



# Transmission and control of an emerging influenza pandemic in a small-world airline network

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## ABSTRACT

The avian influenza virus H5N1 and the 2009 swine flu H1N1 are potentially serious pandemic threats to human health, and air travel readily facilitates the spread of infectious diseases. However, past studies have not yet incorporated the effects of air travel on the transmission of influenza in the construction of mathematical epidemic models. Therefore, this paper focused on the human-to-human transmission of influenza, and investigated the effects of air travel activities on an influenza pandemic in a small-world network. These activities of air travel include passengers' consolidation, conveyance and distribution in airports and flights. Dynamic transmission models were developed to assess the expected burdens of the pandemic, with and without control measures. This study also investigated how the small-world properties of an air transportation network facilitate the spread of influenza around the globe. The results show that, as soon as the influenza is spread to the top 50 global airports, the transmission is greatly accelerated. Under the constraint of limited resources, a strategy that first applies control measures to the top 50 airports after day 13 and then soon afterwards to all other airports may result in remarkable containment effectiveness. As the infectiousness of the disease increases, it will expand the scale of the pandemic, and move the start time of the pandemic ahead.

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## 1. Introduction

In recent years emerging infectious diseases, such as the avian influenza, the 2009 swine flu and severe acute respiratory syndrome (SARS), have rapidly caused many infected cases in humans, negatively affecting human life and the economy. For example, SARS led to an immediate economic loss of close to 2% of the GDP for the East Asian region in the second quarter of 2003 (Brahmbhatt, 2005). Avian influenza virus H5N1 is a potentially serious pandemic threat to the human population (Ferguson et al., 2005). H5N1 may transform into a new human influenza virus through genetic reassortment, and develop the ability for increased and sustained transmission between humans (Capua and Alexander, 2002), possibly being as virulent as it is in the avian population. Most people are easily infected with this new type of influenza because they possibly have no immunity to the emerging disease. In addition, there is no vaccine available that provides effective protection against infection once the disease appears (Ligon, 2005), thereby resulting in a serious pandemic and then obstructing social and economic activities worldwide. Over the past decades, there have been a few

influenza pandemics that spread over the entire globe. The most noted influenza pandemic was the one beginning in 1918 with a mortality rate that resulted in the death of possibly 50 million people worldwide (Ligon, 2005). Influenza pandemics are a serious health threat. It is critical that one understands how an emerging influenza spreads, how to predict the result of a pandemic, and how to design control measures to mitigate the impacts of the disease.

A previous study of SARS indicated that passengers who took the same airplane flight with a SARS patient would possibly become suspect or probable cases of SARS (Centers for Disease Control and Prevention, 2003). Another study also indicated a high rate of transmission of SARS on aircraft (Olsen et al., 2003). These findings show that air travel facilitates the spread of infectious diseases. Although the influence of air travel has been observed in empirical work, past studies that developed mathematical epidemic models have rarely explored this topic, particularly for an emerging influenza. The aim of this study is to help close this gap in the literature.

This paper is different from past studies in that it aimed to explore the transmission of an emerging human influenza via air travel, and evaluate its dynamical evolution and spatial distribution in a small-world<sup>1</sup> airline network. We focused on the human-to-human transmission of influenza, and analyzed the effects of air

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<sup>1</sup> Watts and Strogatz (1998) demonstrate that many biological, technological and social networks in the real world are neither completely regular nor completely

travel activities, including passengers' consolidation, conveyance and distribution in airports and flights, on the influenza pandemic. The purpose of this paper is to develop dynamic transmission models to illustrate the transmission behaviors of the influenza virus in scheduled flights and airport terminals. For the realism of our models, links of the network were weighted by the flying time and the number of passengers, and different values of the infection parameters were designed for flights and airports. We also attempted to investigate how the influenza spreads to different geographic regions based on the connectivity properties of the small-world network. In order to provide helpful insights, the proposed models were further used to assess the expected burden of the influenza pandemic in the absence of control measures, as well as to evaluate the effectiveness of performing the control measures proposed by the present study.

In the literature, some studies have focused on reviewing infectious diseases and analyzing their impacts (Brahmbhatt, 2005; Capua and Alexander, 2002; Donnelly et al., 2003; Ligon, 2005; Meijer et al., 2004), as well as the design and evaluation of control measures (Ferguson et al., 2005; King et al., 2004). For example, Ferguson et al. (2005) modeled the spread of a pandemic in Thailand by incorporating random contacts associated with day-to-day movements to work within the country, and then evaluated the potential effectiveness of containment strategies. In addition, numerous studies have proposed mathematical epidemic models to evaluate and describe the dynamic evolution and the severity of epidemics in the population (e.g. Allen and Burgin, 2000; Colizza et al., 2006, 2007; Massad et al., 2005; Méndez and Fort, 2000), as well as in small-world networks following the work of Watts and Strogatz (1998) (e.g. Kuperman and Abramson, 2001; Saramäki and Kaski, 2005; Small and Tse, 2005). For example, Colizza et al. (2006, 2007) developed a metapopulation stochastic epidemic model on a global scale, and used a stochastic transport operator to describe the dynamics of individuals based on travels between cities. They concluded that a cooperative strategy where countries with large antiviral stockpiles share a part of their resources with other countries results in a global deceleration of the pandemics. However, our study focuses on exploring the influences of air travel activities (i.e. passenger consolidation, conveyance and distribution) and small-world properties of an air transportation network on the spatiotemporal evolution of an influenza pandemic. Few of the previous studies have discussed these issues in detail.

The remainder of this paper is organized as follows. The next section investigates and formulates transmission models on the effects of air travel activities, including passengers' consolidation, conveyance and distribution in airports and scheduled flights. The influence of small-world properties as well as the design and practice of control measures are also discussed in this section. Section 3 presents a case study to demonstrate the effectiveness of the proposed model, and shows the dynamic evolution and spatial distribution of the influenza. Finally, concluding remarks are presented in Section 4.

## 2. Model formulation

This study focuses on the human-to-human transmission of an emerging influenza in a small-world airline network denoted as **G**.

random, but lie somewhere between these two extremes, and refer to them as small-world networks. The structural properties of these networks are quantified by the characteristic path length and clustering coefficient. They also predicted that infectious diseases spread much more easily and quickly in a small-world network than in a regular graph. However, they did not explicitly consider the effects of air travel on an influenza pandemic, and not theoretically formulate the transmission between persons.

In **G**, an airport is defined as a node, and a set of nodes is denoted as **V**. Furthermore, a passenger-flight operated between two airports is defined as a link, and a set of links is denoted as **E**. This study discusses the transmission of influenza between humans occurring in flights and airport terminals, respectively, and formulates two sub-models of transmission for these two situations. Previous studies (Industrial Technology Research Institute, 2005; Zhang, 2005) have recently shown that H5N1 may transmit the influenza virus during the incubation period. As a result, this study applies the susceptible-infected (SI) epidemic model to investigate the transmission of influenza, where the population is partitioned into two possible states, susceptible (S), and infected (I) with infectiousness. There are three assumptions in the transmission model: (1) the influenza is transmitted by contact between an infected individual and a susceptible individual; (2) all susceptible individuals are equally susceptible and all infected individuals are equally infectious; and (3) each individual is initially susceptible to the influenza except for several individuals who are already infected. The first two assumptions are referred to Frauenthal (1980). Once a susceptible individual is infected, she/he becomes an infected individual. The proposed transmission model is derived as follows.

### 2.1. Flights

Based on the operating procedures of a flight, the sub-model for transmission occurring during a flight is further divided into three stages, departure from its origin airport (i.e. passenger consolidation), en route flying (i.e. passenger conveyance), and arrival at its destination airport (i.e. passenger distribution). Let us denote  $I_j(t)$  as the number of infected individuals on flight  $j$  ( $\in E$ ) at time  $t$ , and denote  $t_j$  as the time on which flight  $j$  departs from its origin airport. This study initially investigates the sources of infected individuals of a specific departure flight, one part coming from the upstream flights of the flight, and the other coming from the airport of origin of the flight. Therefore, the initial number of infected individuals on flight  $j$  at time  $t_j$ ,  $I_j^o$ , is defined by Eq. (1):

$$I_j^o \equiv I_j(t_j) = \sum_{j' \in U_j} \alpha_{jj'} \cdot I_{j'}^f + Z_j(t_j) \quad (1)$$

where subscript  $j'$  represents one of the upstream flights connectable to flight  $j$  at the origin airport of flight  $j$ , and the set of upstream flights of flight  $j$  is denoted as  $U_j$ ;  $I_{j'}^f$  is the number of infected individuals on flight  $j'$  when the flight arrives at its destination airport (i.e. the origin airport of flight  $j$ );  $\alpha_{jj'}$  is the proportion of infected individuals on flight  $j'$  who transfer to flight  $j$ ; and  $Z_j(t_j)$  is the number of infected individuals who board the airplane from the origin airport of flight  $j$  at time  $t_j$ . The characteristics and the complexity of land transportation system differ from those of the air transportation system. So, this study uses  $Z_j(t_j)$  to represent those infected individuals from the exterior community of airports, or those individuals from the exterior community who are infected within airports. It should be noted that  $I_j^o$  is not greater than the total number of passengers of flight  $j$ ,  $N_j$ . In addition, the second term of Eq. (1) is determined by Eq. (2):

$$Z_j(t) = v_j \cdot Y_{j^o}(t) \quad (2)$$

where subscript  $j^o$  ( $\in V$ ) represents the origin airport of flight  $j$ ;  $Y_{j^o}(t)$  is the cumulative number of infected individuals in the restricted areas of airport  $j^o$  at time  $t$ , and  $Y_{j^o}(t) \geq 0$ ; and  $v_j$  is the proportion of  $Y_{j^o}(t)$  who board flight  $j$ , and  $0 < v_j < 1$ . Eq. (2) implies that when the cumulative number of infected individuals at a specific airport increases, the possibility that a boarding passenger is an infected individual increases, thereby increasing the expected number of infected individuals who board the airplane at the airport.

After flight  $j$  departs, i.e. en route, the infected individuals will transmit the influenza to susceptible individuals in the cabin of the flight. Let  $S_j(t)$  denote the number of susceptible individuals in flight  $j$  at time  $t$ , and  $\beta$  denote the infection parameter, i.e. the average number of contacts that lead to infection per infected individual per susceptible individual per unit of time. Based on Daley and Gani (1999), the transmission model en route can be formulated as Eq. (3):

$$\frac{dI_j(t)}{dt} = \beta S_j(t) I_j(t) \tag{3}$$

where the right-hand side of the equation is the number of new infected individuals per unit of time in the airplane. Furthermore, since the total population size of flight  $j$  is always  $N_j$ , i.e. it is a closed population, and since all individuals are either susceptible or infected, the equation  $S_j(t) + I_j(t) = N_j$ . In Eq. (3),  $S_j(t)$  can then be replaced by  $N_j - I_j(t)$ , and Eq. (3) can be easily solved by separation of variables, leading to the exact solution of  $I_j(t)$ :

$$I_j(t) = \frac{I_j^0 N_j}{(N_j - I_j^0) \cdot \exp(\beta N_j(t_j - t)) + I_j^0} \tag{4}$$

where  $I_j^0$ , as defined in Eq. (1), is the initial number of infected individuals of flight  $j$  when the flight departs at time  $t_j$ , and is composed of the infected individuals coming from the upstream flights and from the origin airport. Eq. (4) shows that, as the elapsed time for flying increases, resulting in a longer duration during which susceptible individuals are more likely to be exposed to infected ones, the expected number of infected individuals increases. Furthermore, in the case where the flight arrives at its destination airport, let's denote  $F_j$  as the total elapsed flying time of flight  $j$ , and  $\bar{t}_j$  as the time flight  $j$  arrives at its destination airport, i.e.  $\bar{t}_j = t_j + F_j$ . Then at time  $\bar{t}_j$ , the final total number of infected individuals in the cabin of flight  $j$ ,  $I_j^f$ , is as follows:

$$I_j^f \equiv I_j(\bar{t}_j) = \frac{I_j^0 N_j}{(N_j - I_j^0) \cdot \exp(-\beta N_j F_j) + I_j^0} \tag{5}$$

Eq. (5) shows that a link of the network is weighted by the flying time and the number of passengers at the same time. This consideration is different from previous studies (e.g. Colizza et al., 2006), and is more approximate to the real world. After arriving at the destination airport, those infected individuals of flight  $j$  who further transfer to subsequent flights will temporarily stay at the restricted areas of transit terminals, and they may transmit the influenza to susceptible individuals within these places. The new infected cases caused by these transfer passengers with infectiousness inside the restricted areas of the terminals are discussed as follows.

### 2.2. Airport terminals

In airport terminals, we focused on investigating the transmission occurring within the restricted areas of the terminals, while the transmission on other parts of terminals was beyond the research scope of this study. Let  $j^d(\in \mathbf{V})$  denotes the destination airport of flight  $j$ , and  $\rho_{j^d}$  denote the average number of contacts that lead to infection per infected individual per unit of time within the restricted areas of the terminals of airport  $j^d$ . In this study  $\rho_{j^d}$  depends on the total number of passengers of the airport. That is, as the total number of passengers of the airport increases, the number of contacts between susceptible individuals and infected individuals increases, thereby causing more new infected individuals. After flight  $j$  arrives at destination airport  $j^d$ , those infected individuals of flight  $j$  who stay and wait for transfer may start to transmit the influenza within the restricted areas. Let's denote  $X_{j^d}(t)$  as the number of infected individuals within the restricted areas of

destination airport  $j^d$  at time  $t$ . Then the transmission model within the restricted areas can be formulated as Eq. (6) based on Frauenthal (1980):

$$\frac{dX_{j^d}(t)}{dt} = \rho_{j^d} X_{j^d}(t) \tag{6}$$

Since the total population size within the restricted areas changes with time and the number of susceptible individuals is unknown, Eq. (3) is not appropriate herein for describing the transmission, and if applied cannot be solved. On the contrary, the use of Eq. (6) can depict the generation of the new infected cases by infected individuals and the evolution of transmission within the restricted areas. Let  $\hat{j}$  be one of the downstream flights connectable to flight  $j$ ,  $L_j$  the set of the downstream flights of flight  $j$ , and  $\lambda_{\hat{j}j}$  the proportion of  $I_j^f$  who stay and wait for transferring to flight  $\hat{j}$ . At time  $\bar{t}_j$  when flight  $j$  arrives at airport  $j^d$ , it yields  $X_{j^d}(\bar{t}_j) = \sum_{\hat{j} \in L_j} \lambda_{\hat{j}j} I_j^f$ ,

where the right-hand side is the total number of infected individuals of flight  $j$  who will further transfer to downstream flights. For those passengers of flight  $j$  whose final destination is airport  $j^d$ , since they stay at the restricted areas for a relatively shorter time than the transfer passengers, their transmission is not considered in this study, though it should be a subject for future research. Solving Eq. (6) by separation of variables and the condition  $X_{j^d}(\bar{t}_j) = \sum_{\hat{j} \in L_j} \lambda_{\hat{j}j} I_j^f$

leads to the exact solution of  $X_{j^d}(t)$ :

$$X_{j^d}(t) = \sum_{\hat{j} \in L_j} \lambda_{\hat{j}j} I_j^f \cdot \exp[\rho_{j^d}(t - \bar{t}_j)] \tag{7}$$

Nevertheless, for each downstream flight  $\hat{j}$ , the waiting times  $W_{\hat{j}}$  differ. Consequently, Eq. (7) can be further revised as follows:

$$X_{j^d}(t) = \sum_{\hat{j} \in L_j} \{\gamma_{\hat{j}} \lambda_{\hat{j}j} I_j^f \cdot \exp[\rho_{j^d}(t - \bar{t}_j)] + (1 - \gamma_{\hat{j}}) \lambda_{\hat{j}j} I_j^f \cdot \exp[\rho_{j^d} W_{\hat{j}}]\} \tag{8}$$

where  $\gamma_{\hat{j}}$  is an indicator variable,  $\gamma_{\hat{j}} = 1$  if  $\bar{t}_j \leq t < \bar{t}_j + W_{\hat{j}}$ , and  $\gamma_{\hat{j}} = 0$  if  $t \geq \bar{t}_j + W_{\hat{j}}$ ; and  $\bar{t}_j + W_{\hat{j}}$  is the time at which downstream flight  $\hat{j}$  departs. Eq. (8) represents the fact that the infected individuals of flight  $j$  continuously transmit the influenza and cause new infected cases in the restricted areas until they depart from the airport by the downstream flights.

In addition, if several flights arrive at the same airport, called airport  $m (\in \mathbf{V})$ , then the infected individuals of these flights will collectively cause new infected cases in the restricted areas of the airport. In such case, let  $E^m$  represents the set of those flights whose destination airport,  $j^d$ , is airport  $m$ , and the cumulative number of infected individuals in the restricted areas of airport  $m$  up to time  $t$ ,  $Y_m(t)$ , can be formulated as Eq. (9):

$$Y_m(t) = Y_m(0) + \sum_{j \in E^m} [X_{j^d}(t) - \sum_{\hat{j} \in L_j} \lambda_{\hat{j}j} I_j^f] \tag{9}$$

where  $Y_m(0)$  is the initial number of infected individuals in the restricted areas of airport  $m$ . For each downstream flight of flight  $j$ , when it departs from airport  $j^d$ , Eq. (1) can be used to calculate its initial number of infected individuals, and the models developed above can also be used in turn to calculate the number of infected individuals in each circumstance. As a result, the influenza may be spread to various regions all over the globe because the infected individuals can inter-regionally transmit the influenza in the airline network via flights whose origin and destination airports are in nature located in different regions.

Based on the above proposed models, the cumulative number of infected individuals in the whole airline network up to time  $t$ ,  $I(t)$ , can be formulated as follows:

$$I(t) = N_o + \sum_{j \in E} \{ \phi_j [I_j(t) - I_j^o] + (1 - \phi_j) [I_j^f - I_j^o + X_{jd}(t) - \sum_{\hat{j} \in L_j} \lambda_{j\hat{j}} I_{\hat{j}}^f] \} \tag{10}$$

where  $N_o$  is the initial number of infected individuals in the network at time  $t=0$ ; and  $\phi_j$  is an indicator variable,  $\phi_j = 1$  if  $t_j < t < \tilde{t}_j$ , and  $\phi_j = 0$  if  $t \geq \tilde{t}_j$ . Moreover, in the network of worldwide airports the cumulative percentage of airports with infected cases occurring at time  $t$ ,  $H(t)$ , can be formulated as Eq. (11):

$$H(t) = \left( \frac{\sum_{m \in \mathbf{V}} \delta_m}{\|\mathbf{V}\|} \right) \times 100\% \tag{11}$$

where  $\|\mathbf{V}\|$  is the total number of airports in the network; and  $\delta_m$  is an indicator variable,  $\delta_m = 1$  if  $Y_m(t) > 0$ , otherwise  $\delta_m = 0$ . This study assumes that  $Y_m(0) = 0$  for all  $m \in \mathbf{V}$  except for the airport where the initial infected case(s) occurred. Eq. (11) indicates the geographic scope of the influenza transmission at time  $t$  around the network of airports worldwide. By employing a suitable simulation scheme, Eqs. (10) and (11) can be used not only to evaluate the dynamic evolution and spatial pattern of transmission, but also to assess the expected burdens of the pandemic with and without control measures imposed on the simulation of the case study. The simulation is discussed in detail later.

### 2.3. Small-world effects and control measures

The effects of the small-world properties of the airline network on the influenza transmission are discussed as follows. The small-world properties improve the connectivity efficiency of the airline network in two aspects. One is that the properties shorten passengers' travel time by introducing several inter-regional or inter-continental routes that mimic the function of shortcuts in a small-world network. They enable passengers to fly between airports that are located at different regions in an efficient way. The other is that the properties expand the destinations that passengers can reach by scheduled flights, i.e. passengers can further transfer to downstream flights in order to fly to other regions around the globe after they arrive at connecting airports. Nevertheless, the improved connectivity of the airline network contributed by the small-world properties also speeds up the transmission of the influenza in the network. In the absence of inter-regional routes, the infected individuals have a longer travel time for arriving at their destination airports, thereby slowing down the transmission of the influenza to these airports. However, by introducing the inter-regional routes, the flying time of infected individuals,  $F_j$ , can be substantially shortened. This makes the arrival time,  $\tilde{t}_j$ , earlier than before, and as shown in Eq. (8), advances the time at which  $X_{jd}(t) > 0$ , i.e. the influenza is transmitted more rapidly to the destination airports. It further makes  $I(t)$  of the transmission model in Eq. (10) increase more quickly. On the other hand, although the small-world properties expand the number of destinations that passengers can reach, the fact that the destination airports of flights are different from one another enables the infected individuals to spread the influenza to various regions worldwide via flights. In other words, the improved connectivity contributed by small-world properties expands the geographic scope of transmission, i.e.  $H(t)$  in Eq. (11).

In the case of SARS, Bell et al. (2004) pointed out that public health interventions, such as isolating case-patients, issuing travel advisories and screening passengers at international borders, controlled a global epidemic. They used several methods to screen

arrival and departure passengers, including visual inspection to detect symptoms and thermal scanning at international borders (e.g. airports and seaports). This study further designs a control measure to be carried out in airports to constrain the transmission of influenza and reduce its impacts. The control measure is that, the customs and public health officers must inspect all departure passengers at the entrances of restricted areas by such methods as temperature screening. Passengers will be quarantined as soon as their influenza symptoms are identified. This control measure will effectively reduce the possibility that infected individuals will board flights. That is, it decreases the initial number of infected individuals on flights at the departure time,  $I_j^o$ , and consequently, as shown in Eq. (4), diminishes the number of infected individuals on flights,  $I_j(t)$ . As a result, practicing the control measure mentioned above can reduce  $I(t)$  of the transmission model in Eq. (10), and mitigate the influenza transmission.

### 3. Case study

The following case study is presented to demonstrate the application of the proposed models. Since no data is available for large-scale networks, we use a network of previous research (Hsu and Shih, 2008) as our study object. This network covers a total of 265 nodes located throughout major continents, such as America, Asia, Europe and Oceania, and has 2488 links connecting its nodes. The online worldwide flight information provided on the Amadeus website ([www.amadeus.net](http://www.amadeus.net)) is used to determine the travel time of flights operated by different airlines. The one with the shortest travel time among all flights connecting two given nodes is selected to set the travel time between these two nodes. The network has been justified to be a small-world network in the literature (Hsu and Shih, 2008) by using global and local mobility. The procedures for performing the case study are discussed as follows.

First, we collect and then input flight data provided on the Amadeus website. Then, we establish the incidence matrix of nodes. If there are flights between two nodes, then the element of the matrix is equal to the travel time between them, otherwise, it is assumed to be infinite. Next, the parameters applied in the case study are  $N_o = 1$  (person);  $v_j = 0.6\%$ ; and  $\beta = 0.00017$  (per infected individual per susceptible individual per hour) adapted from the data by Ferguson et al. (2005). The value of  $\beta$  is assumed to be 2.5% of that used by Ferguson et al. (2005). Since the infectiousness of the emerging influenza is unknown, we use this underestimated value of  $\beta$  to project the possible situation of the influenza pandemic under the lowest level of infectiousness, and then take it as a baseline scenario for further comparisons.

Moreover, since the total number of passengers within the restricted area of a terminal is much greater than that within the cabin of an airplane, it highly increases the opportunities of interaction and contact between passengers through the use of common facilities (e.g. toilets). This then results in a higher infected probability and a more serious transmission of the influenza within the restricted area. We compare the total number of passengers of all airports according to the statistics published by Airports Council International (ACI).<sup>2</sup> And then, for the airport that has the greatest number of passengers we take  $\rho_{jd} = 0.085$  (per infected individual per hour). Subsequently, for each of the other airports the value of  $\rho_{jd}$  is adjusted downward from 0.085 according to the relative ratio of its number of passengers to the greatest number of passengers on an airport. Finally, based on the data and the parameters mentioned above, we simulate the transmission of the influenza

<sup>2</sup> Source: 2004 Worldwide Airport Traffic Statistics, Airports Council International (ACI).

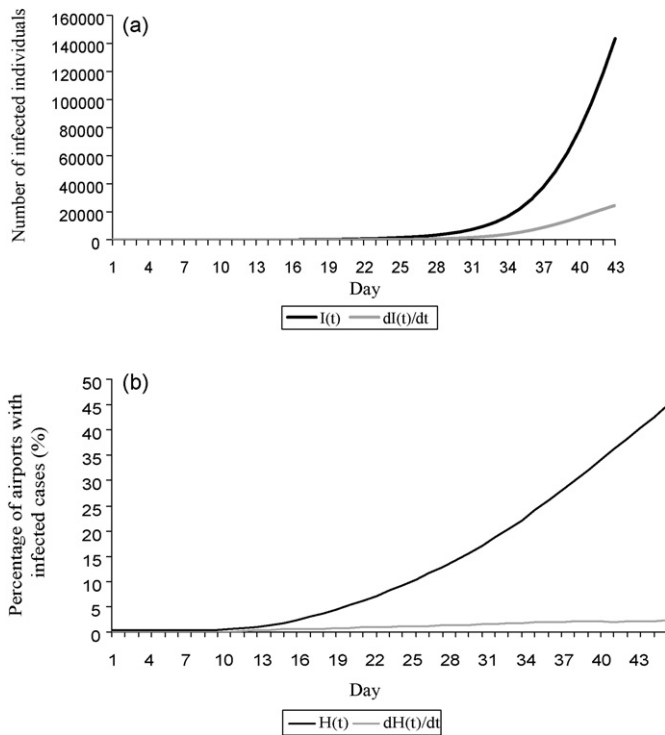


Fig. 1. Average pattern of the influenza pandemic.

in the small-world network, and evaluate its dynamic evolution and spatial distribution. World Bank (2005) said that the avian flu virus could be carried to any region by wild birds or by illegal trade, leading to genetic reassortment and the start of a human flu pandemic in such region. As a result, we simulate various situations of the influenza transmission that could start from any node of the network, and then average these results for analysis.

In the simulation, we determine the downstream flights connectable to flight  $j$  as follows. After the passengers of flight  $j$  arrive at their connecting airport, they may have further waiting time for transferring to other flights. In this study those downstream flights with a transfer time between 1 h and 5 h are considered as being connectable to flight  $j$ . The upstream flights connectable to flight  $j$  can be determined by analogy.

The results of the simulation are discussed as follows. As shown in Fig. 1(a), the number of infected individuals increases rapidly after day 30, and the daily increased number of infected individuals continues to increase over time. Specifically, the daily increased number of infected individuals on day 43 is approximately 20,000 persons. This result is similar to that found in Ferguson et al. (2005)<sup>3</sup> where the daily number of increased cases on day 43 is over 10,000 persons in Thailand, confirming the reasonableness of the result in our study. Furthermore, as shown in Fig. 1(b), the percentage of airports with infected cases increases at an increasing rate, showing both the dynamic evolution and the spatial distribution of the influenza transmission. It also indicates that influenza can spread to other regions all over the world and then increase its geographic scope of transmission at an escalating rate. Since the number of passengers in airport terminals will affect the influenza transmission, we shall further focus on those airports with numbers of passengers ranked among the top 50 airports worldwide. With other words,

<sup>3</sup> The authors collected the sizes and locations of households, workplaces and schools to simulate an outbreak of influenza in Thailand. They also used sensitivity analysis to test unknown parameters, and found that one person infected with a new pandemic virus might averagely infect 1.8 other people.

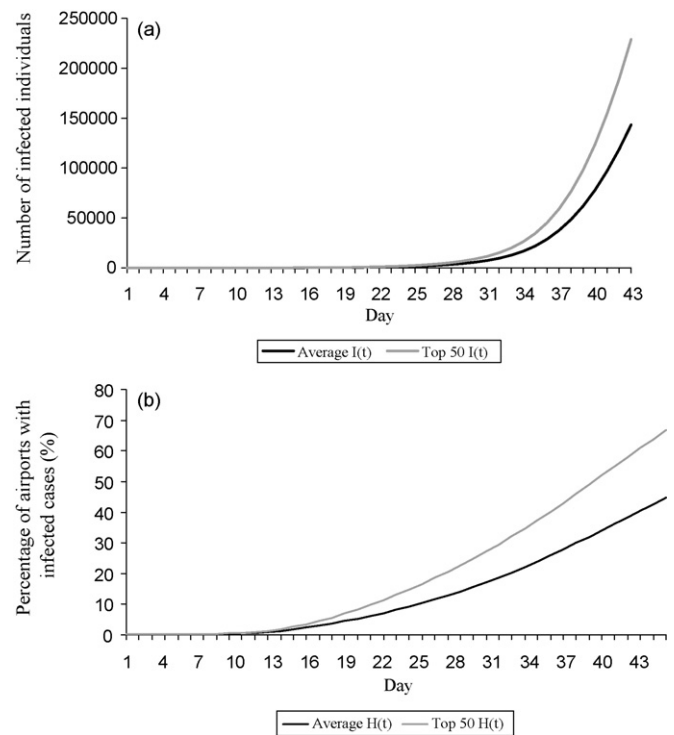


Fig. 2. Comparison of the transmission pattern of the top 50 airports with the average pattern.

we will focus on the pattern of transmission generated by flights whose destinations are the top 50 airports. As shown in Fig. 2, if the destinations of flights that have infected cases are the top 50 airports, then the transmission pattern generated by them will be more serious than the average pattern. This indicates that as soon as the influenza spreads to the top 50 airports, it will accelerate the transmission and result in a larger pandemic.<sup>4</sup>

We then evaluate the influence of control measures on the influenza transmission. When a new strain of influenza appears, people do not immediately recognize the disease for what it is. It may take some time to develop an effective method to detect and respond to it. Considering this initial slow reaction, and the fact that the number of infected individuals increases rapidly after day 30, this study will use the two control measures mentioned above being carried out in all airports after day 30 as an analysis scenario to investigate their effects. As shown in Fig. 3, after day 30 both the daily increased number of infected individuals and the daily increased percentage of airports with infected cases are markedly reduced by these control measures. It indicates that the transmission can be effectively mitigated by the practice of control measures.

However, the resources as well as the capabilities to plan and execute appropriate controls for the prevention of the influenza transmission may vary considerably among airports and countries. As a result, we further investigate the transmission pattern in a situation where the control measures cannot be carried out synchronously for all airports. In the network, such large airports as the top 50 airports have a higher level of network connectivity,

<sup>4</sup> We also evaluated the results for the top 10, top 20 airports, and so on. They generally show similar transmission patterns to the top 50 airports, but the patterns decrease as the top number increases. Here we just picked the top 50 airports as a comparison with the average pattern and only showed their difference in the figure. The total number of passengers of the top 50 airports is around 70% of all airports. So picking the top 50 airports is feasible and representative.

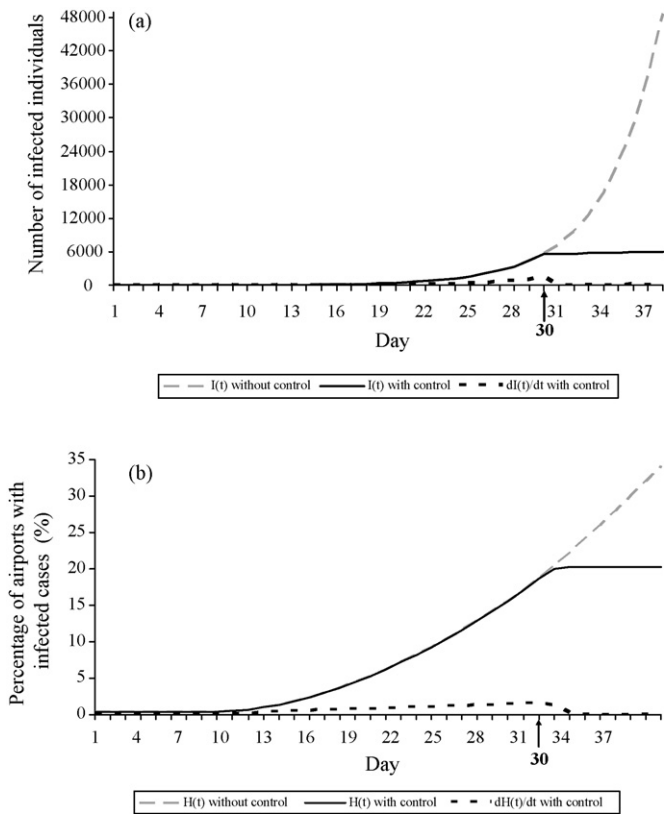


Fig. 3. Influence of the control measures.

but there are fewer large than small airports. So, practicing the control measures at large or small airports may receive different priorities and thereby obtain different containment results. In order to determine which set of priorities results in better containment effectiveness, this study designs various strategies to give different priorities of execution for the control measures based on the size of the airports. Strategies practiced in this study are shown in Table 1, and are described as follows. Strategy 1 stipulates that all airports synchronously carry out the control measures after day 30. Strategy 2 stipulates that the top 50 airports first carry out the control measures after day 30, while other airports execute measures with some time delay due to the constraint of limited resources. It is assumed that these airports will start their control measures 5 days later, i.e. day 35. Contrary to Strategy 2, Strategy 3 stipulates that those airports excluded from the top 50 first carry out control measures after day 30, but that the top 50 airports start executing the control measures after day 35 due to different concerns at various sizes of airports. The results are shown in Fig. 4, indicating

Table 1  
Practice of control strategies.

Strategy no.	Start time for practice	Target of practice
1	Day 30	All airports
2	Day 30 Day 35	Top 50 airports Other airports
3	Day 30 Day 35	Airports excluded from top 50 Top 50 airports
4	Day 13	All airports
5	Day 13 Day 18	Top 50 airports Other airports
6	Day 13 Day 18	Airports excluded from top 50 Top 50 airports

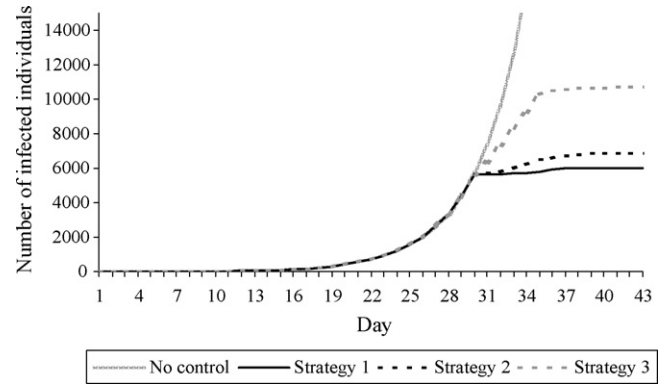


Fig. 4. Comparison of strategies.

that Strategy 1 is the most effective approach for containing the influenza transmission and the pandemic. In addition, Strategy 2 is the second most effective approach with a transmission pattern that is slightly higher than that of Strategy 1. This observation may be helpful in providing an insight to public health authorities, particularly when practicing control measures with limited resources. Compared to Strategy 2, we also run the simulations for carrying out control measures at the top 10, top 20, top 30 airports and so on, and finally at the top 100 airports. The results show that the transmission pattern gradually decreases as the top number increases from 10 to 100. However, as the top number increases over 50, the decrement of the transmission pattern is slight and limited. So 50 can be regarded as a critical number for the choice of the top number of airports in the practice of control measures.

The result of the simulation shows that after day 13, the influenza has spread to two or more airports worldwide, indicating a global outbreak (i.e. a pandemic) appearing in the network. So, we then attempt to start practicing three different strategies after day 13, which give different priorities in executing the control measures according to the size of the airports. This allows us to assess their containment effectiveness and to examine which set of priorities is better for containing the transmission. The different strategies are shown in Table 1, and are described as follows. Strategy 4 stipulates that all airports must synchronously carry out the control measures after day 13. Strategy 5 stipulates that the top 50 airports must first carry out control measures after day 13, and then the other airports start to execute the control measures with 5 days delay, i.e. on day 18. Contrary to Strategy 5, Strategy 6 stipulates that those airports excluded from the top 50 must start the control measures after day 13, while the top 50 airports execute the control measures after day 18. Fig. 5 shows that the influenza pandemic is mitigated more

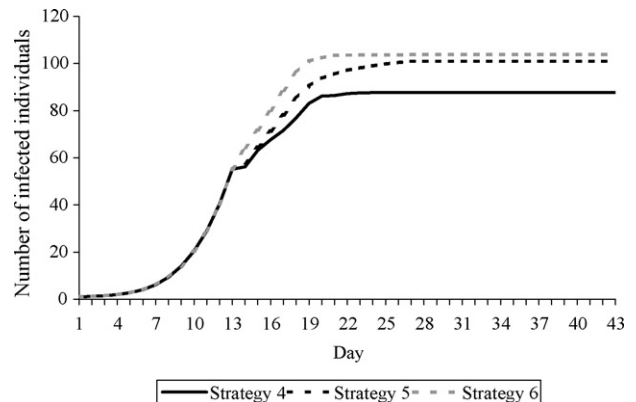


Fig. 5. Practice of strategies after the start time of the influenza pandemic.

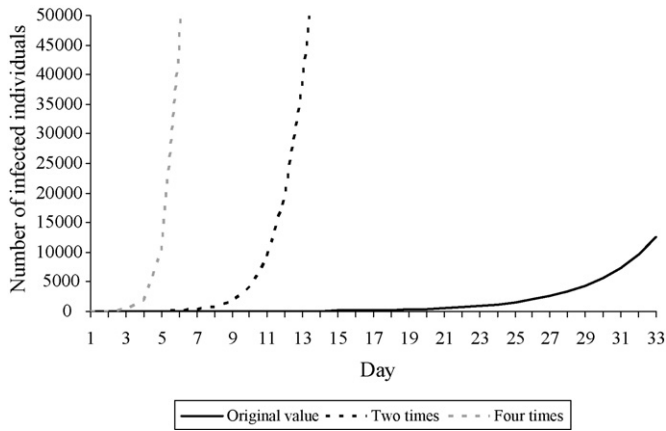


Fig. 6. Sensitivity analysis of the infectiousness.

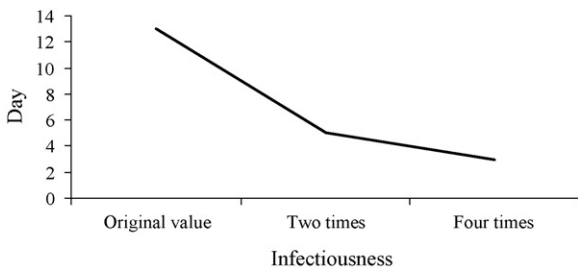


Fig. 7. Start time of the influenza pandemic under various levels of infectiousness.

markedly than Fig. 4, and Strategy 4 results in the highest effectiveness among all the strategies for containing the pandemic. However, under the constraint of limited resources, Strategy 5 can also result in remarkable containment effectiveness. Comparing the results of Figs. 4 and 5 indicate that one should carry out control measures as soon as the pandemic appears so that the transmission can be effectively mitigated.

Since the infectiousness of the emerging influenza is unknown, we performed a sensitivity analysis of the infectiousness in order to determine its effect on the pandemic. We increased the infectiousness from its original value to two and four times that of the original one, as shown in Fig. 6. It shows that the scale of the pandemic increases as the infectiousness increases. At the same time, we also analyzed the start time that the influenza pandemic appears under various levels of infectiousness as shown in Fig. 7. It shows that the start time of the influenza pandemic will be moved ahead from day 13 to day 3 if the level of infectiousness increases. This indicates that when the infectiousness of the influenza becomes stronger, one should carry out control measures earlier.

#### 4. Conclusions

The avian influenza virus H5N1 is a serious pandemic threat to the human population, and previous experience shows us that it may result in serious loss of life for the human population as well as a major disaster for the economy. Empirical investigations have found that air travel facilitates the spread of infectious diseases. However, past studies of mathematical epidemic models have not yet incorporated the effects of air travel on influenza transmission. This paper focused on the human-to-human transmission of influenza, and investigated the effects of air travel activities (passengers' consolidation, conveyance and distribution in airports and flights) on the influenza pandemic in a small-world network. Dynamic transmission models were developed not only to illus-

trate the transmission behaviors of the influenza en route scheduled flights and in airport terminals, but also to assess the expected burdens of the pandemic with and without control measures. This study also investigated how the small-world properties of the airline network facilitate the spread of influenza over all parts of the globe.

The results show that both the number of infected individuals and the percentage of airports with infected cases increase over time. Those flights to the top 50 airports spread the disease more quickly than the same number of flights to all airports. Our findings suggest that the public health authorities should avoid the influenza being spread to the top 50 airports in order to mitigate the impacts of the influenza. Under the constraint of limited resources, control at the top 50 airports first is almost as effective as control at all airports, and control sooner is more effective than control later. The findings may be helpful in providing insights for public health authorities to set priorities. The results of the sensitivity analysis show that as the infectiousness of the influenza increases, the disease spreads more quickly, and the start time of the pandemic is earlier. This means that, once the influenza increases in strength or becomes stronger than expected, the authorities should move the start of the control measures ahead accordingly in order to effectively control the pandemic. However, control measures at larger airports, such as the top 50 airports, are more expensive than at smaller airports. One could consider involving the cost of control measures and its effects for future research.

#### Appendix A.

##### Notation list.

Variable	Definition
$G(V, E)$	A small-world airline network, where $V$ is the set of nodes and $E$ is the set of links
$I_j(t)$	The number of infected individuals on flight $j$ at time $t$
$t_j$	The time on which flight $j$ departs from its origin airport
$I_j^o$	The initial number of infected individuals on flight $j$ at time $t_j$
$j'$	One of the upstream flights connectable to flight $j$ at the origin airport of flight $j$
$U_j$	The set of upstream flights of flight $j$
$I_{j'}^f$	The number of infected individuals on flight $j'$ when the flight arrives at its destination airport
$\alpha_{jj'}$	The proportion of infected individuals on flight $j'$ who transfer to flight $j$
$Z_j(t_j)$	The number of infected individuals who board the airplane from the origin airport of flight $j$ at time $t_j$
$N_j$	The total number of passengers of flight $j$
$j^o$	The origin airport of flight $j$
$Y_{j^o}(t)$	The cumulative number of infected individuals in the restricted areas of airport $j^o$ at time $t$
$v_j$	The proportion of $Y_{j^o}(t)$ who board flight $j$
$S_j(t)$	The number of susceptible individuals on flight $j$ at time $t$
$\beta$	The infection parameter on flights
$F_j$	The total elapsed flying time of flight $j$
$\bar{t}_j$	The time flight $j$ arrives at its destination airport
$I_j^f$	The final total number of infected individuals in the cabin of flight $j$ at time $\bar{t}_j$
$j^d$	The destination airport of flight $j$
$\rho_{j^d}$	The average number of contacts that lead to infection per infected individual per unit of time within the restricted areas of the terminals of airport $j^d$
$X_{j^d}(t)$	The number of infected individuals within the restricted areas of destination airport $j^d$ at time $t$
$\hat{j}$	One of the downstream flights connectable to flight $j$
$L_j$	The set of the downstream flights of flight $j$
$\lambda_{j\hat{j}}$	The proportion of $I_j^f$ who stay and wait for transferring to flight $\hat{j}$
$W_j$	The waiting time needed for transferring to flight $\hat{j}$ from flight $j$
$\gamma_j$	An indicator variable, $\gamma_j = 1$ if $\bar{t}_j \leq t < \bar{t}_j + W_j$ ; $\gamma_j = 0$ if $t \geq \bar{t}_j + W_j$
$E^m$	The set of those flights whose destination airport, $j^d$ , is airport $m$

## Appendix A (Continued)

Variable	Definition
$Y_m(0)$	The initial number of infected individuals in the restricted areas of airport $m$
$I(t)$	The cumulative number of infected individuals in the whole airline network up to time $t$
$N_o$	The initial number of infected individuals in the network at time $t=0$
$\phi_j$	An indicator variable, $\phi_j = 1$ if $t_j < t < \bar{t}_j$ ; $\phi_j = 0$ if $t \geq \bar{t}_j$
$H(t)$	The cumulative percentage of airports with infected cases occurring at time $t$
$\ \mathbf{V}\ $	The total number of airports in the network
$\delta_m$	An indicator variable, $\delta_m = 1$ if $Y_m(t) > 0$ ; otherwise $\delta_m = 0$

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