Preparedness for the Spread of Influenza: Prohibition of Traffic, School Closure, and Vaccination of Children in the Commuter Towns of Tokyo

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ABSTRACT *In Greater Tokyo, many people commute by train between the suburbs and downtown Tokyo for 1 to 2 h per day. The spread of influenza in the suburbs of Tokyo should be studied, including the role of commuters and the effect of government policies on the spread of disease. We analyzed the simulated spread of influenza in commuter towns along a suburban railroad, using the individual-based Monte Carlo method, and validated this analysis using surveillance data of the infection in the Tokyo suburbs. This simulation reflects the mechanism of the real spread of influenza in commuter towns. Three measures against the spread of influenza were analyzed: prohibition of traffic, school closure, and vaccination of school children. Prohibition of traffic was not effective after the introduction of influenza into the commuter towns, but, if implemented early, it was somewhat effective in delaying the epidemic. School closure delayed the epidemic and reduced the peak of the disease, but it was not as effective in decreasing the number of infected people. Vaccination of school children decreased the numbers not only of infected children but also of infected adults in the regional communities.*

KEYWORDS *Influenza, Computer simulation, Commuters, Prohibition of traffic, School closure, Vaccination*

Abbreviations: PT – prohibition of traffic; SC – school closure; VSC – vaccination of school children; PHC – Public Health Center; NIID – National Institute of Infectious Diseases

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INTRODUCTION

If a pandemic influenza were to spread across the capital city of Tokyo, extensive damage to health, life, and the economy could be expected. To reduce the risk of such damage, we must understand the mechanisms of the spread of seasonal influenza in the commuter towns of Tokyo, and we must be prepared for this event. This study is a simulation based on national sentinel surveillance data of seasonal influenza. Simulation is a useful tool for helping administrators plan their actions against influenza. Past experience is of vital importance; however, environmental conditions change with time, and little information is currently available for emerging influenza. It is also very difficult to perform social experiments in the real world.

To design preventative measures against influenza, prohibition of traffic (PT), school closure (SC), and vaccination of school children (VSC) were simulated. Many people who work in Tokyo during the day commute by railroad 1 or 2 h per day. Because the commuters comprise ≈10% of the population of suburban towns, commuters would play an important role in the spread of influenza in the suburbs of Tokyo. PT is a possible candidate for the prevention of disease, but this has not thus far been implemented. Moreover, SC is often adopted when school children contract influenza, but the effect of SC is still undetermined. In Japan, children were mass-vaccinated by law from 1962 to 1987. However, in 1987, this law was relaxed, and it was repealed in 1994 because an efficient flu vaccine was not considered important at that time. A recent study[1] shows the possibility that VSC prevents influenza from spreading in the community; this possibility should be explored by the simulation of new situations and by undertaking new measures.

Many studies of the simulated spread of influenza have analyzed a local seasonal epidemic, without traffic to other regions.[2–7] However, considering the threat of avian flu, whether influenza is contained in a local region or transmitted to other regions will make a great difference. Longini et al.[8,9] investigated the possibility of containing avian flu within a region of Southeast Asia and within the United State. Ferguson et al.[10] also investigated the same possibility in Thailand. The transmission of influenza as a multicity problem in the United States was studied by simulation[11], and a theoretical analysis was performed.[12] These study protocols are useful for simulating the spread of influenza in the commuter towns of Tokyo, where the distinctive feature is the important role played by commuters. Virtual communities along the suburban railroad are constructed for commuter-focused simulation, based on Japanese social statistics: Japanese census data, the statistics of local governments of greater Tokyo, and a survey of Tokyo metropolitan region transportation.

In our simulation, recent real infection data of seasonal influenza during three seasons from 2002 to 2006 was used for understanding the mechanism of the spread of influenza in the suburbs of Tokyo. Influenza infection in Japan is reported from 5,000 sentinel points (designated monitoring points) and data accumulated at regional Public Health Centers (PHC, healthcare centers), then reported to the National Institute of Infectious Disease (NIID). NIID officially announces a seasonal influenza epidemic when the number of patients reported from a sentinel point exceeds 30 per week. For the winter of 2002/2003 and 2003/2004, the maximum number of patients reported per week from a sentinel point was more than 20 but less than 30 in Tokyo. For the winter of 2005/2006, it was greater than 40.

In the present study, we simulated the spread of influenza across the capital city of Tokyo to collect information for measures to mitigate the damage of a pandemic influenza using the individual-based Monte Carlo method. We chose the major suburban

railroad Chuo Line in western Tokyo as a virtual railroad (Figure 1). We analyzed Japanese national surveillance data and used these data to verify our simulations of the mechanism of the real spread of influenza. In addition, we estimated three measures against influenza: (1) PT, (2) SC, and (3) VSC, using the probabilities of the transmission of seasonal influenza in the literature[2–7] because that of emerging influenza is unknown. We also analyzed the effects of low-dose vaccination administered to children in our simulation. Because a short supply of the vaccine due to large-scale distribution during pandemic influenza may result in low-dose inoculation, lower efficiency of vaccination is expected. Finally, the combined effect of these measures was analyzed by simulation.

METHODS

Simulation

We performed Monte Carlo simulation using an individual-based model. We constructed a regional simulated community called the virtual Chuo Line. First, we generated individual people. The number of people in each town was proportional to the number of commuters; the total number of people generated was 8,800. Two thousand people were generated in Hachoji City, 2,600 in Tachikawa City, 2,800 in the Kichijoji area of Musashino City, and the rest were in Shinjuku and Tokyo. Our model was scaled down, but preliminary estimates showed 8,800 people were sufficient for Monte Carlo simulation. These people were connected to many different types of families: singles, couples, fathers, mothers, and children. The ratio of types of families was determined by Japanese census data.

We also constructed "compartments," consisting of 4,040 homes, 60 schools, 658 companies, and 117 stores, using local government statistics. For commuters, the data of the fourth Person Trip Survey of Tokyo Metropolitan Region Transportation was used. In this model, 12% of the people in the suburbs are commuters. We operated trains that moved between stations according to a railroad timetable.
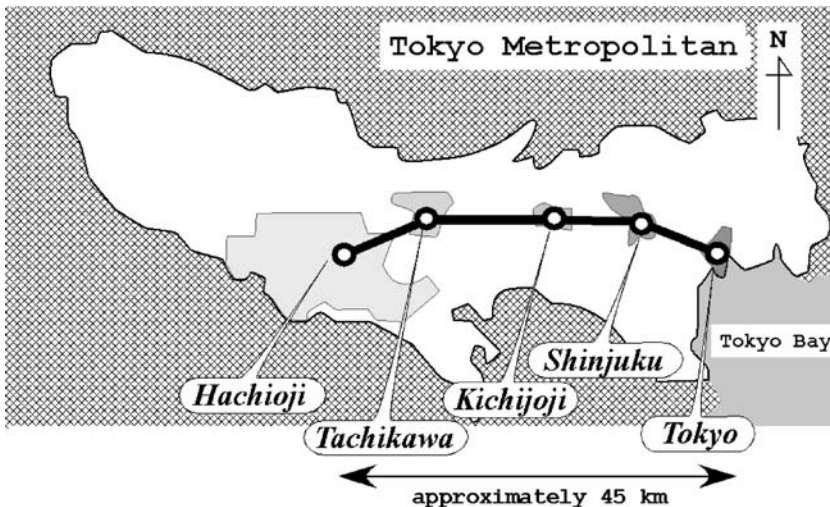
FIGURE 1. Location of stations along the virtual Chuo Line in Tokyo. The Hachioji, Tachikawa, and Kichijoji Stations are located west of Tokyo. The Shinjuku and Tokyo Stations are in the Tokyo central area. The *outlines* are the prefecture boundaries of Greater Tokyo.

Homes, schools, companies, and stores are fixed compartments, and trains are moving compartments. As timetables, we gave people event histories, consisting of movement from one compartment to another. Event histories were constructed using statistical data of the daily life of ≈30,000 Japanese people.[13] In these compartments, people contacted each other stochastically and were occasionally infected. The probabilities of infection we used were 0.005/h for homes, 0.0016 for schools, 0.0125 for trains, and 0.00001 for companies and stores. The width of a time step in our simulation was 1 h, and we used probabilities per hour. The probabilities of infection have been studied in the literature,[2–7] where probabilities are values per day. For homes, schools, companies, and stores, converting each unit with the reasonable assumption that employees are at work from 9:00 A.M. to 5:00 P.M., our values are in the range of those in the literature. For the probability of trains, we assumed they were densely packed. Medical conditions were specified by a scenario of infection in which the latent time was 2 days, and the period of infection was 5 days. In the simulation, all infected people eventually recovered.

### Surveillance Data of Infectious Disease

The Ministry of Health, Labour and Welfare reports surveillance data of infectious disease through registration with the NIID, to which every PHC reports the number of newly infected patients every week. The data of the PHCs come from fixed medical agencies in Japan, consisting of 3,000 pediatricians and 2,000 internists. There are three PHCs in the suburbs along the Chuo Line. The Hachioji PHC is near Hachioji Station; the Tama-Tachikawa PHC, near Tachikawa Station; and the Sugunami PHC, near Kichijoji Station. We analyzed the data from the end of 2002 to the beginning of 2006.

RESULTS

Simulation of the Spread of Influenza in the Suburbs along the Chuo Line in Tokyo

We performed preliminary simulations primarily to specify where the first persons were infected. We tried four situations, in which the first persons infected were in Hachioji, Tachikawa, Kichijoji, or Tokyo. For the situation where the first person infected was in Tokyo, commuters were the first to be infected. In the other three situations, the spread of the epidemic in the town where the first person infected was preceded by infection in the other towns along Chuo Line. This is because the spread of infection among school children in the first town was faster than transmission to the other towns by commuters. When the first person seeded in Tokyo, the causes of the spread of the epidemic almost coalesced in every year examined. Below, we present evidence for this using real data. Our simulation focused on the last situation.

There were similarities among the results of cases where commuters were the first infected. We have discussed the case where ten commuters were the first infected. The graph of a typical result (Figure 2A) shows the number of infected living in the areas of Hachioji, Tachikawa, and Kichijoji Stations. The number of infected living in Hachioji was 572, 914 in Tachikawa, and 1,108 in Kichijoji, respectively. The total number of infected along the Chuo Line, including the initial 10 infected commuters, was 2,915, which is 33% of the population along the Chuo Line. At the beginning of the spread of influenza, there was a period when the number of infected was small, then increased exponentially. The peaks of the number of infected in three towns coalesced ≈6 weeks after the beginning of the spread of influenza.
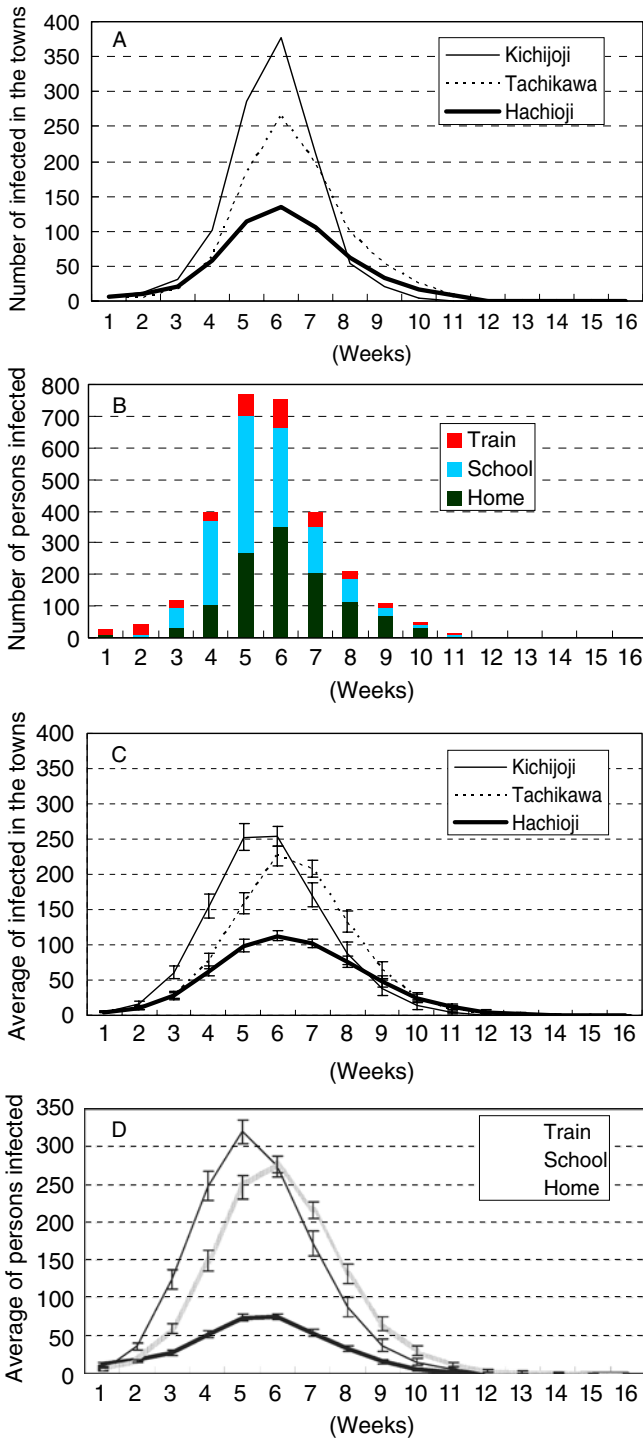
FIGURE 2. Influenza spread along the virtual Chuo Line. **A** The number of infected who live in each commuter town in a typical case. **B** The number of persons newly infected divided by location of a typical case. **C** The average of 100 cases of infected who live in each commuter town. **D** The average of 100 cases of persons newly infected divided by place. *Bars* indicate 95% confidence interval.

Figure 2B shows the number of persons newly infected, including where they became infected. In the beginning, a small number of persons were consistently infected in trains. Infections in schools then increased, followed by homes; there were few occurrences in companies and stores. Figure 2C and D show the average of 100 cases in the Monte Carlo simulation. Because the peaks are out of synchronization, the peak of the average appears lower than that of the typical case.

Real Data of the Spread of Influenza in the Suburbs along the Chuo Line

With the permission of the NIID, we analyzed the number of notifications from the Hachioji, Tama-Tachikawa, and Suginami PHCs from the end of 2002 to early 2006. Type A influenza was detected in the winter of 2002–2003, 2003–2004, and 2005–2006, but in 2004–2005, type A was detected in early winter and type B in late winter. Figure 3 shows the number of notifications from these three PHCs in the winter of 2002–2003, 2003–2004, and 2005–2006. As shown in Figure 3, the data during the period from the 45th week of a given year to the 15th week of next year are shown. The number of patients infected with influenza remained small at the beginning of the season and then increased exponentially. Peaks of infection almost coalesced in each town. These profiles are similar to the profiles of our simulation. In some cases, peaks appeared in early winter and disappeared due to the New Year holidays.

Simulation of Measures Against the Spread Of Influenza

We proposed three measures against the spread of epidemic influenza: (1) PT, (2) SC, and (3) VSC. For each measure, the profiles of the number of persons infected in simulated cases were similar. We utilized the same commuters with the case in Figure 2 as the first persons infected as the basic scenario for this analysis. The scenarios of the simulation in the case in Figure 2 were modified for PT, SC, and VSC. We show the results of a typical case and the average results of 100 cases for each scenario.

For PT, we assumed a 2-week prohibition of the virtual Chuo Line, starting with the fourth week after the beginning of the epidemic. Figure 4A shows the number of persons infected in a typical case divided into specific locations during PT. The total number of persons newly infected is 2,872, without the initial 10. Figure 4D shows the average number of persons newly infected; the total number is 2,837.

For SC, schools were closed for 2 weeks, starting with the fourth week after the beginning of the epidemic. Figure 4B shows the number of persons infected in a typical case. The total number of persons newly infected was 2,813. Figure 4E shows the average number of persons newly infected; the total number is 2,696.

For VSC, we assume children were vaccinated before the influenza season. In this study, instead of conventional vaccination that could not be specified before simulation, we used the fraction of vaccinated children who become immune as a parameter: the percentage of unsusceptible children, x, means x number of 100 vaccinated children would become immune. Figure 4C, a typical case, shows the number of persons infected if 30% of children would become unsusceptible. The total number of persons newly infected is 1,786; Figure 4F shows the average. The average number of persons newly infected in cases of 5–30% of unsusceptible children is shown in Table 1. For 30%, the total number is 1,761. Using the results of the simulation, we define the conventional efficiency of the vaccination of the community in Table 1 as 1 minus the ratio of the number of infected in the community in the case of VSC to the number of infected in the community in the case of unvaccinated children. When the
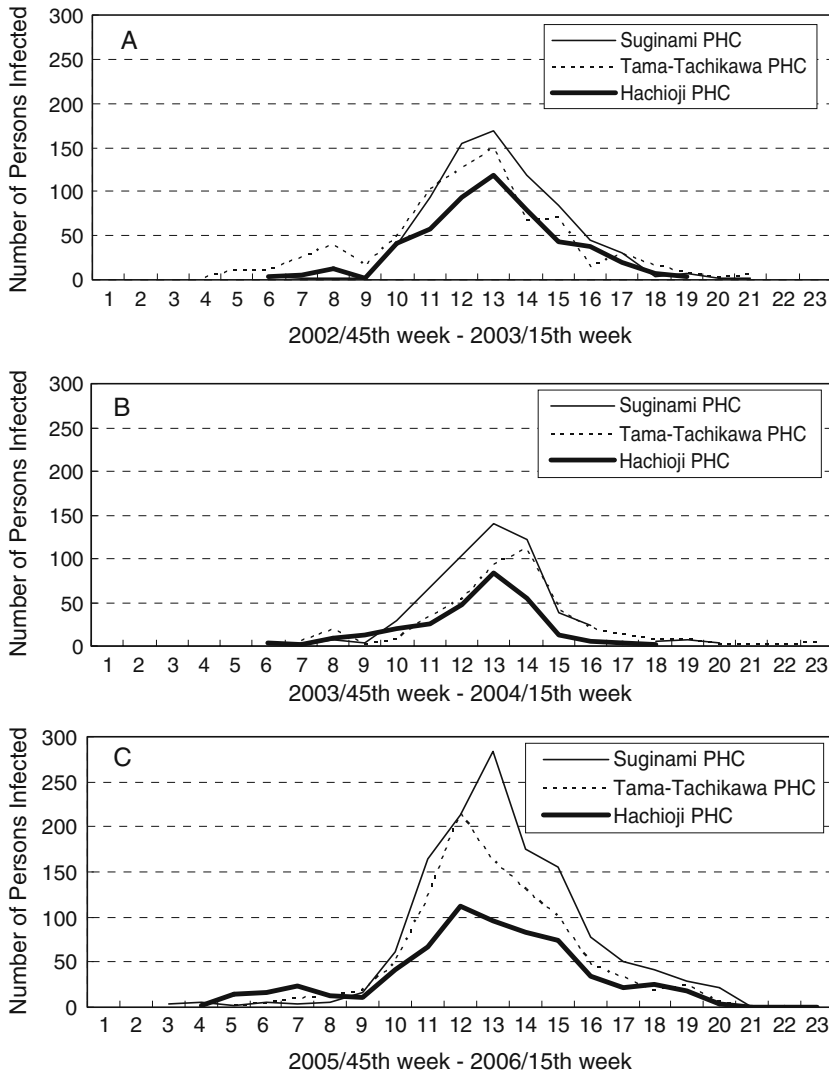
FIGURE 3. Data of notification of influenza from the PHC along the Chuo Line. Data of the Suginami, Tama-Tachikawa, and Hachioji PHCs during the period from the 45th week of a given year to the 15th week of the next year. **A** Data from the end of 2002 to 2003, **B** the end of 2003 to 2004, and **C** the end of 2005 to 2006. Suginami PHC is near Kichijoji Station; Tama-Tachikawa PHC, near Tachikawa Station; and Hachioji PHC, near Hachioji Station.

number of persons infected in the schools decreased, the efficiency of the vaccination of the community increased.

The spread of an epidemic would be affected by PT or SC in the early stages of an epidemic. The numbers of infected if PT started (1) 3 days, (2) 1 week, (3) 2 weeks, (4) 3 weeks, or (5) 4 weeks after the beginning of the epidemic are compared in Figure 5A. The average of the total number of newly infected was 2,909 for (1), 2,943 for (2), 2,915 for (3), 2,874 for (4), and 2,837 for (5). The variation of the total number of persons infected is less than 4% of the number of infected in the case without any implemented preventative measures. For compar-
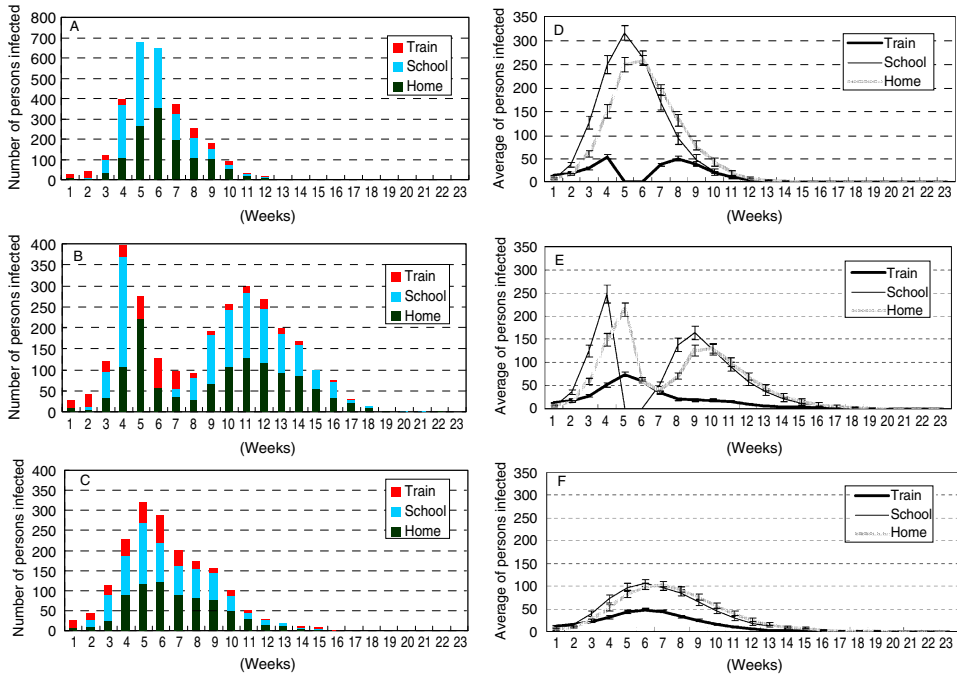
FIGURE 4. Number of persons infected in different anti-influenza scenarios. **A** The number of persons infected in a typical case when traffic was prohibited 4 weeks after the beginning of the epidemic for 2 weeks, divided into locations. **B** SC 4 weeks after the beginning of epidemic for 2 weeks. **C** Vaccination, where the percent of unsusceptible children in C is 30%. **D** The average of 100 cases of persons infected when traffic was prohibited 4 weeks after the beginning of the epidemic for 2 weeks. **E** The average of 100 cases of SC 4 weeks after the beginning of the epidemic for 2 weeks. **F** The average of 100 cases of vaccination, where the percent of unsusceptible children is 30%. *Bars* indicate 95% confidence interval.

TABLE 1.   Number of persons infected when vaccination is implemented

Parameter	Unsusceptible children				
	0%	5%	10%	20%	30%
Infected in trains	376 (371–380)	371 (366–375)	358 (353–362)	344 (339–348)	317 (305–328)
Infected in schools	1,332 (1,327–1,336)	1,234 (1,229–1,238)	1,131 (1,126–1,135)	936 (931–940)	709 (683–734)
Infected in homes	1,227 (1,219–1,234)	1,143 (1,135–1,150)	1,062 (1,054–1,069)	913 (905–920)	722 (696–747)
Newly infected children	1,615 (1,610–1,619)	1,495 (1,490–1,499)	1,371 (1,365–1,376)	1,147 (1,141–1,152)	878 (846–909)
Newly infected adults	2,951 (2,939–2,962)	2,765 (2,753–2,776)	2,567 (2,554–2,579)	2,207 (2,195–2,218)	1,761 (1,698–1,823)
Efficiency of vaccination to community		6.3%	13.0%	25.2%	40.3%

(-) 95% confidence interval.
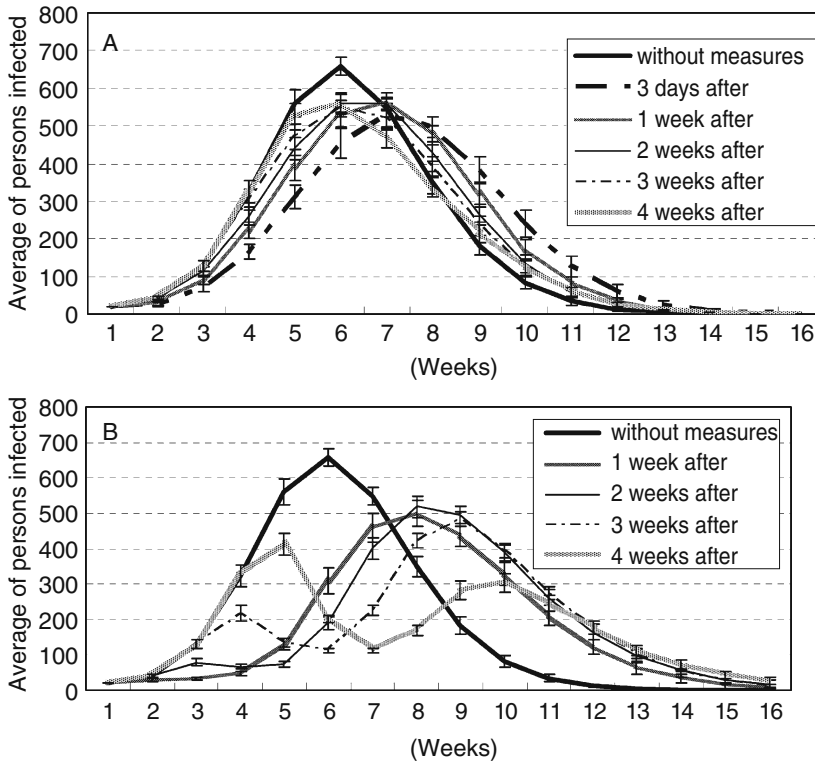
FIGURE 5. Delay and peak shift of newly infected with PT and SC. **A** The average of 100 cases of persons infected with traffic prohibition (1) 3 days, (2) 1 week, (3) 2 weeks, (4) 3 weeks and (v) 4 weeks after the beginning of the epidemic. **B** The average of 100 cases of persons infected if schools were closed for (1) 1, (2) 2, (3) 3, and (4) 4 weeks after the beginning of the epidemic. *Bars* indicate 95% confidence interval.

ison of the effect of the time lag to the closing of schools, SC starting (1) 1, (2) 2, (3) 3, and (4) 4 weeks after the beginning of the epidemic is compared in Figure 5B. The average of the total number of newly infected was 2,756 for (1), 2,895 for (2), 2,820 for (3), and 2,696 for (4). Although there is a noticeable difference in the shapes of the lines in Figure 5B, the variation of the total number of infected in the cases of SC is less than 9% of infected people in the case without any implemented preventative measures.

In Table 2, we show the total number of persons infected, the day of the peak of infection, and the sum of the average numbers of infected before the peak in the case of PT or SC. PT and SC changed only the location of the infected people. The variation of the total number of infected is not large, but both measures delay the peak of the epidemic. PT within 2 weeks after the beginning of the epidemic delayed the peak by 1 week compared to the case without any implemented preventative measures. SC within 3 weeks delayed the peak of the epidemic more than 2 weeks.

We combined PT, SC, and VSC. Figure 6A shows the results of multiple measures. In this case, 2-week PT and 2-week SC started with the fourth week after the beginning of the epidemic. With VSC, 30% of children became unsusceptible.

TABLE 2. Delay and peak shift of newly infected with the implementation of PT and SC

Measure	Total number	First peak		Second peak	
		Week	Sum of infected	Week	Sum of infected
None	2,951	6	1,734	–	–
PT					
3 days	2,909	7	1,567	–	–
1 week	2,943	7	1,884	–	–
2 weeks	2,915	7	1,994	–	–
3 weeks	2,874	6	1,511	–	–
4 weeks	2,837	6	1,598	–	–
SC					
1 week	2,756	8	1,528	–	–
2 weeks	2,895	3	140	8	1,390
3 weeks	2,820	4	408	9	1,784
4 weeks	2,696	5	928	10	1,995

*PT* Prohibition of traffic, *SC* school closure.

The total number of infected is 2,539 with SC and PT, 1,578 with SC and VSC, 1,643 with PT and VSC, and 955 with all three measures. Figure 6B shows the results of VSC in combination with 2-week PT starting with the fourth week after the beginning of the epidemic. Figure 6C shows the results of VSC in combination with 2-week SC starting with the fourth week after the beginning of the epidemic. For VSC, unsusceptible children are assumed to be 5%, 10%, 20%, and 30%.

DISCUSSION

Characteristics of the Spread of a Seasonal Epidemic of Influenza along the Chuo Line in Tokyo and Validity of the Simulation

In our simulation, we analyzed places where people would become infected. When the infection began to spread, people were infected mainly in trains, but this number remained small. Many people then became infected in schools and at home, demonstrating that the spread of influenza along the Chuo Line occurs in two periods, the first beginning 2 weeks after the beginning of epidemic, followed by the second period. During the first period, commuters were infected in trains and then introduced influenza into their towns, and some children were infected at home. During the second period, many children were infected in schools and then in turn infected their parents at home. The number of persons infected increased exponentially during the second period.

In our analysis, profiles of real influenza data in Tokyo for four winter seasons are similar, except in late winter of 2004–2005. This suggests there is a stable mechanism of transmission of influenza along the Chuo Line. The profiles of the simulation are also similar to those of the real data, especially considering that the peaks 6 weeks after the beginning of the epidemic in the simulation almost coincided with that of the real data measured from the beginning of the outbreak. This indicates that the model for the simulation of the spread of influenza reflected the mechanism of the real spread of influenza.
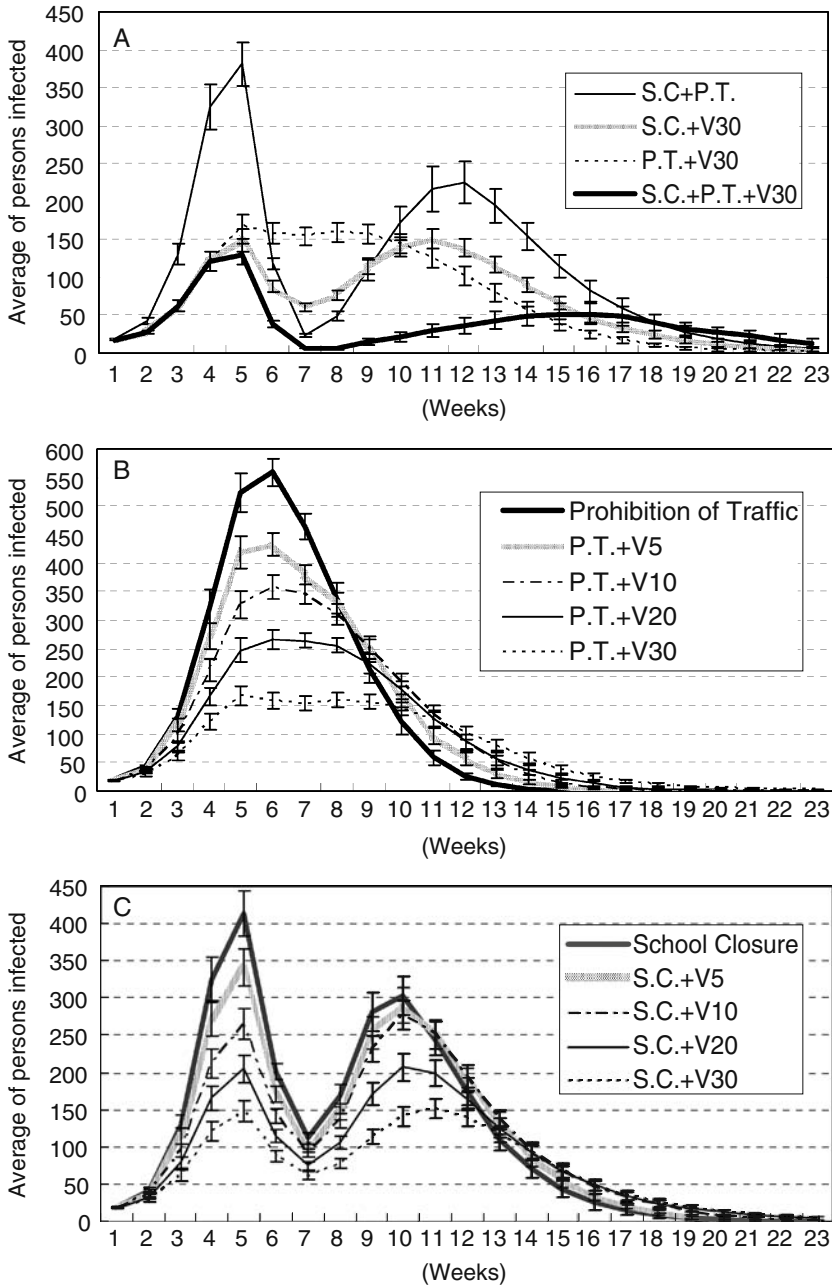
FIGURE 6. Effects of combination of measures, including 2 week PT and 2 week SC beginning in the fourth week, on an average of 100 cases of persons infected. V5-30: vaccination of school children where 5–30% of school children, respectively, become unsusceptible.

On the other hand, the real data of the NIID database provided evidence of the effectiveness of social distancing for protection against influenza. There is a small peak in some of the real data profiles at the beginning of the spread of influenza. The weeks when the peaks declined coincided with the New Year holidays. In Japan, schools are

closed for 2 weeks at this time, and almost all businesses are closed for 1 week; many people in Tokyo return to their home provinces. We conjecture that changes in human behavior during the New Year holidays caused these small peaks.

PT

Influenza was transmitted into commuter towns along the Chuo Line by commuters. However, it would be difficult to prohibit traffic while the number of infected was small; thus in the present study, we prohibited traffic after the pre-epidemic spread of influenza. The profile of the number of infected persons by PT was similar to that without prohibition, and the decrease of the number of infected persons by PT was small. This shows that PT is not effective for protection after the introduction of the spread of influenza into the suburbs. Similarly, Germann et al.[11] demonstrated in their simulation that the number of ill people did not decrease, even though they reduced long-distance travel in the United States to 10% of normal frequency.

We surmised that PT would be effective because influenza is believed to be transmitted in trains used by approximately one tenth of suburban commuters. However, our simulation disproved this supposition. After influenza was transmitted to the suburbs, the number of persons infected in schools and homes was larger than the number of persons infected in trains. Because of the nature of human contact in train compartments, the number of persons infected increased exponentially with the passage of time. Commuters spend 1–2 h in trains, and children spend 6 h or more at school. Thus, children play a more crucial role in spreading influenza than commuters after the influenza is introduced into towns.

These results suggest that towns would be protected from the spread of disease if we could prohibit traffic before the introduction of the epidemic. However, complete protection is difficult because commuters may be already infected before the detection of the spread of influenza. Our results show the spread of the epidemic occurs in the towns even if traffic is prohibited for 3 days after the beginning of the epidemic. However, early PT delays the spread of disease. The increase in the number of infected in cases of 3 days, 1 week, and 2 weeks was smaller than the case without any preventative measures implemented. This indicates that introduction of the epidemic into towns by infected commuters decreased in the early stages in our simulation.

In our simulation, the spread of influenza was initially introduced into local commuter towns by commuters. A similar role of transmission by travelers is discussed using real data. Hollingsworth et al.[23] reported that frequent travelers accelerate the international spread of the epidemic of respiratory disease only if they are infected early in an outbreak, and the outbreak does not expand rapidly. Brownstein et al.[24] demonstrated air travel may be an important mode of long-range dissemination of influenza in the United States. Moreover, Viboud et al.[25] also showed the strong dependence of inter-pandemic influenza spread on workflow implies a key role for adults in the regional dissemination of influenza; at the same time, the long-distance dissemination of influenza between cities or states is captured by movements linked to adults.

SC

In the present study, we closed schools for 2 weeks from the fourth week after the beginning of the epidemic because school was not closed until a certain number of children became infected, and in Japan, the period of SC is usually 1 or 2 weeks. In this case, the peak of the number of children infected was lowered, but the period of the epidemic was prolonged. When we reopened the schools, the number of infected again

increased. While the schools were closed, many infected children recovered. Because children who recovered divided a long linkage of transmission into shorter linkages, the increase of the number of persons infected is slower than before SC, but the decrease of the total number of persons newly infected was small. The results show that SC delays the transmission but somewhat decreases the scale of the epidemic. We achieved the same results in SC in an isolated town, reported elsewhere.[14]

SC 4 weeks after the beginning of epidemic, a conventional measure, is effective in decreasing the peak of infection. A prominent peak appeared in the early stage, but it did not appear in the cases of SC before 2 weeks, and the ripple is small in the case of 3 weeks. This simulation suggests that SC before 3 weeks from the beginning of the epidemic may delay the spread more than 2 weeks.

The characteristics of SC have been studied mainly by simulation. Although their model was designed for enteric virus, Elveback et al.[2] study the effect of opening or closing grade schools. They demonstrate that schools provide additional pathways for the spread of disease between families and between family clusters (neighborhoods or other social groups). Elveback et al.[3] asserted closing school for a few days after an influenza epidemic has begun is more effective in mitigating the duration than the size of the disease. In Asian flu infection in the winter seasons of 1957–1958, Glass et al.[26] reported that closing schools and keeping children and teenagers at home reduced the infection rate by less than 90%. Glass and Barnes[27] showed that closing schools can considerably reduce transmission among children but has only a moderate impact on average transmission rates among all individuals (both adults and children). Also, Ferguson et al.[28] showed SC during the peak of a pandemic can reduce peak infection rates by up to 40% but with little impact on overall infection rates.

The decrease of the number of persons infected by SC for 2 weeks in the simulation seems similar to the real data during the New Year holidays. We can regard the similarity between the real data of surveillance and the simulation of SC as evidence of the effect of the behavior change of children. For real data, Heymann et al.[29] reported evaluation of the effect of SC on the occurrence of respiratory infection among children ages 6–12 years old with a significant decrease in health care services during the period of SC. Vynnycky and Edmunds[30] reported, using the data of Asian influenza, that a modest reduction, e.g., 22%, might be possible if schools were closed early and the basic reproduction number were low. Valleron and Flahault[31] also reported a delay of 10–20 days between school holidays and a decrease in the incidence of influenza diagnoses from 1984 to 2000 in France. The real data show a significant relation between SC and spread of influenza. Based on the simulations, we assert that early SC produces a delay of the spread of influenza and effectively reduces the peak, but that we cannot expect a significant decrease of the total number of persons infected.

VSC

We vaccinated children instead of adults because systematic vaccination of adults seemed difficult due to lifestyle differences. The results of our simulation show that the decrease of the number of persons infected was not proportional to the percentage of unsusceptible children. However, a distinctive trend in the simulation was that the number of persons infected at home decreased when the number of children infected in schools decreased. This strongly suggests that VSC may stop the spread of influenza not only in children, but also in adults because a proportion of vaccinated children who become immune may interrupt the linkage of transmission in the regional community. Although the number of children and adults infected in schools and at home decreased, the number of persons infected in trains did not decrease significantly concomitant

with the VSC. These results suggest that the course of infection primarily among adults in trains is independent of the course of infection in schools and at home.

Our simulation data strongly suggest that VSC is effective in preventing the spread of influenza in the regional community, notwithstanding the important role played by commuters in the initial phase. In Japan, children were mass-vaccinated by law from 1962 to 1987, but in 1987, the law was relaxed and then repealed in 1994. According to research on deaths from pneumonia and influenza from the 1950s to the 1990s, mortality of the elderly decreased when school children were vaccinated,[1] but the effectiveness of VSC is still under discussion.[15–17] The same subject has been studied in the United States.[18–21] These studies assert the effectiveness of school-based influenza vaccination. The Tecumseh case is well known for the effectiveness of vaccinated children in protecting a regional community.[22]

In the present simulation, we analyzed PT or SC, as, under the Japanese Vaccination Law, we cannot prepare for school-based mass vaccination before the influenza season. This study suggests the effectiveness of the combination of different measures. It takes almost 2 weeks for the effect of vaccination to appear. As children are not vaccinated before influenza season, the allowance of time before the spread of the epidemic among children is important for mass vaccination. Delay of spread by SC 2 or 3 weeks after the beginning of the epidemic presents the opportunity for mass vaccination. Our simulation may recommend children be vaccinated before the spread in schools, when we can detect the epidemic in its early stages in trains and then soon close the schools. The effect of mass VSC is expected to decrease the total number of infected in the communities. Ferguson et al.[28] reported that a staged vaccination program has the maximum effect of reducing transmission if children are vaccinated first because school-aged children have the highest transmission rate, while vaccinating the elderly first has the lowest impact on transmission. Germann et al.[11] studied 'dynamic vaccination', in which the vaccine became available incrementally, and showed that the number of ill persons of dynamic child-first vaccination is less than that of dynamic vaccination.

Our results show that VSC has the effect of protecting communities, even if the vaccine is low-efficiency. The problem of low-efficiency vaccine is important, especially when there is a small stockpile of vaccine. Riley et al.[32] reported that substantial reductions in the infection rate are likely to happen and also increase individual-level protection, if vaccines are given to more people at a lower dose. The population-level implications of pre-pandemic vaccine programs should be considered when deciding on stockpile size and dose. Germann et al.[11] compared the recommended two doses, assumed to confer the best protection level, with a strategy in which twice as many people are given a single dose; this assumes that a single dose confers about half the protection of two doses, and that the number of ill persons in the one-dose regimen is less than in the two-dose regimen. Wu et al.[33] reported the problem of the spatial allocation of pre-pandemic influenza vaccination related to the low efficiency of the vaccine.

Multiple Measures

The synergistic effect depends on the combination of measures, i.e., when multiple measures are implemented. When we close schools and prohibit traffic at the same time, the decrease of persons infected in the seventh week is greater than when we combine either SC and VSC or PT and VSC. This is because in our simulation, during an epidemic, people stay home all day and come in contact only with their families.

However, the synergistic effect of combining measures may not always be positive. When combining SC and VSC, the effect of VSC diminished when schools were closed. VSC and SC reduced the spread of influenza in the community by

protecting children. Because there is a similarity in the effect of both measures, a synergistic effect could not be expected. Germann et al.[11] reported that the estimated benefits of preferentially vaccinating children are offset by closing schools. Glass and Barnes[27] reported that immunization of all school children provides only a slight improvement over closing schools, indicating that schools are an important venue for transmission among children. In the combination of PT and VSC in our study, PT did not affect the efficiency of the vaccination. This indicates that the course of infection in trains is independent of the course of infection among children.

Our simulation strongly suggests the following:

1. There are two periods in the spread of influenza in the suburbs of Tokyo. The first period is defined as 2 weeks from the beginning of the epidemic; this is followed by the second period. In the first period, commuters introduce influenza into the suburbs, and in the second, children play an important role in the spread of influenza in the suburbs.
2. PT is not effective after the introduction of influenza into the suburbs. However, the epidemic would be delayed by $\approx$1 week in the early stage of the epidemic if traffic were prohibited within 2 weeks after the beginning of the epidemic.
3. SC would delay the epidemic and reduce peaks of infection. If we could close schools before 3 weeks after the beginning of the epidemic, the epidemic would be delayed by more than 2 weeks.
4. VSC is effective in preventing the spread of influenza, even when commuters spread the disease along a suburban railroad.
5. The synergistic effect of multiple measures depends on a combination of measures; SC offsets the effect of VSC in communities during the period of SC.

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