Abstract

Background: Pandemic influenza, that is, the outbreak of a novel influenza virus that spreads around the world, is a real threat. In order to estimate the spread of pandemic influenza through the whole of Japan, this study applies real individual based model (ribm) to the whole of Japan and simulates how pandemic influenza could diffuse through Japan from the introduction of the first case.

Methods: We used Person-Trip (PT) data for nine regions (the Tokyo Metropolitan area, Kansai, Chubu, Fukuoka, Sendai, Sapporo, Miyazaki, Okinawa, and Northern Ibaragi). PT data is collected from randomly chosen persons and contains information on their locations and their use of all transportation modes including trains, cars, buses, bicycles, and walking. In total, the nine regions have a population of about 72 million; out of these, more than 2.20 million individuals participated in the PT surveys. The probability of movement among the nine PT regions is estimated based on the results of the Third National Survey for Movement in 2003. Disease transmission in each region or in a train is assumed to occur within a 1 meter (1m) radius.

Results: The approximate numbers of new cases arising on day 14 after the first case was infected are estimated at 322000 in Tokyo, 25000 in Kansai, 4800 in Chuukyo, 3600 in Sapporo, 2600 in Fukuoka, 600 in Sendai, 17 in Okinawa, and 300 in Miyazaki. The spread of the disease seems to occur more slowly in smaller cities such as Miyazaki and Okinawa than in big cities such as Tokyo and Kansai.

Conclusion: Area quarantines may help to contain outbreaks in smaller cities, though they will probably not help in larger cities. Because this study demonstrates that ribm is useful in simulating the spread of pandemic influenza in Japan, it is hoped that this

modeling technique will be used in creating future preparedness plans.

1. 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 start to get infected by or sick from a new influenza virus 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 pandemic influenza. The Spanish Flu of 1918 was the most serious pandemic in recent history. It caused the deaths of at least over 40 million people worldwide. The most recent pandemic influenza were the Asian Flu in 1957 and the Hong Kong Flu in 1968.

It is not known when the next pandemic influenza will occur or how severe it will be. The World Health Organization (WHO) warns that there is a substantial risk of a pandemic influenza within the next few years. A pandemic influenza 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: it could require restrictions on travel, alterations to normal business operations, and dismissal of students from schools to help the slow the spread of infection. Thus, in addition to its impact on human health, the possibility of a pandemic influenza presents a major threat to the world economy.

Research on this topic is therefore extremely urgent and, accordingly, a considerable number of studies have already been conducted. Many of the recent studies on the pandemic influenza and spread of it have used 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 were cited in the WHO containment strategy and the pandemic plan of the US. 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 the practice of 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 US and the UK, respectively, but both of these studies ignore commuting as a possible risk factor. In contrast, our new 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 potential to be the finest and most realistic mathematical model of infectious disease.

ribm has already been used in the preparation of preparedness plans for pandemic influenza or a bio-terrorism attack in the Tokyo metropolitan region [1]. This paper applies ribm to the whole of Japan. Specifically, it simulates how an initial case in Tokyo could spread out into 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, Chubu, Fukuoka, Sendai, Sapporo, Miyazaki, Okinawa, and Northern Ibaragi. Since no previous studies have concentrated on the transmission of 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 be helpful to the government of Japan and to policy-makers in forming a preparedness plan for all of Japan.

2. Material and Methods

The PT data for each region contains data on all transportation modes, including cars, trains, buses, bicycles, and walking, as well as the location 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 33.00 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 5 years old. Each location is reported as one of 1,648 zones, each of which is 1 square kilometer ($1km^2$) on average, and each place within each location is reported as either 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 got the train and where they got off, and their time of departure and arrival.

In addition to the Tokyo Metropolitan Region, this study used PT data from Kansai, which has a population of 19.20 million; Chuukyo, which has a population of 9.54 million; Fukuoka, which has a population of 4.80 million; Sendai, which has a population of 1.55 million; Miyazaki, which has a population of 0.50 million; Okinawa, which has a population of 1.00 million; Sapporo, which has a population of 2.30 million; and Northern Ibaragi, which has a population of 0.90 million. In total, these regions have a population of about 72.00 million. Survey year, survey items, and sampling rate were not the same among the regions, but they are similar enough that, in principle, the resulting data should be comparable to that obtained for the Tokyo metropolitan region. More than 2.20 million individuals participated in these surveys.

The surveys have allowed us to pinpoint the location of all participating individuals every six minutes. 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 in contact with, in their own households and in other locations including trains. Moreover, we assume movement among the 9 PT regions using the probabilities reported by the third National Survey for Movement in 2003, conducted by the Ministry of Land, Infrastructure, Transportation, and Tourism. Assumptions about each patient's history, the time at which each patient is infected, the rate of infectiousness of asymptomatic patients, and the typical withdrawal rate are borrowed from our own previous research [1]. The basic reproduction number (R_0) 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-meter radius. In the case of the Tokyo Metropolitan Region, which is divided into zones, contact in a particular zone is estimated to be $n \times 3.14 \times 37.00/1000^2$, 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 1000^2 is the area of an average zone in square meters. Likewise, contact on a train is defined as $n \times 3.14 \times 37.00/1200$, where n is the number of people on that train at a given time, and 1200 is the total area of the train, assuming each train car has an area of 4m×30m and 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 $30m^2$. These calculations reflect assumptions about transport in the Tokyo metropolitan region; our assumptions about the average size of zones 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 was available.

The probability of transmission is assumed to be $100\times\alpha\%$ for a person who is around a symptomatic patient for more than one hour within a distance of less than 1m, where α is infectiousness at home or in that area. The probability is assumed to decline proportionally along with the length of time the person is around the patient: for example, if the person were to stay around the patient for 6 minutes, the probability of infection is assumed to be $10\times\alpha\%$. 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 R_0 at home or in an area is the same as in those previous studies, namely, 1.6-2.4 [4-8, 10]. Yet because our model factors in the risk of infection in crowded trains, we assume a higher value of R_0 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/his family residing in Hachiouji, one of the largest bedroom communities in the Tokyo region. Her/his workplace is proposed to be at Marunouchi, one of the biggest business centers in Tokyo, which is more than 90 minutes away from Hachiouji by heavily crowded train. This person commutes by train on day 4, when s/he is exhibiting symptoms. On day 5, s/he visits a doctor. The doctor suspects H5N1 from her/his travel history and orders tests from the local public laboratory. At least one 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, 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 and Transport, and with prefecture map information produced by ESRI Japan.

3. Results and Discussion:

Figure 1 shows the locations of the 9 PT regions. Figure 2 indicates the location of the initial case at Hachiouji. 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, Chuukyo, Fukuoka, Sendai, and Miyazaki appear on day 8, and those in in Okinawa and Sapporo appear on day 9. The approximate numbers of new cases appearing on day 14 are estimated to be 322000 in Tokyo, 25000 in Kansai, 4800 in Chuukyo, 3600 in Sapporo, 2600 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 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 movements 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 one 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 on 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 computation 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 counter-measures such as antiviral prophylaxis, school closures, and/or vaccinations have never been examined. The estimated effects of these counter-measures 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 counter-measures in a model makes it even more necessary for that model to simulate the entire course of an influenza pandemic, for, though effective counter-measures may reduce the intensity 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 the 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 this data from certain censuses which record methods of commuting from home to school or to workplace and which classify this information by city or town. Finding a way to extend ribm to regions without PT data is a challenge that we must overcome if our research is to be useful on a nationwide scale.

4. Conclusion

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.

Acknowledgements: The authors are very thankful to the Traffic Planning Committees in each of the 9 regions for permitting us to use their data in this study.

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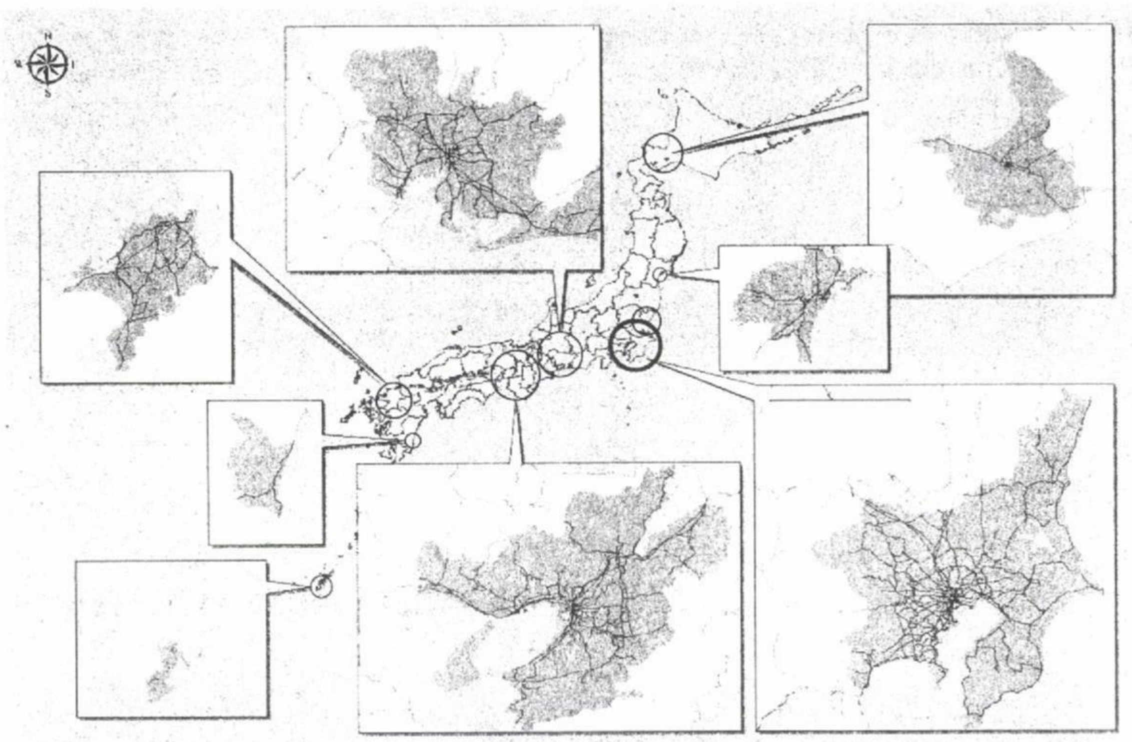

Figure 1: The 9 Regions for which PT data was available. We used PT data from the regions of (clockwise from upper right)**8** Sapporo, Sendai, Tokyo (along with Northern Ibaragi), Kansai, Miyazaki, Okinawa, Fukuoka, and Chuukyo.

Figure 2: Day 3 after initial case is infected. This figure and those following show the persons newly infected 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 persons newly infected 3 days after the initial case was infected.

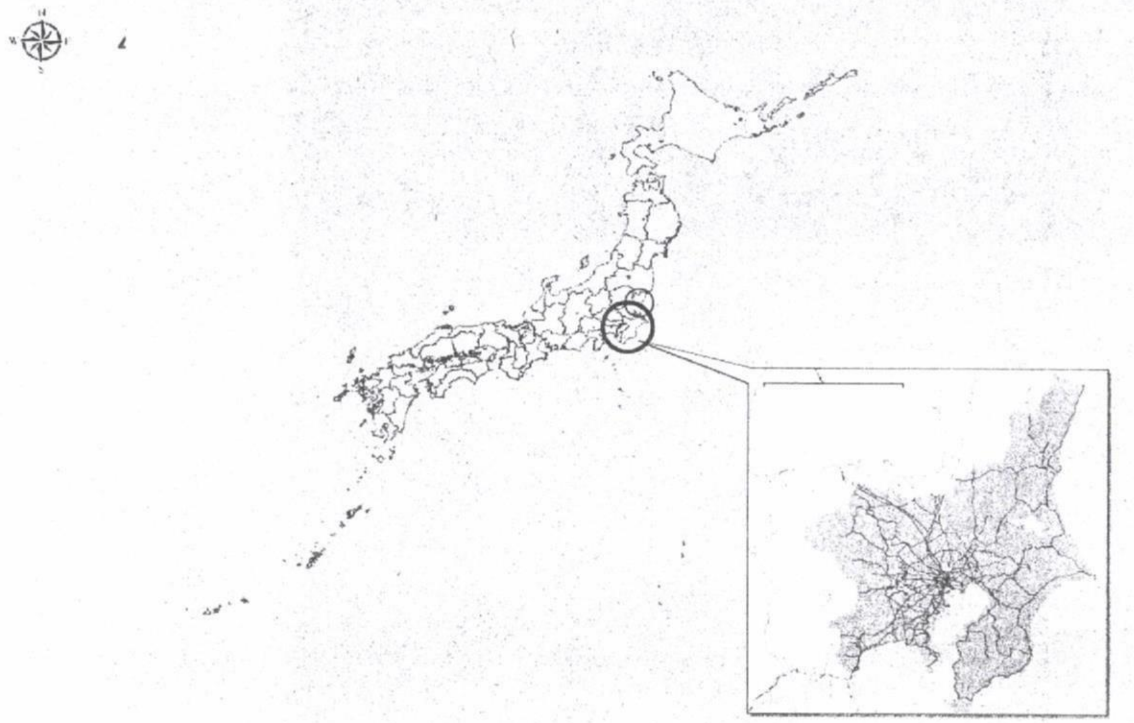

Figure 3: Day 4 after initial case is infected. This figure shows the persons newly infected 4 days after the initial case was infected.

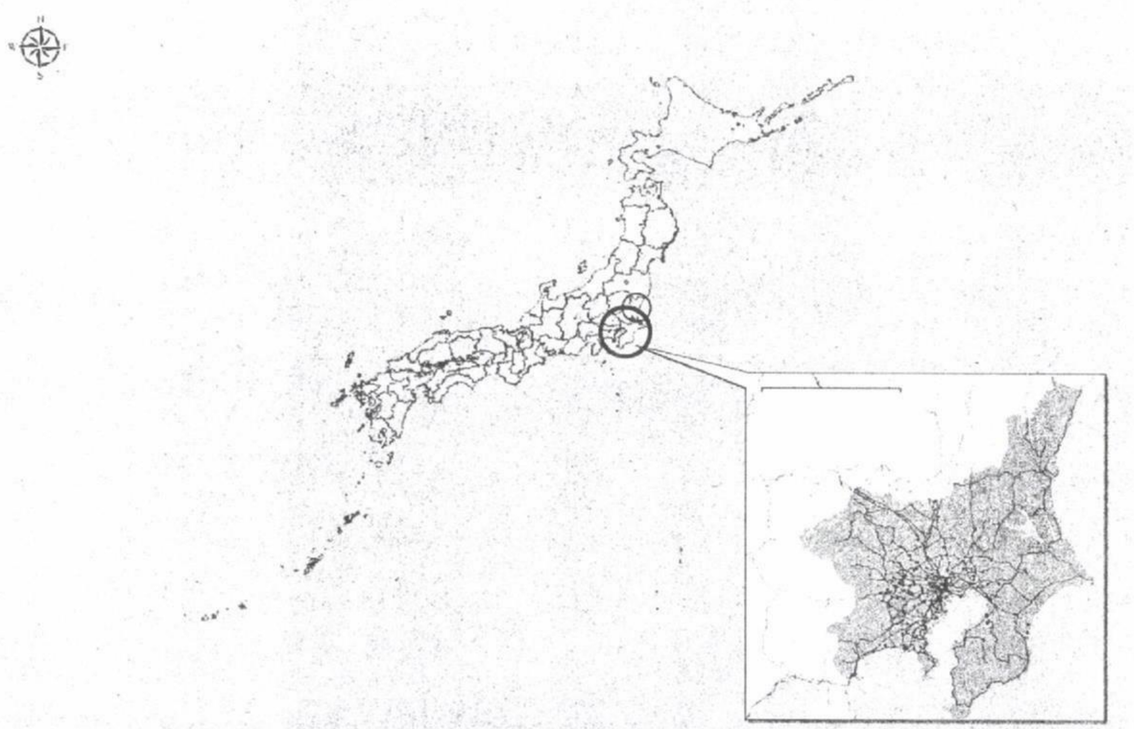

Figure 4: Day 5 after initial case is infected. This figure shows the persons newly infected 5 days after the initial case was infected.

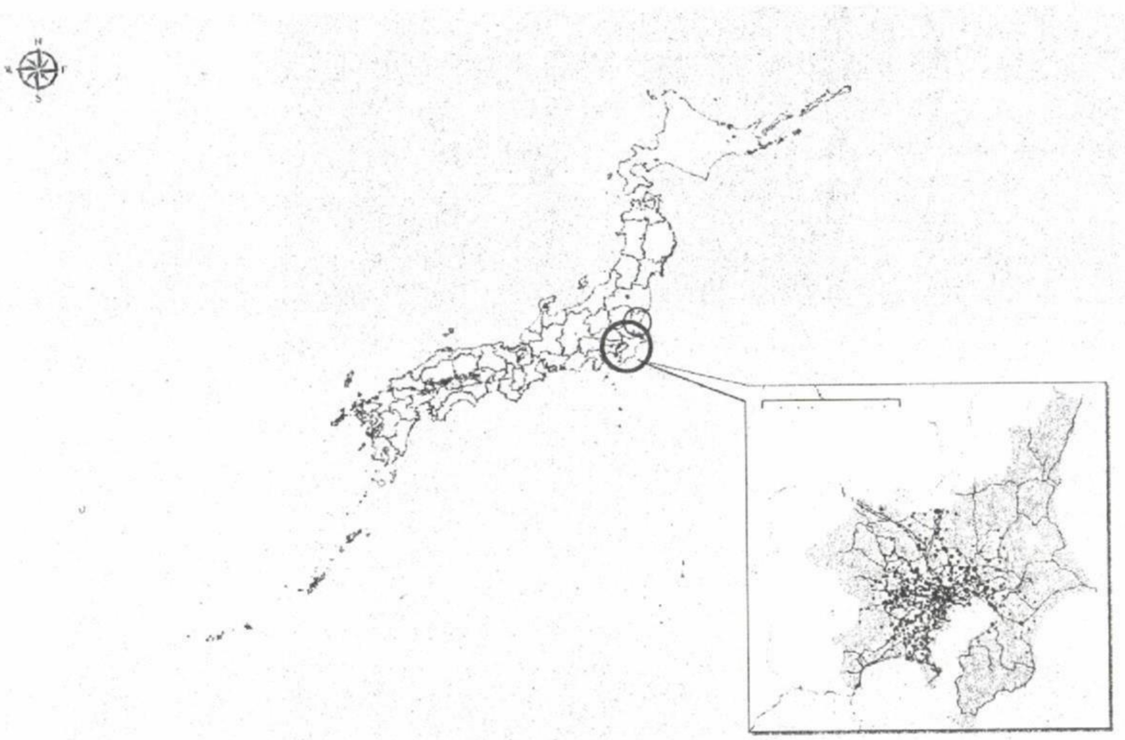

Figure 5: Day 6 after initial case is infected. This figure shows the persons newly infected 6 days after the initial case was infected. Note that, in our model, this is the earlier day on which the initial case could be diagnosed.

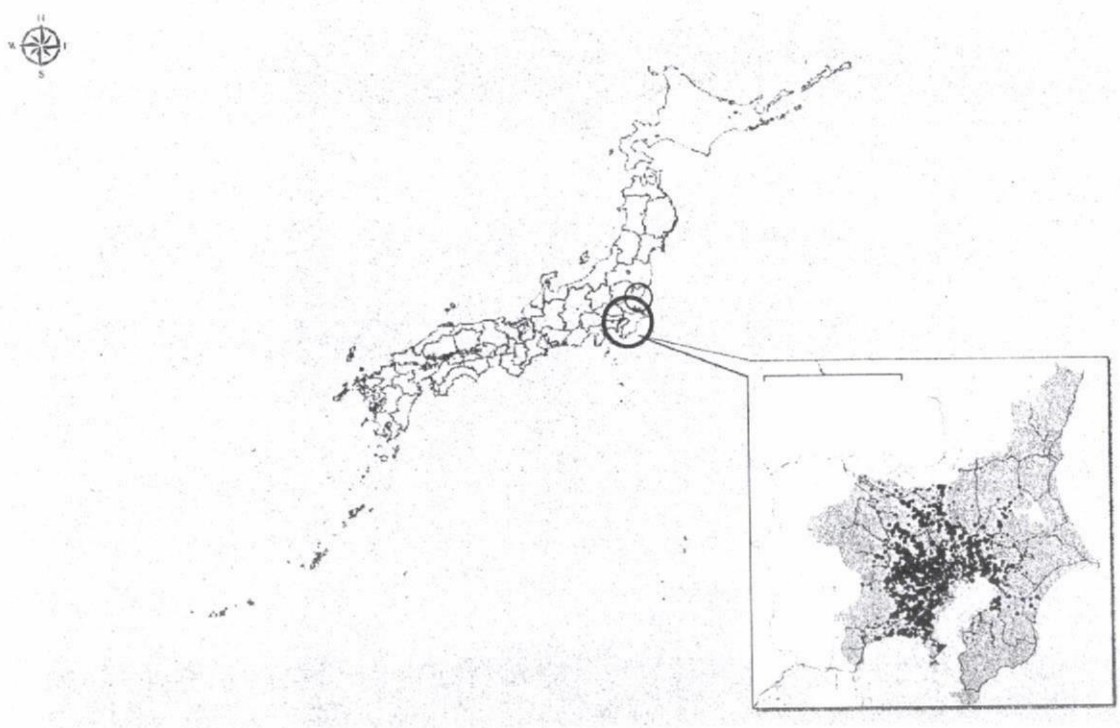

Figure 6: Day 7 after initial case is infected. This figure shows the persons newly infected 7 days after the initial case was infected.

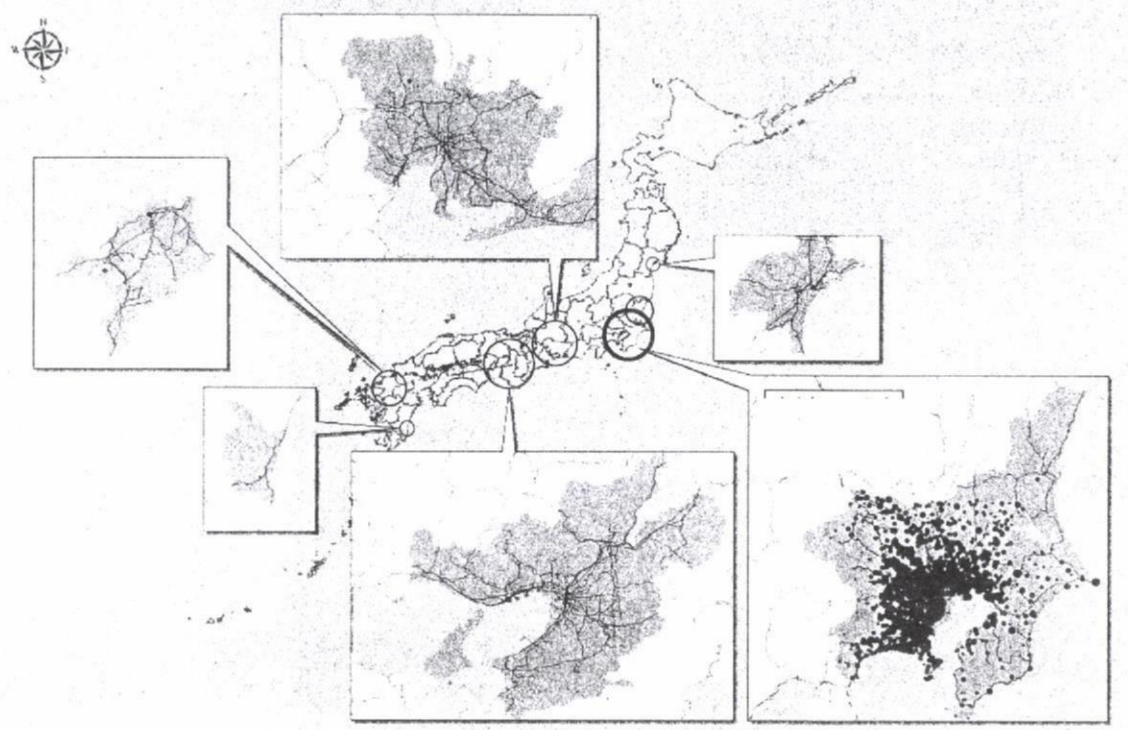

Figure 7: Day 8 after initial case is infected. This figure shows the persons newly infected 8 days after the initial case was infected. Note that the disease has now spread to other cities.

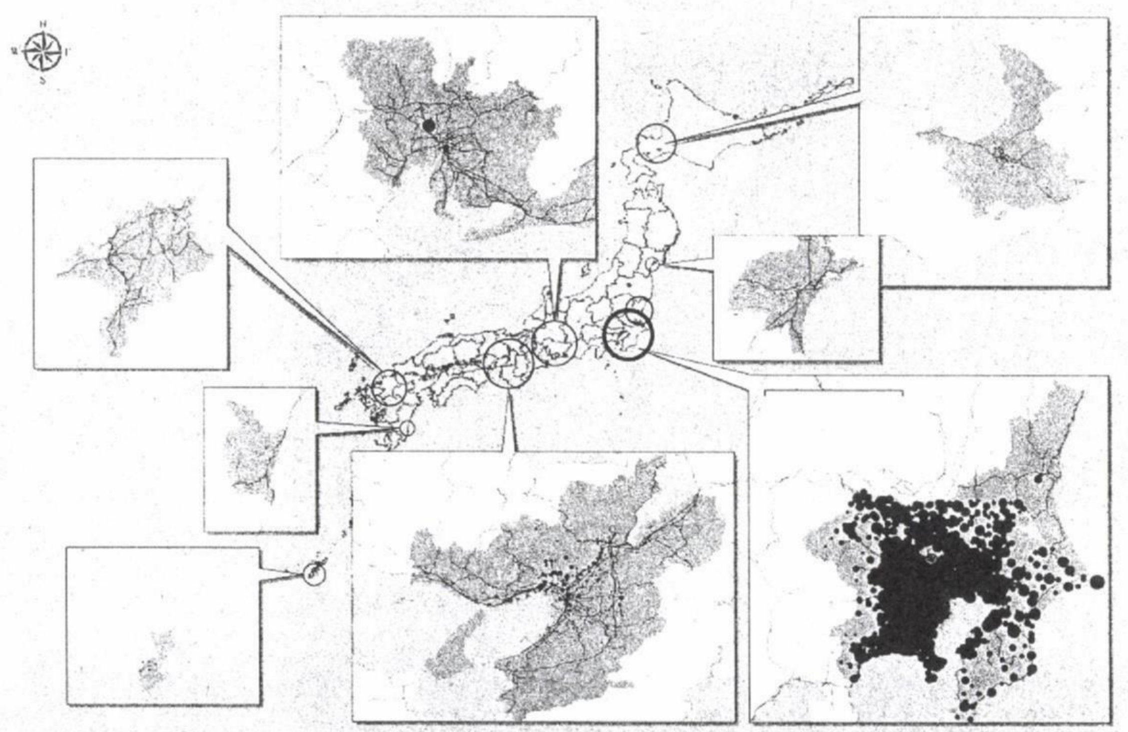

Figure 8: Day 9 after initial case is infected. This figure shows the persons newly infected 9 days after the initial case was infected.

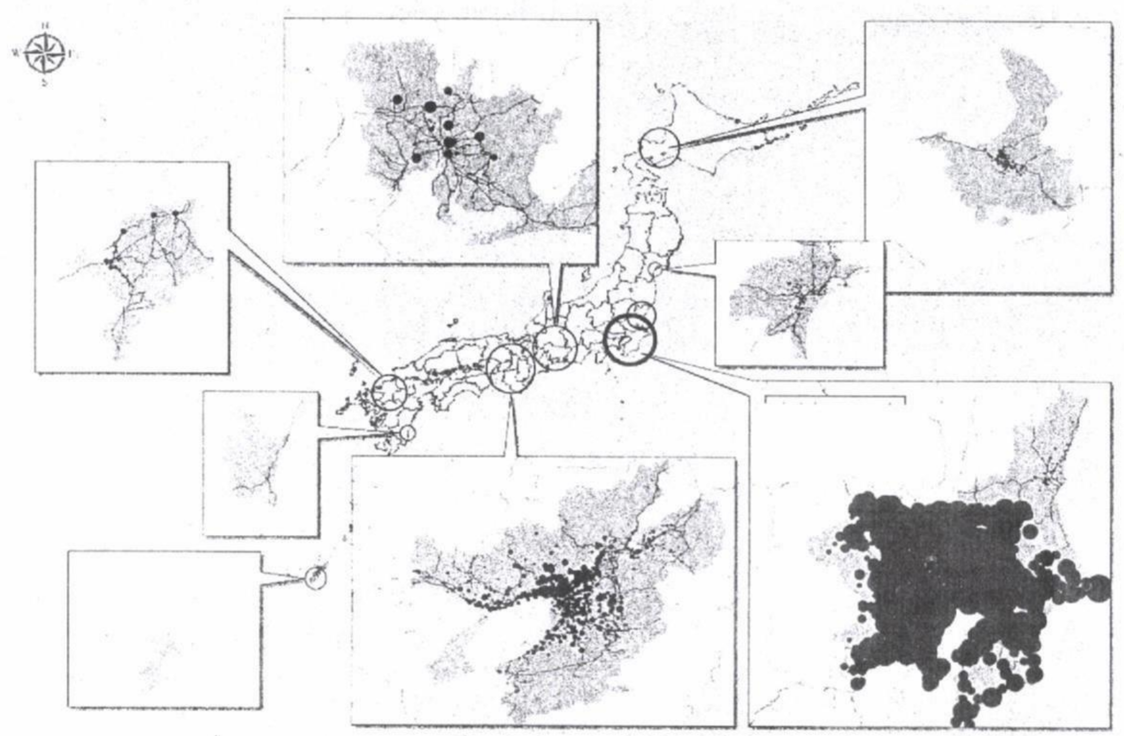

Figure 9: Day 10 after initial case is infected. This figure shows the persons newly infected 10 days after the initial case was infected.

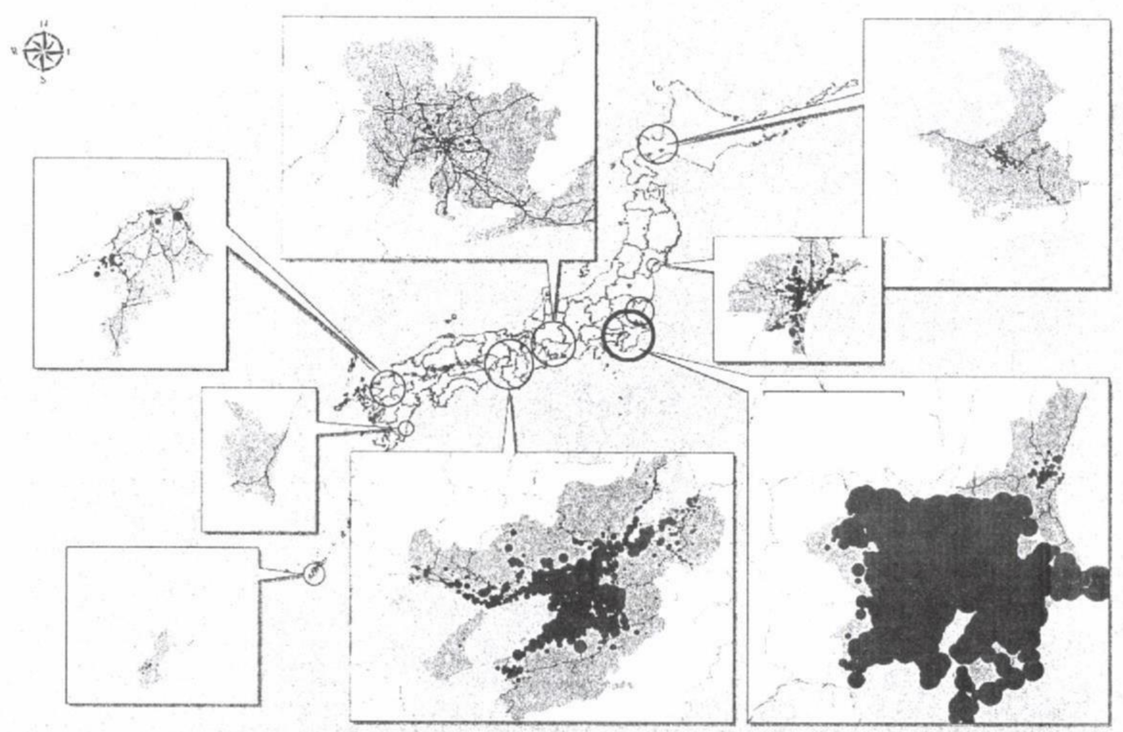

Figure 10: Day 11 after initial case is infected. This figure shows the persons newly infected 11 days after the initial case was infected.

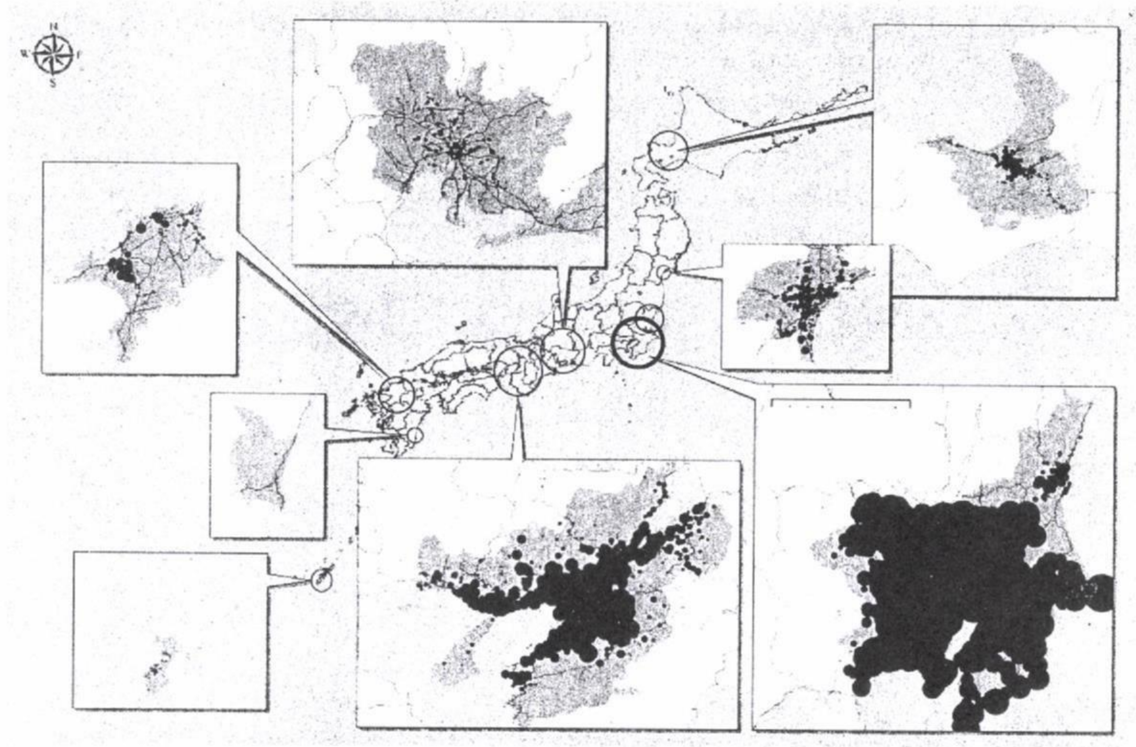

Figure 11: Day 12 after initial case is infected. This figure shows the persons newly infected 12 days after the initial case was infected.

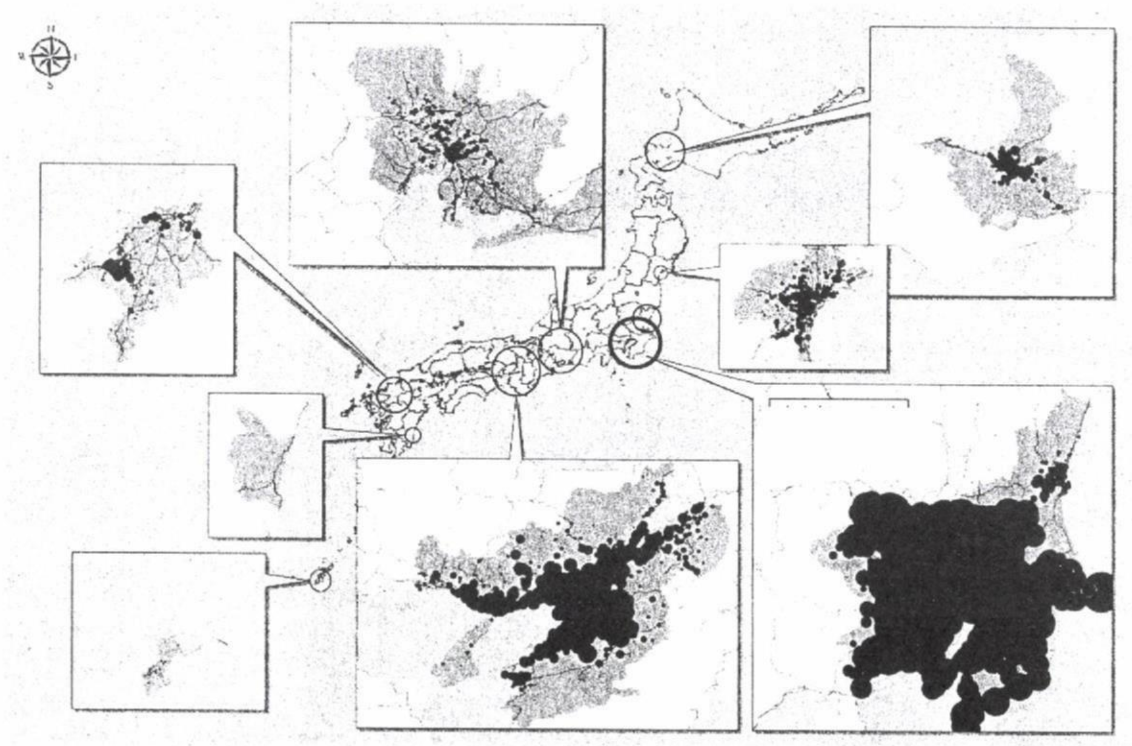

Figure 12: Day 13 after initial case is infected. This figure shows the persons newly infected 13 days after the initial case was infected.

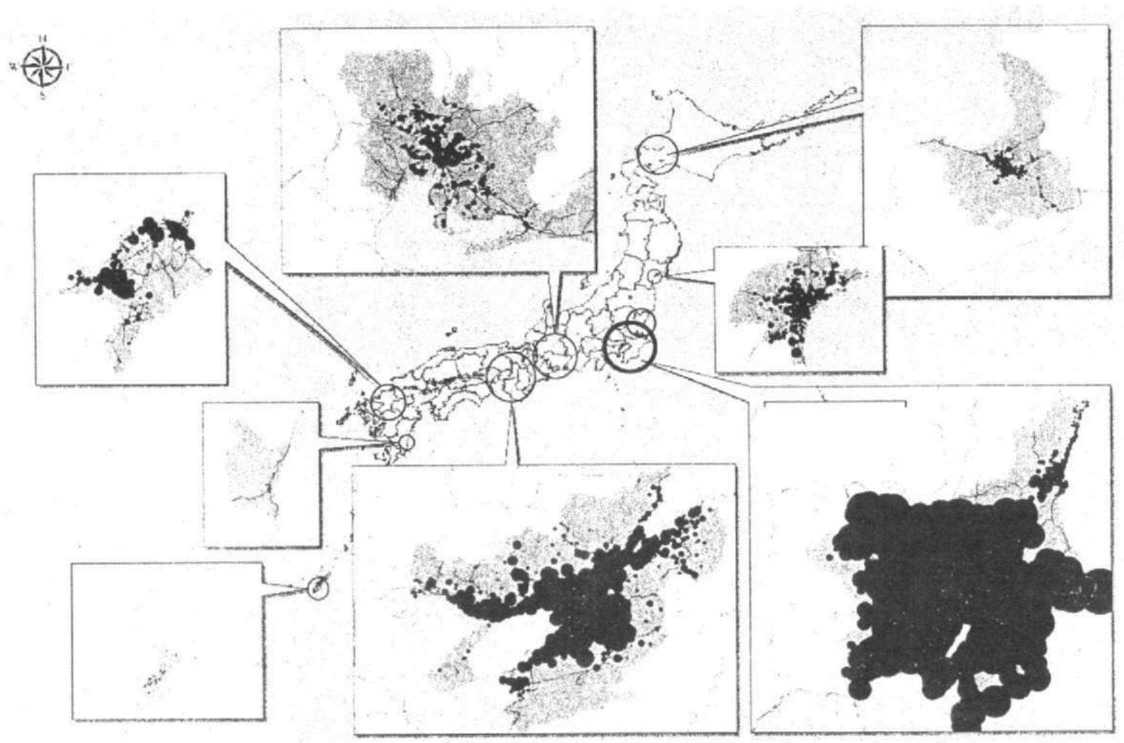

Figure 13: Day 14 after initial case is infected. This figure shows the persons newly infected 14 days after the initial case was infected.

Assessing the Potential Effectiveness of Shutting Down Transportation Systems to Contain Pandemic Influenza in a Megacity Area

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Abstract

This study was aimed at assessing the potential effectiveness of shutting down transportation systems against pandemic influenza and comparing this with the effectiveness of other measures, such as facility closure and area quarantine. An individual based model populated with 900,000 individuals was employed for this analysis. Shutting down the train system starting at a specified cumulative number of cases appeared to be 2.16% effective, but closing all facilities at the same threshold reduced the number of clinically apparent infections more efficiently. Moreover, if these measures are combined at an early stage of the epidemic, it was shown that the shutdown of transportation systems did not have particular influence on the number of cases. However, it was also demonstrated that the shutdown can increase the probability of successful containment by 20% if the transmission probability within trains is high compared to no transmission within trains.