Cost-Effectiveness of Workplace Closure and Travel Restriction for Mitigating Influenza Outbreaks: A Network-based Simulation

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ABSTRACT

Background: Social distancing strategies, such as workplace closure and travel restriction, have been widely considered as alternative measures to contain influenza viruses, particularly when vaccines and antiviral drugs are under development. However, their cost-effectiveness in large urbanized populations is poorly understood.

Method: To fill this knowledge gap, this research builds a spatially-explicit network-based model to simulate influenza transmission, mitigation strategies, and their associated costs. This model represents a spatio-temporal network of individuals' daily contacts, which enables the simulation of local infection and long-distance dispersion of influenza. The workplace closure and travel restriction strategies, as well as their combinations with antiviral prophylaxis, are incorporated into this model to estimate their cost-effectiveness in mitigating seasonal flu and pandemic flu. The metropolitan area of Buffalo, NY, USA, with a population about 1 million, is selected as the study area.

Results: Without any intervention, the seasonal flu and pandemic flu cost $234.1 million and $331.1 million, respectively. The closure of 30% affected workplace is the most cost-effective single strategy with $12.9K per case averted for seasonal flu and $34.9K for pandemic flu. The travel restriction is not cost-effective if applied alone, but a 50% travel restriction in combination with antiviral prophylaxis and workplace closure forms the best strategy, which only costs $10.6K per cases averted for seasonal flu and $13.5K for pandemic flu.

Conclusions: For a large urbanized area, the closure of affected workplaces could be an effective and cost-saving strategy to mitigate influenza outbreaks, while the highest cost-effectiveness can be achieved by combining the travel restriction with antiviral prophylaxis and workplace closure.

Categories and Subject Descriptors

I.6 [**Simulation and Modeling**]: I.6.5 Model Development, I.6.6 Simulation Output Analysis.

General Terms

Algorithms, Design, Economics, Human Factors.

Keywords

Influenza, Mitigation Strategies, Cost-Effectiveness, Social Network, GIS, Agent-based Simulation

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1. INTRODUCTION

Recent outbreaks of influenza around the world, such as the H5N1 bird flu and new H1N1 flu, have triggered a new wave of exploring effective mitigation strategies [1]. A wide variety of strategies has been tested for their effectiveness in disease control, including pharmaceutical strategies, for example, the vaccination and antiviral prophylaxis, and non-pharmaceutical social-distancing strategies, such as the workplace/school closure and travel restriction [2-4]. In addition to their control effectiveness, the economic costs of these strategies are also of importance for health policy makers to consider, for instance, monetary costs of vaccines and loss of productivity from work absenteeism. A strategy that brings extremely heavy burden to the socio-economy is often not recommended, even though it is effective to control disease spread. A feasible mitigation strategy should not only be effective, but also cost-effective. A prior knowledge on the cost-effectiveness of different mitigation strategies is essential for influenza risk management.

In the current literature, cost-effectiveness has been primarily evaluated for pharmaceutical strategies through medical experiments [5-8]. Due to resource limits, these studies were often focused on a small group of population (100~1000 people in size), for example, healthcare workers, school children, and elderly people. The costs and benefits of pharmaceutical strategies remain unknown for large populations. Further, social distancing strategies, such as the city-wide workplace/school closure and travel restriction, are difficult to experiment in real practice, and their cost-effectiveness is poorly understood. The lack of such knowledge may cloud decision makers when facing influenza epidemics in a large city, or nationwide pandemics.

With the recent rise of computer-based epidemic simulation models, there have been a small number of studies attempting to estimate the cost-effectiveness of influenza mitigation strategies for large populations. For instance, Scuffham and West had evaluated vaccination and antiviral prophylaxis for elderly populations in three European countries [9]. This work employed a linear epidemic model, and thus could not account for the dynamic, nonlinear effects of interventions in infectious diseases, likely underestimating the cost-effectiveness [10]. To improve, Sander et al. [11] and Perlroth et al. [12] had proposed stochastic agent-based models to simulate the spread of influenza and mitigation strategies in the United States. However, both studies assumed a hypothetic population with an age and sex make-up matched to the overall US average. Hence, their results may not be applicable to dense urban populations where demographic characteristics and contact patterns are distinct [12]. Further, many details of populations were highly simplified, such as the geographic location of workplaces and the daily travel behaviors of people. The latest work by Milne et al. [13] intended to gauge mitigation strategies in a realistic town population in Australia, but the details about workplaces and human mobility were not considered either. The lack of these details prevents these studies from evaluating the workplace closure and the travel restriction strategies, which are widely recognized as potential policies to contain influenza outbreaks [3].

To fill the knowledge void, this article intends to evaluate the cost-effectiveness of workplace-closure and travel restriction in mitigating influenza outbreaks for a realistic urban area. A spatially-explicit network-based model is developed as a tool for evaluation. The section that follows introduces the structure of the model with three major components, including a flu simulator, a cost calculator, and mitigation strategies. The third section presents the simulation results and identifies cost-effective strategies. The last section concludes this article with discussion.

2. MATERIALS AND METHODS

In health economics, the cost-effectiveness of a mitigation strategy is commonly measured as a ratio between incremental costs and averted consequence of this strategy, as given in Equation 1:

$$\begin{aligned} CER(i) &= \frac{\Delta Costs(i)}{\Delta Consequence(i)} \\ &= \frac{StrategyCost(i) - Savings\ from\ health\ outcomes\ averted}{No.of\ cases\ averted(i)} \\ &= \frac{StrategyCost(i) - [FluCosts(0) - FluCosts(i)]}{No.of\ cases\ averted(i)} \end{aligned} \quad (1)$$

where i denotes a specific mitigation strategy and $CER(i)$ is its cost-effectiveness ratio ($ per case averted). The incremental or net costs of a strategy $\Delta Costs(i)$ includes the cost of the strategy $StrategyCosts(i)$ minus the savings from health outcomes averted by the strategy. The savings are the difference between the costs of influenza without mitigation strategies $FluCosts(0)$ as a baseline scenario, and those with the mitigation strategy $FluCosts(i)$. The denominator $\Delta Consequence(i)$ is expressed as the number of influenza cases averted by the strategy i, i.e., the differences in case numbers between the baseline scenario and the strategy i. Following Equation 1, a computer model is designed to simulate the influenza spreading process, the mitigation strategy against influenza, and the resulting costs, respectively. Therefore, the model has three major components: a flu simulator, a cost calculator, and a set of mitigation strategies (Figure 1).

2.1 Component 1: Flu simulator

The flu simulator takes an agent-based approach to simulate the daily travel of individuals, their social contacts, and resulting

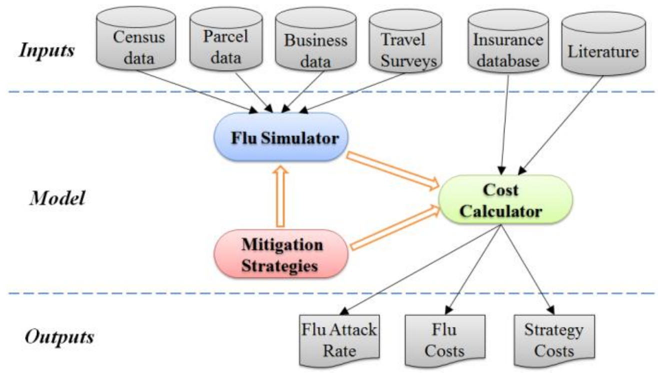

Figure 1. Structural design of the simulation model. The model is composed of three major components, including a flu simulator, a cost calculator, and a set of mitigation strategies. The simulation involves several databases as inputs, and produces flu attack rates, flu costs, and strategy costs for cost-benefit analysis.

influenza transmission in the study area (Buffalo, NY). This approach involves stochastic simulation, discrete time steps, and spatially explicit representation of individual mobility. Each of the 985,001 individuals is conceptualized as a modeling unit with a set of characteristics (e.g., age, occupation, infection status, time and location of daily activities) and behaviors (e.g., traveling between locations for activities and having contact with other individuals). They are first grouped and allocated to 400,870 household locations in 967 census block groups under the constraints of census data, so that the modeled population matches the age and household structure of the real study area. These individuals are further modeled to travel between homes and 36,839 business locations (schools, workplaces, or service places) to carry out their daily activities, such as working, shopping, and recreation, which expose them to the risk of infection. The assignment of individuals to locations utilizes a business database released by ReferenceUSA Inc. and a travel survey report from the Greater Buffalo-Niagara regional transportation council. The implementation adopts an algorithm developed by Mao and Bian [14], which is not a focus of this research. As illustrated in Figure 2, each 3D trajectory represents an individual's travel behavior of a day. Vertical segments on a trajectory indicate a stay at a location for some time, while horizontal segments indicate travel from one location to another. The intersections between trajectories, as circled in the map, imply that individuals meet at the same time and location, and may have contacts with one another that allow influenza transmission. Since individuals travel over time and location, this model represents a spatio-temporally

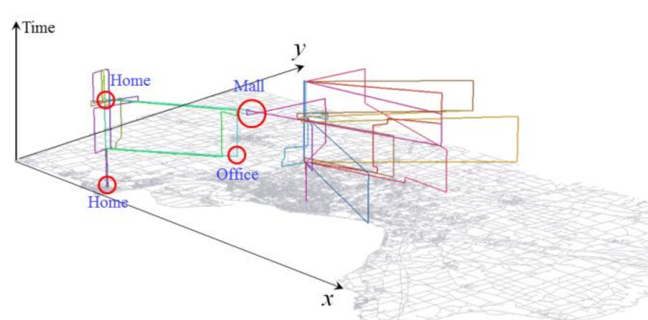

Figure 2. 3D travel trajectories of 10 individuals in a day. The X and Y axis represent a geographic space of the study area, and the Z axis showing time.

varying contact network woven by individual mobility.

The transmission of influenza from one individual to another is stochastically simulated based on such a network. Each individual is allowed to take one of four infection status during a time period, namely, susceptible, latent, infectious, and recovered [15]. The progress of infection status follows the natural history of influenza, including the latent, incubation, and infectious periods. During the infectious period, individuals being infected may manifest symptoms and become symptomatic. Details on influenza parameter setting are provided in Table 1.

Table 1. Key parameters for simulating influenza spread

Parameters	Values	Literature
Basic reproduction Number R_0	1.3– 1.4	[16, 17]
Infection rates per contact I_{age}	Children (under 5): 0.1 Youth (6-17): 0.08 Adults (18-64): 0.08 Senior (65+): 0.09	Calibrated based on R_0
Likelihood of symptom manifestation	0.5	[18]
Latent period	2 days	[19]
Incubation period	3 days	[19, 20]
Infectious period	Children: 7 days Youth: 4 days Adults: 4 days Senior: 4 days	[19, 21]

To initiate the disease transmission, five infectious individuals are randomly seeded into the study area at the first day of simulation, which then lasts for 150 days. In each day, the model traces susceptible contacts of infectious individuals, and simulates the next generation of infections using the Monte-Carlo method. The model had been validated using the CDC weekly reports of confirmed cases in 2004–05 flu season in the study area [14].

2.2 Component 2: Flu Cost Calculator

The flu simulator described above identifies symptomatic individuals (influenza cases) during every simulation day. For each influenza case, a flu cost calculator is triggered to value the monetary costs of this case in response to influenza, following a tree-structured flowchart shown in Figure 3.

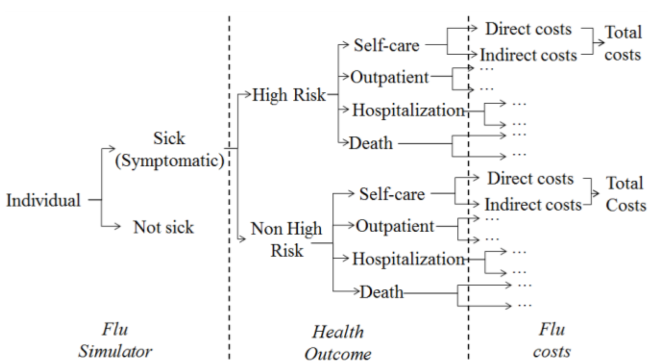

Figure 3. Workflow of flu cost calculator in the simulation model to estimate flu costs to an influenza case. The flu simulator first determines the sickness of an individual. The cost calculator, then, uses the probabilities on branches to determine the associated health outcome and costs (from Table 2 to 4).

Except for the first branch on the left in Figure 3, all other branches in the flow chart are determined by probabilities adopted from the literature [22, 23], as shown in Table 2. Influenza cases are separated into five age groups: under 5, 5–17, 18–49, 50–64, and over 65 years. According to an age-specific probability, each case is then categorized as either a high risk case or non high-risk case. For either category, an influenza case may develop one of four possible outcomes: self-care, outpatient, hospitalization, and death with probabilities estimated by Molinari et al. [22] from the literature, medical records, and reports. Those in the high-risk category have greater chance to develop severe outcomes, such as hospitalization and death [24].

Table 2. Nationwide influenza parameters and distributions by age group, by risk and by health outcomes, all adopted from Molinari et al. [22]

Influenza Parameters	Age Group	Mean	Standard Deviation
Likelihoods of high-risk influenza cases			
	0-4	0.052	0.890
	5-17	0.106	0.360
	18-49	0.149	0.340
	50-64	0.330	0.700
	65+	0.512	0.730
Pr (Outpatient visit| flu infection)			
Non-High risk cases	0-4	0.455	0.098
	5-17	0.318	0.061
	18-49	0.313	0.014
	50-64	0.313	0.014
	65+	0.620	0.027
High risk cases	0-4	0.910	0.250
	5-17	0.635	0.167
	18-49	0.625	0.118
	50-64	0.625	0.118
	65+	0.820	0.093
Pr (Hospitalization| flu infection)			
All risks	0-4	0.0141	0.0047
	5-17	0.0006	0.0002
	18-49	0.0042	0.0014
	50-64	0.0193	0.0064
	65+	0.0421	0.0140
Pr (Death| flu infection)			
All risks	0-4	0.00004	0.00001
	5-17	0.00001	0.00000
	18-49	0.00009	0.00003
	50-64	0.00134	0.00045
	65+	0.01170	0.00390
Pr (Self-care| flu infection)			
Non-High risk	0-4 5-17 18-49 50-64 65+	Pr (Self-care| flu infection) =1- Pr (Outpatient visit| flu infection)- Pr (Hospitalization| flu infection)- Pr (Death| flu infection)	
High risk	0-4 5-17 18-49 50-64 65+	Pr (Self-care| flu infection) =1- Pr (Outpatient visit| flu infection)- Pr (Hospitalization| flu infection)- Pr (Death| flu infection)	

When the health outcome of an influenza case is determined, the direct and indirect costs associated with this outcome are estimated, and then summed into the total influenza costs to this individual (Figure 3). The direct costs come from the medical expenditure in response to influenza (e.g., hospitalizations, outpatient visits, and drug purchases), and vary over age groups, risk categories, and outcomes. Details about the direct costs by age group, risk category, and health outcome are given in Table 3.

Table 3. Direct costs of influenza by age group, by risk and by health outcome, all adopted from Molinari et al. [22]

Cost per health outcome by age and risk group	Medical (Direct) cost ($)		
	Mean	S.D.	Distribution
Self-care			
All risks			
0-4	3	2	Log normal
5-17	3	2	Log normal
18-49	3	2	Log normal
50-64	3	2	Log normal
65+	2	2	Log normal
Outpatient visit			
Non-High risk			
0-4	167	307	Log normal
5-17	95	258	Log normal
18-49	125	438	Log normal
50-64	150	766	Log normal
65+	242	1,544	Log normal
High risk			
0-4	574	1,266	Log normal
5-17	649	1,492	Log normal
18-49	725	1,717	Log normal
50-64	733	1,307	Log normal
65+	476	1,131	Log normal
Hospitalization			
Non-High risk			
0-4	10,880	36,189	Log normal
5-17	15,014	86,804	Log normal
18-49	19,012	44,636	Log normal
50-64	22,304	95,727	Log normal
65+	11,451	23,128	Log normal
High risk			
0-4	81,596	123,626	Log normal
5-17	41,918	50,393	Log normal
18-49	47,722	85,644	Log normal
50-64	41,309	74,798	Log normal
65+	16,750	32,091	Log normal
Death			
Non-High risk	Mean	S.D.	Distribution
0-4	28,818	24,483	Log normal
5-17	28,818	24,483	Log normal
18-49	76,336	91,654	Log normal
50-64	118,575	333,879	Log normal
65+	41,948	96,467	Log normal
High risk			
0-4	267,954	221,130	Log normal
5-17	267,954	221,130	Log normal
18-49	75,890	65,267	Log normal
50-64	118,842	345,973	Log normal
65+	33,011	61,904	Log normal

The indirect costs include the loss of productivity due to work/school absenteeism and due to death. The loss of productivity due to work/school absenteeism is calculated by multiplying the length of days absent from work with the daily wage of a person ($145/day in Buffalo). For influenza cases ending with deaths, the productivity loss is estimated as the present value of lost earnings (PVLE), the projected earnings until retirement based on a person's current salary. The average lengths of work/school absenteeism and the PVLE by age group, along with their statistical distributions, are shown in Table 4.

Table 4. Indirect costs of influenza by age group, by risk and by health outcome, all adopted from Molinari et al. [22]

Cost per health outcome by age and risk group	Lost productivity (days)		
	Mean	Distribution	
Self-care			
All risks			
0-4	1.0	Poisson	
5-17	0.5	Poisson	
18-49	0.5	Poisson	
50-64	0.5	Poisson	
65+	1.0	Poisson	
Outpatient visit			
Non-High risk			
0-4	1	Poisson	
5-17	1	Poisson	
18-49	1	Poisson	
50-64	2	Poisson	
65+	3	Poisson	
High risk			
0-4	6	Poisson	
5-17	4	Poisson	
18-49	2	Poisson	
50-64	4	Poisson	
65+	7	Poisson	
Hospitalization			
Non-High risk			
0-4	8	Poisson	
5-17	9	Poisson	
18-49	12	Poisson	
50-64	13	Poisson	
65+	13	Poisson	
High risk			
0-4	31	Poisson	
5-17	23	Poisson	
18-49	21	Poisson	
50-64	24	Poisson	
65+	18	Poisson	
Death	**Present value of lost earnings ($)**		
Non-High risk	Mean	S.D.	Distribution
0-4	1,074,866	222,803	Log normal
5-17	1,276,012	900,934	Log normal
18-49	1,374,115	2,754,332	Log normal
50-64	521,083	1,588,835	Log normal
65+	185,846	597,639	Log normal
High risk			
0-4	1,074,866	222,803	Log normal
5-17	1,276,012	900,934	Log normal
18-49	1,374,115	2,754,332	Log normal
50-64	521,083	1,588,835	Log normal
65+	185,846	597,639	Log normal

Since estimates in Table 3 and 4 chose 2003 as the base year, this research inflated all the costs from 2003 to 2010 according to the consumer price index (CPI) of these two years. The CPI ratio between year 2010 and 2003 was set to 1.185 as reported by the

Bureau of Labor. After inflation, the costs of each influenza case can be valued. The sum of costs to all influenza cases is the total costs of influenza to the study area, i.e., the *FluCosts* variable in Equation 1.

2.3 Component 3: Influenza mitigation strategies and their costs

Table 5 shows the design of three mitigation strategies and their combinations. This research mainly focuses on two social-distancing strategies, namely, the workplace closure and travel restriction. A targeted antiviral prophylaxis (TAP) strategy is added to examine the cost-effectiveness of combined strategies. The baseline scenario represents an influenza epidemic without any mitigation strategy, and is designed to compute *FluCosts(0)* in Equation 1.

Table 5. Design of mitigation strategies and low-high scenarios

Strategy \ Scenario	Low	High
Baseline	No Interventions	No Interventions
Workplace/School Closure (WSC)	100% schools +10% workplaces	100% schools+33% workplaces
Travel restriction (TR)	10% trips	50% trips
Targeted Antiviral Prophylaxis (TAP)	30% cases	60% cases
Combined	Combination of all above	Combination of all above

The workplace/school closure strategy (WSC) shuts down a proportion of workplaces and schools where influenza cases are detected. Following Ferguson et al. [3], workplaces and schools would be closed for 3 weeks once 1 case is detected. After reopened, they can close again if new cases occur. To account for the compliance issue, this research considers a low scenario (10%WSC) that closes 10% affected workplaces along with 100% affected schools in a day, and a high scenario (30%WSC) that closes 30% affected workplaces along with 100% affected schools. The costs of this strategy are measured as the loss of productivity due to work/school absenteeism. For each closed place, the loss of productivity is the product of the number of employees, the daily wage per person ($145 on average), and the length of closure in days. The school absenteeism also causes loss of productivity of one parent because he/she needs to be absent from work to take care of children. The sum of productivity loss for all closed places is the total costs of this strategy, i.e., *StrategyCost(i)* in Equation 1.

The travel restriction strategy (TR) aims to reduce the trips into and out of affected communities [3, 25]. Each of the 967 census block groups in the study area is treated as a community. The restriction is assumed to last 2 weeks after the first case is detected in a community. Once the restriction is lifted, a community can be restricted again if new cases are identified. Following Germann et al. [26], a low-level scenario (10% TR) restricts 10% trips into and out of all affected communities, while a high-level scenario prohibits 50% trips (50% TR). The costs of this strategy come from the loss of productivity due to work/school absenteeism, because some pupil and staff cannot travel to schools and workplaces that are out of their residential communities. The costs to a restricted individual who cannot travel to workplace/school are the product of the average daily wage ($145) and the length of being restricted in days. The total costs of this strategy, *StrategyCost(i)* in Equation 1, are the sum of costs to all restricted individuals in the study area.

The TAP strategy identifies influenza cases every day, searches their household members (up to 10), and then targets antiviral drugs to all these individuals [26]. If an individual takes antiviral drugs, the chance of being infected and infecting others can be reduced by 70% and 40%, respectively [27, 28]. Each targeted individual is simulated to takes 20 Capsules of Tamiflu for 10 days with a market price of $130 in total. Thus, the total cost of this strategy, *StrategyCosts(i)*, is the total number of targeted individuals multiplied by $130. To account for limited health personnel, this research evaluates two scenarios. The low scenario assumes that only 30% of influenza cases (30%TAP) can be identified during a day, while the high scenario assumes 60% (60%TAP), both following the design in Germann et al. [26].

In addition to testing the three control strategies individually, their combinations are also evaluated. A low-level combination scenario (referred to as the Combined-Low) includes all three strategies at their respective low levels. Likewise, a high-level combination (referred to as the Combined-High) contains all three strategies at high levels. The total costs of a combined strategy are the sum of costs from all individual strategies. The TAP strategy is assumed to be implemented at the time when the total number of influenza cases exceeds 0.5‰ of the population (≈500 cases), and last until the end of the epidemic. The workplace/school closure and travel restriction strategies are assumed to be applied under a more severe situation that the case number exceeds 1‰ of the population (≈1,000 cases).

2.4 Cost-benefit analysis

Each scenario in Table 5, as a strategy *i*, is incorporated into the flu simulator and the cost calculator to measure the *FluCosts(i)* and *StrategyCosts(i)*. The simulation is performed 50 realizations per scenario to reduce randomness in results. The averaged *FluCosts(0)*, *FluCosts(i)*, and *StrategyCosts(i)* of a strategy scenario are then plugged into Equation 1 to estimate the cost-effectiveness ratio *CER(i)*. The comparison between scenarios would suggest the most cost-effective way to control influenza with minimum disruptions on socio-economy.

2.5 Sensitivity analysis

To account for the uncertainties of influenza outbreaks, all scenarios in Table 5 are further tested in a context of pandemic influenza. The methods are the same as described above, but the basic productive number R_0 is set to 2.0 to represent a highly infective flu strain that may lead to pandemics. The infection rates per contact by age group are the calibrated to this R_0 for flu simulation, while all other model parameters remain unchanged.

3 RESULTS

3.1 Cost-effectiveness of mitigation strategies

Without any intervention (the baseline scenario), the seasonal influenza (R_0=1.4) may cause sickness to an average of 18.6% population (Table 6). This reasonably falls within the range of seasonal flu attack rate from 5~20% reported by the Center for Disease Control and Prevention (CDC) [21]. The total economic burden can be amounted to $231.4 million in the study area. Among the four non-pharmaceutical scenarios, the restriction of 10% travels (TR10%) is not recommended, because it even increases the influenza attack rate to 20% and aggravates the outbreak. This is a "spending money but getting worse" situation. A possible reason is that a low level restriction of travels is not sufficient to prohibit the penetration of influenza into other communities, but meanwhile it intensifies the frequency of household contacts, leading to more infections. The rest of three scenarios do produce mitigation effects on influenza outbreak. The WSC10% is the most expensive strategy with the highest costs per case averted ($37.2K), but it does not reduce infections remarkably. The WSC30% is quite effective in reducing the flu attack rate from 18.6% to 6.7%, and meanwhile its net costs are $349 million lower than the WSC10%. A higher level of travel restriction (TR50%) seems to moderately contain the spread of influenza (the attack rate drops 28%), but its high net costs ($1.65 billion) neutralize its control effectiveness. In summary, the workplace closure strategy is more cost-effective than the travel restriction. If the policy maker plans to choose a single strategy to control the flu outbreak, the WSC30% is a cost-effective choice with $12.9K per case averted. This is particularly useful when no pharmaceutical treatments are available at early outbreaks of new influenza viruses.

Table 6. Simulated economic costs of influenza control scenarios under R_0=1.4

Scenario	Disease Attack Rate (%)	Net Costs/Returns* (Million $)	Costs Effectiveness Ratio-CER ($/case averted)
Baseline	18.6	N/A	N/A
WSC10%	13.5	1866.3	37,151
WSC30%	6.70	1517.2	12,944
TR10%	20.01	345.4	N/A
TR50%	13.3	1653.2	31,667
TAP30%	14.5	-19.3	-478
TAP60%	12.9	-41.9	-746
Combined-Low	8.8	1742.3	18,048
Combined-High	1.4	1796.6	10,604

*=FluCosts-StrategyCosts. Positive values indicate net costs, while negative values are net returns.

In contrast to the non-pharmaceutical scenarios, two pharmaceutical scenarios (TAP30% and TAP60%) could even save $400-800 for each averted case. This is not surprising because the closure of workplaces and schools causes the loss of productivity every day, and so does the travel restriction. If a workplace is closed for 21 days, the loss of productivity for a person can be amounted to $3,045, while treating this person with antiviral drugs only costs $130. However, these two TAP scenarios only produce 4~6 point drop in the disease attack rate, and neither could significantly mitigate the influenza outbreak. It is also noteworthy that the TAP strategy requires a large stockpile of antiviral drugs, which may not be available at the early stage of influenza outbreaks. Therefore, the TAP strategy is suggested to be combined with social distancing strategies, rather than deploying alone. In the case that health resources allow a combined strategy, the high-level combination of three individual strategies (Combined-High) is recommended, because it almost eliminates the outbreak with only a little higher net costs than the Combined-Low strategy. The costs per averted case are around $10K, the lowest among all scenarios.

3.2 Sensitivity analysis

To test the sensitivity of recommendations made above, those control scenarios are also simulated in a pandemic flu context (R_0=2.0). For a highly infective influenza strain, about 8% more people would feel sick due to infection, leading to a total flu costs of $331.1 million (Table 7). As a result, the costs per case averted are doubled or even tripled for most mitigation scenarios. In the case that antiviral prophylaxis was not available, the WSC30% would still be a cost-effective option due to its relative lower costs per averted case ($35K) among individual scenarios. A low level (10%) restriction of individual travels would again worsen the situation, and even the high-level restriction produces few mitigation effects (the attack rate only drops 14%). The WSC10% and TR50% produce similar mitigation effects, but both require a pretty high investment. The Combined_High scenario is the only one that reduces the attack rate under 10%. Meanwhile, the costs per averted case only increases 30% from $10.6K for the seasonal flu (R_0=1.4) to $13.5K for the pandemic flu. This is the most effective and cost-effective strategy to combat both seasonal and pandemic flu.

Table 7. Simulated economic costs of influenza control scenarios under R_0=2.0

Scenario	Disease Attack Rate (%)	Net Costs/Returns* (Million $)	Costs Effectiveness Ratio-CER ($/case averted)
Baseline	26.4	N/A	N/A
WSC10%	23.4	2622.5	88,748
WSC30%	18.4	2750.9	34,910
TR10%	27.2	296.2	N/A
TR50%	22.8	1775.9	50,082
TAP30%	22.9	-5.9	-171
TAP60%	21.4	-17.6	-357
Combined_ Low	19.8	2699.1	41,518
Combined_ High	6.2	2679.4	13,466

*=FluCosts-StrategyCosts Positive values indicate net returns, while negative values are net costs.

4 DISCUSSION

In practice, health administrators need to balance the costs and benefits when choosing a mitigation strategy. This study shows that for a metropolitan area of 1 million people, an outbreak of seasonal influenza would cost $260 million, and approximately 8-10 times of such amount may need to totally invert its health outcomes. The pandemic influenza costs more, and requires more investments for mitigation. The results suggest that closing 30% affected workplaces every day could be a single cost-effective strategy to mitigate both seasonal and pandemic flu. If resources and manpower allow a combined strategy, the high level implementation of targeted antiviral prophylaxis and the two social distancing strategies (workplace closure and travel restriction) would be the best strategy to combat influenza.

The workplace closure and travel restriction strategies have been widely considered as alternative measures to contain emerging influenza viruses, particularly when vaccines and antiviral drugs are under development [2]. However, their cost-effectiveness in large urbanized populations is poorly understood because few current models have explicitly considered the spatial location of workplaces and the travel behaviors of individuals between homes and workplaces. This study is the first attempt to evaluate the cost-benefits of workplace closure and travel restriction strategies, and thus complement current understandings on social distancing strategies. Further, the model is implemented for a realistic urban population, rather than an US average population, and therefore the outcomes are more informative and appropriate to guide influenza containment in areas where the influenza is the most communicable. Although influenza has been taken as an example, the proposed model can be easily extended to other emerging pathogens, such as the severe acute respiratory syndrome (SARS), by manipulating model parameters.

Similar to any modeling analysis, this research has a number of limitations. First, the simulation model focuses on one US metropolitan area. It is possible that the model outcomes vary between cities with different demographics and standards of living. The interpretation of model outcomes should be limited to the study area, or other similar areas. Nevertheless, the proposed model can be modified to fit other urban areas by changing input census, business, and travel survey data. Second, the model has not considered the active prevention of healthy individuals, assuming that they would not take any action to protect themselves unless being intervened. A coupled model of disease transmission and human preventive behavior could be considered to deal with this limit. Third, many model parameters used to calculate costs, such as the likelihood of being a high-risk case and the length of work absenteeism, were estimated from a nationwide database by previous work, not specifically for the study area. The differences may bias the quantitative estimates, but may not be sufficient to mislead the qualitative comparison between strategies. Last, a more comprehensive analysis of cost-effectiveness should have included intangible costs, such as the loss of social values due to death and the long-term effects of workplace/school closure. All these limitations warrant a future study.

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