Effects of Temporal Factors in Combined Intervention of School Closure and Workforce Shift for Mitigating the Spread of Influenza

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It is believed that combined interventions may be more effective than individual interventions for mitigating epidemic. However there is a lack of quantitative studies to investigate the performance of the combination of individual interventions under different temporal settings. To better understand the problem, we develop an individual-based simulation model running on top of contact networks based on real-life contact data in Singapore. We model and evaluate the spread of influenza epidemic with intervention strategies of school closure, workforce shift and their combination respectively, and examine the impact of temporal factors, namely the trigger threshold and duration of the intervention. By comparing simulation results for intervention scenarios with the temporal factors, we find that combined interventions do not always outperform individual interventions and are more effective only when the duration is longer than 6 weeks or school closure is triggered at the 5% threshold; combined interventions may be more effective if school closure starts first when the duration is less than 4 weeks or workforce shift starts first when the duration is longer than 4 weeks. We therefore conclude that identifying the appropriate timing configuration is crucial for achieving optimal or near optimal effect of mitigation for the spread of influenza epidemic. The results of this study are useful to policy makers in deliberating and planning individual and combined interventions.

Keywords: school closure, workforce shift, combined intervention, simulation, contact network, influenza

1. INTRODUCTION

Past influenza pandemics and the recent H1N1 pandemic alert people the unpredictability and potentially overwhelming impacts of influenza outbreaks. While it is certain that next pandemic will arrive in human societies, it is almost impossible to predict the virus type, transmission manner, and attack and mortality rates etc. Such unpredictability seriously challenges the public health system. Supplies of vaccine and pharmaceuticals may not be available or in shortage for a few months or even longer while a substantial number of infected cases has been reported. Under such critical circumstances, non-pharmaceutical interventions are usually considered in the first place, aiming at mitigating the spreading and lowering the attack rate and fatality.

Schools and workplaces are both crucial community structures in epidemic control and mitigation planning. High contact rates and long contact duration in schools and workplaces may prompt the transmission among school and workforce population. As a conventional non-pharmaceutical intervention (Wallinga et al. 2008), school closure had been widely evaluated in epidemic and pandemic control (Milne et al. 2008; Halder et al. 2010; Neil M. Ferguson et al. 2006; B. Y. Lee et al. 2010). In a recent article (S. Cauchemez et al. 2009), multiple aspects of school closure were reviewed, and it concluded that there are still many uncertainties on mitigation benefits of school closure as a public health policy. Historical school closure implementation data in real world epidemic mitigation also showed contradictory conclusions. In March 2008, Hong Kong school officials made an abrupt decision to close all primary schools for 2 weeks, as an effort to block a rising wave of seasonal influenza. However, a follow-up study (Cowling et al. 2008) reported that no substantial effect was obtained by the school closure. On the other hand, Israel school closure data from January 16 to January 28 of 2000 supported the effectiveness of school closure on reducing the respiratory infections (Heymann et al. 2004).

Comparing to school closure, closure of workplaces causes more significant disruption to economic activities and social functioning. Therefore a large-scale of workplace closure is hardly seen in the history of infectious disease control. In order to reduce contacts in workplace during epidemic, policy makers may seek alternative interventions, such as workforce shift. In workforce shift intervention, a portion (work team) of workforce is scheduled away from workplaces for a certain time span and then return by shifting with others. Workforce shift has been planned in real-life epidemic control. UK influenza contingency plan suggested 25% of employees taking 5-8 days off to increase social distancing (M E J Newman 2002); in the Singapore guideline of infectious disease control for workplace, dividing employees into work teams with minimum contacts between teams by shift system is suggested (Ministry of Health Singapore). To our knowledge, there are no studies on evaluating policies similar to workforce shift for influenza mitigation. We therefore investigate how effective team-based rotational workforce shift is. As school closure and workforce shift target different portions of the population, the combination of the two strategies may achieve better mitigation for influenza epidemic. As mass social distancing strategies, school closure and workforce shift may result in the considerable economic and social costs. Any decision on intervention combination should be cautiously deliberated. This calls for quantitative evaluations on the effectiveness of combined intervention strategies.

Combined interventions for influenza epidemic have been evaluated widely in the literature. Germann et al (Timothy C. Germann et al. 2006), Carret et al (Carrat et al. 2006) and Milne et al (Milne et al. 2008) assumed that combined interventions are implemented before the outbreak of epidemic and lasted until the end. Halder et al. (Halder et al. 2010) evaluated combined interventions with limited durations (how long an intervention lasts). Longni et al (Ira M. Longini et al. 2005) and Ferguson et al (Neil M. Ferguson et al. 2006) studied how different effectiveness and coverage of interventions could impact the attack rate and peak incidence. Halloran et al (Halloran et al. 2008) and Rizzo et al (RIZZO et al. 2008) simulated the epidemic by implementing multiple strategies simultaneously at different time points with their own fixed durations. Duerr et al (Duerr et al. 2007) tested the combination of two interventions in which one started at the beginning of epidemic and the other may start at different time points but lasted to the end of the epidemic.

In this study, we evaluate a series of scenarios under school closure, workforce shift and their combinations, with different trigger thresholds and durations. To our knowledge, this is the first study evaluating combination effects of school closure and workforce shift for influenza mitigation. In comparison with the timing configuration in other studies, our study is novel in three aspects: 1) trigger thresholds are defined in terms of the proportion of symptomatic cases in the overall population rather than specific time points; 2) trigger thresholds of individual interventions in the combination can be configured independently; 3) durations of the combined interventions can be varied. Through simulation evaluations, we aim to provide a more comprehensive view on the impact of temporal factors in social distancing interventions for influenza epidemic, helping to answer three key questions: a) *how do trigger threshold and duration affect the outcome of intervention?* b) *does a combined intervention outperform an* *individual intervention?* c) *does the implementation sequence in a combined intervention make a difference in its effectiveness?*

Considering the importance of social structure in infectious disease spread, network-based models (M E J Newman 2002; Del Valle et al. 2007; Meyers et al. 2005) have been commonly used for exploring the effectiveness of interventions in a heterogeneous-structured population for assisting policy makers to make the corresponding decisions. In this work, we use a contact-network-based simulation model to carry out the evaluations based on Singapore's social structure.

2. METHOD

We adopt an agent-based simulation model running on top of a social contact network. The network represents the statistical properties of interpersonal contacts that may lead to disease transmission in a community. We also investigate two intervention policies – school closure and workforce shift – via simulations to study the effectiveness of individual interventions as well as their combinations, with different trigger thresholds and implementation durations.

2.1 Contact network construction

In a heterogeneous structured population, human-to-human contacts are represented in a contact network. The contact network is formed through the connections of vertexes, i.e., each person is represented by a vertex and each contact between two individuals is linked by an edge. Thus, the disease transmission between two individuals can be simulated through the probabilistic propagation of viruses via the connecting edges. A person who is with more contacts in a society might be with a higher probability to be infected and subsequently cause more secondary infections. The number of contacts that a person has is also called the contact degree of the person. In a contact network, the number of edges emanating from a vertex is equal to the contact degree of the corresponding person. The distribution of the degrees of vertices, also called degree distribution, is a fundamental quantity in network theory, playing a critical role in estimations of outbreak size and epidemic probability in a network (M E J Newman 2002).

The contacts take place at various community structures. In this study, we take into account the contacts at schools, workplaces, hospitals, shopping places, households and public transportation (**Error! Reference source not found.**1). From the network perspective, community structures can be represented as clusters of vertices which have denser connections internally than outside. This clustering phenomenon may significantly affect the topology of contact network and the transmission of diseases in a community (Girvan & M. E. J. Newman 2002).

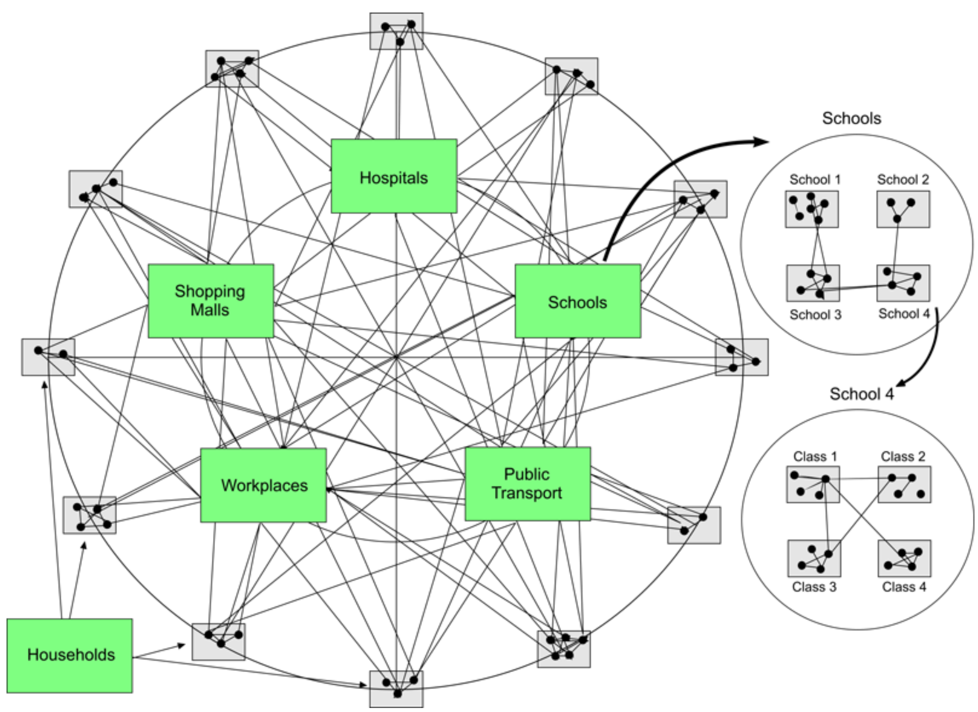

Figure 1 Schema of contact network in the urban setting. Dots denote people and lines connecting between dots denote the interpersonal contacts that may lead to disease transmission.

Using HPCgen model (Zhang et al. 2009), we construct a contact network based on Singapore's social structure. The model contains 100,000 households according to Singapore household size distribution, household structure and age distribution (Department of Statistics Singapore 2010), which yields approximately a population of 480,000. The scale-down network model is carefully set such that its contact distribution keeps good consistency with that of the overall society. Specifically, according to household members' ages, they are assigned to occupy the schools and workplaces by following the school size distribution and company size distribution in Singapore. The individuals are also assigned to visit other community structures such as shopping places and hospitals based on shopper traffic statistics and ward bed occupancy records. Public buses and trains are the primary transportation modes for the commuters in Singapore, with daily ridership up to 5,000,000 passenger-trips in 2008 to 2009 (Land Traffic Authority Singapore 2010). In contact network generation, public transport is assumed as a giant community structure in which all the commuters are mixed to make contacts randomly. Within each community structure, we create the random connections between pairs of individuals by assuming a Poisson degree distribution (Meyers et al. 2005) with the mean contact degrees acquired from our social contact surveys. Each school and hospital is further divided into sub-units, i.e. classes and wards. Each individual in the sub-units is assumed to have a higher probability to contact with someone from the same sub-unit than from the other sub-units. Teachers and healthcare workers are also assigned to the classes and wards to contact with students or patients. The applied data and their sources are:

- Household data: household size distribution and household structure, collected from Singapore public cencus year 2000 and our survey results
- Hospital data: hospital and ward size distribution, contact rate, caregiver allocation, collected from local hospitals
- School data: school and class size distribution, contact rate, teacher allocation, collected from Singapore Ministry of Education and survey results
- Workplace data: workplace size distribution and contact rate, collected from Singpaore Ministry of Manpower and survey results
- Shopping place data: visitor traffic and contact rate, collected from local shopping mall and survey results
- Public transport data: commuter traffic and contact rate, collected from Singapore Land Transport Authority and survey results

We had designed a survey form containing 45 questions to conduct the social contact survey among the public of Singapore in 2008. There are totally 1040 pieces of survey data collected. The number of contacts at different locations is estimated through the social survey data. The derived average numbers of contacts are summarized in Figure 2. The average number of contacts in the households is excluded in the figure as we assume every household is fully connected.

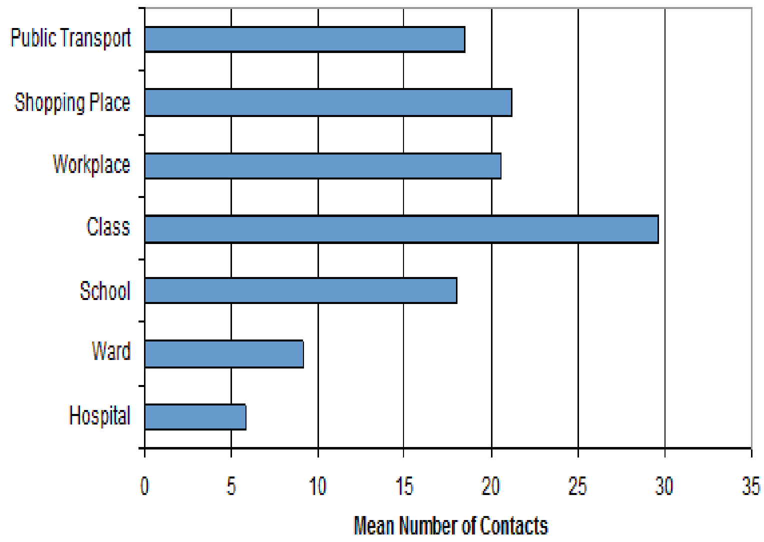

Figure 2 Mean number of contacts at different types of community structures

2.2 Intervention Policies

Intervention polices are implemented to contain and mitigate the transmission of disease. There are two categories of intervention: pharmaceutical and non-pharmaceutical interventions. Pharmaceutical interventions are mainly associated with vaccines and anti-viral drugs; and non-pharmaceutical interventions include isolation/quarantine, social distancing, etc. As vaccine production and anti-viral stockpiling often require substantial time after a pandemic occurs, non-pharmaceutical interventions are necessary to delay and dampen the pandemic before pharmaceuticals become available (U. S. Department of Health and Human Services 2010). School closure and workforce shift are the examples of social distancing interventions and will be evaluated in our work.

1) School Closure

School closure is a typical social distancing policy for mitigating the spread of infectious diseases among the student population. The student population (usually refers to less than fifteen years old) is often considered as more vulnerable to the risk of infection. The reasons are firstly children are less capable in self-care compared to adults; and secondly their immunity system may not be prepared as much as adults. In the 2009 H1N1 pandemic, 60% of infected cases were found to be 18 years old or younger (Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team 2009; Christophe Fraser et al. 2009). There are different types of school closure: 1) class closure, i.e., a class is closed if there is a diagnosed case; 2) individual school closure, i.e., a school is closed if there are diagnosed cases, and 3) all-school closure, i.e., all schools are closed simultaneously if a threshold number of cases are diagnosed. All three types of school closure had been implemented in the real-world interventions in countries like Australia, UK, USA, and Japan to mitigate the spread of pandemic influenza (M E J Newman 2002; Del Valle et al. 2007; Meyers et al. 2005).

In this study, we implement all-school closure in our simulations with different trigger thresholds and implementation durations. We assume: 1) all schools are closed immediately after the trigger threshold is reached; 2) all contacts taking place in schools are removed from the contact network during the period of school closure; 3) school closure does not cause an increase of contacts in other community structures.

2) Workforce Shift

In many countries, working adults occupy the largest portion in the population, and make close contacts with their co-workers in their daily activities. Closing workplaces has significant economic and social costs; so it is one of the least favorable choices that policy makers may consider. Another social distancing measure is *workplace non-attendance*, in which each worker has a 50% chance each day to choose either staying at home or attending to work. This policy is hard to realize as random and voluntary attendance of workers may cause chaos in the workplace.

Although workplace closure is seldom implemented in practice, policy makers do consider and suggest alternative workplace control, like workforce shift, for mitigating disease spread when necessary. In this study, we evaluate the *workforce shift* policy, i.e. each company or institution splits its employees to two work teams and implements 7-day rotation among the teams for simplicity. So in every 7-day time span, one team stays at home and the other team attends to work.

2.3 Models for Disease Spread and Intervention

Figure 3 describes the host progression is the process of infectivity development of influenza illness within the host person. Any susceptible person has a chance (transmission probability) to be infected if he/she has at least one infectious contact. If the person (denoted as p) is infected, p is exposed but has no infectivity as well as any symptom yet. Then after the period of incubation, p becomes infectious. Moreover, p also has a chance (symptomatic rate) to develop the clinical symptoms of influenza and turns into symptomatic infectious, or turn into asymptomatic infectious if without any symptoms. After the infectious period elapses, p is finally removed, i.e. either recovered from influenza or dead.

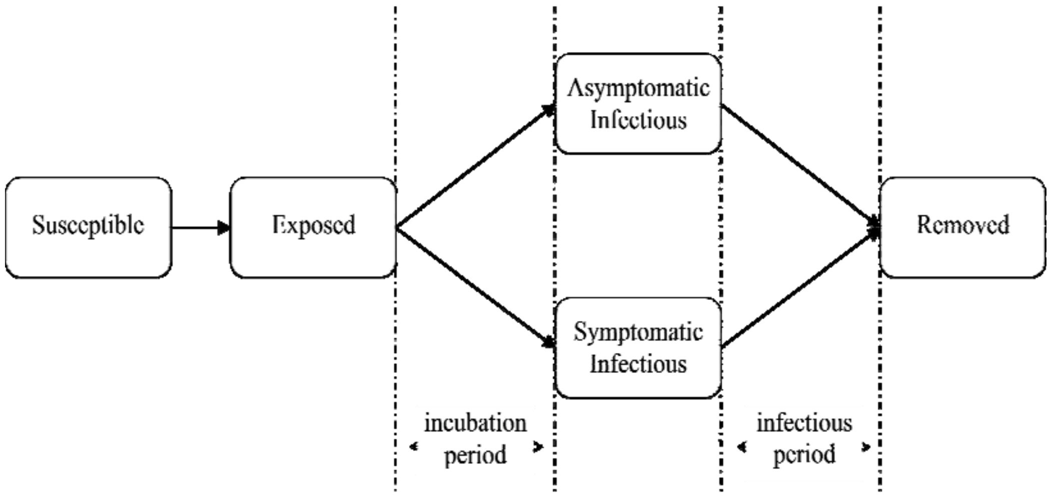

Figure 3 Dynamics of influenza progression within host individuals

Besides modeling the dynamics of the disease spread, the focus of this study is on investigating the effectiveness of intervention polices under different scenarios. We parameterize an intervention policy by six parameters: *trigger threshold, duration, target, control level, compliance rate and shift length*:

- *Trigger threshold* is a percentage of diagnosed (symptomatic) cases in the overall population, which is used to determine the starting time of intervention. For example, trigger = 0.1% means an intervention will be implemented when 0.1% of the population is diagnosed as symptomatic cases of influenza.
- *Duration* refers to how long an intervention will be implemented.
- *Target* specifies what type of contacts is targeted by an intervention, such as school contacts, workplace contacts etc.
- *Control level* is used to differentiate the interventions performed at the different levels of a community structure, e.g. school-level closure and class-level closure.
- *Compliance rate* refers to the percentage of contacts that is removed by an intervention. As compliance rate is often affected by other interventions (e.g. workplace absenteeism will improve compliance rate during the school closure as the adults will stay at home to take care of the children), we assume the 100% compliance rate for all-school closure to simplify our simulation scenarios.

- *Shift length* refers to the time span between team rotations.

3. RESULTS

The evaluation results of uncontrolled epidemic in the contact network are the baseline results. Different school closure scenarios with different trigger thresholds and implementation durations are simulated based on the individual-based contact network simulation model. We then evaluate and compare impacts of different scenarios on the effectiveness of school closure.

3.1 Experiment Settings

The basic reproductive number, R_0, is defined as the average number of secondary infections produced by a randomly selected infected person in a fully susceptible population (Diekmann et al. 1990). Previous estimates of R_0 in the past pandemic influenza were 1.4-1.6 from Mexico data (Christophe Fraser et al. 2009) and 2.3 from Japan data (Nishiura et al. 2009) of the 2009 pandemic influenza, 1.89 from Hong Kong data of 1968 (Rvachev & Longini Jr 1985), 1.5-1.7 from UK data of 1957 (Neil M. Ferguson et al. 2006), and 2.0-3.0 from US data of 1918 (Mills et al. 2004). We determine R_0 empirically by assuming a scenario in which one individual is randomly infected where everyone else is susceptible and not able to transmit the disease, and count the number of secondary infections. The process is repeated by 10,000 times and R_0 is then obtained as the average number of secondary infections. Thus, R_0 in our simulations is estimated to be 1.9 (95% Confident Interval (CI) 1.871 – 1.924), and the mean generation time is 2.522 days (95% CI, 2.489 – 2.508). It is comparable to estimates of 1.3 – 2.71 days for the 2009 influenza pandemic (Christophe Fraser et al. 2009). We use 66.7% of symptomatic rate (Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team 2009) in the simulations as well. We also assume 1/3 of generation time is latent and the rest is infectious (Christophe Fraser et al. 2009). The base transmission probability in the simulations is 0.04, which gives the threshold determining whether an asymptomatic infectious person may infect his/her susceptible contacts; the transmisson probability is doubled if the person is symptomatic infectious, and meanwhile, half of the contacts is randomly removed due to self-isolation or self-shielding.

In this study, we focus on examining the impact of trigger thresholds and duration length of interventions on the effectiveness of mitigating the influenza epidemic. The test scenarios are tabulated in **Error! Reference source not found.**. Each of those scenarios including the baseline case is simulated for 200 days and iterated for 100 times. All the results described in the following section are thus average values among 100 simulation runs.

Table 1 Intervention scenario description

Parameters	**School Closure**	**Workforce Shift**
Trigger Threshold	0.02%, 0.25%, 1.5%, 5%	0.02%, 0.25%, 1.5%, 5%
Duration	2,4,6,8,10 weeks	2,4,6,8,10 weeks
Target	school contacts	workplace contacts
Control Level	schools	workplaces
Compliance Rate	100%	100%
Shift length	NA	7 days

Every simulation starts at *day* 0 with 10 infectious persons seeded into a susceptible population that is assumed without prior immunity to the influenza virus. In our experiments, there are four trigger thresholds and five implementation durations available to choose for an intervention scenario. Hence there are totally 120 scenarios: 20 scenarios for all-school closure, and another 20 scenarios for workforce shift, and 80 scenarios for the combined interventions (we assume the individual interventions in each combination scenario share the same length of implementation duration).

The effectiveness of interventions is examined by evaluating attack rate (AR), peak incidence (PI), and peak day (PD). Attack rate refers to the cumulative proportion of symptomatic cases of influenza infection in the overall population; peak incidence refers to the highest number of the daily incidence of symptomatic cases; peak day refers to the day when the peak incidence happens. In the public health perspective, attack rate indicates the size of epidemic and the overall burden on the public health system due to an epidemic; and peak incidence and peak day display the challenge to an effective response to patient surges in public health system.

3.2 Influenza Spread without Intervention

Error! Reference source not found. shows the average epidemic curves of the 100 simulation runs. The epidemic reaches its peak at *day* 26 and fades out on *day* 73. The total attack rate *(AR)* is 44.47% (95% CI, 44.45% - 44.48%); peak incidence (*PI*) is 42.45 per 1000 people (95% CI, 41.72 – 43.17). This result is comparable with 43.5% attack rate found in (Timothy C. Germann et al. 2006). It is noted that the trigger thresholds {0.02%, 0.25%, 1.5%, 5%} are reached at *day* {7, 13, 17, 20} respectively.

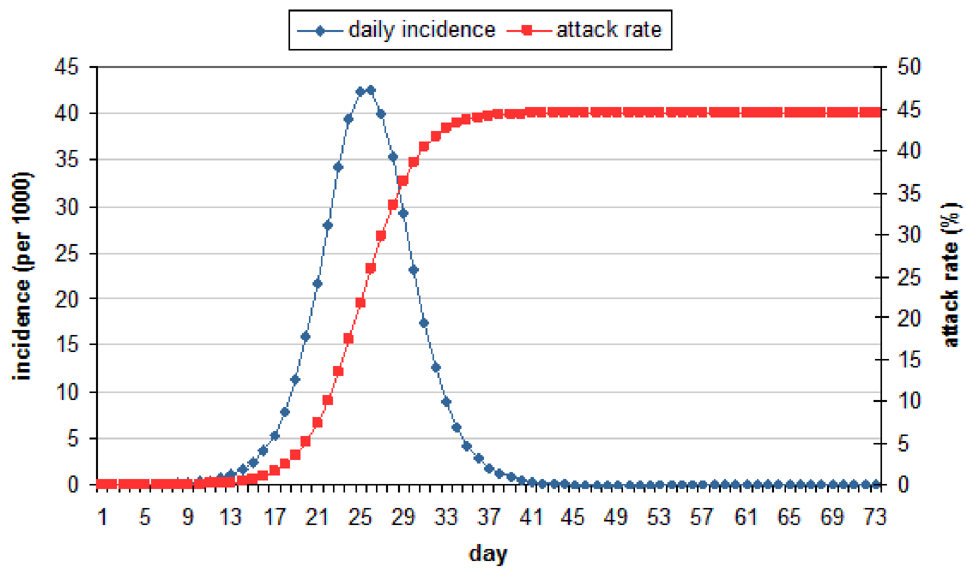

Figure 4 Average attack rate and daily incidence of baseline simulation in 100 runs (R0 = 1.9)

3.3 Impact of All-school Closure

Error! Reference source not found. shows varying thresholds and durations affect the outcome of all-school closure. The attack rates after implementing school closure range from 40.42% to 44.45%, 0.05% to 9.10% reduction compared to the baseline. The lowest attack rate occurs when 10-week school closure is triggered at 0.02%. It is observed from the CI that our results of *AR* in the 100 runs have very small variation. We note that, in all of our tested scenarios, similar small variations are observed in all averaged quantities. We do not show the 95% CI in the following results.

The simulated results help policy makers address the uncertainty in the proposed interventions. For example, for the cost-cautious reason, policy makers may prefer a shorter intervention and it is then recommended to start school closure by a longer delay since outbreak; if policy makers aim to minimize the size of epidemic, they should implement school closure as early as reasonable and last for more than 6 weeks. We also note that the variation of attack rates due to varying thresholds is much more significant for a shorter closure. So when a shorter duration is favored, making a wise choice of the trigger threshold becomes more critical, e.g. it saves an extra 6.05% of the overall population from the infection at no cost by just choosing the correct trigger threshold for the 2-week all-school closure.

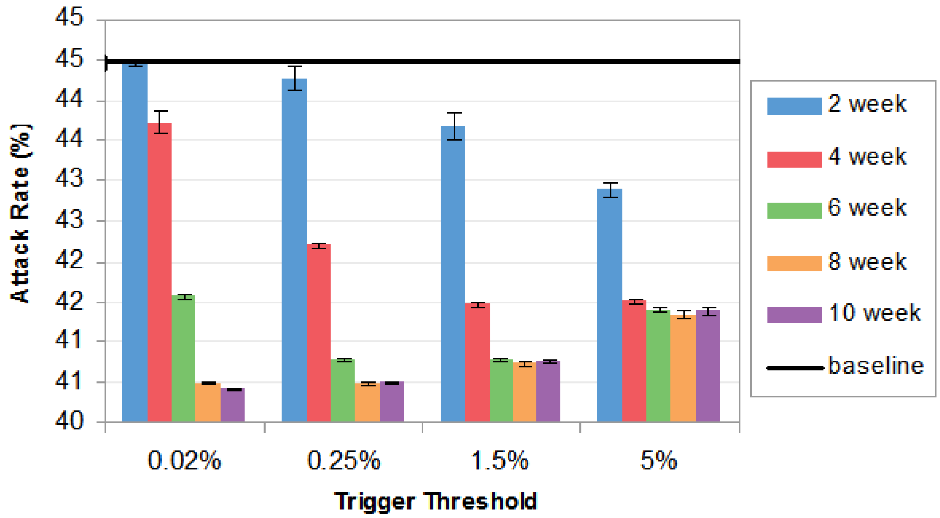

Figure 5 Attack rate with all-school closure. The black error bars indicate the 95% confidence intervals of the mean *AR* in 100 runs.

Error! Reference source not found.6 shows all-school closure has clear impact on reducing peak incidence of the epidemic. The lowest peak incidence under school closure is 30.75 per 1000 people, a 27.55% reduction compared to the baseline. It is achieved when the 6-week closure is triggered at 0.25%. We note that 4-week closure is sufficient for reducing the peak incidence, as a more extended closure does not bring any significant additional benefit on easing the stress to the public health system.

Error! Reference source not found.7 shows all-school closure has the constant trend of delaying the peak day. We observe that the peak day is significantly affected by trigger threshold, yet different durations make hardly any difference. When the threshold rises from 0.02% to 5%, peak day steadily moves earlier. The longest delay obtained is 5 days to the baseline. It is achieved when any closure longer than 2 weeks is triggered at 0.02%.

Combining the results from attack rate, peak incidence and peak day, we find that, if it is a cost-cautious situation in which short intervention is preferred, all-school closure of 2-week should be implemented at a higher threshold (a later time); if the epidemic size is the top priority, it will be wise to implement a longer school closure (more than 6 weeks) as early as reasonable. With regard to the public health system, an earlier school closure (more than 2 weeks) is always favorable because of lower peak incidence and later peak day.

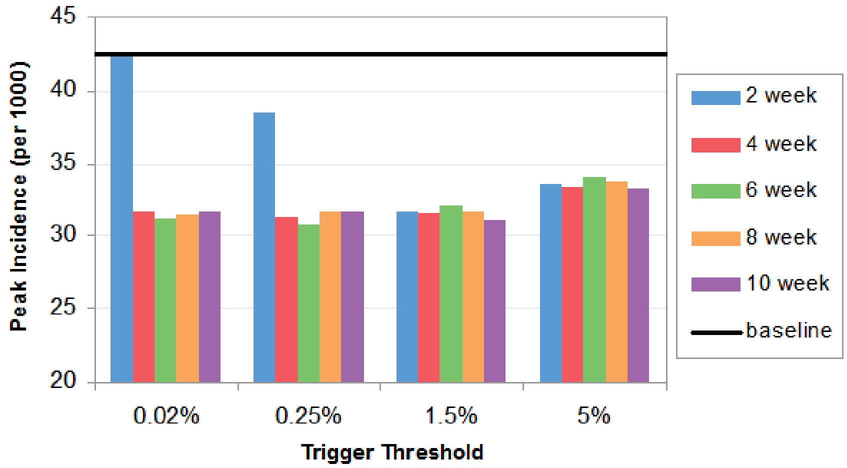

Figure 6 Peak incidence with all-school closure.

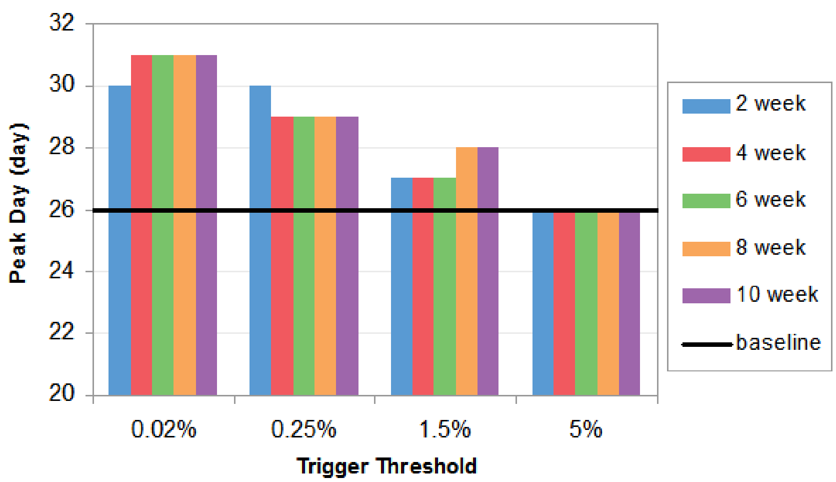

Figure 7 Peak day with all-school closure

3.4 Impact of Workforce Shift

As shown in **Error! Reference source not found.**8, workforce shift is more effective on reducing the attack rate of the epidemic compared to all-school closure. The attack rates under workforce shift are in range from 36.51 to 44.21, a

0.59% to 17.90% reduction compared to the baseline. The lowest attack rate takes place when the 10-week workforce shift is triggered at 0.02%, which is the same configuration when school closure achieves the lowest attack rate.

Similar to school closure, the difference of attack rates at the different thresholds but the same duration declines when the threshold increases. But the magnitude of the difference is larger for workforce shift compared to school closure. An extra 11.55% of the overall population can be saved from infections by choosing the appropriate trigger threshold for 2-week workforce shift.

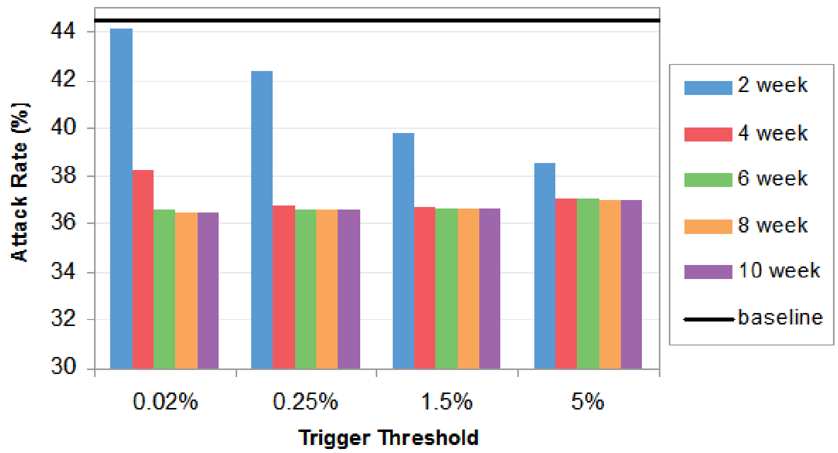

Figure 8 Attack rate with workforce shift.

Error! Reference source not found.9 shows that workforce shift has the remarkable impact of suppressing the peak incidence of influenza epidemic. The peak incidences under workforce shift range from 29.8 to 34.66 per 1000 people, a 18.34% to 29.63% reduction compared to the baseline. The lowest peak incidence occurs when the 2-week workforce shift is triggered at 1.5%. It is noted that 4 weeks are sufficiently long for reducing the peak incidence as no additional reduction is gained by extending the intervention.

Error! Reference source not found.10 shows that workforce shift has a mixed impact on peak day. Consistent with peak day results from school closure, varying durations makes no effect on peak day; and trigger threshold is the dominant factor for peak day. When trigger threshold rises from 0.02% to 5%, a constant decline of peak days is observed. It could be explained that when workforce shift is implemented at a higher threshold, a larger number of the population has been infected and the more potential transmissions will be blocked. Therefore, it sooner reaches the cutoff point at which the disease is unable to sustain the growth trend of incidences, so the peak would occur earlier. On the other hand, when workforce shift is implemented at a lower threshold, there are fewer infectious cases within the population and the amount of susceptible contacts left is still tolerable to maintain the chain of infections. Therefore, the daily incidence could be still growing but at a lower pace, subsequently leading to a later peak day. **Error! Reference source not found.**11 shows divergent impact of workforce shift on peak day. 6-week workforce shift triggered at 5% advances the peak incidence by 2 days compared to the baseline; on the other hand, 6-week workforce shift triggered at 0.02% reaches the peak incidence 1 day later than the baseline.

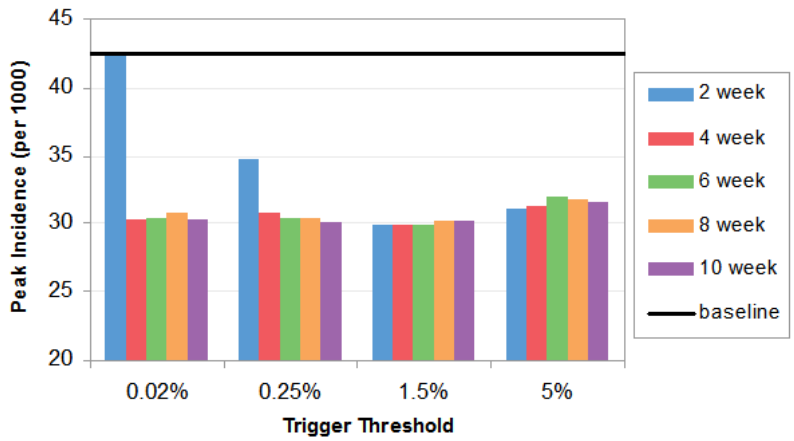

Figure 9 Peak incidence with workforce shift (per 1000 people).

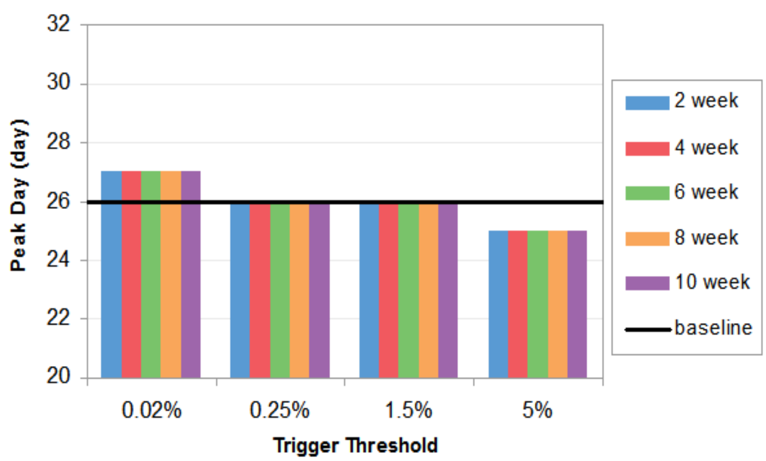

Figure 10 Peak attack day with workforce shift

3.5 Impact of Combined school Closure and Workforce Shift

We then examine the combined intervention of all-school closure together with workforce shift. We are interested in the effectiveness of the combined intervention as well as the impact of the temporal sequence of individual interventions in a combination.

Error! Reference source not found.12 A-E show that the lowest attack rate (*AR)* under the combined intervention is 31.07%, achieved when school closure and workforce shift are both triggered at 5% and lasted for 10 weeks. In the single interventions, the lowest *AR* from all-school closure is 40.42% (10-week closure triggered at 0.02%), and 36.51% from workforce shift (10-week shift triggered at 0.02%). 12.24% of population can be further saved from the infection by applying the combined intervention compared to the single interventions.

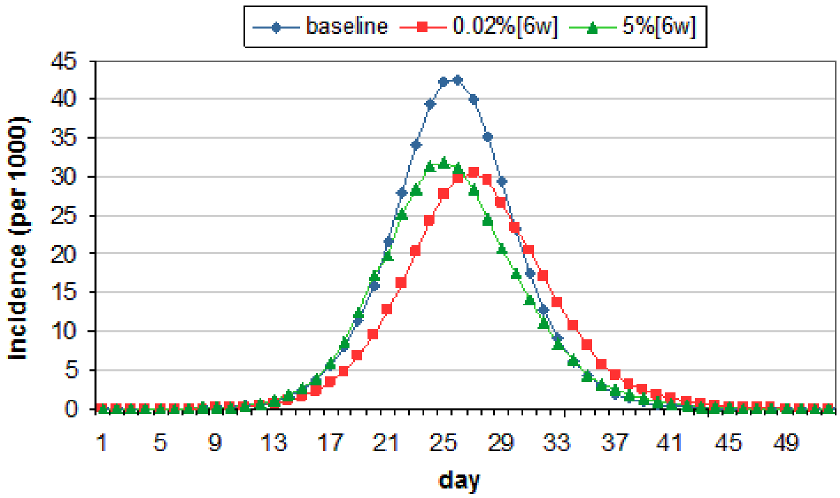

Figure 11 Daily symptomatic incidence from day 1 to 52, from baseline v.s. 6-week workforce shift triggered at 1.5% and 5% respectively

Error! Reference source not found.12 F-J show that the lowest peak incidence (*PI)* occurs when 10-week school closure and workforce shift are triggered at 0.02% and 5% respectively. Comparing the lowest *PI* from single interventions (30.75 from school closure; 29.87 from workforce shift), the combined intervention is able to further reduce *PI* to 16.48.

Error! Reference source not found.12 K-O show that the combined intervention can delay the peak day (*PD*) by 12 days compared to the baseline. It is longer than *PD* in individual interventions, i.e. 7-day delay by school closure and 10-day delay by workforce shift.

In the followings, we summarize our results in an attempt to answer the three questions asked in the earlier section:

(a) Do combined interventions always outperform single interventions?

It is commonly believed that combined interventions will outperform single interventions. But we notice some cases in which combined interventions lead to higher attack rates than single interventions at the same trigger threshold and duration. The worst case is observed when the 4-week school closure and workforce shift are both triggered at 0.02%. If we apply only workforce shift at 0.02% threshold and 4-week duration (*Scenario A – single intervention*), the *AR* is 38.25%; on the other hand, *AR* from the combined intervention (*Scenario B – Combined intervention*) is 43.12%, which is 4.87% higher.

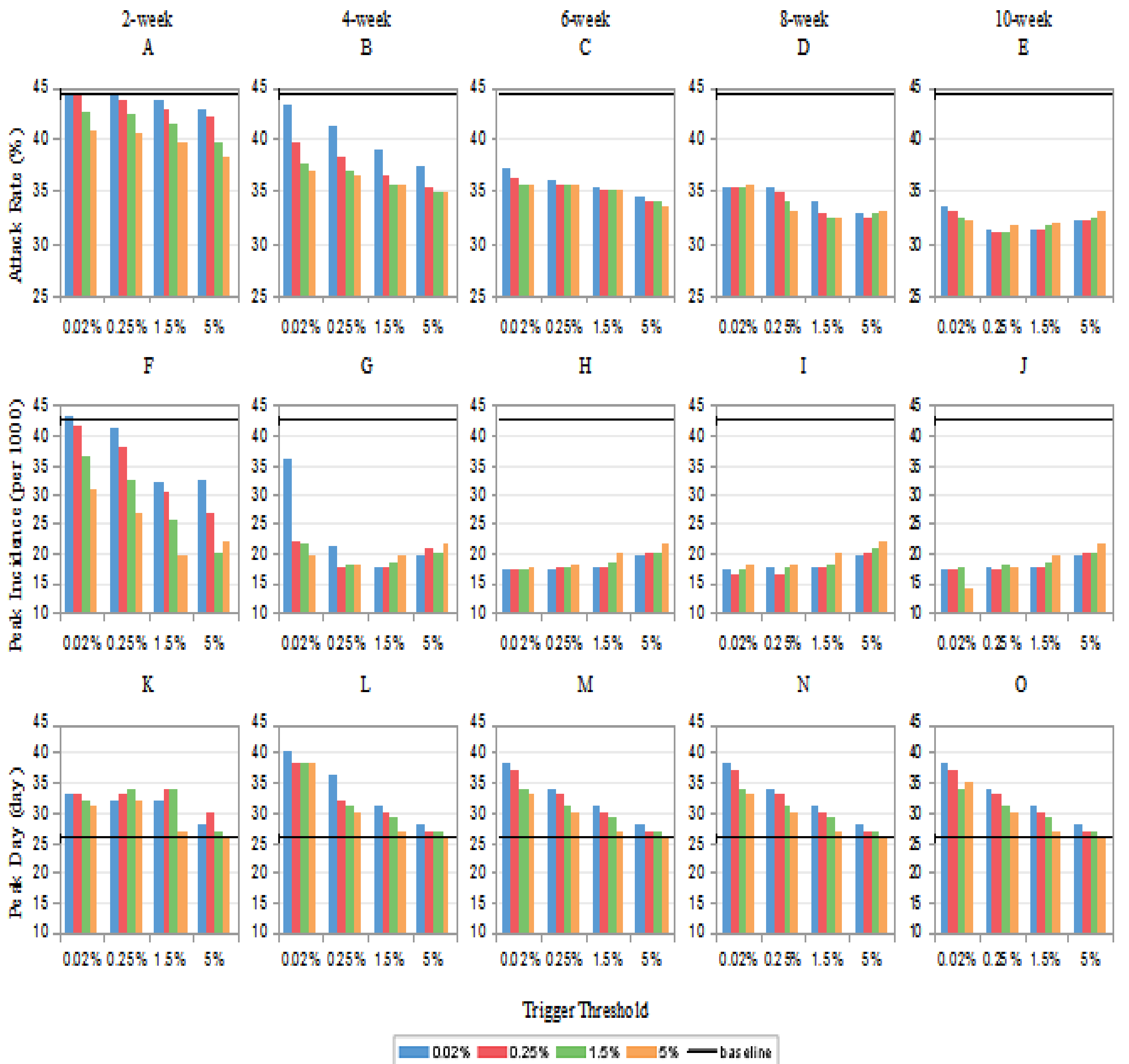

Figure 12 Total attack rate, peak daily incidence and peak attack day with hybrid control (x-axis shows school closure's triggers, colored bar indicates workforce shift's triggers; In each row, duration = 2/4/6/8/10 weeks from left to right)

Error! Reference source not found.13 further describes what happens in *Scenario A* and *B*. On *day* 7, the trigger threshold (t = 0.02%) is reached and the epidemic curve of the combined intervention grows much slower than the single intervention because more contacts have been removed and chance of infection is lower. On *day* 35, the interventions in the both scenarios ends and the removed contacts are restored. Because the growth of infected cases is much slower in *Scenario B*, there is more susceptible left in the population. Specifically, on *day* 35, 49.65% and 85.88% of population are susceptible in *Scenario A* and *B* respectively. This nearly doubled size of susceptible population determines more disease-causing contacts and higher chance of infection in *Scenario B* compared to *Scenario A*, leading to the divergent development of the epidemic after *day* 35 – the incidence continues to decline and gradually fades out in *Scenario A*; and oppositely in *Scenario B*, the incidence number grows exponentially until *day* 40 and a large number of infections take place after the intervention.

It is observed that 11 combined scenarios of 2-week intervention underperform 2-week single interventions out of 16 scenarios, 7 of 16 scenarios of 4-week interventions and 1 out of 16 scenarios in 6-week interventions. Apparently combined interventions with a longer duration (>=6 weeks) are less prone to underperform, meaning combined interventions have to be maintained long enough to prevent the rapid spread of influenza after the intervention period.

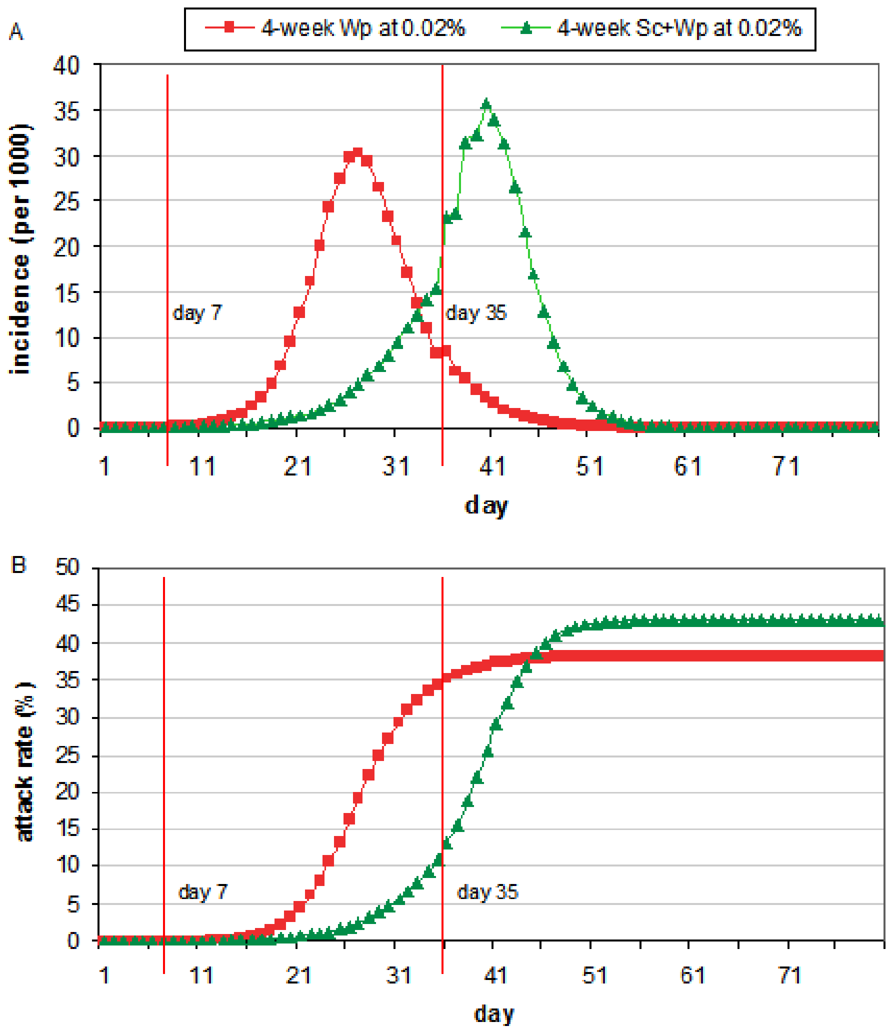

Figure 13 Comparison on daily incidence (A) and attack rate (B): red line denotes 6-week workforce shift (Wp) triggered at 0.02%; green line denotes 6-week school closure + workforce shift (Sc+Wp) triggered at 0.02%

b) How trigger and duration affect the impact of combined interventions?

The performance of combined interventions can be affected by both trigger and duration. When the duration increases, *AR* and *PI* decline consistently. When trigger threshold rises, *AR* and *PI* drop if the duration is shorter than *d* weeks (*d* = 8 for *AR*; *d* = 4 for *PI*); if the duration is longer than *d* weeks, *AR* and *PI* increase instead. In **Error!**

Reference source not found.12 E and G, convex curves clearly show the existence of the above trends. For the peak incidence time, the *PD* drops when the triggers rises with $d >= 4$weeks. It also shows that a longer duration of intervention (> 4 weeks) does not bring in any further contribution to the delay of peak incidence time.

c) Does the implementation sequence in a combined intervention make a difference in its effectiveness?

The temporal implementation sequence of individual interventions within the combined strategy may also affect the outcome of intervention. The maximal differences of *AR* among sixteen threshold combinations are {6.13%, 8.24%, 3.47%, 3.21%, 2.59%} with {2, 4, 6, 8, 10}-week durations respectively. The performance of the *synchronized interventions* (two individual interventions start from the same threshold) increases when the trigger rises. Comparing to asynchronized combinations (individual interventions start at different thresholds) with the same duration, their relative performance is changed from "underperformance" to "outperformance" when the trigger rises from 0.025 to 5% subject to the condition that duration is within 8 weeks. When the duration is longer than 8 weeks, synchronized interventions underperform in most of the scenarios and so it is wise to start them at different thresholds in the implementation.

For asynchronized interventions, the sequence order of single interventions can affect the *AR* as well. The difference between attack rates of different pairs of the asynchronized interventions are {2.13%, 1.31%, 1.55%, 2.73%, 1.66%} for {2, 4, 6, 8, 10}-week durations respectively. It is observed that school closure should be implemented later when duration is less than 4 weeks; and workforce shift should start later when duration is long than 4 weeks.

4. DISCUSSION

Using an individual-based simulation model based on the social structure of Singapore community, we investigate the effectiveness of school closure and workforce shift as well as their combination as a means to mitigate the spread of influenza. Specifically, the impact of interventions has been investigated through evaluating the total attack rate and daily incidence as well as the delay of peak incidence time quantitatively.

Both school closure and workforce shift are social distancing measures that aim to reduce disease-causing contacts between individuals and the risk of infection so as to reduce consequent secondary infections. As the production of vaccine and stockpiling of anti-viral drugs usually take considerable time, the shortage of pharmaceuticals has ever been the challenge in the preparedness planning for pandemic influenza and might not be ready at the time of influenza outbreak.

Our simulation results show that both all school closure and workforce shift are able to lower attack rate and daily incidence as well as delay the epidemic in most intervention scenarios. Such social distancing through enforcement from administration is necessary to mitigate the diffusion of influenza virus among the communities, especially when a large number of asymptomatic cases exist in the community.

Our experiments provide guidance on choices of trigger threshold and length of duration for implementing school closure, workforce shift and their combination intervention measures. These results will be relevant to future contingency plan for influenza pandemic, which is estimated to be more pathogenic and might have higher case fatality rates than that shown in 2009 H1N1 pandemic flu (Halder et al. 2010). We find that the durations of 8 weeks and 6 weeks are sufficiently long for school closure and workforce shift respectively. Short interventions should be implemented after a longer delay since outbreak; in contrast, long interventions should start as early as reasonable. The cutoff values between long and short duration are 6-week for school closure and 4-week for workforce shift, if attack rate is the priority.

Comparing the effect of school closure with workforce shift, we observe that workforce shift is generally more impactful. One of the main reasons is because of the difference in the number of people that can be affected by school and workplace interventions. In our contact network, school closure removes the school contacts from ~53,000 people; workforce shift affects ~148,000 people at any time during the intervention. So there is around 2.8 times more population controlled in the workforce shift.

Furthermore, we examine combined interventions as temporal combinations of single policies. We fix the duration shared by single policies in combination for simplicity; but allow different trigger threshold so that the two policies may be implemented either one after another or at the same time. Our results show that the combined interventions do not always outperform the single interventions while varying trigger threshold and duration. It is shown that short closures (less than 6 weeks) are more prone to underperform compared to the workforce shift only. Moreover, the influence of varying trigger threshold and duration has the similar pattern for the combined interventions with the single polices. Generally longer duration can improve the effect of interventions. When duration is short (compared to the corresponding cutoff values), a higher threshold is preferred for lower attack rate and peak incidence; when duration is long, a lower threshold will be favorable instead. Lastly, we show that switching the order of single policies in combination can make a difference in the effect of intervention. Planning multiple interventions in the appropriate order is able to strengthen the mitigation to the spread of epidemic at no additional cost.

Among all choices of combined interventions examined, the near-optimal policy happens when all school closure and workforce shift are both implemented at the 0.25% trigger threshold and lasted for 10 weeks (31.17% attack rate; peak incidence of 17.42 per 1,000 people at *day* 33).

Enforcing a social distancing policy always associates with considerable cost, on both economic and social aspects. For example, the major cost of school closure comes from absenteeism of working parents who have to stay home to take care of their children. A UK study (Sadique et al. 2008) estimated 16% of UK workforce was the main carers of dependent children and likely to be absent due to school closure. This percentage could further climb to 30% if counting healthcare workers only, meaning more absenteeism could happen in public healthcare system which has been already stressful during an epidemic. Besides, there are also problems about social justice, ethical issues etc as the social consequence of school closure (S. Cauchemez et al. 2009). On the other hand, workforce control will lead to a lack of manpower, lower productivity and inevitable economic lost. In this study, through examining the effectiveness of workforce shift and its combined strategies, we conclude that the 50% workforce shift might be a choice for workforce control during epidemic when considering the social and economic cost. It is also noted that it is not necessary to implement the 50% workforce shift in all societies. Policy makers may evaluate the social and economic costs together with the disease burden when planning for workforce shift which may also help improve the compliance rate of school closure. The planned workforce shift would definitely help companies and other institutions to plan better than unexpected mass absenteeism and minimize the lost in productivity and economic cost as well. Nowadays, accessible infrastructure for telecommunication is widely available at many workplaces. Tele-working has become more and more feasible and can be equipped in advance along with the planned workforce shift. It makes workforce shift with longer duration more feasible.

In lack of information about the compliance rate of school closure, we have assumed a 100% compliance rate in all relevant intervention scenarios in this study. However, in a real-world school closure, the student compliance rate for social distancing may be at a lower value. The compliance rate of students for social distancing would be increased when implementing workforce shift together with school closure. We ignore the variation of compliance rate for not complicating the analysis on the combined interventions. A higher compliance rate is definitely preferred in real-world interventions and needs the coordination among education agency, health agency and communities to achieve.

The evaluation of intervention scenarios in this study is based on Singapore's social structure. The results presented here should be interpreted with the following caveats in mind. First, the Singapore community is not a closed system. There are millions of visitors arriving in Singapore (e.g., a peak of 10 million visitors in 2007). Singapore has a population size of around 4.9 million. The large volumes of visitors flowing into the country implicitly indicate that the influence of imported cases should be considered when planning intervention strategies. However, the influence of visitors is not considered in our research as we focus on investigating and comparing the effectiveness of the individual and combined intervention scenarios. We note that it is desirable to further analyze the influence of visitors on the disease spread in the community for combating future pandemic. On the other hand, Singapore is a highly urbanized city and population density is among the top in the world, which will definitely lead to high contact numbers in different community structures. The best intervention scenario in terms of control timing may vary when the social structure is dramatically different from the social structure studied in this paper, as the heterogeneity of social structure is a significant factor affecting disease spread and therefore affecting mitigation planning strategies as well.

5. CONCLUSION

Though the combined intervention strategy outperformed its individual strategies in most cases, it is found that combined intervention strategies underperform its individual intervention strategies under inappropriate timing configuration. Our results suggest that trigger threshold and duration are critical to the effectiveness of the combined intervention, specifically, for lowering attack rate and daily incidence as well as longer peak delay. Our studies also show that the implementation order of individual interventions in the combination could affect the effect as well. Exploring correct timing configuration is therefore crucial to achieving optimal or near optimal effect of mitigation for influenza epidemic. Such an evaluation is recommended for assisting policy makers in influenza preparedness planning with their specific situation and constraints.

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