials should target vaccination to those that contribute the greatest transmission, i.e., schoolage children and their parents [7].

In China, the impact of pandemic influenza A (H1N1) transmission at school also emerges. For example, from 18th to 25th Sep 2009, schools in Hunan (a province of China) had reported 19 collective infections with 73 confirmed cases [8]; some had taken interventions such as suspending classes, closing campuses, quarantining confirmed cases and vaccinating.

Campuses in China, particularly most university/college campuses for bachelor students, are somewhat different from those elsewhere with respect to the students' residential and alimentary characteristics, which makes them at-high-risk areas for virus propagation. Students are usually assigned to dormitories after enrollment. During semesters, each student moves daily between the dormitory, crowded refectories and classrooms on campus. Generally, a few refectories are located scatteredly within the campus and provide meal services during rush hours, so that for each meal students choose one from those refectories taking into consideration locations, distances and preferences etc.. Altogether, students have close contacts with acquaintances in dormitories, and many casual contacts with teachers, schoolmates and personnel in classrooms and refectories. Therefore, the whole population living within the campus compose a large cluster during the course of a campus outbreak of airborne influenza A (H1N1).

Although the basic biology [9], practical advice for clinicians in terms of case definitions and treatments [10] and surveys of public knowledge and misconceptions [11] of this novel flu has been well studied, there has been relatively little work on individual-based quantitative simulation and forecast of pandemic influenza A (H1N1) spreading. Current quantitative studies on the spread of pandemic influenza A (H1N1) are mostly focused on mathematical models [e.g. 6, 12], in which a strong assumption is existent that all members of the population contribute equally to the spread of the disease. Nevertheless in reality, the likelihood of spreading virus varies across members.

In this paper, we model the pandemic influenza A (H1N1) transmission through campus contacts and then forecast the effectiveness of interventions, tailoring a previously presented Complex Agent Network model for simulating infectious diseases [1] according to the characteristics of pandemic influenza A (H1N1) spreading. In our model, the campus population is modeled as a social network with nodes representing individuals and edges representing contact between two people, and each individual (node) with heterogenous disease progression is further modeled as a host agent. Thus, the probability of infection for a susceptible individual is determined by the connectivity (degree) of the individual (node) and the infection status of his/her partners (neighboring nodes) in the networks. Subsequently, three categories of experiments with no intervention taken, confirmed cases quarantined and confirmed cases quarantined plus randomly chosen people vaccinated, respectively, are conducted to evaluate the effectiveness of interventions.

2. Model

2.1. Basic Assumptions

In the 2009 influenza A (H1N1), the virus isolated from patients in the United States was found to be made up of genetic elements from four different flu viruses: North American swine influenza, North American avian influenza, human influenza and swine influenza virus typically found in Asia and Europe – “an unusually mongrelised mix of genetic sequences” [9, 13]. The influenza A (H1N1) virus is highly transmissible but of no greater virulence than seasonal influenza to date [10, 14].

To tentatively investigate the impact of pandemic influenza A (H1N1) on campus, we elaborate on some simplifying assumptions as follows.

1. Each infected individual is equally infectious, excluding the case of super infectors.
2. The virulence of the pandemic influenza A (H1N1) virus remains changeless during the course of spreading.
3. The immunity and susceptibility of each individual is identical regardless of his/her age. This means an assumption of homogeneous immunity and susceptibility structure in the population, which holds for our study.
4. The duration of incubation follows a uniform distribution of 1-2 days, and patients at this period are assumed to be non-infectious.

5. The duration of symptomatic period follows a uniform distribution of 1-7 days. An individual will get diagnosed immediately after the symptoms appear and finally get recovered at the end of the symptomatic period with no mortality.
6. The infectiousness of an infected individual remains changeless during the course of symptomatic period (asymptomatic excluded).
7. We consider no demographical effect, i.e., ignoring the influence of people's inflow and outflow on the virus spreading. We believe that after a pandemic influenza A (H1N1) outbreak, the inter-contacts within the population rather than the inter-contacts between the population and the outside accounts for the greatest contribution to pandemic influenza A (H1N1) spreading. Additionally, schools might close campuses and urge confirmed/suspected students to stay in a hospital or dormitory, which further enlarges the contribution.
8. Individuals become immune to pandemic influenza A (H1N1) virus with no exception either after getting recovered from previous infection or with a delay of 14-21 days after vaccinated.

2.2. Model Construction

2.2.1. Agent-based Host Model

We construct the host model of individuals by using agent-based modeling. Agent-based Modeling, or Individual-based Modeling, are used to study complex systems through a so-called bottom-up or micro-macro methodology. Unpredictable however realistic system emergence is expected to occur based on the aggregation of simple individual behavior through interactions between individuals [15].

The infection progression of a host is shown as Fig. 1. Each susceptible host can be infected by people with whom he/she interacts with on campus. After the infection, his disease status transfers to the incubation with assumed non-infectiousness and then the symptomatic period with infectiousness. An individual finally can get recovered or die (excluded in Sec. 2.1 for our simulations) from the infection. Aside from this, a susceptible individual can refrain from getting infected by vaccination. Therefore, individuals can become immunized by either natural immunization (recovery from the previous infection) or random vaccination.

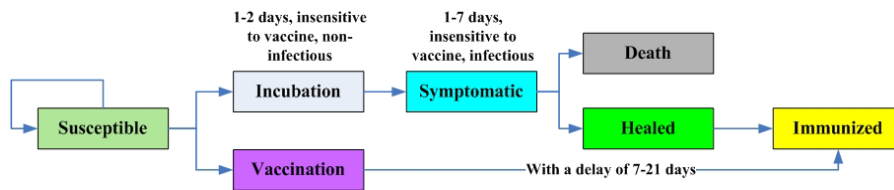


Figure 1: Infection Progression of a Host Agent

2.2.2. Contact Model between Hosts

We use social networks, a subgroup of complex network [16, 17], to abstract the complex contacts between hosts. A social network is a set of people or groups of people with some pattern of contacts or interactions between them [17]. The topological structure of a network implies sociological and epidemiological statistical achievements on the contacting rules in a given social community. An edge, representing interaction between two hosts who are depicted as nodes, denotes a possible occurrence of infection.

A schematic illustration of virus spreading in a network is shown as Fig. 2. The possible statuses of a host agent form a set of being susceptible, at incubation, at symptomatic period, recovered, vaccinated, immunized and dead. The transition of intra-host status depends on the host's infection progression and treatment. Please note, the edges in Fig. 2 remain unchanged except the cutoff of those connecting to a dead individual; while in our simulations some edges are removed or rewired with time steps to achieve high stochasticity.

On condition that we lack realistic statistical data on the interested population, we adopt scale-free networks with small exponents to represent the complex interactions between hosts since many social networks are scale-free

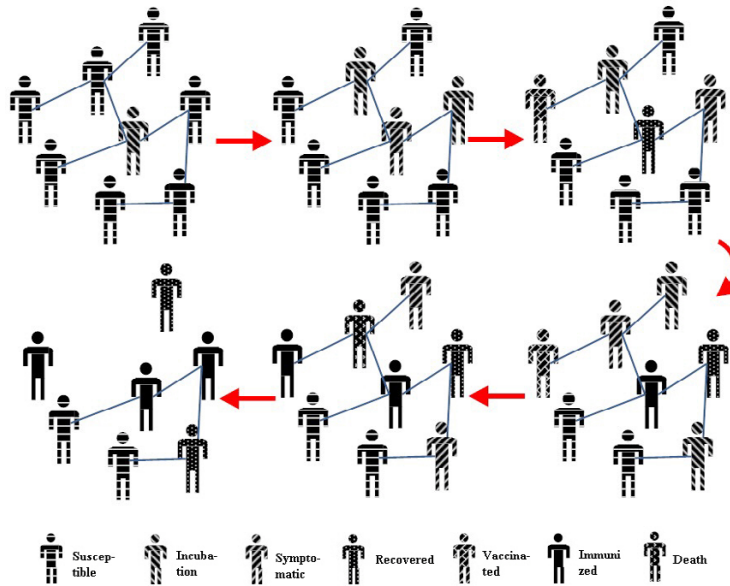


Figure 2: Virus Spreading in a Network

[18, 19, 20, 21, 22, 23, 24]. The degree distribution of nodes follows a power-law distribution $p_k = Ak^{-\gamma}$, where A is a normalization factor. Due to the high clustering of individuals on campus, we set the distribution with small exponents ($\gamma \in [1.6, 1.8]$).

We denote the transmission probability within a given period of time, say one day, across an edge which connects an infected individual and a susceptible individual as P , and the number of infected contacts with whom this susceptible individual interact within one day as n_i ($\leq k_i$ which is the degree of the corresponding node), the susceptible individual gets infected with a probability

$$TP_i = 1 - (1 - P)^{n_i}.$$

3. Simulation Results

We perform pandemic influenza A (H1N1) spreading simulations in a population of 10000 representing the campus community. Initially, a randomly chosen individual is set to be infected and the time step is set to be one day.

3.1. No Intervention Taken

4 sets of simulations are performed by setting γ as 1.6 and 1.7, and P as 0.01 and 0.02, respectively, **with no intervention taken**. Fig. 3 shows the temporal involution of the number of infected individuals within 90 days (averaged over 30 realizations).

According to the curves of the number of the infected shown in Fig. 3, pandemic influenza A (H1N1) on campus dies out even though that many people might get involved during the course and no intervention has been taken. This is most likely due to the non-difficult recovery from infection within a short period (in days or weeks) and the consequent natural immunization, besides the intrinsically changing diffusivity of networks themselves for virus spreading. At the beginning, networks display low diffusivity when the infected are few. Then the diffusivity increases with the increase in the number of the infected. After days, the diffusivity drops again with the decrease in the number of the

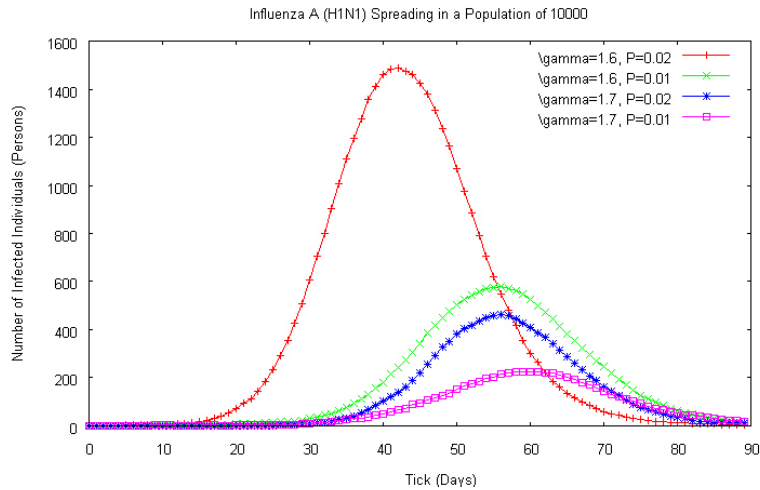


Figure 3: Simulated Results with no Intervention Taken

susceptible and the increase in the number of the naturally immunized. Therefore, each curve peaks only once in the middle when recovery instead of infection turns to be dominant. For example, the peak at 1487 infected occurs on the 42nd day when $\gamma = 1.6$, $P = 0.02$ and the peak at 578 occurs on the 56th day when $\gamma = 1.6$, $P = 0.01$. Additionally, the simulated result of the number of the infected is primarily sensitive to the exponent of pow-law degree distribution and secondarily to P .

3.2. Confirmed Cases Quarantined

With fixed values of $\gamma = 1.6$ and $P = 0.02$, 4 other sets of simulations are performed by *starting quarantine all confirmed cases from the 5th, 13rd, 23rd and 33rd day onwards*, namely with a delay of, respectively, 2, 10, 20 and 30 days after the first case confirmed. Fig. 4 shows the temporal involution of the number of infected individuals within 90 days (averaged over 30 realizations).

As shown in Fig. 4, the earlier quarantine is started, the more effective it is to interdict pandemic influenza A (H1N1). The peak at 1396 infected occurs on the 50th day with confirmed cases quarantined from the 33rd day onwards, which delays the epidemic peak for 8 days (from 42nd to 50th) but shows no significant decrease in the number of the infected at the peak, compared to the corresponding result simulated with no intervention taken. If quarantine is started from the 23rd day onwards, the peak at 514 occurs on the 54th day. Moreover, if quarantine is started from the 5th day onwards, pandemic influenza A (H1N1) will be interdicted entirely.

3.3. Confirmed Cases Quarantined plus Randomly Chosen Susceptible People Vaccinated

Aside from *quarantining confirmed cases from the 33rd day on, 100 randomly chosen susceptible individuals are vaccinated on 20th, 30th and 50th day, respectively*, to perform 3 other sets of simulations. Fig. 5 shows the temporal involution of the number of infected individuals within 90 days (averaged over 30 realizations).

On the basis of quarantine, additionally vaccinating a group of randomly chosen susceptible individuals can further decrease the number of the infected occurring at the peak. As shown in Fig. 5, following quarantine from the 33rd day onwards, the peak at 1189 occurs on the 49th day with 100 susceptible vaccinated on the 30th day and the peak at 765 occurs on the 46th day with 100 vaccinated on the 20th day.

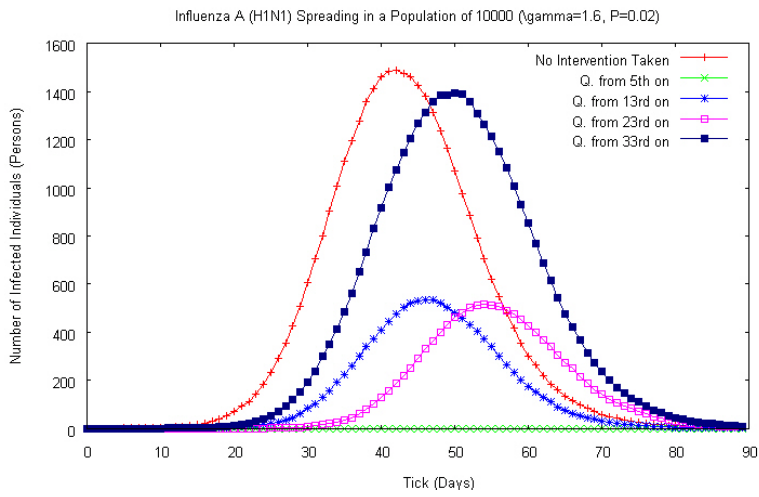


Figure 4: Simulated Results with Confirmed Cases Quarantined (abbr as Q.)

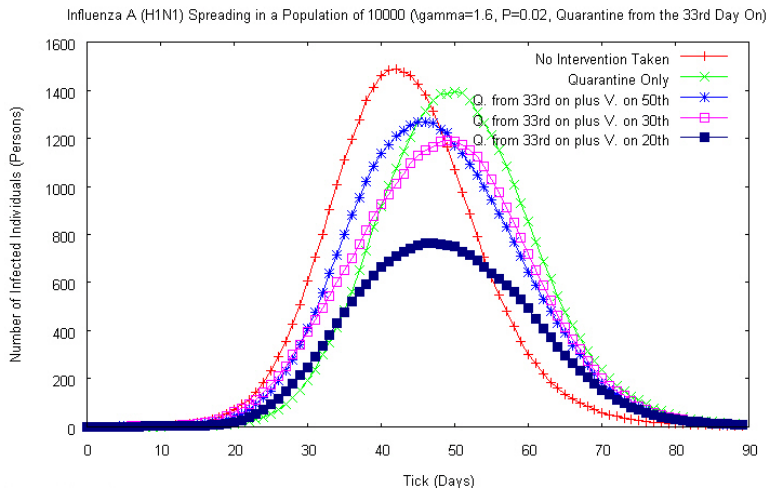


Figure 5: Simulated Results with Confirmed Cases Quarantined plus Randomly Chosen Susceptible Individuals Vaccinated (abbr as V.)

4. Conclusions

In this study, we present an approach for quantitatively evaluating interventions in the Influenza A (H1N1) epidemic on China campus grounded on individual-based modeling and simulation. It can be used as an alternative method for tentatively modeling the spreading of pandemic influenza A (H1N1) or other seasonal influenza on China campus, with heterogeneity in personal disease progression and number of contacts considered.

Our simulated results suggest that pandemic influenza A (H1N1) on campus will die out even with no intervention taken; the most effective intervention is still quarantining confirmed cases as early as possible and, in addition, vaccinating susceptible people can further decrease the maximum daily number of the infected.

However, placing people in quarantine is not good for economics [25]. People that have to stay home or in some sort of quarantine cannot work. Also, closing schools will mean that many parents are forced to stay home and cannot work. The pandemic influenza A (H1N1) is mild, but putting people in quarantine is therefore very drastic which we usually decline during a normal seasonal flu.

Our study is limited because of the assumption that the transmission probability across an edge which connects an infected individual and a susceptible individual within a given period of time is identical. However, the transmission probability is various with respect to age, the infected individual's infectiousness and the susceptible individual's susceptibility. Therefore, much more needs to be known about the interactions between people through which transmissions arise and realistic mixing patterns in a population, before our model will be possible to accurately predict an epidemic on China campus.

Acknowledgements

The authors would like to acknowledge the support of the severe infectious diseases spreading research based on social networks (Chinese grant 2008ZX10004-013) and the European DynaNets (www.dynanets.org) grant (EU Grant Agreement Number 233847).

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