Does separating vaccinated and unvaccinated students in schools result in better health outcomes? An agent-based model for mumps

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ABSTRACT

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A rise in unvaccinated children and subsequent uptick in vaccine-preventable disease has led to a vigorous public debate regarding vaccination status, with some physicians and parents calling for unvaccinated children to be banned from clinics or schools. We simulated a mumps outbreak in a small school system and evaluated how key disease dynamics were impacted by instituting a policy of separating vaccinated and unvaccinated children into different schools. In addition, we evaluated the impact of school separation when used concurrently with physical distancing, self-isolation, school closure, and mandatory isolation.

We used Agent Based Simulation to model mumps outbreaks among students in a small city. Agents move between the school, home and other places on a daily basis. Mumps parameters are modeled based on current literature on infectious diseases. Multiple control strategies were investigated in terms of infection rate, outbreak length, and total costs.

Our motivation for this work was to evaluate the disease impact of a school separation strategy. Given the potential ethical and legal complications, the associated health benefits would have to be significant to persuade policy makers to adopt such a policy. Our results do not suggest that a school separation strategy should be adopted in most of the scenarios since this strategy increases the number of infected students, the chance of outbreaks, and the associated cost in the majority of them. In addition, our work demonstrates that educating students on the benefits of adopting physical distancing and self-isolation is effective in controlling the mumps outbreak size and cost in a population with 90% vaccine coverage, and confirms that mandatory isolation in this population is an effective strategy for managing outbreaks.

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Table of Contents

List of Figures:

List of Tables:

1. Introduction

Vaccination programs have been hugely successful in reducing infectious disease outbreaks; however, rising vaccine hesitancy has limited the ability of vaccination programs to successfully control outbreaks. A variety of non-pharmaceutical interventions have been evaluated, including the effect of social patterns and individual behavior on lowering the infection rates and controlling the outbreaks. They suggest that in some contexts, restricting population contact rates could be a potential useful control measure [1,2,3]. Markel et al. recommend isolation, school closure, and cancellation of public gatherings, which are all non-pharmaceutical interventions, in parallel with vaccination and medication for severe influenza pandemics [4]. Moreover, using a mathematical model for smallpox, Del Valle et al. suggest if behavioral change is combined with other interventions, it can reduce the number of infections and outbreak duration[5].

Social distancing, in which individuals avoid crowded places in order to reduce the chance of infection, has been examined by many researchers [6, 7,8]. The goal of social distancing is to decrease attack rates and mortality rates and also delay peak period in order to better control the virus. Kelso et al. suggest that social distancing can have a critical role in control of a pandemic if implemented quickly and maintained [7]. School closure is one instance of social distancing. High levels of interactions between students in schools makes them a critical place for virus transmission and explains the academic and policy interest in educational facilities [9]. Hyman et al. recommend school closure for controlling influenza pandemic as their results show school closure reduces upper respiratory illness [8]. Using a large-scale social contact survey, Hens et al. show that school closure can reduce infectious disease spread [10]. Isolation of infectious individuals is another intervention which is investigated in a number of researches [11,12,13]. Fergguson et al. suggest that, if feasible, a quick case isolation strategy could reduce the infectiousness of individuals significantly in an influenza pandemic [13] and Wang et al. show that patient isolation delays influenza spread [12]. If isolation is practiced voluntarily, it is called self-isolation, that could be staying at home and avoiding contacts with others. Holmberg et al. reveal that about one third of the U.S. states in 2005-2006 had plans to recommend self-isolation to adults including staying at home [14]. Physical distancing, the idea which suggests avoiding close contacts with others, is another personal protective behavior that could have a significant impact on the severity of an outbreak [15]. Physical distancing has already been practiced in previous outbreaks in the world such as H1N1(2009) and SARS (2003) in Singapore [16] . Karimi et al. showed that physical distancing combined with other protective behaviors can significantly reduce attack rate and peak number of infections in a university setting [15].

Prevention strategies are not limited to these measures. Many states in the U.S. have policies that give schools the authority to exclude those students who are not vaccinated for a limited time during outbreaks which, as a result, control the spread of the virus and reduce number of infections in the population [17]. These interventions could be considered as a type of nonvoluntary social distancing [18].

Another approach that has recently been focused in the media is the practice of dismissing unvaccinated families by some family physicians and pediatricians. Although the Center of Disease Control and Prevention (CDC) is not in favor of this approach, dismissing these families is not uncommon [19]. In a survey done by Flanagan-Klygis et al. in 2005, 38% of physicians declared they would not provide service for families who refused all vaccinations and 28% would dismiss families in case they did not accept specific vaccinations [20]. A newer study suggests that, while there is variation by region, families who refuse vaccination are dismissed by 20% of the pediatricians [19]. Diekema suggests that this approach is not beneficial for the public health [21]. However, physicians who don't accept these families claim that unvaccinated children pose an infection risk to other children and staff in the clinic, and if they dismiss this group of families, the infection probability in the waiting room is minimized [22]. Research by O'Leary et al. support the idea that this policy may raise vaccine uptake by underscoring vaccine significance [19]. However, no research has yet evaluated the impacts of this policy on disease dynamics during an outbreak [23].

Although several control measures have been proposed and investigated in epidemiological research, more effective and cost-efficient measures are needed to better control and prevent the epidemics. In this research, we propose a novel approach for social intervention and analyze its effects by means of simulation and cost analysis. The idea of dismissing unvaccinated children in clinics led us to consider a similar strategy for separating unvaccinated children into different schools. We implement a strategy where unvaccinated students are separated from vaccinated students by transferring them to a different school. This approach is called Separation strategy in this thesis. We compare separation strategy with no separation strategy, where vaccinated and unvaccinated students are not separated.

There are a variety of practical and ethical issues involved in implementing this policy. The beauty of simulation, and particularly agent-based simulation, is that it allows us to create experiments to evaluate the implication of policies without involving human subjects. These policies will likely be most important for low vaccination communities. Agent Based Modeling and Simulation (ABMS) allows us to create a community of individuals with a low rate of vaccination. We model the implementation of school closure at the beginning of a possible outbreak in the unvaccinated school. This school will be prepared for small signals of an outbreak and will close the school as soon as number of infections passes a threshold. From a purely disease control perspective, if the combined policy of school separation and school closure can control the outbreak successfully, or at least does not result in an adverse effect in a potential outbreak in the separated school, this policy could be considered beneficial for public health. Moreover, the separation might encourage resistant families to vaccinate their children in order to avoid the possible difficulties of sending their children to a specific school either for convenience or health reasons, which as a result, would increase the vaccine coverage of the population in long term.

By removing unvaccinated students from most schools, the chance of a large scale outbreak in those schools might decrease considerably. In this research, we evaluate this notion by creating a model city and simulating school attendance for high school students in different parts of the city using an agent based model. During the simulation, an outbreak is initialized to infect several individuals. The model runs until the outbreak is eradicated. By running different scenarios and combining them we investigate the benefit of each approach. The efficacy of each measure is analyzed by comparing the attack rates and anticipated costs of each approach with the baseline scenario and other policy measures.

Throughout this research, we consider other prevention policies such as social distancing, self-isolation, and physical distancing. We evaluated the effects of implementing these social patterns in both the separation and no separation strategies.

We investigate the outbreaks of mumps in our analysis. A study by Van Loon, F. P., et al. shows that implementation of mumps vaccine in 1967 had a huge impact in protection of US citizens [24]; however, the risk of its outbreaks raised in recent years through a drop in vaccine uptake and one of its important causes appears to be the rise of non-vaccinators and vaccine hesitant parents [25, 26]. It is now evident that governments are worried about the practice of vaccine hesitancy by individuals [26]. The anti-vaccination movement, which first originated in the 19^{th} century and was strengthened again in 1990s as a result of some unproven publications about the negative effects of measles, mumps and rubella vaccine (MMR) on children's health, has provoked a trend of hesitation and vaccine bypassing in families during the last two decades [25,27,28]. Consequently, it resulted in an increased probability of Mumps outbreaks. There are also other important elements which negatively impact vaccine uptake such as poor access to health care [25]. However, mumps outbreak emergence could be a result of intense exposures, overwhelming the protection offered by the vaccine, waning immunity, etc. [29]. Several mumps outbreaks have occurred in different countries in the last decade [30]. In fact, the populations with routine mumps vaccination have not completely removed the chance of an outbreak. The UK and the USA have had large outbreaks [31] and the mumps detection rate in Denmark has increased by a factor of 10 in the last decade [30].The United Kingdom faced an epidemic of mumps during 2004-2005 with more than 56000 reported cases in England and Wales [32]. Many individuals of this group were students and their illness was related to outbreaks in universities and colleges across this area [33]. Universities and schools are a prime location for the spread of Mumps, mainly because of the high rates of social interaction and shared accommodation [34]. In order to prepare for such an outbreak and minimize the probable costs, information about the spread of mumps and its consequences in educational settings is necessary.

Mumps is a contagious vaccine preventable disease with a medium to high level of contagiousness. Its main symptom is a characteristic facial swelling, while inflammation of other body parts such as ovaries is the additional potential complication. In extreme cases, infertility, meningitis, hearing loss, or even death are possible, though severe complications are scarce [31,35,36]. Direct contact, contamination of fomites, or droplet spread are major routes of mumps' transmission. Its incubation period is between 15 to 24 days with a median of 19 days [37]. The virus is highly contagious 1 to 2 days before the onset of symptoms and this status is maintained for several days [38]. The infectiousness period starts 3 days before the appearance of symptoms and lasts for 12 days [39]. If people get mumps, they have a high chance of acquiring lifetime immunity; however, JP Gut et al. suggest there is still a possiblity that individuals get infected again [40].

A wealth of mathematical modeling research focuses on vaccine-preventable infectious diseases, in particular Influenza, and some of this research specifically concentrate on educational settings [41,42,43,44]. However, little research exists on mathematical or simulation modeling of mumps [45,46, 47]. Moneim analyses a number of infectious diseases including mumps using simulation while importance of latent period, the time from infection to infectiousness, is his target [45]. Kanaan et al. use mathematical modeling for mumps and rubella, and by the use of matrix models, estimate the basic reproduction number for these diseases [47]. Simoesa, J. M. simulates a mumps outbreak in Portugal using agent based model and provides a spatial pattern of infection [46]. Nonetheless, existing research does not thoroughly explore the dynamics of mumps. Besides, the authors could not find a research concerning simulation of mumps in educational environment. Hence, considering the existing risk of mumps outbreaks, the necessity of practicing mumps modeling specially in students' community is evident. Accordingly, we examined the spread of mumps in this research. We obtained some mumps parameters from existing literature and calculated a number of others based on literature from other diseases.

2. Research Methodology

In order to analyze the impact of separation strategies and protective behaviors, we constructed an agent based simulation which represents the occurrence of a mumps outbreak among high school students in a city using Matlab 2015a software. The structure of the disease and elements of its behavior such as latent period and vaccine effectiveness were modeled based on the literature on mumps and other infectious diseases. Some basic elements of mumps were calculated based on influenza literature.

The size of the city and number of stations where the students attend are made based on assumptions. The participation of students in the stations was acquired based on literature and assumptions.

The agent based simulation was run for several scenarios including baseline scenario, school closure scenario, communicable disease safety initiative scenario, and mandatory isolation scenario. These scenarios are discussed in section 4.2. Each scenario is run with and without implementing separation strategy which requires unvaccinated students to study in a separated school.

The scenarios and the effect of separation strategy on them were analyzed regarding the number of infections, and the costs associated with infections such as healthcare costs, and prevention costs. These costs were obtained from literature.

The protective behavior of students and their attitude towards implementing them after a communicable disease safety initiative were grasped using a previous research in which bachelor students at Concordia Universitry were surveyed [15]. Since the age difference between bachelor students and high school students is negligible, we used the data from this research.

One of the key challenges of this literature is the paucity of disease transmission parameter values on mumps in the literature. In the next sections we describe how we derived these values.

Finally, the results of these scenarios are compared in terms of attack rate and costs, and suggestions about the implementation of these approaches are provided.

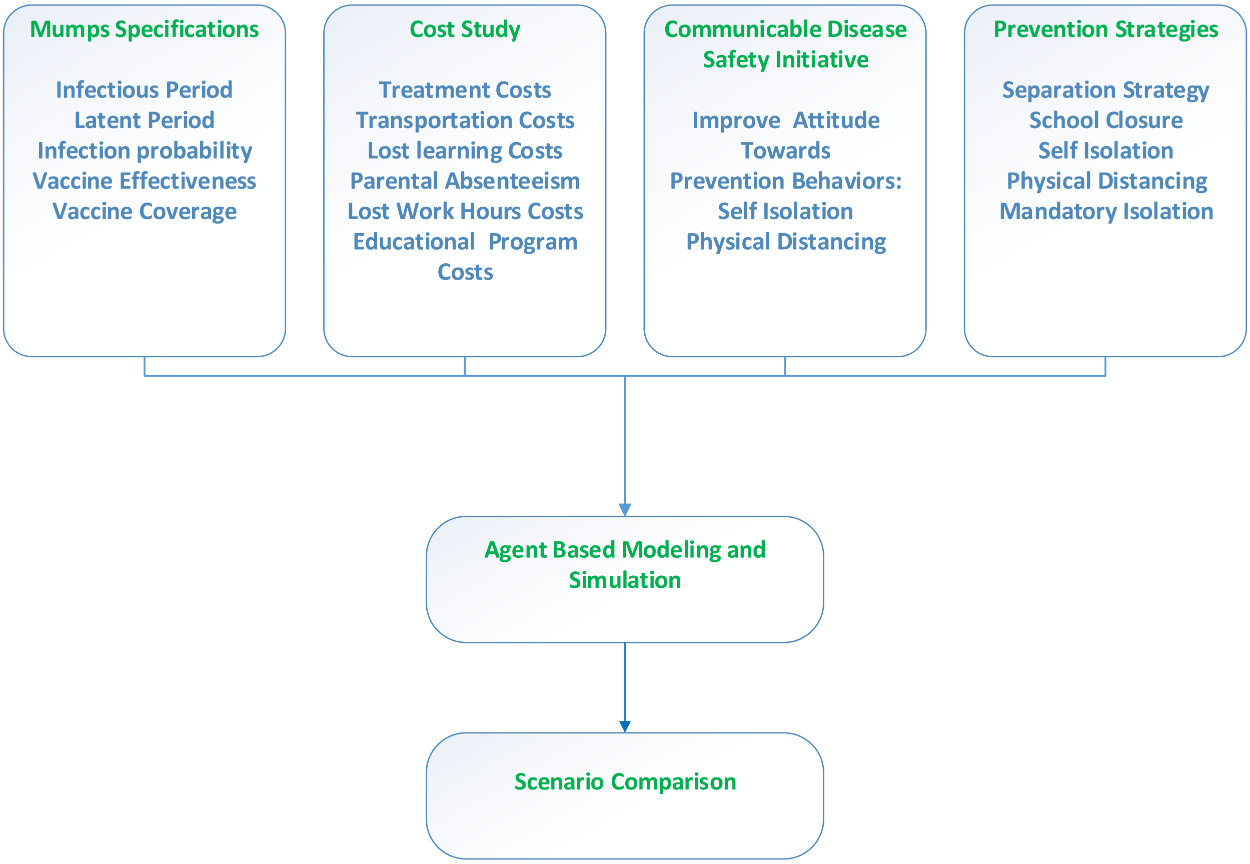

Figure 1: Modeling structure

2.1. Mumps Transmission Dynamics

2.1.1. Spread pattern

Susceptible agents in the system are capable of receiving the virus from potential infectious agents around them. Transmission is achieved by an effective contact between the virus carrier and a susceptible agent. Successful transmission can only happen when a susceptible agent comes within a minimum distance of an infectious agent.

During the simulation process, a susceptible agent enters a location in which there would be possibly a number of infectious agents. It stays there for an amount of time, and during this period, there is a possibility of virus communication. This chance, which would be calculated when the agent exits the station, depends on a set of infectious agents in the station which have satisfied the distance constraint discussed above. This radius, in our simulation, is assumed to be 4 meters. However, agents who are within 2 meters of the infectious agent have a higher chance of infection than those who are between 2 to 4 meters. We assumed that chance of infection, if the susceptible agent is within 2 to 4 meters of an infectious agent, is only 20% of the chance of infection when an agent is within 2 meters distance. We reached this number based on calibration of the transmission probabilities so that the simulated attack rates were close to observed rates in real outbreaks.
In addition, the duration of contact is an important decisive factor for increasing the infection probability. According to Haber's work on influenza [48], contact length has a positive effect in raising the chance of virus spread .The probability of infection between two people for specific time t could be calculated using cumulative distribution function of exponential distribution:

$$P(\mathrm{t})=1-e^{-\lambda t} \tag{1}$$

Where λ is the transmission rate of the disease i.e. the probability of virus transmission between two infectious and susceptible adults in one minute. Mumps is also spread by droplet and fomite contact, and as such, should follow the same equation structure laid out in Equation 1.

In reality, a student has several contacts with other infectious students in a specific location and considering the effect of them, as a whole, is necessary. Thus, by developing the previous formula, we can include the contact duration of the susceptible agent with all the infectious students in the station [48] and then calculate the infection probability as the agent exits the place:

$$P_{infection}=1-e^{-\lambda(\sum_{i=1}^{n} t_i)}$$

Where n is the number of infectious agents in the station. If we assume that the duration of contact with all the infectious agents in one location is the same amount *t*, then we can say:

$$P_{infection}=1-e^{-n\lambda t}$$

2.1.2. Mumps transmission rate

In this section, we obtain the transmission rate of mumps based on transmission rate of Influenza. The reason for implementing the influenza value is the fact that we could not find this value in the literature, and obtaining this value by biological experiment, which would be the best method, is beyond the scope of this research. However, with regards to the existence of other values for mumps, we can find estimation for the desired parameter by getting the help of influenza transmission rate which is available in the literature.

The basic reproductive number which in epidemiology is defined as "the number of individuals infected by a single infected individual during his or her entire infectious period, in a population which is entirely susceptible" [49], is calculated as follows [50]:

$$R = c\,\lambda\,d \qquad (2)$$

Where

c is the average number of contacts per unit time,
λ is the transmission rate, and
d is the duration of infectiousness.

Therefore, we will have the following equations for the two diseases:

$$R_{influenza} = c_i \lambda_i d_i$$

$$R_{Mumps} = c_m \lambda_m d_m$$

As our model is based on a previous simulation modeling of Influenza outbreak in an educational setting [44], and contact patterns are almost similar in different educational environments, the number of contacts per unit time (c) in Eq. 2 remains consistent for influenza and mumps. We used the average contacts of students for this value. Thus:

$$c_i = c_m$$

We consider the duration of infectiousness for both diseases. Mumps is contagious for approximately 7 days [51,52,53] while influenza is contagious for approximately 4.1 days [54].

$$d_i = 4.1$$

$$d_m = 7$$

We also used the basic reproductive number for both diseases. The basic reproduction number for mumps is roughly twice that of influenza, 4-7 versus 2-3 [55,56].We used the midpoints of these two diseases for calculating the factor:

$$R_{Mumps} = 5.5 \ , R_{influenza} = 2.5$$

$$\frac{R_{Mumps}}{R_{influenza}} = 2.2$$

$$c_m \lambda_m d_m = 2.2 * c_i \lambda_i d_i$$

Since $c_i = c_m$ we will have:

$$\lambda_m d_m = 2.2 * \lambda_i d_i$$

$$\lambda_m * 7 = 2.2 * \lambda_i * 4.1$$

$$\lambda_m = 1.29 * \lambda_i$$

Haber et al. [48] suggest that the probability of influenza infection between infectious and susceptible adults in one minute is 0.00032 for people between 18 and 64. We could not find this number for children, and assumed that high school students are more similar to adults in our calculation. By using influenza transmission rate in our equation, we extracted the mumps transmission rate:

$$\lambda_m = 1.29 \; * 0.00032 = 0.00041$$

2.1.3. Length of Disease Stages: latent and infections period

In order to simulate the virus transmission, we needed to know the latent period and infectious period. Latent period is defined as the duration of a patient's exposed state in our SEIR model. We calculated the latent period using the reported incubation period which is defined as the time from exposure to onset of disease [57]. Incubation period is similar to latent period, but it is longer since it is defined as the time that an asymptomatic individual sheds the virus. The range of incubation period for mumps is 12-25 days with an average of 16-18 days [36].

3 days before the appearance of symptoms, the infectiousness arises [39]. Therefore, we estimate latent period by subtracting this amount from the incubation ranges and average discussed above. Subsequently, we can write a triangular distribution for the latent period:

$$a=9,\ c=14,\ b=22$$

Where a and b are the ranges and c is the average of mumps latent period.

We also reviewed the literature to construct a distribution function for mumps infectious period, which was used as patient's infectious state length in our model. Infectiousness starts 3 days before symptoms emerge and continues till 9 days after the onset, which makes the estimated total duration of infectiousness 12 days [39]. However, the probability of virus transmission doesn't remain the same in different days. Polgreen et al. developed a function which represents the probability of transmission from an infected individual. *t* is the number of days following [51] :

$$\mathbf{log}\left(\frac{p(t)}{1+p(t)}\right) = -0.954 - 0.234(t)$$

After the emergence of symptoms, we can observe a quick decrease in the chance of virus transmission as time passes. It is expected that the majority of infected individuals who observed the symptoms don't communicate the virus after 5 days of symptoms' appearance. The percentage of the individuals who communicate the virus after this period can be placed between 8% to 15% [51]. By using the average of these numbers in our model, we assumed that only 11.5% of infected individuals remain infectious after 5 days.

Previous studies have suggested that virus from saliva specimens of people infected with mumps could be cultured more than 5 and up to 9 days after parotitis, which is the emergence of parotid gland inflammation [51]. We also know that high level of mumps infection appears 1 to 2 days before the onset of symptoms [38] and continues 5 days after the parotitis onset [36]. Based on our review of the literature, most individuals are infectious for 6 to 8 days, but some are infectious for 9 to 12 days. Therefore, we assigned a uniform distribution to the length of infectious period. We considered 6-8 days for 88.5% of infected cases and used the longer period of 9-12 days for 11.5% of them.

Infectious Period	Probability	distribution
6-8	88.5%	uniform
9-12	11.5%	uniform

Table 1: Infectious period specifications

Day after onset	Point estimate (Wald 95% CI)	
0	0.282	(0.236-0.333)
1	0.237	(0.205-0.271)
2	0.196	(0.170-0.225)
3	0.162	(0.135-0.193)
4	0.132	(0.102-0.169)
5	0.107	(0.076-0.148)
6	0.087	(0.056-0.131)
7	0.07	(0.041-0.115)
8	0.056	(0.030-0.102)
9	0.044	(0.022-0.089)
10	0.035	(0.016-0.079)
11	0.028	(0.011-0.069)
12	0.022	(0.008-0.061)
13	0.018	(0.006-0.053)
14	0.014	(0.004-0.047)
15	0.011	(0.003-0.041)

Table 2: Probability of virus shedding after onset of symptoms [51]

2.2. Vaccine Effectiveness

One of our main goals in this research was to discover the effect of mumps vaccine in an outbreak. A lot of students in the schools were vaccinated against mumps during their childhood. Thus, we considered the effect of vaccine in our system by searching for mumps vaccine related parameters in the literature. At the beginning of our simulation, in the vaccine-based scenario, the agents are assigned as vaccinated or not vaccinated with a certain probability. This probability is based on immunization coverage which is the percent of people in the society who have received vaccine [58]. We used vaccine coverage to create the fraction of students in the university who have taken mumps vaccine. The vaccinated agents do not necessarily have immunity, and still a chance of infection threatens them. To show this possibility in our model, we implemented vaccine effectiveness from mumps literature, which is "the percentage reduction in the frequency of influenza infections among people vaccinated compared with the frequency among those who were not vaccinated, assuming that the vaccine is the cause of this reduction" [59]. Vaccine effectiveness could be obtained based on final attack rate, which is the ratio of the final number of infected people in an outbreak to the number of primary susceptible individuals [60]. We can also use infection probabilities [61]:

$$VE\ (\%) = \frac{ARU - ARV}{ARU} \times 100$$

$$VE = 1 - \frac{ARV}{ARU} = 1 - \frac{P_{.1}}{P_{.0}} \quad [60,61]$$

Where ARU and ARV are used as the final attack rates in groups of unvaccinated and vaccinated people, and $P_{.0}$ and $P_{.1}$ are the probabilities of infection for unvaccinated and vaccinated people.

While this paper examines mumps infection solely, the vaccine that has been used against mumps since 1960s is a three-in-one Measles-Mumps-Rubella (MMR) vaccine [24]. The median coverage for 2 doses of MMR vaccine among kindergartners in USA in 2014-2015 was 94%. Coverage ranged from 86.9% in Colorada to 99.2% in Mississipi [62]. In Quebec, the coverage of one dose MMR had been more than 95% between 1980 until 1999 [63]. Other data demonstrates that the average MMR vaccine coverage for the children who were born in 1988-1989 in Quebec was between 93% to 96.1% while this number was about 92.4% for the children who were born in 1996-1998 [64].We used both 90% and 95% vaccine coverage in our simulations.

Accepted recommendations suggest getting two doses of this vaccine [65]. Although, previously some people received only one dose of the vaccine, gradually, a more intense trend was observed for receiving two dose vaccines especially after 1996 in Canada. For one dose of MMR vaccine, estimates of vaccine effectiveness have been between 62%-85%, while for two doses, vaccine effectiveness estimates ranged from 76% to 95% [66]. The generally agreed upon effectiveness of two doses is 88% [67,68]. Literature information implies that most individuals born after 1992 in Ontario, forming about 90% of them, took the two-dose vaccine of mumps and the rest took one dose [66]. In our model, we assumed that all the vaccinated students received two doses of the MMR vaccine.

3. Cost Study

Costs were calculated based on several factors related to each scenario. Depending on the prevention strategy used in the model, there are different costs. In this research, self-isolation costs include lost work hours, lost productivity, and communicable disease safety initiative. Communicable disease safety initiative consists of holding classes to develop the knowledge of students about mumps and prevention strategies. Social distancing costs are basically related to class cancellation and school closure which includes lost work hours and lost productivity. Communicable disease safety initiative cost is the only cost that we considered for physical distancing. In addition, school separation involves extra cost of transportation. It actually involves the higher cost that students need to pay when their school is changed. In our model, we assumed that students participate in the closest school to their home. Therefore, any policy to change their school would bring them an extra transportation cost. We also assumed that only the unvaccinated students would pay this extra cost. Although, in reality, the costs of these scenarios might also include social and psychological difficulties, we did not include them in our research as it is hard to quantify those elements in monetary concept.

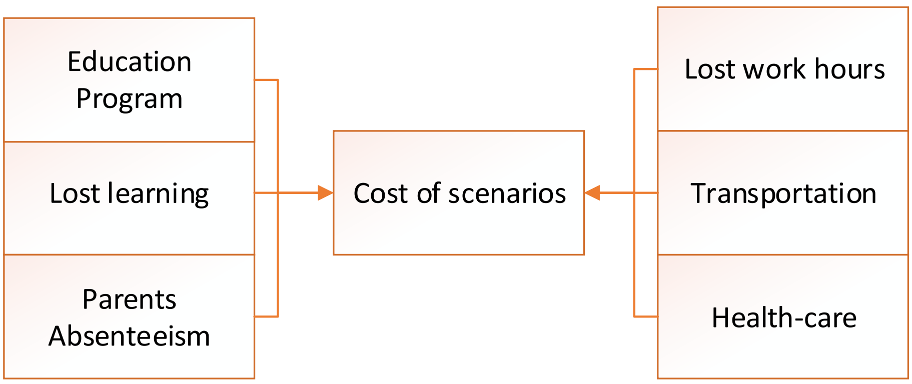

Figure 2: Cost of scenarios

The costs evaluated in this research are as follows:

3.1. Lost wage

Among high schools and colleges in United States, about 4 out of 5 students work with average of 19 hours a week [69]. When students get sick they would lose the opportunity to do their job. To calculate the lost wage, we assumed that 80% of students work. We also used a normal distribution for the students' wage. Since we could not find a source for high school students' wage in U.S., we assumed that mean wage is 7.25 dollars per hour which is the minimum wage in the United States, and standard deviation is assumed to be 1 dollar. By the use of the wage information, we calculate the lost wage per day for every student in the model. This daily cost was applied for all ill students who were assigned to stay at home during their illness.

3.2. Lost learning

We considered the cost of lost classes (lost learning) for those students who don't attend school in their illness period. When a student misses a school class, he is missing an amount of money which is previously paid for him through government or his family. In order to obtain a reasonable understanding of the missed classes cost, we considered the human capital method which calculates the value of school based on all the payments to employees in a school. This method is based on the assumption that the sum of all the educators' earnings is equal to the value of formal education. Lempel et al found that the sum of all employees' income in elementary or secondary schools is $7.3 billion per week. They estimate that the cost of lost learning as a result of school closure policy in United States is $6.1 billion per week [70]. The cost of lost learning for each student during school closure was calculated from the total number of elementary and secondary school students, 55 million in 2010 [71]. Therefore, we can estimate that the cost of one week lost learning during school closure for a student is $110.5 and for one school day is $22.1 ($24.41 in 2015 dollars). We assumed the cost of lost learning for one student during school closure is equal to the cost of lost learning for each sick student while school is open.

3.3. Healthcare cost

Healthcare costs are the highest costs associated with the mumps outbreaks. Mumps complications have a considerable cost of hospitalization which would eventually result in a high cost for an infected individual. However, the probability of complications' occurrence is not high and it could even be as low as 0.005% (for deafness) [72]. No specific treatment exists for the mumps virus other than analgesics for pain and swelling, however, treatment for complications can result in considerable cost [72,73].

There are several possible complications for mumps which based on their severity and hospitalization days, the costs are different. Central nervous system involvement is a common result of most frequent complications of mumps which are orchitis, mastitis, meningitis and encephalitis, oophoritis, deafness, and pancreatitis [72]. The probability of complications, hospitalization, and cost of hospitalization for age group of greater than 15 years old are shown in Table 3:

Complication	Probability of occurrence	Probability of hospitalization	Cost of hospitalization	Cost of outpatient visit
Uncomplicated	51.49 %	1%	8898$	124.31$
Aseptic meningitis	7.5%	25%	18,983$	143.63$
Encephalitis	0.01%	100	29,556$	337.95$
Orchitis	38% (male)	1%	7,184$	115.04$
Pancreatitis	4%	10%	18,752$	70.63$
Deafness	0.005%	10%	24,132$	207.49$
Mastitis	31% (female)	1%	9,138$	195.25$
Oophoritis	5% (female)	10%	15,896$	356.85$

Table 3: Mumps complications [72] (2001 dollars)

Most of the patients would not have any complication (48.51%). We assumed that all patients visit a clinic or hospital after symptoms arise. We also assumed that all the patients with complication, who don't become hospitalized, do an outpatient visit. The cost of an uncomplicated mumps outpatient visit based on Hinman et al study is 124.31$ [72]. The costs of all the complications according to their probabilities were considered in the model to calculate the medication costs. We did not include long term costs associated with the complications in our calculations. We used the probability of complication occurrence and probability of hospitalization for every infected individual to calculate the medical cost in our model.

3.4. Communicable disease safety initiative

We analyzed a scenario in our simulation where a communicable disease safety initiative is assumed to be implemented. In this scenario, we assumed that a communicable disease safety initiative is held in every class of every school in the city so as to increase students' knowledge about self-isolation and physical distancing, and we also assumed that this knowledge will encourage them to do self-initiated protective behaviors. Through these sessions, an expert explains mumps and self-initiated preventive behaviors to students. Students are assumed to gain an increased tendency for doing self-isolation and physical distancing after this class. This increased tendency was implemented from a research by Karimi et al. in which a cross sectional study was done for influenza control using Health Belief Model (HBM) [15]. HBM investigates different psychological and behavioral factors associated with a health action including perceived susceptibility, perceived severity, perceived benefits, and perceived barriers [74]. In the Karimi et al. research, a health specialist provided some information about self-initiated preventive behaviors to some of undergraduate students at a university and the effect of this session on students' protective behavior was investigated [15]. The results of their research suggest that the held session was effective to raise self-isolation and physical distancing by 41% [15]. We applied this rate as the effect of a communicable disease safety initiative in our model. We were able to apply these results to our model by using results from questions that did not specifically target influenza, and it makes sense that students might have the same concepts about using self-isolation and physical distancing when they face any kind of outbreak in school.

In order to calculate the cost of the communicable disease safety initiative, it was assumed that it takes an hour work of a health specialist. The median of a public health specialist's hourly salary in U.S. is 19$ [75]. We used this amount as the cost of communicable disease safety initiative for each class in every school, or 100 total classes.

3.5. Parental Absenteeism

When children are ill, parents will in some cases stay home or hire a babysitter. Based on data from literature, Sander et al assume that when a child (<12) is sick, the affected household stays at home for 2.5 days each week [76]. As the average infectiousness period of a person infected by mumps is around one week, we assumed that all the affected households of students in high school also stay at home for 2.5 days.

We used the average income of individuals in United States as the income of parents in our analysis. Per capita personal income in U.S. in 2014 was $46,129 [77]. By using the monthly income of an individual, we calculated the cost of parental absenteeism.

Parental Absenteeism cost per week (one individual)= 1/12 * $46,129 * 2.5/30= $320.3 ($327.01 in 2015 dollars)

3.6. Transportation

We used the cost of transportation to compare separation strategy and no separation strategy. When unvaccinated students are separated from vaccinated students, it is assumed that they have moved to other school, and that their originally assigned school was the closest school to the student's home. Under the separation strategy, only one school accepts unvaccinated students, so it is reasonable to assume that when a student's school is changed, the cost of transportation is increased.

The average expenditure for every student transported in United States at public expense (2010-2011) was 928 dollars ($1008.7 in 2015 dollars) [78]. We assumed that all the students in our model use public transportation and the cost of students' transportation in the no separation strategy is equal to the average cost in United States. In the separation strategy, students who change their school have an additional cost of transportation because their school is located further away. We estimated the additional cost based on the costs of bus transportation under school district consolidation. Hanley suggests that school consolidation in state of Iowa has an increased cost of 0.6% to 10.6% [79]. We used this range for school separation strategy since school district consolidation requires many students to travel a greater distance than they used to travel before, which is similar to the school separation strategy. We implemented uniform distribution by using the above range.

4. Model Development

In order to analyze the separation strategies and the effect of protective behaviors on the outbreaks, we modeled a mumps epidemic in a city using an agent-based simulation. Using object oriented programming in Matlab R2015a, we created our model based on implementing agents in the simulation. Each agent represents a unique student in the model and has several attributes which are assigned to it including vaccination status, infectious period, school and home ID, complication status, treatment cost, etc.

We constructed a synthetic city with population of 3000 high school students. Only students are considered in the model and we assumed that other individuals do not infect the students. We also assumed that students' ages are greater than 15 years old and that half of the population in the model is female and the other half is male.

In this model, each individual is given a random schedule based on Table 4 at the beginning of every day and would follow these schedules to go to different stations through end of the simulation.

The stations include School, Home, Hub, and Clinic. The model includes 10 schools, 3000 Homes, 100 Hubs and 30 clinics. In this research, Hub is a representation of any place that a student would go in the city except school, home and clinic which would let him to have contact with other students. In fact, by using a simplifying assumption, we considered all the malls, playgrounds, libraries, street, etc. that have a potential of infection as hubs.

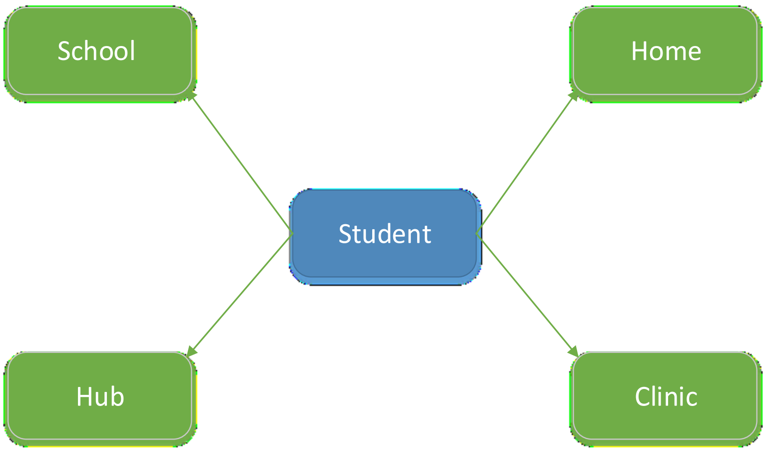

Figure 3: Model's stations

In this model, the student should necessarily be in one of the stations at a time. Every student leaves a location in each break and enters to another place based on probabilities. Each student attends a specific school every day (except weekends) which is assigned randomly at the beginning of the simulation. S/he would stay there for a few hours during the day. When students finish their school, they have the choices to go to a Hub, Home or clinic and after choosing one of these options; they would again go to other station or choose to stay at the current station. All of these decisions are made based on assigned probabilities to each station type. These decisions are included in the daily schedule at the beginning of each day. Chances of going to stations are different from each other. The probability of going to home or staying at home, in our model, is considered to be more than going to hub and going to hub is much more likely than going to a clinic. Every student, after finishing school, would have to do decision making for a number of times each day. Every time, s/he might choose to go or stay at home for a 70% chance, go to a hub for a 29% chance, and a clinic for a chance of 1%. This assumption was based on a research on children's activity pattern which suggested that children spend 70% of their time at home [80]. We also considered the annual doctor consultation per capita to estimate the probability of going to a clinic. According to a Common wealth fund article , the average annual physician visits per capita in United States was 4 times in 2010 [81] which could mean that a person visits a doctor about every 3 months on average and would visit a doctor by the chance of 1% in a typical day. We assumed that students who go to clinic would don't visit doctor again for at least 2 days.

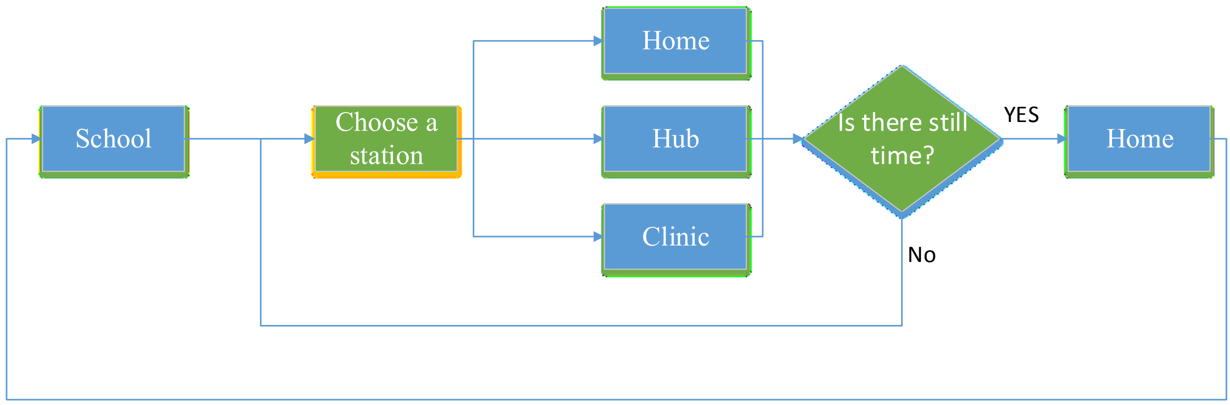

Figure 4: Weekday routine decisions

The amount of time which the students spend at each station is assigned randomly every time they choose a station according to Table 4. We assumed that students spend at least two hours and at most four hours at home and hub stations and one to three hours in the clinic station based on a uniform function. As a rule, all the students would spend a fixed time of 7 hours at school. We also included weekends in the simulation so students don't attend school on these days.

Station	Number of stations	Probability of selection	duration in each stay
School	10	_	7 hours
Home	3000	70%	2 to 4 hours
Hub	100	29%	2 to 4 hours
Clinic	30	1 %	1 to 3 hours

Table 4: Stations specifications and probabilities

Every student is assigned to a specific school randomly and would attend the same school throughout whole the simulation. Students are also assigned to a specific home. Nonetheless, students are not assigned to a specific hub or clinic.

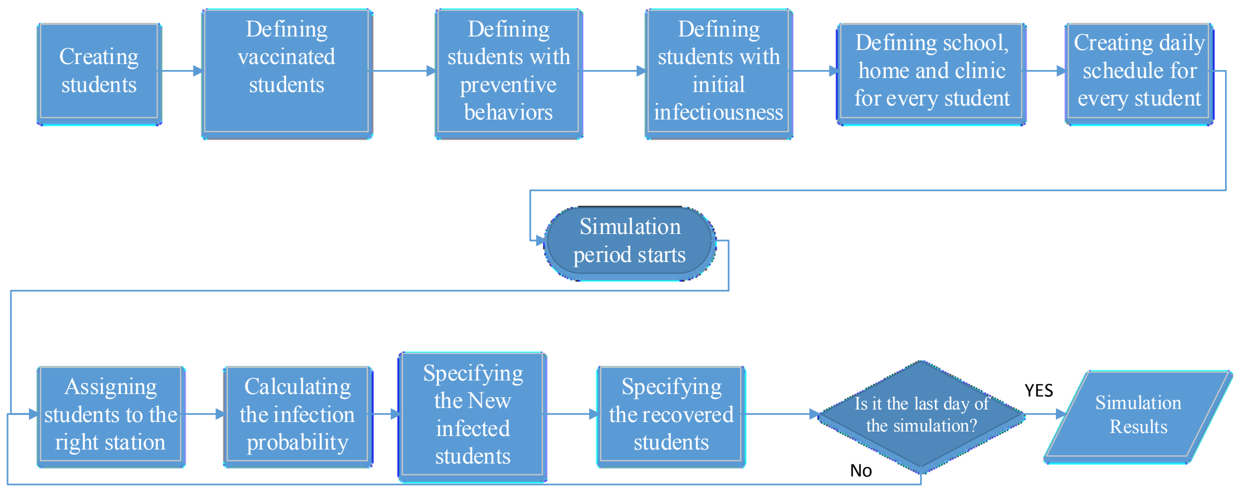

Figure 5: Simulation stages

When students are in school, their time is divided between attending classes and breaks. All students are assigned to a friendship group of between 10 and 20 students. These groups consist of a student's friends in school and during school breaks. Friends are randomly selected from all classes within the assigned school.

Students in hubs, clinics and school classes are assumed to be seated in a fixed grid pattern for the period of time they are assigned to that station. Depending on their position they would have different chances of receiving the virus from infectious agents around them.

Infected students in all the stations (school classes, hubs and clinic) can only infect students within a specific range. Those who are very close to the infectious person (less than 2 meters) have a higher chance of infection than those who are in farther distance. We assumed that students who are farther than 4 meters would not get the virus.

The number of students within the infectious range (4 m) of an infected student varies and depends on the location of the infectious student in the station. Infectious students located at the center of a full station could infect 12 students within 2 meters and 48 students within 4 meters. In other circumstances, the number of potential students for infection decreases. For instance, when an infectious student is located at the corner of a station, the infection range could cover 3 and 12 students for 2 meters and 4 meters respectively, and could even reach zero if there is no other person in the station.

Students who develop the disease don't change their routine behavior until symptoms appear, and once symptoms appear may or may not cancel their routine. Students who decide to take sick leave do so as soon as symptoms appear. We assume that 25% of infected students stay at home for the whole infectiousness period. This assumption is based on the fact that among mumps infections 20-40 percent are asymptomatic and about half of them only have non-specific or primarily respiratory symptoms [82].

For the communicable disease safety initiative scenario, students would become more likely to remain home while symptoms remain.

Students who implement physical distancing are assumed to avoid sitting close to other students in the classes and also avoid close contacts in hubs and clinics. These students sit at the back of the class with a maximum distance from other students and also make distance in hubs and clinics from others.

4.1. Disease Stages

Our simulation model is based on a SEIR model stages which are Susceptible, Exposed-Infectious, and Recovered states. SEIR models have been widely used in mathematical modeling of infectious diseases [55,83,84,85] . In our agent based model, we employ these states for every agent singularly and analyze the disease stage for every one of them. This gives us the opportunity to define the behavior and reactions of every agent based on different situations.

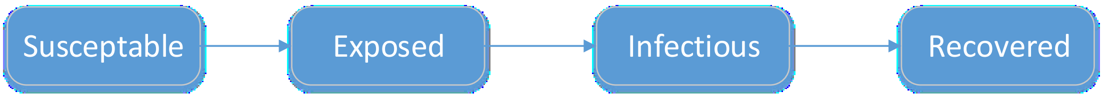

Figure 6: SEIR stages

Every student is considered as an agent in the system. Each agent, at the beginning of the simulation, is susceptible to the disease, except one agent who is infected at the starting point. The susceptible agent, based on a probability which is achieved by considering the time passed with other infectious agents and the distance from them, has a potential to receive the virus. As soon as the agent takes the disease and becomes infected, it switches from the first state to the second which puts it in the Exposed cluster. In this stage, the agent carries the virus but it cannot spread that yet, due to the fact that the disease has a latent period which is the time from infection to infectiousness. When the latent period is passed, the agent goes to the infectious state, letting it to communicate the virus to others. The amount of time agent stays in this state is infectious period. Finally, after this interval, the agent is recovered and becomes resilient to the virus. We assumed that all the recovered agents gain immunity. The parameter values for the exposed and infectious periods are obtained from the literature and the probability of transmission is discussed in section 2.1.

4.2. Simulation Platform

After acquiring all the necessary information about mumps, building the city structure and constructing the outbreak model, the simulations were coded and run in Matlab software version R2015a on the Orwell server at Concordia University.

We consider four scenarios, shown in Figure 7.

1. In the Baseline scenario, no interventions are applied.
2. In the school closure scenario, schools are closed in the case of an outbreak above a given threshold.
3. Under the voluntary isolation/distancing scenario, students are educated on the value of self-isolation when they are ill, and physical distancing to keep themselves healthy or avoid spreading the disease when they are ill and must come into contact with others.
4. Under the mandatory isolation scenario, unvaccinated students are kept away from school during an outbreak.

Each of these scenarios is modeled for no separation strategy and a separation strategy. No separation strategy assumes that vaccinated and unvaccinated students are mixed, while under the separation strategy, non-vaccinated students are assigned to a separate school. For each scenario and strategy combination, every simulation is run for 35 iterations in order to get the most reliable results.

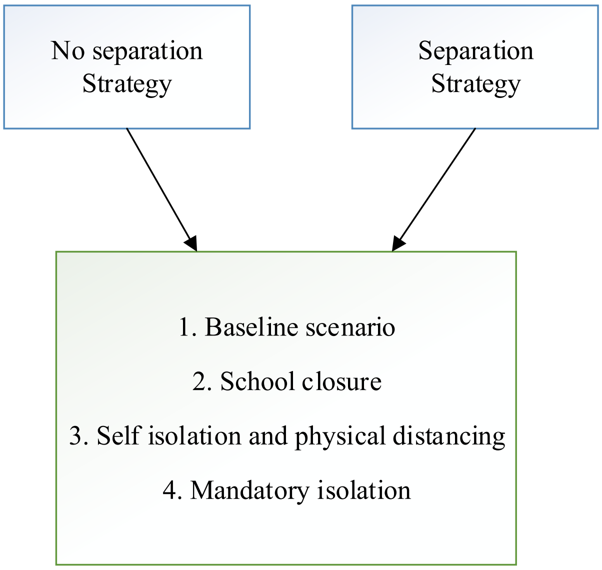

Figure 7: Simulation scenarios

All combinations of scenarios and strategies were run for vaccine coverage values of 90% and 95% in order to determine the effect in less vaccinated areas.

4.3. Model Validation

In order to validate our model, we compared our simulated attack rate and basic reproductive number with several mumps outbreaks in 2005 and 2006. Attack rate was considered among vaccinated and unvaccinated individuals. We ran 15 different simulations using no separation strategy under the baseline scenario and 95% vaccine coverage. We considered the low attack rate simulations separately from the high attack rate simulations. In 9 out of 15 simulations, less than 25 of 3000 students became ill, with an average attack rate of 1.1 % for unvaccinated students and 0.24% for vaccinated students. The average length of these outbreaks was 66.2 days. These results are reasonable because in a high vaccinated population, outbreaks tend to be very small or not evolve as the chance of infection is low.

These results are consistent with numerous records of mumps outbreaks throughout the world in which number of infections was very small with a minimum of only one infection [86].

The high attack rate results (6 out of 15 simulations) represent much longer outbreaks. The average attack rate among vaccinated individuals in the simulations is 4.71% with a range of 2.24% to 5.75%. This is comparable with Cortese et al.'s assessment of the attack rate among undergraduate students at Kansas State University in 2006. In this outbreak, the secondary attack rate among roommates with a history of receiving 2 doses of vaccine ranged from 2.2% to 7.7% [87]. Our results are also consistent with attack rate of an outbreak which occurred among college students in Iowa where the attack rates for students with records of 2 doses vaccine were 3.3% and 6.7% in 2 colleges with vaccine coverage of 98% and 84% accordingly [88].

Observational studies report that mumps attack rate among unvaccinated household members (without a history of mumps) has been in the range of 31%-48% [87]. In the research done by Marin et al., in which an outbreak in 2006 among 2 colleges at Iowa was investigated, attack rate among unvaccinated students was 23.1% [88]. In 2005, a mumps outbreak in a summer camp had an attack rate among unvaccinated children of 42.9% [89]. Our simulation results are within the range of these data as we found that average attack rate is 34.64% for unvaccinated students with a range of 25.3% to 40.66% in the outbreaks that we synthesized.

The other important factor in our validation is the basic reproductive number (R_0) which is the number of infections caused by one infectious individual in a population assuming that nobody has been vaccinated. In order to acquire this value, we ran the simulation with 0 percent vaccine coverage for 20 simulations. We used the validation approach to find R_0. In this approach, the number of secondary infections caused by only the first infected agent is counted and considered as basic reproductive number [15,54]. The average basic reproductive number in our simulations was 9.4 with a range of 2-17. This result is consistent with the mumps R_0 range found in the literature. Fan et al. found a mumps R_0 of 3.8-18.2, Kanaan et al. found a range of 4.0-31.5, and Farrington, C. P. et al. found a range of 3.3-25.5 [47,90,91].

5. Experiments and Results

To understand the impact of the school separation strategy, we implemented it under different scenarios including baseline scenario, school closure scenario, communicable disease safety initiative scenario, and mandatory isolation scenario. The scenarios were analyzed and compared, in terms of number of infections, outbreak length, and cost, for both no separation strategy and separation strategy. Our model did not approve school separation in most of the scenarios since it did not decrease number of infections or cost. In fact, we realized that separating vaccinated and un-vaccinated students, in the majority of the scenarios, increases the average number of infected students, the chance of outbreaks, and the associated cost.

Every scenario is run for 35 iterations and the results are compared among scenarios. We used the average of infections, outbreak length, and cost in addition to Wilcoxon signed rank test to compare the scenarios. Within each set of the iterations, the size and length of outbreaks may vary greatly in size, while in others no virus transmission occurs. Simulation runtime varies based on length of outbreaks in iterations and sits somewhere between about one minute to 2 hours.

5.1. Comparison in terms of attack rate and outbreak length

5.1. 1. School separation without other interventions

In this section, we analyze the outcome of separation strategy under the baseline scenario. We evaluated the effect of the school separation by comparing the difference between the number of infections in the no separation strategy and the separation strategy. We simulated the outbreak for the baseline scenario using both separation strategy and no separation strategy.

Vaccine coverage	Strategy	Number of infection	Length of outbreak
90%	No separation	225±96	289±110 days
90%	Separation	234±110	129±56 days
95%	No separation	34±30	134 ±74 days
95%	Separation	85±59	105±58 days

Table 5: Separation strategy and No separation strategy under baseline scenario

Implementing the separation strategy for 95% vaccine coverage resulted in an increase in average of infections by a 2.5 factor while the average length of outbreak decreased by 21.6%. However, for 90% vaccine coverage, average number of infections increased only by 4% and average length of outbreak decreased by 55.3%. As the results in table 5 show, separation strategy does not have a considerable effect on the average number of infections in 90% vaccine coverage population and it has a very bad effect on the average number of infections in 95% vaccine coverage population. In both the populations, if an initial infection occurs in an unvaccinated school, almost all the students in this school get infected. However, the average length of outbreaks is decreased in both of the populations when separation is implemented. Regarding the average length of outbreak, separation is more effective when used in less vaccinated populations than used when vaccine coverage is very high (95%). We also tested the simulation samples based on Wilcoxon signed rank test. According to this test, separation did not have a significant effect on number of infections in both the populations. It didn't also have a significant effect on outbreak length in 95% vaccine coverage population. However, we observed a significant effect on reduction of outbreak length in 90% vaccine coverage population (p value of .000) .

5.1.2. School closure

School closure scenario was analyzed in both no separation strategy and separation strategy to investigate the impact of school closure when a mumps outbreak occurs in schools and also realize the effect of separation strategy when combined with school closure.

In our model, school closure was implemented when 3 individuals in the school got infectious (about 1% of each school). We used school closure in two different approaches: 1- closing any school that reaches this threshold 2- only closing the separated school (unvaccinated students) when reaches the threshold. We also used different periods of school closure to check the effect of closure length on the outbreak.

Vaccine coverage	Strategy	Number of infections	Length of outbreak
90%	No separation	50±53	141±94 days
90%	Separation	172±101	114±56 days
95%	No separation	9±7	62±27 days
95%	Separation	46±47	80± 52 days

Table 6: Separation strategy and No separation strategy under school closure scenario (closure for 2 weeks)

Vaccine coverage	Strategy	Number of infections	Length of outbreak
90%	No separation	44±52	114±72 days
90%	Separation	94±82	91±49 days
95%	No separation	7±4	60± 26 days
95%	Separation	15± 22	59± 39 days

Table 7: Separation strategy and No separation strategy under school closure scenario (closure for 1 month)

Vaccine coverage	Strategy	Number of infections	Length of outbreak
90%	No separation	50±53	141±94 days
90%	Separation	201±111	126±60 days
95%	No separation	9±7	62±27 days
95%	Separation	80±58	121±69 days

Table 8: Separation strategy and No separation strategy under school closure scenario – only closing the separated school (closure for 2 weeks)

Vaccine coverage	Strategy	Number of infections	Length of outbreak
90%	No separation	44±52	114±72 days
90%	Separation	155±106	120±64 days
95%	No separation	7±4	60± 26 days
95%	Separation	52±50	105±57 days

Table 9: Separation strategy and No separation strategy under school closure scenario – only closing the separated school (closure for 1 month)

Compared to the no separation strategy under the baseline scenario, for a 95% vaccine coverage population, if school closure was used for a period of 2 weeks, it was effective to decrease average number of infections by 74% and average length of outbreak by 54%. If school closure was used for one month, it was able to reduce average number of infections by 80% and average length of outbreak by 55%.

For a 90% vaccine coverage population, 2 week school closure reduced average number of infections by 78%, and one month school closure reduced the average number of infections by 80%. Also, 2 week school closure reduced average length of outbreak by 51%, and one month school closure reduced it by 61%. Significance test showed that one month school closure had a significant effect on reduction of infections (p value of 0.000 and 0.021 for 90% and 95% vaccine coverage) and outbreak length (p value of 0.000 and 0.01). Besides, significance test showed that 2 week school closure, in 90% vaccine coverage population, had a significant effect on reduction of infections and outbreak length (p value of 0.000 for infections and 0.001 for outbreak length). In 95% vaccine coverage population, two week school closure did not have a significant effect on infections (p value of 0.051) but had a significant effect on reduction of outbreak length (p value of 0.022). These results suggest that school closure, in the majority of the scenarios, could substantially decrease the intensity and length of a mumps outbreak.

We also used school closure combined with separation strategy. By comparing the results with no separation strategy under school closure scenario, we realized that separation strategy, when used in parallel with the school closure, was not effective to reduce number of infections, and length of outbreak did not significantly change. According to significance tests, all the p values for number of infections and outbreak length were greater than 0.05 in our comparisons.

In addition, we implemented school closure for the case that only the unvaccinated school would be closed when number of infections goes beyond the threshold. The results in table 8 and table 9 show a 18.6% decrease in average number of infections for a population with 90% vaccine coverage and 24.7% decrease for a population with 95% vaccine coverage. The average outbreak length is also decreased by 56.5% and 29.3% for 90% and 95% vaccine coverage populations.

5.1.3. Communicable disease safety initiative

We investigated the effect of communicable disease safety initiative by assuming that all the schools implement a communicable disease safety initiative held by a specialist. According to Karimi et al., a health promotion session was successful to increase students' physical distancing and self-isolation by 41% for influenza [15]. We used the same parameter in our model assuming that students' behavior change would be the same in response to a mumps outbreak. In the baseline scenario, we didn't include the practice of physical distancing. However, in the educational scenario in our model, 41% of infectious students avoid close contacts with other students. Besides, students are 41% more likely to stay the whole period of the infectiousness at home.

Vaccine coverage	Strategy	Number of infections	Length of outbreak
90%	No separation	13±13	63±33days
90%	Separation	92±78	68±40 days
95%	No separation	6±4	45±12 days
95%	Separation	29±33	52±33 days

Table 10: Separation strategy and No separation strategy under communicable disease safety initiative scenario

Our results show that the physical distancing and self-isolation behavior, which were encouraged by a communicable disease safety initiative, were considerably successful to reduce the average number of infections and outbreak length. The information in table 10 demonstrates that the resulted self-isolation and physical distancing decreased average number of infections by 82% (for 95% vaccine coverage) and 94% (for 90% vaccine coverage). The outbreak length was also reduced by 66% (for 95% vaccine coverage) and 72% (for 90% vaccine coverage). Significance tests also demonstrate that this intervention significantly reduces number of infections (p value of 0.000 for 90% vaccine coverage and 0.002 for 95% vaccine coverage) and outbreak length (p value of 0.000 for 90% vaccine coverage and 0.002 for 95% vaccine coverage). This information suggests that communicable disease safety initiative, specifically an increase in self-initiated behaviors among students can have major effects on mumps outbreak control.

The effect of separation strategy was also analyzed when physical distancing and self-isolation were applied to the model. As we observe in Table 10, average number of infections and outbreak length were smaller when we didn't implement school separation.

For 90% vaccine coverage, separation strategy enlarges the average number of infections by a 7 factor, and increases average outbreak length by 7%. For 95% vaccine coverage, separation strategy enlarges the average number of infections by a 4.8 factor, and increases the average outbreak length by 16%. However, the significance tests suggest that separation did not have a significant effect on number of infections and outbreak length.

5.1.4. Mandatory isolation of unvaccinated students

Mandatory isolation of unvaccinated students was also implemented as a type of social distancing measure in our model. In this scenario, whenever an outbreak enters a school and passes a threshold (3 infections), the school goes into emergency condition and requests the unvaccinated students to not attend the school for a certain period of time. We analyzed this scenario by considering isolation periods of 2 weeks and one month.

Vaccine coverage	Strategy	Number of infections	Length of outbreak
90%	No separation	155±87	272±130 days
90%	Separation	201±111	126±60 days

95%	No separation	26±29	108±71 days
95%	Separation	80±58	121±69 days

Table 11: Separation strategy and No separation strategy under mandatory isolation scenario (2 weeks)

Vaccine coverage	Strategy	Number of infections	Length of outbreak
90%	No separation	95±67	234±123 days
90%	Separation	155±106	120±64 days
95%	No separation	13±10	87±49 days
95%	Separation	52±50	105±57 days

Table 12: Separation strategy and No separation strategy under mandatory isolation scenario (1 month)

By using table 11 and table 5, we compared no separation strategy under 2 week mandatory isolation scenario with no separation strategy under the baseline scenario. The results show a 31% decrease (for 90% vaccine coverage) and a 24% decrease (for 95% vaccine coverage) in average number of infections, and a 6% reduction (for 90% vaccine coverage) and a 19% reduction (for 95% vaccine coverage) in the average outbreak length.

Moreover, by evaluating one month mandatory isolation scenario and comparing the outputs of table 12 with table 5, for 90% vaccine coverage, we observed a 58% decrease in the average number of infections and 19% decrease in the average outbreak length.

For 95% vaccine coverage, we noticed a 62% decrease in average number of infections and a 35% decrease in average outbreak length.

The significance tests suggested that there was no significant change in number of infections and outbreak length for 95% vaccine coverage population. However, for 90% vaccine coverage population, number of infections significantly decreased for both 2 week and 1 month mandatory isolation (p value of 0.006 for 2 week period and 0.000 for 1 month period). Outbreak length didn't have a significant change in 90% vaccine coverage population. This gives us the notion that mandatory isolation could be more effective in less vaccinated populations.

We also evaluated the separation strategy in conjunction with mandatory isolation.

By comparing separation strategy with no separation strategy, under the mandatory isolation scenario, we noticed that, when we used 2 week isolation, separation strategy had 30% higher average number of infections for 90% vaccine coverage and 207% higher average number of infections for 95% vaccine coverage. However, it had 54% lower average outbreak length for 90% vaccine coverage and 12% higher average outbreak length for 95% vaccine coverage.

When we used one month isolation, separation strategy had 63% greater average number of infections for 90% vaccine coverage and 4 times greater average number of infections for 95% vaccine coverage. It also had 49% lower average outbreak length for 90% vaccine coverage and 20% greater average outbreak length for 95% vaccine coverage compared to no separation strategy.

Significance tests did not show a significant change in number of infections and outbreak length in 95% vaccine coverage population. For 90% vaccine coverage, the tests didn’t demonstrate a significant increase in number of infections either. However, outbreak length significantly decreased in 90% vaccine coverage population. On overall, these results do not suggest that separation strategy was effective to reduce the average number of infections.

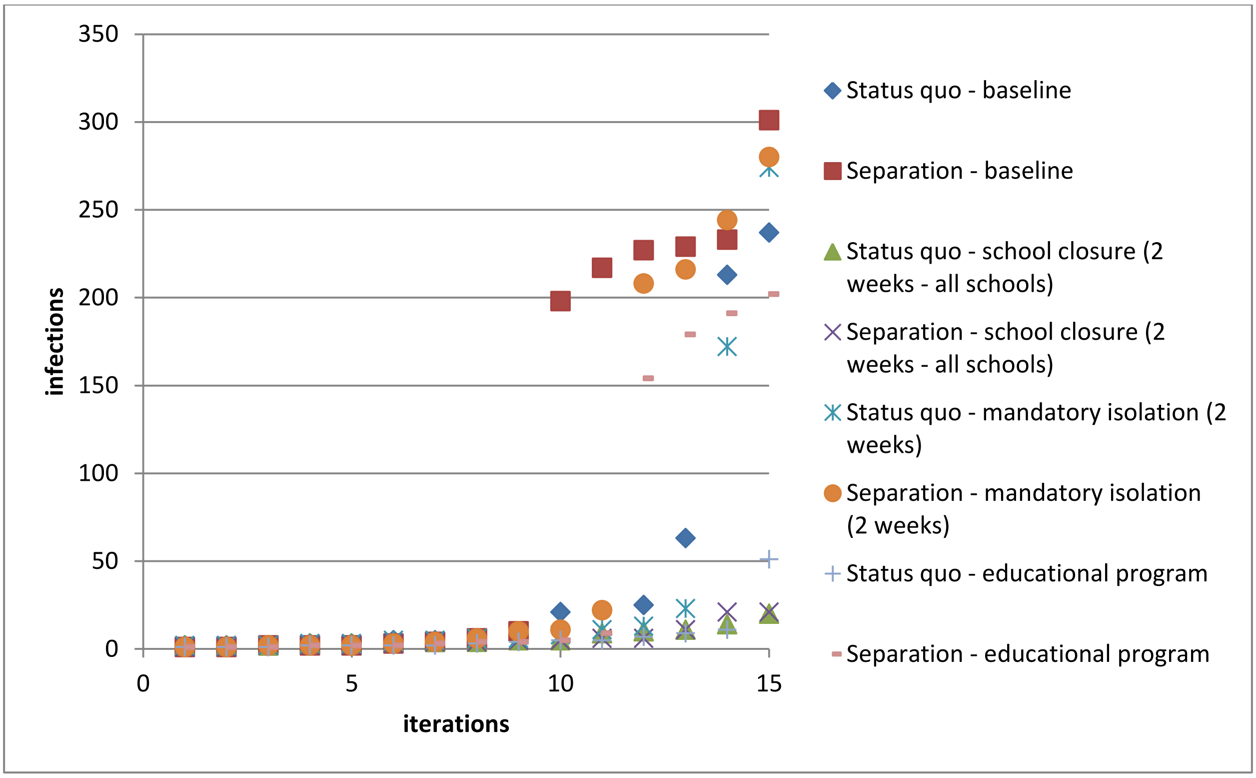

Figure 8: Number of infections in each iteration for different strategies – 95% vaccine coverage (iterations are sorted from smallest number of infections to largest)

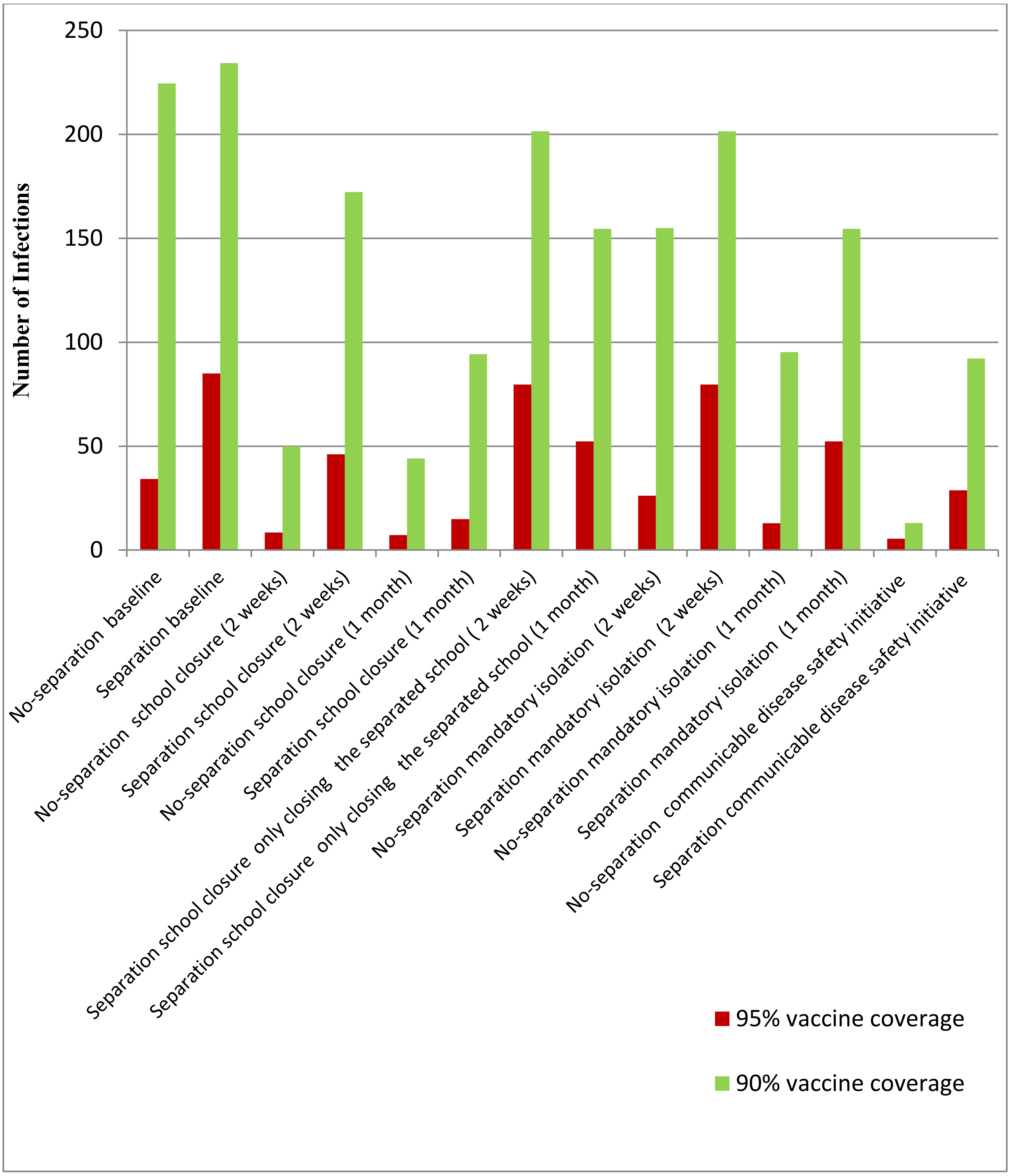

Figure 9: Number of infections in different scenarios

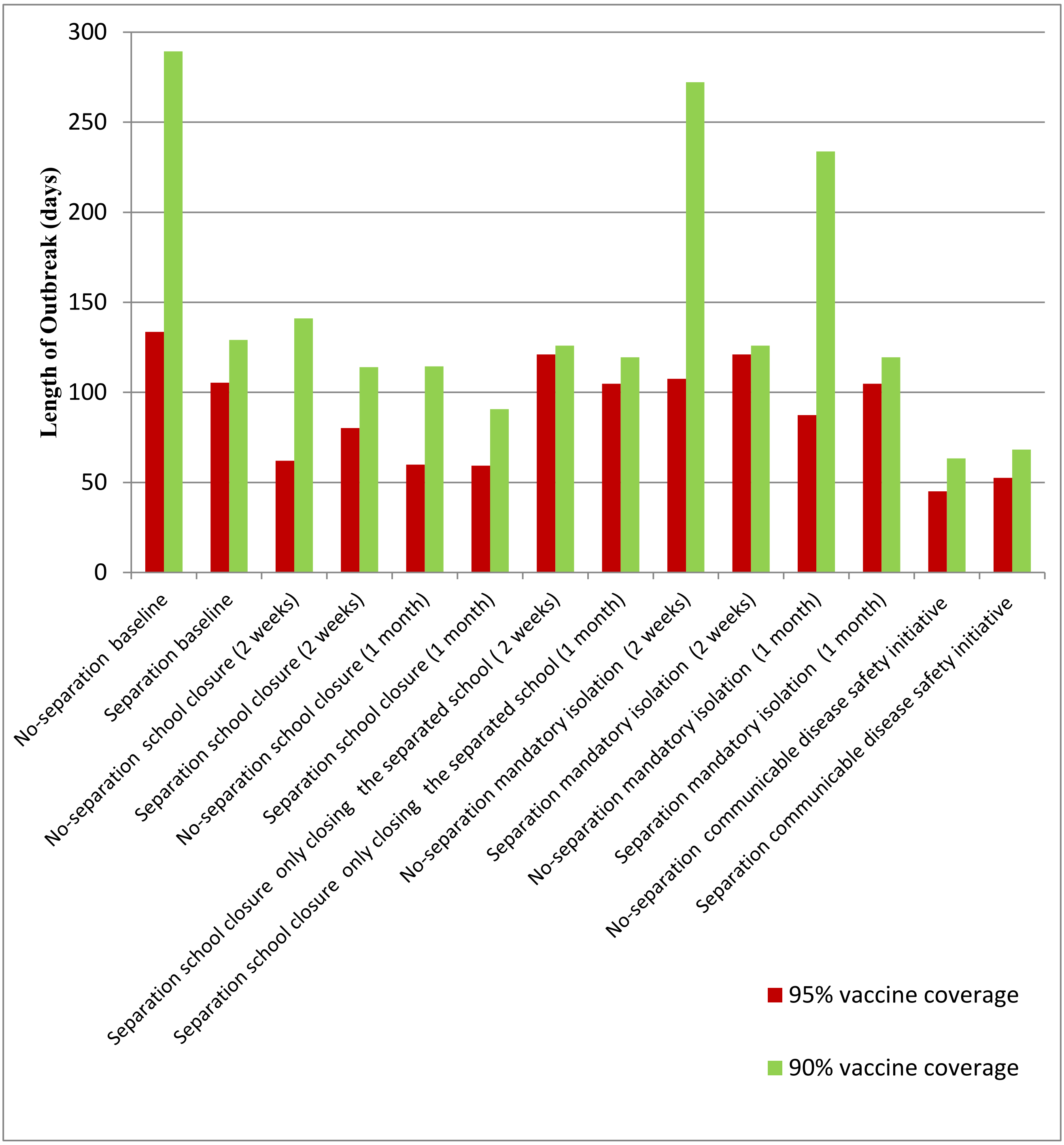

Figure 10: Length of outbreaks in different scenarios

5.2. Comparison in terms of costs

In this section, we compared the estimated costs of separation strategy and no separation strategy when they are employed under different scenarios. Our calculations are based on the costs of lost wages, lost learning, medication, communicable disease safety initiative, parental absenteeism, and transportation which were discussed in section 3. Although there should be some hidden costs other than what we considered, the cost difference between scenarios provides a useful sight to the decision makers. Our results show that separation strategy, on the whole, is more costly than no separation strategy in most of the scenarios. Moreover, mandatory isolation and implementing a communicable disease safety initiative are less costly than the no separation strategy under the baseline scenario for 90% vaccine coverage population which underscores their importance.

5.2.1. School separation without other interventions

Based on the results in table 13, when the school separation strategy is implemented, the average cost is increased by 16% in a 90% vaccine coverage population and increased by 176% in a 95% vaccine coverage population. We observed a significant increase in the cost for 95% vaccine coverage population (p value of 0.023) and no significant increase for 90% vaccine coverage population (p value of 0.112). Hence, there is an additional cost for utilizing separation strategy for baseline scenario and this difference is significant when separation is used in 95% vaccine coverage population. This gives us the idea that implementing school separation strategy in a population with less vaccination coverage might be more acceptable than using the separation in highly vaccinated populations.

Vaccine coverage	Strategy	Estimated cost
90%	No separation	\$190,000±85,000
90%	Separation	\$221,000±100,000
95%	No separation	\$29,000±29,000
95%	Separation	\$80,000±54,000

Table 13: The costs of Separation strategy and No separation strategy under baseline scenario

5.2.2. School closure

Our results demonstrate that using separation strategy under school closure scenario requires a higher cost than no separation strategy under baseline scenario.

According to table 14 and table 13, no separation strategy under school closure scenario for 2 weeks for 90% and 95% vaccine coverage populations requires 1.79 and 2.27 times greater budget compared to no separation strategy under baseline scenario. This cost increase is significant (p value of 0.000).

Separation strategy under one month school closure scenario for 90% vaccine coverage population, on average, is more costly than no separation strategy under one month school closure scenario by 22%. It is also 8% more costly for 95% vaccine coverage.

Significance tests show that, in 90% vaccine coverage population, separation strategy under school closure scenario for 2 weeks and one month significantly increased the costs (p value of 0.000) compared to no separation strategy under school closure scenario. In 95% vaccine coverage population, separation with one month closure significantly increased the cost (p value of 0.001) but the cost increase for separation with 2 week closure was not significant (p value of 0.404).

According to table 14 and 15, one month school closure, on average, is more costly than 2 week school closure by a factor of 1.95 for 90% vaccine coverage population. One month school closure, on average, is more costly than 2 week school closure by a factor of 2.78 for 95% vaccine coverage and this difference is statistically significant.

Vaccine coverage	Strategy	Estimated cost
90%	No separation	\$340,000±46,000
90%	Separation	\$525,000±84,000
95%	No separation	\$79,000±6,000
95%	Separation	\$111,000±38,000

Table 14: The cost of Separation strategy and No separation strategy under school closure scenario (closure for 2 weeks)

Vaccine coverage	Strategy	Estimated cost
90%	No separation	\$665,000±59,000
90%	Separation	\$816,000±69,000
95%	No separation	\$220,000±5,000
95%	Separation	\$238,000±20,000

Table 15: The cost of Separation strategy and No separation strategy under school closure scenario (closure for 1 month)

We also considered school closure for only the separated school. According to table 16 and 17, using separation strategy under school closure scenario for 1 month, compared to the same strategy with a 2 week period, involves 10% less average cost for 90% vaccine coverage population and 7% more average cost for 95% vaccine coverage population.

The cost increase for the population with 95% vaccine coverage is significant (p value of 0.018) but the cost difference is not significant for 90% vaccine coverage population (p value of 0.280).

Vaccine coverage	Strategy	Estimated cost
90%	No separation	$340,000±46,000
90%	Separation	$226,000±92,000
95%	No separation	$79,000±6,000
95%	Separation	$103,000±46,000

Table 16: The cost of Separation strategy and No separation strategy under school closure scenario – only closing the separated school (closure for 2 weeks)

Vaccine coverage	Strategy	Estimated cost ($)
90%	No separation	$665,000±59,000
90%	Separation	$204,000±88,000
95%	No separation	$220,000±5,000
95%	Separation	$111,000±40,000

Table 17: The cost of Separation strategy and No separation strategy under school closure scenario – only closing the separated school (closure for 1 month)

5.2.3. Communicable disease safety initiative

We calculated the total cost for the scenario in which we applied the effect of communicable disease safety initiative. The communicable disease safety initiative was supposed to increase self-isolation and encourage physical distancing by 41% among students. By comparing table 18 with table 13, we understand that using communicable disease safety initiative is highly effective in reducing the outbreak costs. Our results show that No separation strategy under communicable disease safety initiative reduces the average cost by 93% in a 90% vaccine coverage population, and it reduces the average cost by 79% in a 95% vaccine coverage population. Significance test also shows that communicable disease safety initiative significantly reduces the cost in 90% vaccine coverage population (p value of 0.000) but Cost decrease is not significant in 95% vaccine coverage population (p value of 0.074). This shows that using communicable disease safety initiative in a less vaccinated population was more effective to reduce the cost.

Vaccine coverage	Strategy	Estimated cost
90%	No separation	$ 13,000±12,000
90%	Separation	$ 98,000± 69,000
95%	No separation	$ 6,000±4,000
95%	Separation	$ 38,000±34,000

Table 18: The costs of Separation strategy and No separation strategy under communicable disease safety initiative scenario

We also see that separation strategy under communicable disease safety initiative scenario compared with no separation strategy under the same scenario increases the average cost hugely by a factor of 7.5 and 6.3 for 90% and 95% vaccine coverage populations. The significance tests also demonstrate that this cost increase is significant for both the populations (p value of 0.000). As the results show, the adverse effect of separation strategy on cost is evident in this scenario.

5.2.4. Mandatory isolation of unvaccinated students

Table 19 and table 13 show that if no separation strategy under mandatory isolation is used for 2 weeks in a 90% vaccine coverage population, it decreases the average cost by 34% compared to no separation strategy under baseline scenario and if it is used for 95% vaccine coverage, it decreases the average cost by 35%.

According to table 20 and table 13, if no separation strategy under mandatory isolation is used for one month in a 90% vaccine coverage population, it decreases the average cost by 20.7% compared to no separation under baseline scenario. If this strategy is used in a 95% vaccine coverage population, it decreases the average cost by 60%. We observe that mandatory isolation successfully decreased the average cost in both the populations.

These results show that mandatory isolation of unvaccinated students was effective to reduce the total cost of outbreaks. Moreover, rising the isolation period to one month was almost less costly. In no separation strategy, one month mandatory isolation compared to 2 week mandatory isolation is, on average, 50% less costly for 95%

vaccine coverage population and 39% less costly for a 90% vaccine coverage population.

Vaccine coverage	Strategy	Estimated cost
90%	No separation	$ 125,000±70,000
90%	Separation	$ 182,000±94,000
95%	No separation	$22,000± 26,000
95%	Separation	$88,000±57,000

Table 19: The costs of Separation strategy and No separation strategy under mandatory isolation scenario (2 weeks)

Vaccine coverage	Strategy	Estimated cost
90%	No separation	$ 76,000±55,000
90%	Separation	$ 138,000±85,000
95%	No separation	$11,000±12,000
95%	Separation	$54,000±44,000

Table 20: The costs of Separation strategy and No separation strategy under mandatory isolation scenario (1 month)

Separation strategy, when implemented with mandatory isolation, increased the average cost. It magnified the average cost by 45% (2 weeks) and 82% (1 month) for 90% vaccine coverage population. It also enlarged the average cost by a factor of 4 (2 weeks) and a factor of 4.9 (1 month) for 95% vaccine coverage.

Wilcoxon signed rank test shows that mandatory isolation significantly reduced the cost for 90% vaccine coverage population (p value of 0.028 for 2 week mandatory isolation and p value of 0.000 for 1 month mandatory isolation). However, it did not have a significant effect on the reduction of cost for 95% vaccine coverage population (p value of 0.18 for 2 week mandatory isolation and p value of 0.15 for 1 month mandatory isolation). Besides, separation strategy significantly increased the cost for 95% vaccine coverage population (p value of 0.003 for 2 week period and 0.002 for 1 month period). For one month mandatory isolation, it also significantly increased the cost in 90% vaccine coverage population (p value of 0.047) but its effect on cost reduction was not significant for 2 week mandatory isolation (p value of 0.062).

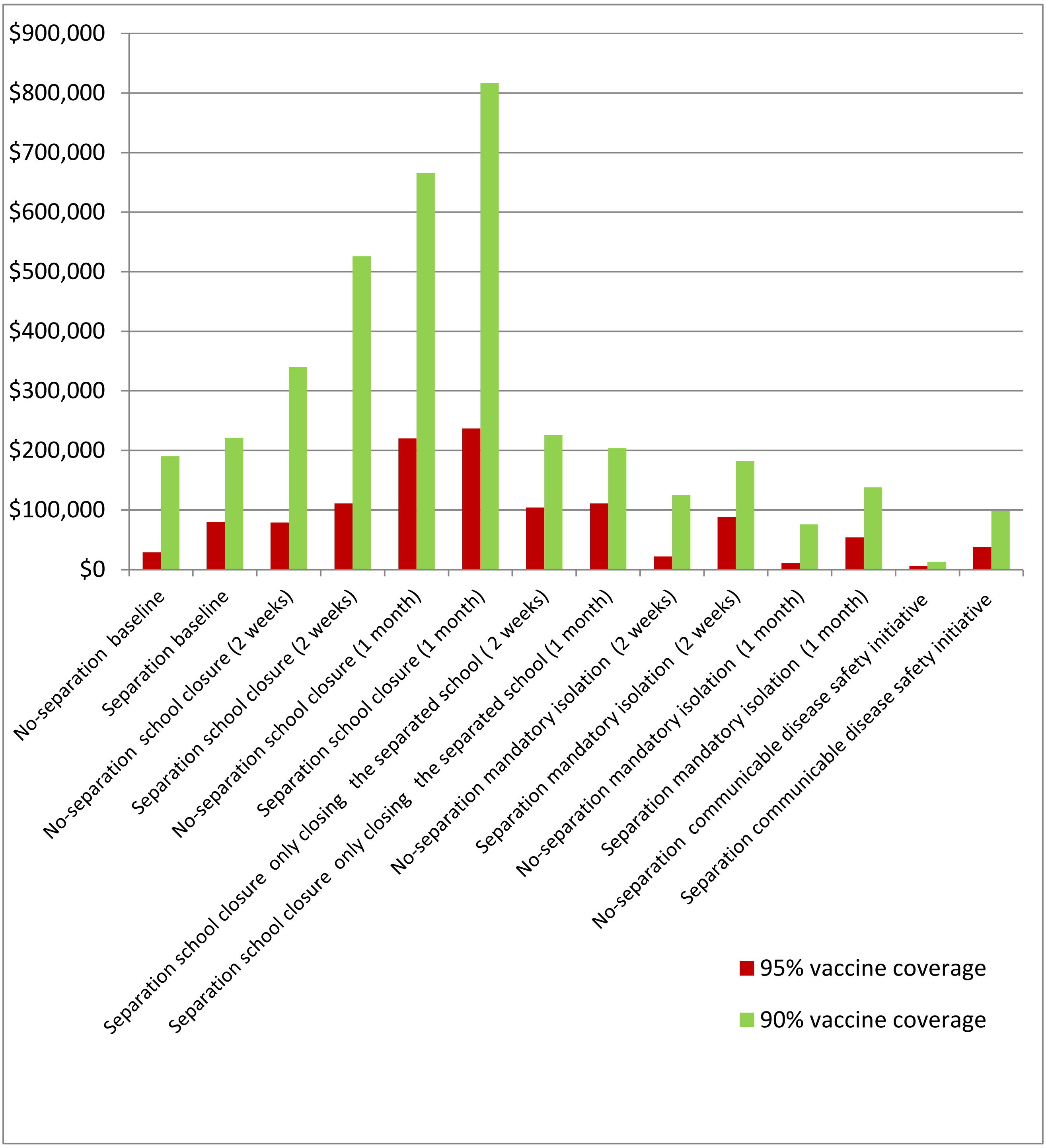

Figure 11: Cost of different scenarios

Our results showed that increasing the length of an approach such as school closure or mandatory isolation had different outcomes. In no separation strategy under school closure scenario, increasing the period of school closure from 2 weeks to 1 month decreased the average number of infections by 22% for 95% vaccine coverage and 12% for 90% vaccine coverage. However, this decrease was not significant (p value of 0.721 for 95% vaccine coverage and 1.0 for 90% vaccine coverage). Moreover, increasing the period resulted in a significant increase in the cost for both 90% and 95% vaccine coverage (p value of 0.000). This information shows that increasing the closure period increased the cost while the infections didn't significantly change. Therefore, 2 week closure could be preferred based on our model.

In separation strategy under school closure scenario, increasing the period of school closure from 2 weeks to 1 month decreased the average number of infections by 67% for 95% vaccine coverage and 45% for 90% vaccine coverage. This decrease was not significant for 95% vaccine coverage (p value of 0.071) but was significant for 90% vaccine coverage (p value of 0.006). Moreover, increasing the period resulted in a significant increase in the cost for both 90% and 95% vaccine coverage (p value of 0.000). This information shows that, for 95% vaccine coverage population, increasing the closure period increased the cost while the infections didn't significantly change. Hence, 2 week closure could be preferred for 95% vaccine coverage population. However, for 90% vaccine coverage, we had a decrease in number of infections while observing an increase in the cost. To relate the cost of this approach with the impact in terms of illnesses, note that increasing the closure period to 1 month reduces the average number of infections by 78 but this reduction in illness is accompanied by a cost of $291,000 which results in the cost of $3,700/infection. If this cost is acceptable for preventing an individual from infection, this approach could be approved for this population.

In separation strategy under school closure of unvaccinated school, increasing the period of school closure from 2 weeks to 1 month decreased the average number of infections by 35% for 95% vaccine coverage and 23% for 90% vaccine coverage. However, this decrease was not significant (p value of 0.117 for 95% vaccine coverage and 0.098 for 90% vaccine coverage). Moreover, increasing the period resulted in a significant increase in the cost for 95% vaccine coverage (p value of 0.018) and no significant increase for 90% vaccine coverage (p value of 0.28). This information does not suggest the increase of the closure period for 95% vaccine coverage.

In no separation strategy under mandatory isolation of unvaccinated students, increasing the period of school closure from 2 weeks to 1 month decreased the average number of infections by 50% for 95% vaccine coverage and 39% for 90% vaccine coverage. However, this decrease was not significant (p value of 0.345 for 95% vaccine coverage and 0.106 for 90% vaccine coverage). Moreover, increasing the period did not resulted in a significant increase in the cost (p value of 0.07 for 95% vaccine coverage and p value of 0.055 for 90% vaccine coverage). Although we didn't notice a significant change in infections and cost, based on this information, increasing the mandatory isolation period could be suggested since the average number of infections and cost were both reduced.

6. Discussion

This research uses Agent Based Simulation to investigate the effect of school separation strategy in parallel with vaccination and different measures of social distancing to control mumps outbreaks. Multiple scenarios, with and without considering school separation, were investigated in terms of infection rate, outbreak length, and total costs associated with each of them. Then, the advantage and disadvantage of them were compared with each other. We aimed to provide solutions which could be utilized by decision makers in disease control departments to minimize the intensity of outbreaks and the total costs associated with controlling and preventing them.

In this study, separation strategy was analyzed as a potential tool to control the outbreaks. However, we realized that it is almost an inappropriate measure for controlling mumps outbreak since in most of the scenarios it provides higher number of infections and higher total cost. While the separation strategy, in the majority of the scenarios, resulted in shorter outbreaks, this is not necessarily better if it means that the same number or more students get sick in a shorter period of time. In fact, a longer outbreak with the same number of infections could be preferred since it provides more time to vaccinate unvaccinated individuals and take proper actions by the government. Moreover, it reduces number of patients' visit to the hospitals during peak periods. If separation strategy results in a shorter outbreak while imposing more cost than no separation strategy, it would give us another sign that separation strategy is not appropriate for that scenario.

By evaluating the number of infections, cost, and outbreak length for different scenarios, we realized that using separation strategy under most of the scenarios is not a useful measure to control the outbreaks. According to figure 13 and 14, the outcomes of separation strategy for different scenarios, when they are compared to no separation strategy for the same scenarios, are discussed as follows:

- Baseline

School separation strategy produced higher average costs for both 90% and 95% vaccine coverage populations. It caused higher average number of infections for 95% vaccine coverage and almost the same number of infections for 90% vaccine coverage. It also reduced the average outbreak length in both of the populations which is not satisfactory for outbreak control if number of infections is the same or higher. This information does not approve that separation strategy should be adopted in the baseline scenario. As discussed in the results section, in baseline scenario, Wilcoxon signed rank test did not show a significant change in number of infections, outbreak length, and cost except that separation significantly reduced outbreak length for 90% vaccine coverage (p value of 0.000) and cost for 95% vaccine coverage (p value of 0.023).

- School closure
  - 90% vaccine coverage

    The average cost of school separation strategy was higher in all the school closure scenarios (2 week closure, 1 month closure) except the scenario which involved closure of only unvaccinated school. The average number of infections was higher in all the scenarios in this group. The average outbreak length was shorter in all of the scenarios (2 week closure, 1 month closure, and 2 week closure of unvaccinated school) except the scenario which involved 1 month closure of unvaccinated school. The significance tests showed that separation didn't have a significant effect on the increase of infections (p value of 0.66 for 2 week closure and p value of 0.7 for 1 month closure) and didn't reduce the outbreak length significantly (p value of 0.72 for 2 week closure and 0.74 for one month closure). However, the cost was significantly increased (p value of 0.000).
  - 95% vaccine coverage

    The average cost of school separation strategy was higher in all the scenarios except one month closure of unvaccinated school. The average number of infections was higher in all of the scenarios. The average outbreak length was higher in all the scenarios except two week closure of unvaccinated school in which the outbreak length was almost the same as no separation strategy.

    The significance tests showed that separation didn't have a significant effect on the increase of infections (p value of 0.92 for 2 week closure and p value of 0.96

for 1 month closure) and didn't reduce the outbreak length significantly (p value of 0.60 for 2 week closure and 0.53 for one month closure). The cost didn't significantly increase for 2 week closure (p value of 0.404). However, it was significantly increased for 1 month school closure (p value of 0.001).

These results show that school separation cannot be approved in most of the school closure scenarios:

- School separation with school closure for 2 weeks in both 90% and 95% vaccine coverage population could not be approved since it increases both the number of infections and cost.

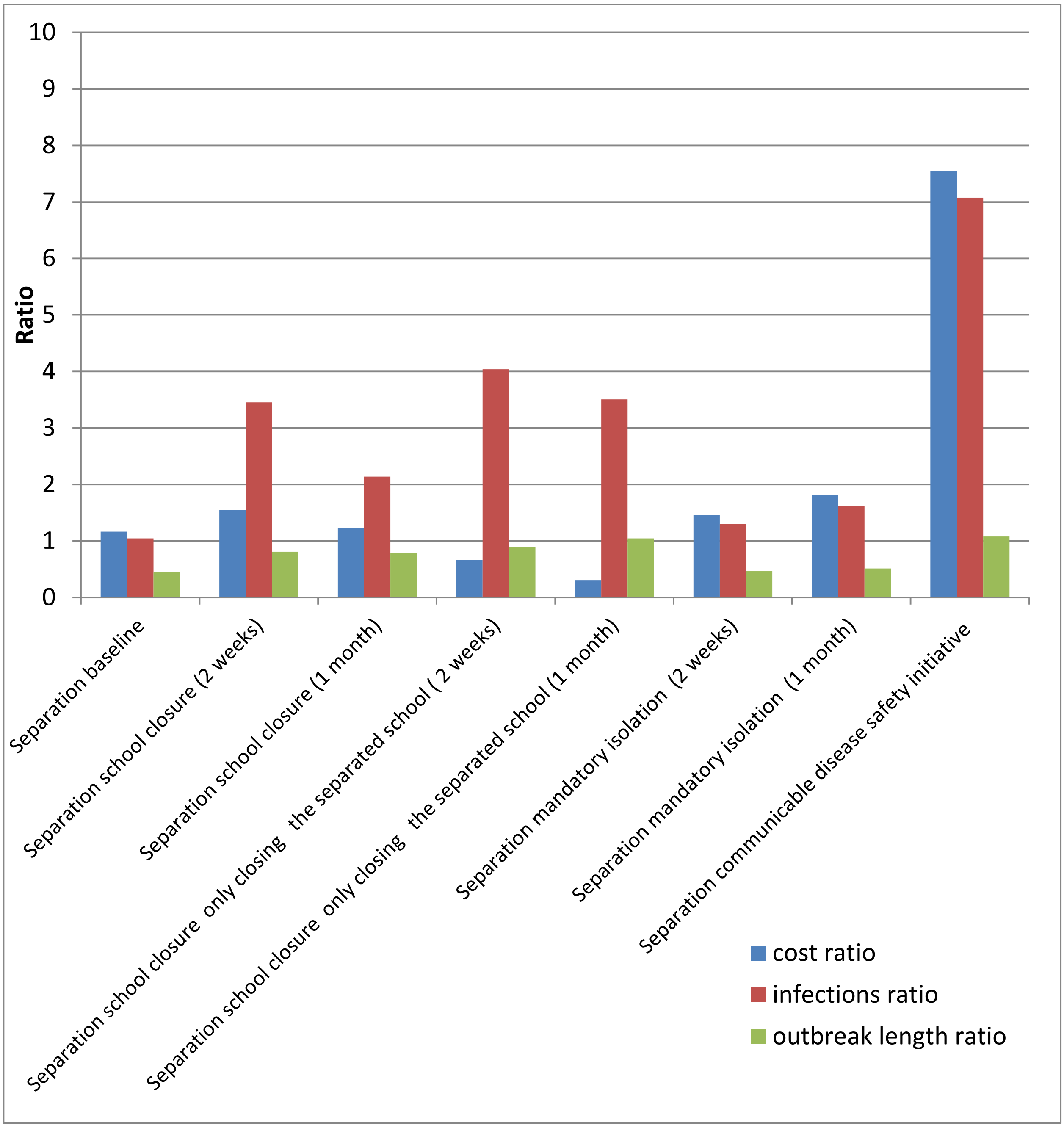

Figure 12: Ratio between separation strategy and no separation strategy in terms of number of infections, outbreak length, and cost for different scenarios (90% vaccine coverage population)

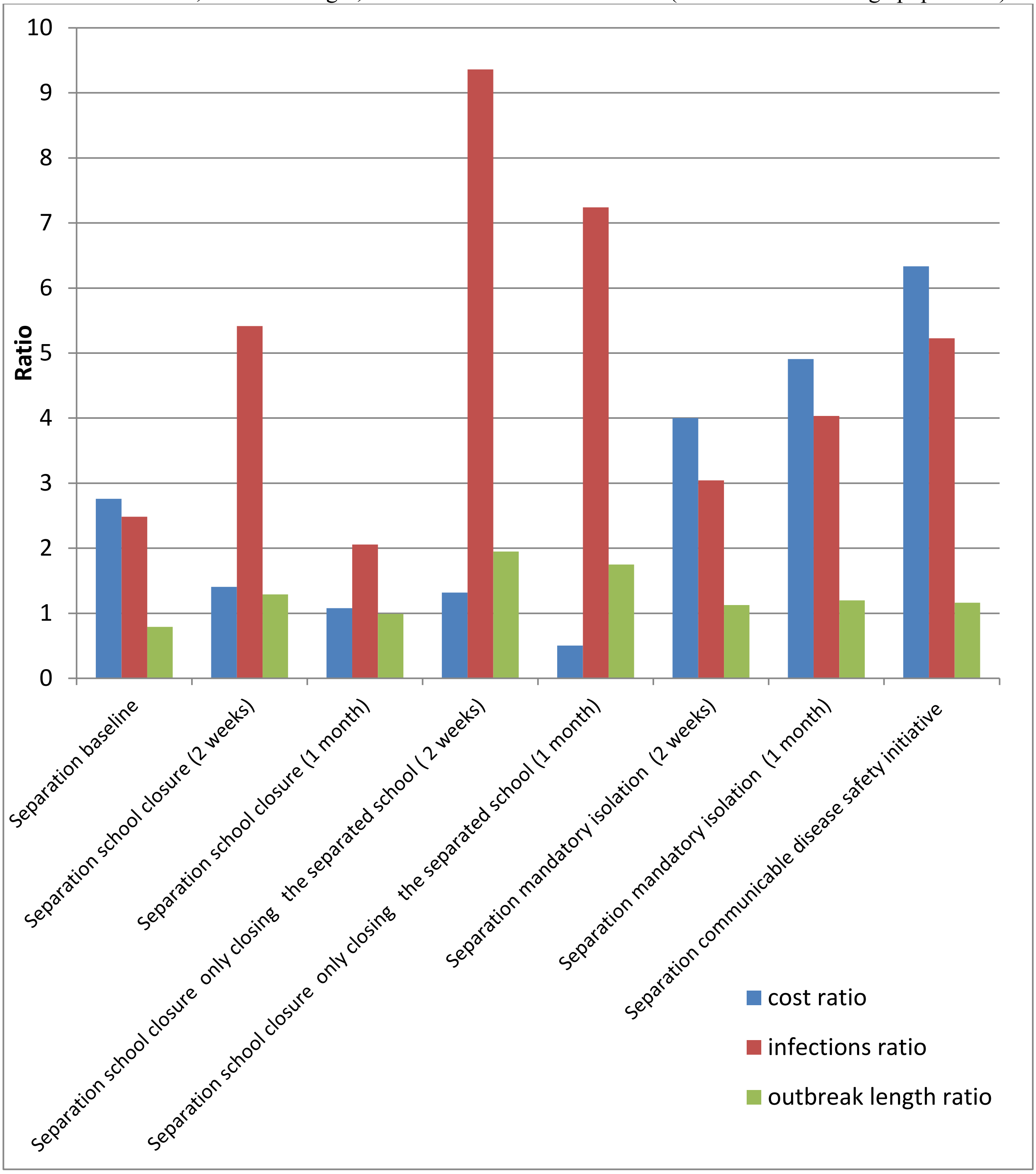

Figure 13: Ratio between separation strategy and no separation strategy in terms of number of infections, outbreak length, and cost for different scenarios (95% vaccine coverage population)

- School separation with school closure for 1 month in both 90% and 95% vaccine coverage population could not be approved since it increases both the number of infections and cost.
- School separation with 2 week closure of unvaccinated school in 95% vaccine coverage population cannot be approved since it increases both number of infections and cost. To relate the cost of separation with the impact in terms of illnesses for 90% vaccine coverage population, note that according to table 8 and table 16, separation reduces the cost by $114,000 but this decrease in cost is accompanied by an increase in number of infections by 151, or $755/infection. If the cost per infected person is considered high, separation could be approved for this population.
- School separation with 1 month closure of unvaccinated school, in both the populations, increases number of infections while reducing the cost. The outbreak length is increased in both the populations. To relate the cost of separation with the impact in terms of illnesses for 90% vaccine coverage population, note that according to table 9 and table 17, separation reduces the cost by $461,000 but this decrease in cost is accompanied by an increase in number of infections by 111, or $4,153/infection. If this cost is acceptable for preventing an individual from infection, separation could be approved for this population. To relate the cost of separation with the impact in terms of illnesses for 95% vaccine coverage population, note that according to table 9 and table 17, separation reduces the cost by $109,000 but this decrease in cost is accompanied by an increase in number of infections by 45, or $2,422/infection. If this cost is acceptable for preventing an individual from infection, separation could be approved for this population.

- Mandatory isolation of unvaccinated students

  School separation strategy resulted in higher average number of infections and costs for both the populations. It also caused shorter average outbreak length in 90% vaccine coverage and almost the same outbreak length in 95% vaccine coverage population. As a result, we could not approve the separation strategy for this scenario.

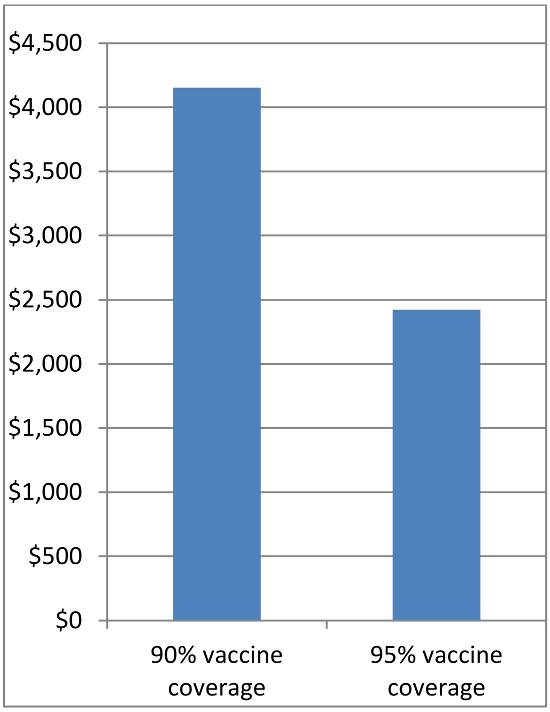

Figure 14: Cost per infection for switching from no separation strategy to separation strategy under one month school closure of separated school scenario

As discussed in the results section, separation didn't significantly increase the number of infections and didn't significantly decrease outbreak length (except 2 week mandatory isolation). However, it significantly increased the cost for most of the scenarios except 2 week mandatory isolation (p value of 0.067).

- Communicable disease safety initiative

  School separation strategy resulted in higher number of infections and costs for both the populations. It caused almost the same outbreak length for both of the populations. This information does not recommend the separation strategy for communicable disease safety initiative scenario. Based on the significance test, separation didn't significantly increase the number of infections and the outbreak length but it significantly increased the cost (p value of 0.000).

As a result of school separation, unvaccinated students had a high rate of interaction with each other. Our results show that if an infection occurs in an unvaccinated school, the chance of outbreak spread goes much higher. Although not every outbreak which is initiated in another school can reach the unvaccinated school, the chance of outbreak expansion is very high if a student from unvaccinated school gets infected through the interactions with students from other schools. In fact, our results demonstrated that in 60% and 40% of the iterations (for 90% and 95% vaccine coverage accordingly), unvaccinated school was affected by the virus. When this happened, almost all the students received the virus.

Separating students not only increases the chance of infections in most of the scenarios, but also results in a higher amount of cost in the majority of them. The costs associated with separation of students such as transportation and healthcare cost make the total cost of separation strategy higher than no separation strategy in most of the scenarios. The rate of the cost increase, in most of the scenarios, is even higher if separation strategy is implemented in a 95% vaccine coverage population, compared to a 90% vaccine coverage population.

Our results also suggest that no separation strategy under school closure scenario can significantly reduce the intensity and length of a mumps outbreak in most of the school closure scenarios. For a 95% vaccine coverage population, compared to baseline scenario in no separation strategy, school closure was effective to decrease average number of infections by 74% and average length of outbreak by 54% if used with 2 weeks closure, and if used with one month closure it was able to reduce average number of infections by 79% and average length of outbreak by 55%. When we analyzed 2 week school closure for 90% vaccine coverage population, we noticed a 78% decrease in average number of infections and the average outbreak length was also decreased by 51%.

Besides, no separation strategy under communicable disease safety initiative, which provided an increase in self-initiated behaviors among students, can have a significant effect on controlling of the mumps outbreak. We realized that the increase of self-isolation and physical distancing, as a result of communicable disease safety initiative, decreased average number of infections by 82% (for 95% vaccine coverage) and 94% (for 90% vaccine coverage). The outbreak length was also reduced by 66% for 95% vaccine coverage, and was reduced by 78% for 90% vaccine coverage.

Moreover, no separation strategy under mandatory isolation of unvaccinated students reduces outbreak infections and the reduction is significant for 90% vaccine coverage. For example, when mandatory isolation was applied for a length of 2 weeks, it resulted in a 31% decrease in number of infections for 90% vaccine coverage, and 24% decrease for 95% vaccine coverage. Besides, it resulted in a 6% decrease in outbreak length for 90% vaccine coverage, and also a 19% decrease for 95% vaccine coverage.

Comparing the average of costs shows that no separation strategy under mandatory isolation and communicable disease safety initiative are less costly than no separation strategy under baseline scenario for 90% and 95% vaccine coverage population. However, the significance tests demonstrate that the cost reduction as a result of these interventions for 95% vaccine coverage population is not significant but they are significantly less costly if used in 90% vaccine coverage population.

7. Conclusion

Our motivation for this work was to evaluate the disease impact of a school separation strategy. Given the potential ethical and legal complications, the associated health benefits would have to be significant to persuade policy makers to adopt such a policy. Our results do not suggest that a school separation strategy should be adopted in most of the scenarios since this strategy does not decrease the number of infected students and the associated cost is increased in the majority of them. Our finding can shed light on the recent debates among physicians and parents calling for unvaccinated children to be banned from schools or clinics. The decision makers and parents should be aware that, if banning unvaccinated students from the schools would result in school separation, it could impose a high risk to the unvaccinated students. Based on our results, we can hypothesize that any intervention which involves gathering of unvaccinated individuals might end in an unfavourable outcome. Our results showed that separating students into different schools could have an adverse effect on the outbreaks. We might expect similar outcomes for separation of children into different clinics. However, future research is required to specifically investigate the outcome of separation strategy in different settings such as clinics. In addition, our work demonstrates that educating students on the benefits of adopting physical distancing and self-isolation is effective in controlling the mumps outbreak size and costs in a population with 90% vaccine coverage, and confirms that mandatory isolation in this population is an effective strategy for managing outbreaks.

8. Future research

This is the first research that investigates the effect of school separation in parallel with other social distancing measures. Future research could analyze the simultaneous effects of separation and various control measures on other infectious diseases. Besides, this is the first research that inspects mumps outbreaks among students using agent based models. A complementary research can extend the simulation modeling for all the individuals in a city and check the effect of social distancing measures for different social groups like employees at work. Besides, future research can specifically investigate the outcome of separation strategy in the clinics. Moreover, we only examined 90% and 95% vaccine coverage. Future work can extend the range of vaccine coverage to investigate the effects of separation and social distancing measures on the populations that have low vaccine coverage. Besides, future research can specifically focus on separation under school closure scenario by evaluating the effect of different school closure thresholds on number of infections and total costs. Moreover, future research can also evaluate the impact of MMRv vaccine (mumps, measles, rubella, and varicella) on mumps outbreak control.

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Appendix

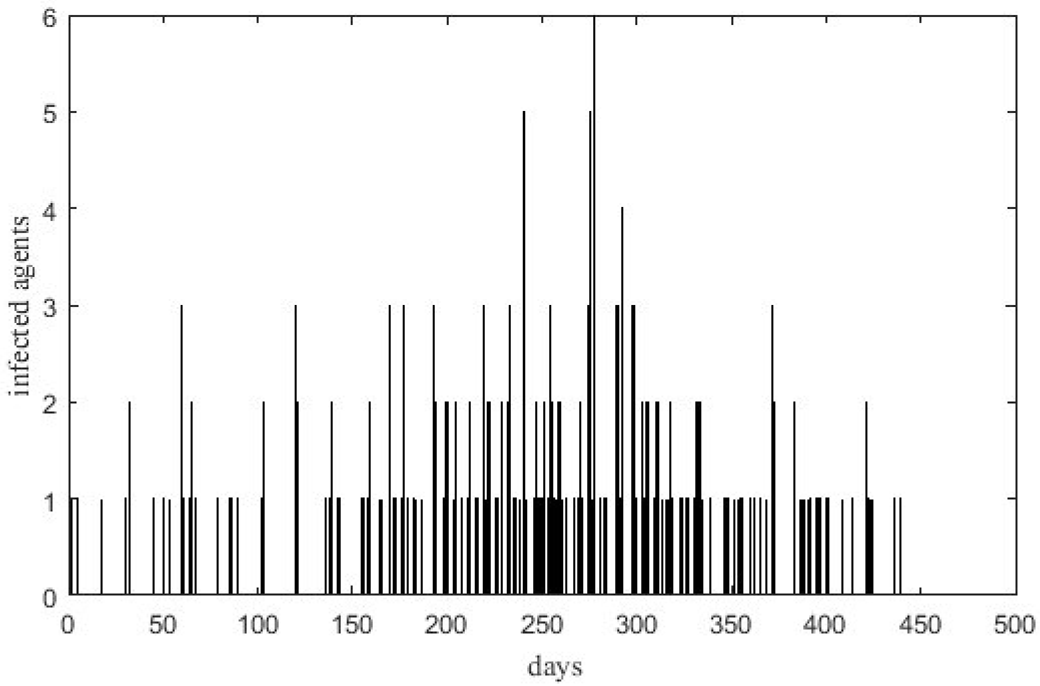

Figure 15: New infections in no separation strategy under baseline scenario (a sample iteration for 95% vaccine coverage, attack rate of vaccinated students: 6%, attack rate of unvaccinated students: 44%)

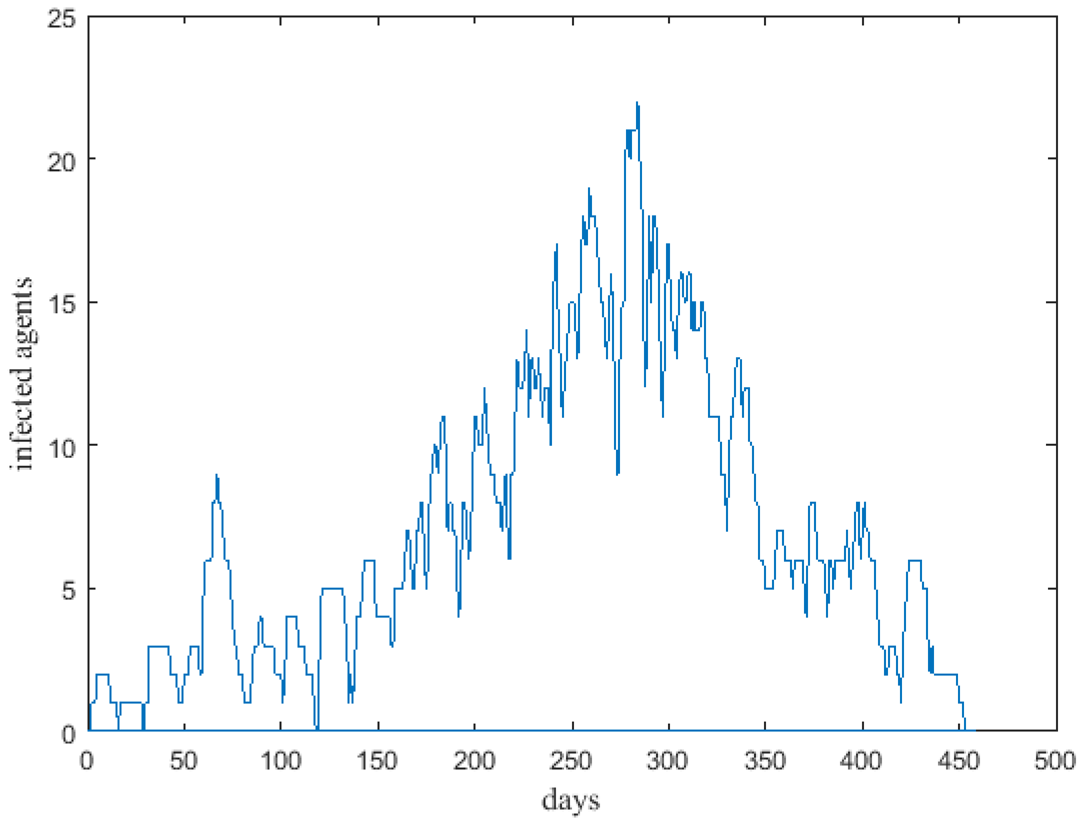

Figure 16: Total infections in no separation strategy under baseline scenario (a sample iteration for 95% vaccine coverage, attack rate of vaccinated students: 6%, attack rate of unvaccinated students: 44%)

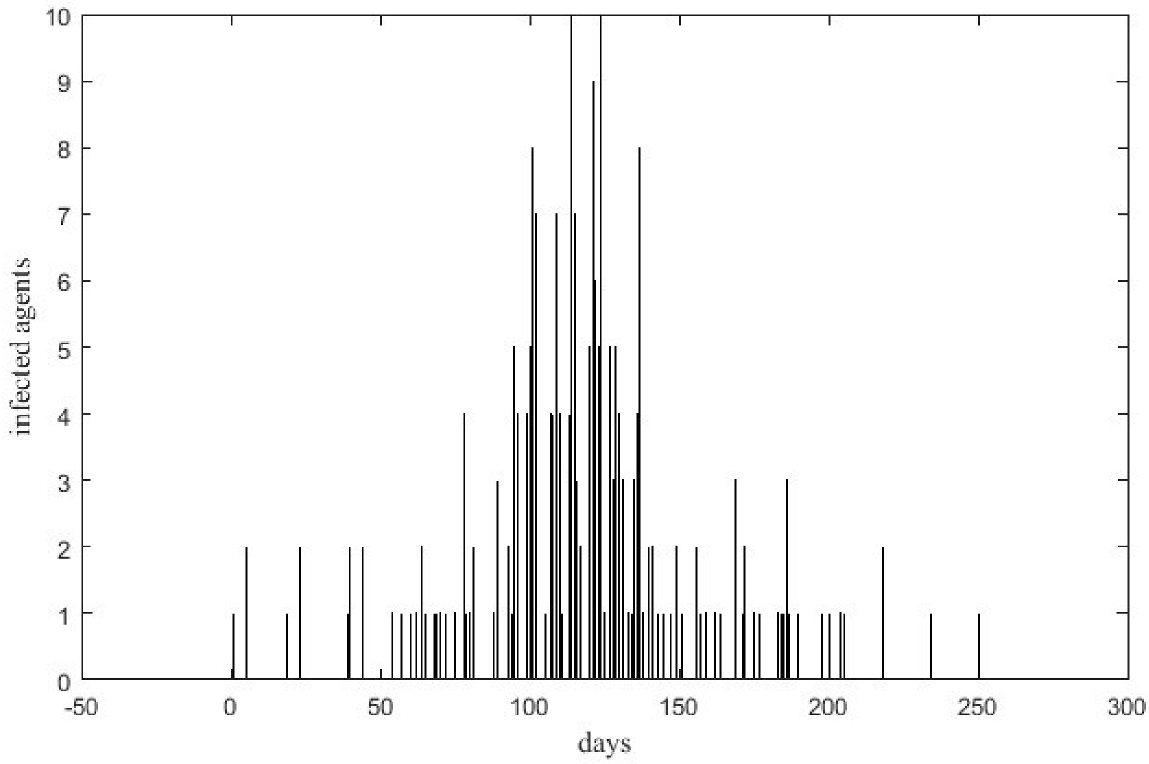

Figure 17: New infections in separation strategy under baseline scenario (a sample iteration for 95% vaccine coverage, attack rate of vaccinated students: 2.94%, attack rate of unvaccinated students: 99.33%)

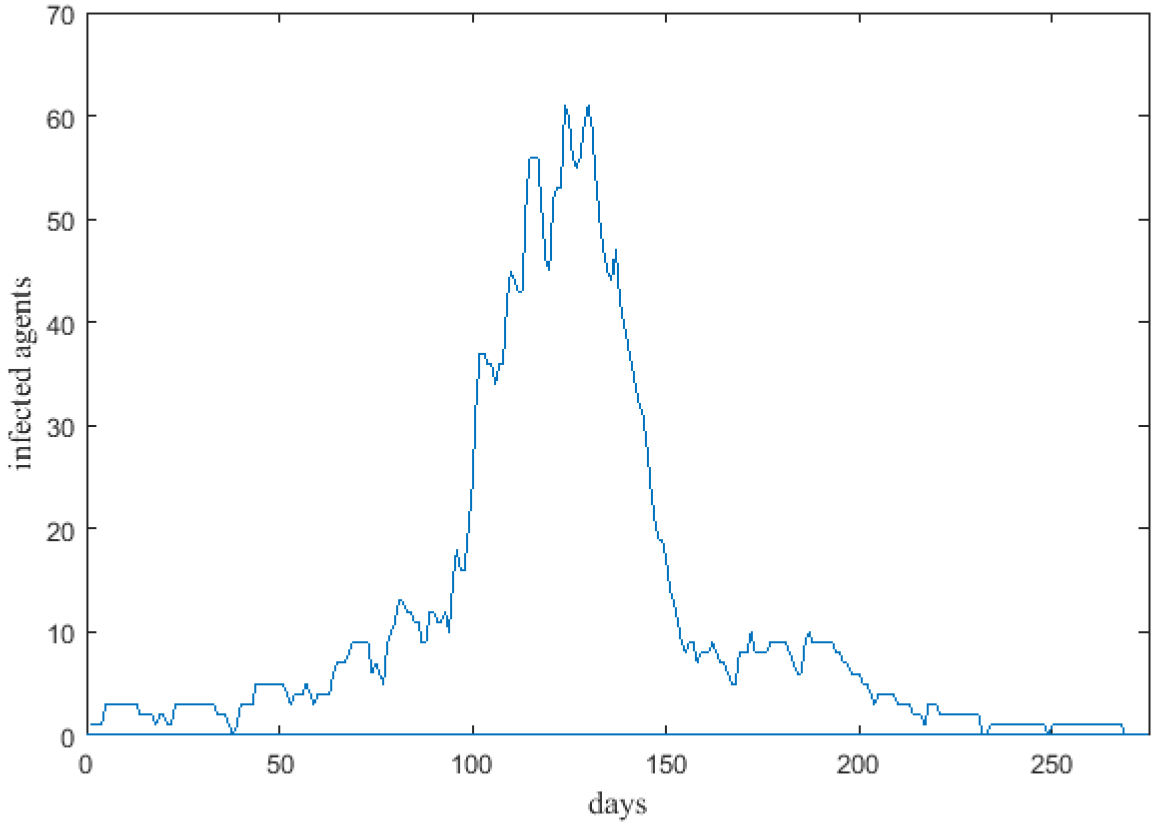

Figure 18: Infections in separation strategy under baseline scenario (a sample iteration for 95% vaccine coverage, attack rate of vaccinated students: 2.94%, attack rate of unvaccinated students: 99.33%)

Scenario	Period	Estimated cost ($)	
		90% vaccine coverage	95% vaccine coverage
No-separation baseline		$190,000	$29,000
Separation baseline		$221,000	$80,000
No-separation school closure	2 weeks	$340,000	$79,000
Separation school closure	2 weeks	$526,000	$111,000
No-separation school closure	1 month	$666,000	$220,000
Separation school closure	1 month	$817,000	$237,000
Separation school closure only closing the separated school	2 weeks	$226,000	$104,000
Separation school closure only closing the separated school	1 month	$204,000	$111,000
No-separation mandatory isolation	2 weeks	$125,000	$22,000
Separation mandatory isolation	2 weeks	$182,000	$88,000
No-separation mandatory isolation	1 month	$76,000	$11,000
Separation mandatory isolation	1 month	$138,000	$54,000
No-separation communicable disease safety initiative		$13,000	$6,000
Separation communicable disease safety initiative		$98,000	$38,000

Table 21: Estimated costs of different scenarios

Comparison of Separation scenarios with No separation scenarios using Wilcoxon Signed Ranks test

Number of Infections for 95% vaccine coverage
(Comparison of Separation scenarios with No separation scenarios)

	Baseline	School closure (2 weeks)	School closure (1 month)	Mandatory isolation (2 weeks)	Mandatory isolation (1 month)	Communicable disease safety initiative
Z	-.999[b]	-.090[b]	-.049[c]	-1.198[b]	-1.138[b]	-.145[c]
Asymp. Sig. (2-tailed)	.318	.929	.961	.231	.255	.885

a. Wilcoxon Signed Ranks Test

b. Based on negative ranks.

c. Based on positive ranks.

Number of Infections for 90% vaccine coverage
(Comparison of Separation scenarios with No separation scenarios)

	Baseline	School closure (2 weeks)	School closure (1 month)	Mandatory isolation (2 weeks)	Mandatory isolation (1 month)	Communicable disease safety initiative
Z	-.679[b]	-1.841[b]	-.384[b]	-1.365[b]	-1.113[b]	-.487[b]
Asymp. Sig. (2-tailed)	.497	.066	.701	.172	.266	.626

a. Wilcoxon Signed Ranks Test

b. Based on negative ranks.

Outbreak length for 95% vaccine coverage
(Comparison of Separation scenarios with No separation scenarios)

	Baseline	School closure (2 weeks)	School closure (1 month)	Mandatory isolation (2 weeks)	Mandatory isolation (1 month)	Communicable disease safety initiative
Z	-.885[b]	-.513[b]	-.614[b]	-.450[c]	-.885[c]	-.180[b]
Asymp. Sig. (2-tailed)	.376	.608	.539	.652	.376	.858

a. Wilcoxon Signed Ranks Test

b. Based on positive ranks.

c. Based on negative ranks.

Outbreak length for 90% vaccine coverage
(Comparison of Separation scenarios with No separation scenarios)

	Baseline	School closure (2 weeks)	School closure (1 month)	Mandatory isolation (2 weeks)	Mandatory isolation (1 month)	Communicable disease safety initiative
Z	-3.690[b]	-.348[b]	-.322[b]	-2.984[b]	-2.055[b]	-.676[b]
Asymp. Sig. (2-tailed)	.000	.728	.748	.003	.040	.499

a. Wilcoxon Signed Ranks Test

b. Based on positive ranks.

c. Based on negative ranks.

Cost for 95% vaccine coverage
(Comparison of Separation scenarios with No separation scenarios)

	Baseline	School closure (2 weeks)	School closure (1 month)	Mandatory isolation (2 weeks)	Mandatory isolation (1 month)	Communicable disease safety initiative
Z	-2.277[b]	-4.373[b]	-3.259[b]	-2.981[b]	-3.079[b]	-3.915[b]
Asymp. Sig. (2-tailed)	.023	.000	.001	.003	.002	.000

a. Wilcoxon Signed Ranks Test

b. Based on negative ranks.

Cost for 90% vaccine coverage
(Comparison of Separation scenarios with No separation scenarios)

	Baseline	School closure (2 weeks)	School closure (1 month)	Mandatory isolation (2 weeks)	Mandatory isolation (1 month)	Communicable disease safety initiative
Z	-2.277[b]	-4.373[b]	-3.259[b]	-2.981[b]	-3.079[b]	-3.915[b]
Asymp. Sig. (2-tailed)	.023	.000	.001	.003	.002	.000

a. Wilcoxon Signed Ranks Test

b. Based on negative ranks.

Comparison of No separation scenarios with No separation under baseline scenario using Wilcoxon Signed Ranks test

Number of infections for 95% vaccine coverage
(Comparison of scenarios with No separation under baseline scenarios)

	School closure (2 weeks)	School closure (1 month)	Mandatory isolation (2 weeks)	Mandatory isolation (1 month)	Communicable disease safety initiative
Z	-1.949[b]	-2.302[b]	-1.287[b]	-1.451[b]	-3.151[b]
Asymp. Sig. (2-tailed)	.051	.021	.198	.147	.002

a. Wilcoxon Signed Ranks Test

b. Based on positive ranks.

Number of infections for 90% vaccine coverage
(Comparison of scenarios with No separation under baseline scenarios)

	School closure (2 weeks)	School closure (1 month)	Mandatory isolation (2 weeks)	Mandatory isolation (1 month)	Communicable disease safety initiative
Z	-4.204[b]	-4.203[b]	-2.731[b]	-3.543[b]	-4.452[b]
Asymp. Sig. (2-tailed)	.000	.000	.006	.000	.000

a. Wilcoxon Signed Ranks Test

b. Based on positive ranks.

Outbreak length for 95% vaccine coverage
(Comparison of scenarios with No separation under baseline scenarios)

	School closure (2 weeks)	School closure (1 month)	Mandatory isolation (2 weeks)	Mandatory isolation (1 month)	Communicable disease safety initiative
Z	-2.293[b]	-2.561[b]	-1.535[b]	-1.589[b]	-3.110[b]
Asymp. Sig. (2-tailed)	.022	.010	.125	.112	.002

a. Wilcoxon Signed Ranks Test

b. Based on positive ranks.

Outbreak length for 90% vaccine coverage
(Comparison of scenarios with No separation under baseline scenarios)

	School closure (2 weeks)	School closure (1 month)	Mandatory isolation (2 weeks)	Mandatory isolation (1 month)	Communicable disease safety initiative
Z	-3.289[b]	-4.102[b]	-.368[b]	-1.435[b]	-4.468[b]
Asymp. Sig. (2-tailed)	.001	.000	.713	.151	.000

a. Wilcoxon Signed Ranks Test

b. Based on positive ranks.

Cost for 95% vaccine coverage
(Comparison of scenarios with No separation under baseline scenarios)

	School closure (2 weeks)	School closure (1 month)	Mandatory isolation (2 weeks)	Mandatory isolation (1 month)	Communicable disease safety initiative
Z	-2.195[b]	-2.565[b]	-1.343[b]	-1.441[b]	-1.785[b]
Asymp. Sig. (2-tailed)	.028	.010	.179	.149	.074

a. Wilcoxon Signed Ranks Test

b. Based on positive ranks.

Cost for 90% vaccine coverage
(Comparison of scenarios with No separation under baseline scenarios)

	School closure (2 weeks)	School closure (1 month)	Mandatory isolation (2 weeks)	Mandatory isolation (1 month)	Communicable disease safety initiative
Z	-3.821[b]	-4.076[b]	-2.197[b]	-3.625[b]	-4.128[b]
Asymp. Sig. (2-tailed)	.000	.000	.028	.000	.000

a. Wilcoxon Signed Ranks Test

b. Based on positive ranks.