Original Article

Simulation Model of Pandemic Influenza in the Whole of Japan

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SUMMARY: An influenza pandemic—an outbreak of a novel influenza virus that spreads around the world—is a real threat. To predict the spread of an influenza pandemic across the whole of Japan, this study applies a real individual-based model (ribm) to the whole of Japan and simulates how a single case of influenza could spark pandemic influenza throughout Japan. We used Person-Trip (PT) data for nine regions (the Tokyo metropolitan area, Kansai, Chukyo, Fukuoka, Sendai, Sapporo, Miyazaki, Okinawa, and northern Ibaragi). PT data were collected from randomly chosen persons and contain information on their locations and their uses of all transportation modes including trains, cars, buses, bicycles, and walking. In total, the nine regions have a population of about 72 million, of whom more than 2.2 million individuals participated in the PT surveys. Estimates on the probability of movement among the nine PT regions are based on the results of the Third National Survey for Movement in 2003. Disease transmission in each region or on a train is assumed to occur within a 1-m radius. The approximate numbers of new cases arising on day 14 after the arrival of the first infected person are estimated to be 322,000 in Tokyo, 25,000 in Kansai, 4,800 in Chukyo, 3,600 in Sapporo, 2,600 in Fukuoka, 600 in Sendai, 17 in Okinawa, and 300 in Miyazaki. The disease seems to spread more slowly in smaller cities such as Miyazaki and Okinawa than in big cities such as Tokyo and Kansai. Area quarantines may help to contain outbreaks in smaller cities, but probably not in larger cities. Because this study demonstrates that ribm is useful for simulating the spread of pandemic influenza in Japan, it is hoped that this modeling technique will be used in the creation of preparedness plans.

INTRODUCTION

An influenza pandemic is an epidemic of the influenza virus that spreads on a worldwide scale and infects a large proportion of the human population. Pandemic influenza begins when people become infected with or sick from a new influenza virus, or one that had not previously been harmful to people. Because the virus is new to everyone, no one is immune and everyone is at risk of contracting the disease. Thus this type of influenza spreads easily from person to person and can cause many people to become very ill or die.

Pandemic influenza may come and go in waves that can last for months at a time. In contrast to the regular seasonal epidemics of influenza, these pandemics occur irregularly and may cause high levels of mortality. Over the last 100 years, there have been three influenza pandemics, the most serious of which was the Spanish Flu of 1918. It caused the deaths of more than 40 million people worldwide. The pandemic influenza pandemics of Asian Flu in 1957 and Hong Kong Flu in 1968.

It is not known when the next influenza pandemic will occur or how severe it will be. The World Health Organization (WHO) warns that there is a substantial risk of one within the next few years. Such an outbreak would cause a large number of people, including children and young adults, to fall ill and possibly die. It would also have a significant negative impact on society, possibly to include restricting travel, altering normal business operations, and dismissing students from schools to slow the spread of infection. Thus, in addition to its impact on human health, the possibility of pandemic influenza presents a major threat to the world economy.

Research on this topic is therefore extremely urgent, and a considerable number of studies have already been conducted. Many of the recent studies on pandemic influenza and its spread have used the individual-based model (ibm) (1-8); two very well-known examples are the papers by Ferguson et al. (6) and Longini et al. (5), both of which are cited in the WHO containment strategy and in the United States’ pandemic plan. No matter how finely we can construct such models, however, they are only models—they are only hypothetical, and they cannot mimic the real world precisely. Moreover, the models so far proposed do not take into account exposure among people commuting by train, which is a very popular and very crowded means of transportation in Tokyo and other large cities in Asia. Germann et al. (7) and Ferguson et al. (8) have constructed models for the United States and the United Kingdom, respectively, but both of these studies ignore commuting as a possible risk factor. In contrast, our new model, real individual-based model (ribm) (1), was designed from an urban-engineering perspective. It uses real data on transportation modes and locations, and simulates the diffusion of an infectious disease through human travel. Thus it has the potential to be the finest and most realistic mathematical model of the spread of infectious disease.

ribm has already been used in the formulation of preparedness plans for pandemic influenza or bio-terrorism attacks in the Tokyo metropolitan region (1). The present paper applies ribm to the whole of Japan. Specifically, it simulates how an initial case in Tokyo could spread to the other regions of Japan. We believe this information will be useful in creating a nationwide preparedness plan for pandemic influenza and/or bio-terrorism. For this purpose, we have been permitted to use Person-Trip (PT) data from the following nine regions: Tokyo metropolitan region, Kansai, Chukyo, Fukuoka, Sendai, Sapporo, Miyazaki, Okinawa, and northern Ibaragi. Since...
no previous studies have concentrated on the transmission of the influenza virus in crowded trains, though Mangili and Gendreau have reported on disease transmission in airplanes (2), this study focuses especially on how pandemic influenza may spread in trains. It is our goal that this study will help the government of Japan and policymakers to formulate a preparedness plan for all of Japan.

MATERIALS AND METHODS

The PT data for each region contain data on all transportation modes, including cars, trains, buses, bicycles, and walking, as well as on the locations of a number of randomly chosen persons in that region. For example, in the case of the Tokyo metropolitan region, which has a population of 33 million, about 0.88 million randomly chosen persons participated in this survey. In other words, the actual behavior of about 2.70% of the population was surveyed for urban planning purposes. The information gathered includes all of the transportation modes used and all of the locations occupied in one day by all family members over the age of 5 years. Each location is reported as one of 1,648 zones, each of which is 1 km² on average, and each place within each location is reported as either a household, school, workplace, or other. Moreover, if one or more family members rode a train that day, we know the name of the station where they boarded the train and where they deboarded, as well as their departure and arrival times.

In addition to the Tokyo metropolitan region, this study used PT data from Kansai, which has a population of 19.20 million; Chukyo, 9.54 million; Fukuoka, 4.80 million; Sendai, 1.55 million; Miyazaki, 0.50 million; Okinawa, 1.00 million; Sapporo, 2.30 million; and northern Ibaragi, 0.90 million. In total, these regions have a population of about 72 million. The survey year, survey items, and sampling rate were not the same among the regions, but they were similar enough that, in principle, the resulting data should be comparable to those obtained for the Tokyo metropolitan region. More than 2.20 million individuals participated in these surveys.

The survey results have allowed us to pinpoint the locations of all participating individuals every 6 min. Location is defined as the zone that a person occupies and/or the train that he or she takes. Using this information, we are able to determine how many other people each of these individuals comes into contact with, in their own households and in other locations including trains. Moreover, we assume movement among the nine PT regions using the probabilities reported by the third National Survey for Movement in 2003, conducted by the Ministry of Land, Infrastructure, Transport and Tourism. Assumptions about each patient’s history, the time at which each patient is infected, the rate of infection among asymptomatic patients, and the typical withdrawal rate are borrowed from our own previous research (1). The basic reproduction number (R₀) at home or in a specific area is also assumed to be the same as in the previous research, namely, 1.60–2.40. Transmission in each location or train is assumed to occur within a 1-m radius. In the case of the Tokyo metropolitan region, which is divided into zones, contact in a particular zone is estimated to be n × 3.14 × 37.00/1,000², where n is the number of people in that zone at a given time, 37.00 is the reciprocal number of the sampling rate, which is 2.70% for the Tokyo metropolitan region, and 1,000² is the area of an average zone in square meters. Likewise, contact on a train is defined as n × 3.14 × 37.00/1,200, where n is the number of people on that train at a given time, and 1,200 is the total area of the train, assuming each train car has an area of 4 m × 30 m and that each train in a large city has 10 cars. In the case of smaller cities, we assume that each train has 2 cars rather than 10. We calculate the transmission probability in buses in the same way; the area of each bus is assumed to be 30 m². These calculations reflect assumptions about transport in the Tokyo metropolitan region. Our assumptions about the average zone size and the average number of cars in each train are adjusted to match the situation in each of the other eight regions for which PT data were available.

The probability of transmission is assumed to be 100 × α% for a person who is around a symptomatic patient for more than 1 h within a distance of 1 m, where α is infectiousness at home or in that area. The probability is assumed to decline in proportion to the length of time the person is around the patient: for example, if the person were to stay around the patient for 6 min, the probability of infection is assumed to be 10 × α%. Assumptions about each patient’s history, the period when the patient is infectious, the rate and level of infectiousness of asymptomatic patients (2), and the withdrawal rate (3) are borrowed from previous studies. Because the value of α is determined by these parameters, the R₀ at home or in an area is the same as in those previous studies, namely, 1.6–2.4 (4-10). Yet because our model factors in the risk of infection in crowded trains, we assume a higher value of R₀ than the previous studies did.

We have performed a simulation assuming the following scenario: the initial case is infected in an affected area outside Japan on day 1, then returns to Japan on day 3. This person then infects her or his family (henceforth we assume this person is male) residing in Hachioji, one of the largest bedroom communities in the Tokyo region. His workplace is proposed to be at Marunouchi, one of the biggest business centers in Tokyo, which is more than 90 min from Hachioji by heavily crowded train. He commutes by train on day 4, when he is exhibiting symptoms. On day 5, he visits a doctor. The doctor suspects H5N1 based on his travel history and orders tests from the local public laboratory. At least 1 day will pass before the test results can be obtained, and thus any response aiming to contain the spread of the disease could start no sooner than day 6 even if such decisions are made as quickly as possible.

Some simulation results are shown in the maps below. These were generated using ArcGIS with map information from numerical map 25000, produced by the Geographical Survey Institution of the Japanese Ministry of Land, Infrastructure, Transport and Tourism, and with prefecture map information produced by ESRI Japan.

RESULTS AND DISCUSSION

Figure 1 shows the locations of the nine PT regions. Figure 2 indicates the location of the initial case at Hachioji. Figures 2 to 13 show the locations of cases newly infected on days 3 to 14 after the initial case was infected. The first new cases in Kansai, Chukyo, Fukuoka, Sendai, and Miyazaki appear on day 8, and those in Okinawa and Sapporo appear on day 9. The approximate numbers of new cases appearing on day 14 are estimated to be 322,000 in Tokyo, 25,000 in Kansai, 4,800 in Chukyo, 3,600 in Sapporo, 2,600 in Fukuoka, 600 in Sendai, 17 in Okinawa, and 300 in Miyazaki.

It has been proposed that the initial case visits a doctor on day 5 and that the response starts as soon as possible on day 99.
Fig. 1. The nine regions for which Person-Trip (PT) data were available. We used PT data from the regions of (clockwise from upper right) Sapporo, Sendai, Tokyo (along with northern Ibaragi), Kansai, Okinawa, Miyazaki, Fukuoka, and Chukyo.

Fig. 2. Day 3 after initial case is infected. This figure and the following show the locations of new infection on the stated day as circles centered on their home addresses. The size of each circle indicates the number of newly infected people at that location. Figure 2 shows the locations of new infections 3 days after the initial case was infected.

7. Nevertheless, the geographic diffusion of the influenza soon expands to the whole of the Tokyo metropolitan region, as shown in Figure 7. It would obviously be very difficult to prevent the spread of influenza outside Tokyo by enforcing a quarantine there. It would be nearly impossible to restrict the movement of so many people, and the smaller quarantines proposed in previous studies (2–4), containing areas 5.00 to 20.00 km in radius, would fail to contain the disease. Moreover, starting on day 8, newly infected cases appear in other cities, and by day 9, newly infected cases appear in Sapporo.
and Okinawa. Because the initial case is not detected until day 6, there is only 1 day between its detection and the appearance of the first cases in other cities, and this is not enough time to put a quarantine into effect. Thus it is probably not feasible to place a quarantine in Tokyo. Other regions, however, might benefit from a quarantine: in smaller cities like Miyazaki and Okinawa, the disease seems to spread more slowly than it does in big cities such as Tokyo or Kansai. Quarantines in these regions may help to contain the local outbreaks.

This simulation has many limitations. First, due to the limits of our computational resources, we cannot simulate the whole course of an influenza pandemic. Though the early phase is regarded as the most important period to plan for, the entire
duration and specifically the time when the number of cases peaks are also important. To properly evaluate the entire course of the pandemic will require more computer resources and the efficient use of parallel computing.

A second limitation is that the effects of countermeasures such as antiviral prophylaxis, school closures, and/or vaccinations have never been examined. The estimated effects of these actions on a pandemic are usually taken into account in the formation of preparedness plans by individual countries and by WHO. In principle, we can factor these elements into our model as well, but we must caution that including countermeasures in a model makes it even more necessary for that model to simulate the entire course of an influenza pandemic, for, although effective countermeasures may reduce the in-
Fig. 7. Day 8 after initial case is infected. This figure shows the locations of new infections 8 days after the initial case was infected. Note that the disease has now spread to other cities.

Fig. 8. Day 9 after initial case is infected. This figure shows the locations of new infections 9 days after the initial case was infected.

tensity of a pandemic’s peak, they can also sometimes extend its duration, and we will not be able to observe their overall effect if we cannot simulate the whole course of the pandemic.

Moreover, the results of other simulation studies are usually shown as averages, with distributions, of the results obtained in several iterations. As mentioned above, our computer resources are limited; we were not able to perform several iterations of our simulation. This is a particularly significant limitation in ribm, because variation in the assumed scenario of the initial case is a potential source of variation in the outcome. To overcome this limitation, we must gain access to increased computer resources and make use of parallel computing. Even with our present resources, however, we can guess that, although the timing of the peak may
vary among the iterations, the number of cases at the peak of the pandemic and the cumulative total number of infected persons will vary less, because these outcomes are more strongly influenced by such factors as city layouts and transportation patterns.

In addition to correcting these limitations, a natural next step in our research is to extend our application of ribm to other regions of the country. Yet because PT surveys have not yet been conducted in other regions, we must find another way to acquire data on commuting and transportation. One option is to obtain such data from certain censuses that record means of commuting from home to school or workplace and that classify this information by city or town. We must find a way to extend ribm to regions without PT data if
our research is to be useful on a nationwide scale. This study applied ribm to a potential influenza pandemic in Japan. ribm offers the most realistic simulation of the speed and direction of the spread of infection, and it is hoped that this study will encourage its use in the creation of preparedness plans for pandemic influenza (11).

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REFERENCES


