Challenges in Formulating Evidence-based Strategies for School Closures

Studies in Japan and other countries

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Asami SASAKI*1

Once children are infected with a virus or bacteria, there is no knowing whether this will develop into bronchitis, pneumonia, or even encephalitis. Doctors see patients who have become sick and treat them one by one. Public health focuses on preventing groups of people from becoming sick. Having the experience of working as a pediatrician, I felt that more children could be prevented from becoming infected, which might even save their lives. I started studying in the Department of Public Health, Niigata University in Niigata Prefecture, Japan in 2003. I have studied the epidemiology of infectious diseases, especially influenza and measles, and my principal areas of knowledge and skill concern respiratory viruses, such as viral isolation and identification, and molecular virology.[1,2] In my studies I learned how surveillance in vivo and in vitro is important in controlling influenza outbreaks.[3–5]

Given the golden opportunity of studying in the 2008/09 Takemi Program at the Harvard School of Public Health, I researched "School closures," which is one measure for preventing influenza outbreaks in groups of children and local areas.

In this paper, I review studies of school closures in influenza outbreaks and pandemic planning undertaken in Japan and other countries and present a summary of the findings of my school closure study.

History of Pandemic Influenza

Influenza is an infectious disease caused by RNA viruses of the family Orthomyxoviridae that is transmitted by the aerosols generated by coughs or sneezes of infected people.

The most famous influenza pandemic in history is the 1918 Spanish flu Pandemic, which caused 80 million deaths around the world. This pandemic was caused by the H1N1 virus making its first appearance, and the strain has remained as seasonal influenza. Kawana et al. reported a high death rate (6–8%) in hospitalization registries of Japanese army hospitals during this pandemic, even though patients were otherwise healthy male adults.[6]

In 1957, the Asian influenza virus (H2N2) caused two million deaths, but disappeared after the pandemic. The H3N2 virus, known as the Hong Kong influenza strain in Japan, first appeared in 1968, when it caused one million deaths. This strain also remains as a seasonal influenza virus.

In 2009, the H1N1 changed its form, becoming a combination of the pig, bird, and human influenza viruses. The death rate has still not been established. The term "Seasonal influenza" is now commonly used for regular influenza viruses, which mostly occur in winter time, to distinguish them from new influenza strains such as the new H1N1 or avian influenza.

As a measurement of the susceptibility to infection for any infectious diseases, the reproductive Number (R_0) is often used; The reproductive number is the number of people who are infected by one patient. Measles is often given as an example of a strongly infectious virus whose R_0 is 10 to 15. The R_0 for seasonal influenza is around 1.3. For Spanish influenza, the R_0 is estimated

*1 Division of Health and Nutrition, University of Niigata Prefecture, Niigata, Japan (asammy@unii.ac.jp). Takemi Fellow (2008–2009), Harvard School of Public Health, Boston, MA, USA.

to have been 1.8–2.0 and 1.5–1.7 for Asian influenza.[7] The R_0 for the New H1N1 virus is estimated to be 1.4–1.6 in Mexico.[8]

The Japanese School System

In Japan, the school health care system was introduced in 1958. Two regulations concerning infectious control were included in the School Health Law. These regulations were influenced by the 1957 Asian influenza epidemic due to the large number of deaths and school closures reported during this period. One regulation is the "School infectious disease attendance prevention standards" (Article 19, School Health Law). Under these standards, when children are infected with influenza, they have to stay home till two days after the fever has lowered and need a doctor's permission letter to go to school again. This is possible because all children in Japan are covered by health insurance and will go to a doctor when they experience flu symptoms.

Since diagnostic tests are commonly used in Japan, school absentees can be clearly divided into students diagnosed with influenza and students diagnosed with another infection. With this system of self-reporting from infected students, Japan has a good school surveillance system.

The other regulation introduced after the Asian influenza pandemic is the "Temporary school closing system" (Article 21, School Health Law). Under this regulation, school principals have the right to close part or all of the school when it is necessary for the prevention of infectious diseases. Thus Japanese schools commonly close in units of "class," "grade" or "school" in influenza outbreaks every flu season, but some schools do not close even in a large outbreak depending on the policy of the school's principal.

In April 2009, a new "School Health and Safety Law" was implemented. Now the decision of whether or not to close a school is made by the school's founder. Over 98% of Japanese elementary schools are public schools, and so now local education boards decide if and when to close a school, enabling more standardized rules; most prefectural education boards close their schools when the absentee rate per day is around 10%. This percentage is decided arbitrarily and not in accordance with evidence-based strategies.

The Importance of School Closures and Research on Japanese School Closure

As we are experiencing with the new H1N1 virus, vaccines are not available for all as is not possible to produce them with automated manufacturing and as yet there is no knowing how much vaccine would protect people from becoming infected. Also, there is concern that drug-resistant strains of influenza might spread all over the world in the near future.[9–11] Under non-pharmaceutical plans, "social distancing methods" such as personal travel restrictions and school closure are the main strategies for reducing people-to-people contact, and attention has been focused on "School closures" as a measure to inhibit the spread of the virus in a pandemic.[12]

In Japan, mass school vaccination programs started in 1962, influenced by the Asian influenza pandemic. Because of the side-effects caused by vaccination, the program ended in 1994. Sugaya et al. reported that, following the program, vaccinating school children against influenza had reduced the rate of mortality of elderly people due to influenza.[13]

Thus controlling outbreaks at schools might not only protect school children themselves but also reduce the rate of infection in other age groups in the local community.

Though school closures are commonly carried out every winter season, few Japanese studies discuss its effectiveness in controlling influenza outbreaks. Based on actual records of Asian influenza in Japan, Fukumi et al. reported that with school closures of five to six days, only a small number of schools reported a second outbreak of the disease in the school. When schools closed for over seven days, they did not have another outbreak.[14] A pediatric study group in Ishikawa Prefecture has suggested that two days of school closure was not effective in controlling the outbreak, but that 3 days or more days of closure might be effective.[15]

In simulations of pandemic influenza spreading patterns, using "person trip data" Ohkusa et al. showed how fast the virus could spread throughout the country when one new influenza-infected patient came back to Tokyo from outside Japan. Using R_0 1.6–2.4, his analysis showed that influenza patient numbers increase to 127,000 in a week in Tokyo. Moreover, when the

virus is spreading around Japan, densely populated cities spread much faster than sparsely populated cities.[16]

In the early outbreak of H1N1 in Japan in May 2009, the estimated R_0 was as high as 2.3 in the transmission in the virus amongst high school students in Hyogo and Osaka Prefectures.[17] This is a much higher number than the estimated data which R_0 was 1.4–1.6 in Mexico.[8] Infection may have spread much faster than other countries because of the high population density and train congestion in urban areas. From May 18, all the schools in Hyogo and Osaka Prefectures were closed for seven days. Nishiura reported that this school closure intervention reduced the R_0 to below 1, decreasing patient numbers significantly.[17]

Kawaguchi et al. reported that the prefecture-wide school closure strategy may have been effective in not only reducing virus transmission and preventing successive large outbreaks but also generating greater public awareness about the need for preventive measures.[18]

Studies in Other Countries Describing Different Methods

Social network studies

Social network study is one method of measuring social distancing in which people's behavior patterns are tracked and checked for who they have met. Infections continue if an infected person meets people who are not infected and do not have immunity to the disease. Different age groups will have different social environment background such as schools, business offices, hospitals, or other places where people meet.

Glass et al. found in their social network study that high-school students may form the local transmission backbone in a pandemic, and so closing schools and keeping students at home during a pandemic would remove the transmission potential within this age group and thwart the spread of the virus within a community.[19] A high school student outbreak happened in Japan in the early stages of the H1N1 influenza outbreak in Osaka and Hyogo[17,18,20] and social network studies on different age groups to observe their contact patterns and range of activity in Japanese society may be needed.

From studies of social contact patterns of primary school children in Germany, Mikolajczyk et al. found that school children would come in contact with people in different age groups from their own more on the weekend.[21] Thus we need to consider who children might come in contact with during a school closure which may differ between societies.

Scenario simulation

Factors such as R_0, Case Fertility Rate (CFR), vaccination rate, medication stocks, and social distancing methods are used in scenario simulation. Numbers for each factor are needed for policy making so that policy makers know what tools we have and how effectively we can use these tools in controlling the outbreak. Furgson et al. proposed that school children have the highest transmission rate.[22] In the case of R_0 'moderate' (R_0 1.7 Asian influenza) and 'high' (R_0 2.0 Spanish influenza), schools closing even as early as a day after the first case is reported will not effectively control the outbreak as a single intervention. In such cases, additional intervention using antiviral drugs is needed. Germann et al reported that in cases of low R_0, vaccination or antiviral drugs might be effective in controlling the outbreak. When R_0 is high, a combination of multiple strategies is needed to control the outbreak.[23] Carrat described intervention using school closure in which schools and workplaces were closed when a threshold number of infections (5/1000 subjects in the example) had been reached in the population and were reopened 10 days after the last observed case of infection.[24] Vynnycky et al. identified 3 different R_0: R_0 1.8, which is similar to that of the Asian influenza pandemic, and R_0 2.5 and R_0 3.5, which is a much higher transmission rate. Their analysis showed that the closure of schools/childcare centers could reduce the scale of the epidemic by only a very small amount (<10%) if R_0 is high (e.g. 2.5 or 3.5), and modest reductions (e.g. 22%) might be possible if the R_0 is low (1.8) and schools are closed early.[25] Using mathematical models, Glass et al. showed that closing schools can reduce transmission among children considerably, but has only a moderate impact on average transmission rates among all individuals (both adults and children) under most scenarios. Much of the benefit of closing schools can be achieved if schools are closed by the time that 2% of children are infected.[26]

These studies are of school closures in which

schools are generally closed after the first case of infection is reported and for over a month in the case of pandemic influenza, so we can not directly apply their results to Japanese school closure systems. Still, there is possibility that when R_0 is low, school closure may be effective in itself. If with the high transmission rate is high, multiple interventions such as vaccination and antiviral drugs are recommended.

The problems in the simulation studies are that the values for the factors used (such as vaccination rate and its effectiveness and age groups in the community) will change the results of the study. The values for the factors used in one simulation study have mostly been taken from other, different studies or are estimates. Halloran et al. has written that, "Because of the current lack of data on which to base such models, further field research is recommended to learn more about the sources of transmission and the effectiveness of social distancing measures in reducing influenza transmission."[27]

Evidence of school closures in existing data

There are few studies based on data showing the effects of school closure in actual outbreaks. The case of a school closure in Israel during an influenza outbreak is an interesting example of the possible effectiveness of school closure.

From January 16 to 28, 2000, during an influenza outbreak, there was a nationwide closure of elementary schools due to an isolated organized labor dispute by teachers. During this period, there were significant decreases in the diagnosis of respiratory infections (42%), visits to physicians (28%) and emergency departments (28%), and medication purchases (35%).[28] In Israel, children comprise 33.8% of the population and this might have increased the effectiveness of the school closure.

Analysis conducted by Furgson et al. showed that spring holiday in France prevents 16–18% of influenza cases overall, and 18–21% of influenza cases in children. People's age and behavior patterns according to the situation are important determinants; holidays affect children's contact patterns.[29] In Hong Kong during the large influenza outbreak, schools were closed for two weeks. Analysis did not show significant effectiveness of the school closure as the influenza season was already in a natural decline. Also, the study indicated that better surveillance is needed for schools and local communities to monitor outbreaks.[30]

This kind of study shows us more realistic results than estimation. Knowing more and more about what effect the school closure have in seasonal influenza would be very important in estimating the pandemic.

Social factors

Carrying out school closures involves many social factors in and outside the schools.

Seasonal influenza studies based on questionnaires indicate that school principals' and teachers' concerns when schools were closed were mostly about education and not about controlling the infection: too many days closed would delay classes. In addition, working parents want their children to be at school if they are not ill.[31,32] The impact of school closures would be reduced if maintaining low contact rates among children for a prolonged period became difficult.[29] Education at home such as internet-based studies might be needed when closing schools for a prolonged period and keeping the children at home.

A UK study calculated that during a pandemic wave of 12 weeks, the cost of school closure would be 0.2–1% of GDP (£0.2 billion to1.2 billion per week).[33] A US study estimated a high economic cost of about US$27 million per 1,000 population, or 6% of GDP, and that strategies involving school closure would be between 14 and 21 times as costly as intervention strategies using antiviral drugs or pre-vaccination alone. The greatest productivity loss (60%) during school closure can be attributed to parents being unable to work.[34]

Research in the Takemi Program

The purpose of my research in the Takemi Program was to create a strategy for school closures in Japan using real outbreak data.[35] Closing schools for more than two weeks may enable the control of outbreaks and is a suitable strategy if the virus has high transmission and mortality rates.

For seasonal influenza or 2009 H1N1, for which the mortality rate is not so high,[20] school closure of two weeks to a month is not realistic in terms of social and economic factors.

Using the daily influenza absentee data for 54 elementary schools in one city in Niigata Pre-

fecture, Japan, in the influenza season for each between May 2004 and August 2007, we analyzed the timing of school closure. We focused on the first outbreak reported in each of the 54 elementary schools in each influenza season because when the outbreak spreads inside a school or community, it is difficult to see the spreading pattern. Sometimes there could be two or three outbreaks in one school in one season. These could be different outbreaks or recurrences of the first outbreak, and it is difficult to identify the patterns.

We considered three scenarios: a single-day scenario in which daily influenza-related absentee rates are observed for the first time above a given threshold for one day; a double-day scenario in which rates reached a given threshold for the first time for two consecutive days, with the second day at the same rate or higher than the first; and a triple-day scenario in which rates reached a given threshold for the first time for three consecutive days, with the second and third days at the same rate or higher than the first. Each scenario was evaluated at nine different threshold percentages for influenza-related absentees per school per day: 1%, 2% . . . 9%. The results showed that a single-day observation at a threshold influenza-related absentee rate of 5%, double-day observations of >4%, and triple-day observations of >3% are the optimal levels for alerting school administrators to the need to consider school closure. The double- and triple-day scenarios performed similarly, and provided better results than those for the single day. Thus, the double-day scenario may be the preferred early warning trigger.

On September 24, 2009, Japan's Ministry of Health, Labour and Welfare presented recommendations for two school closure plans. One is an active school closure plan. If there is still no outbreak in the local community and if only one person was infected in the class, the class or school should be closed for five to seven days. If the outbreak is already widespread in the local community, passive school closure is said to be sufficient. Most Japanese schools are now closing when the influenza-related absentee rate is over 10%. The results of our EID study of intervention in the early stages of an outbreak support these recommendations.

As stronger and more serious pandemic influenza strains may appear in the near future, this H1N1 outbreak is providing good practice for discussing strategies for controlling outbreaks. It has also reconfirmed that "school closure" is an important measure in pandemic planning. As schools are at the center of communities in most countries, society type may affect the efficacy of school closure as a strategy for controlling disease outbreaks. More studies from different areas might be needed to formulate evidence-based "school closure," which would support pandemic planning.

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(http://www.hsph.harvard.edu/research/takemi/)

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