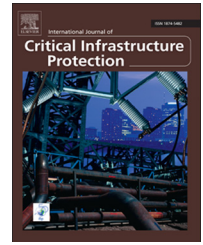


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# Effect of air travel on the spread of an avian influenza pandemic to the United States

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## ABSTRACT

The highly pathogenic avian influenza (HPAI) strain H5N1, which first appeared in Hong Kong in 1997, achieved bird-to-human transmission, causing a severe disease with high mortality to humans [18]. According to the World Health Organization (WHO), a total of 637 cases were reported in fifteen countries, including 378 deaths, corresponding to a case fatality rate of nearly 60% [19]. Avian influenza continues to be one of the deadliest diseases that jumps from animals to humans. Epidemiologists believe that it is likely to cause the next major global pandemic that could kill millions of people.

The 2002 outbreak of severe acute respiratory syndrome (SARS) demonstrated that international air travel can significantly influence the global spread of an infectious disease. This paper studies the effects of air travel on the spread of avian influenza from Asian and Australian cities to the United States. A two-city mathematical model involving a pandemic strain is used to derive the basic reproduction number ( $\mathcal{R}_0$ ), which determines if the disease will spread and persist ( $\mathcal{R}_0 > 1$ ) or go extinct ( $\mathcal{R}_0 < 1$ ). Real air travel data is used to model the disease spread by individuals who are susceptible to or are infected with pandemic avian influenza. Analysis of the two-city model helps understand the dynamics of the spread of pandemic influenza when the cities are connected by air travel. Understanding these effects can help public health officials and policy-makers select the appropriate disease control measures. Also, it can provide guidance to decision-makers on where to implement control measures while conserving precious resources.

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## 1. Introduction

The avian influenza virus belongs to a group of viruses known as Influenza A that circulate in many avian and mammalian species, including humans [2]. The highly pathogenic avian influenza (HPAI) strain H5N1 achieved bird-to-human transmission and caused a severe disease to humans with high mortality [18]. HPAI first appeared in 1997 in Hong Kong, where it infected eighteen humans and caused six deaths. To date, a total of 637 cases in fifteen countries have

been reported to the World Health Organization (WHO), including 378 deaths with a case fatality rate approaching 60% [19].

Interestingly, there has been no decline in the mortality rate since the first appearance of HPAI. In March 2013, China reported several confirmed cases involving the H7N9 strain that had not been seen previously in humans [20]. Most patients showed flu-like symptoms, and a throat swab taken from a patient in Jiangsu Province revealed the presence of the H3N2 human influenza virus and the H7N9 avian influenza

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virus [19]. Avian influenza continues to be one of the deadliest diseases that links humans and animals. Indeed, it is expected to cause the next major influenza pandemic.

An influenza pandemic occurs when a new strain of virus circulates among humans, potentially killing millions of people. Aside from its high mortality rate, avian influenza is monitored closely for a pandemic because Influenza A type viruses can evolve rapidly and jump between species. The viruses evolve through evolutionary mechanisms such as drift and shift. Drift involves small, gradual changes to surface proteins while shift involves abrupt major changes to the influenza virus. Shift evolution occurs through reassortment, the mixing of two influenza viruses (e.g., avian influenza and human influenza) into a new strain that carries properties from both strains. Shift typically occurs when a patient gets infected with both strains of the influenza virus. Recent outbreaks in China show that shift evolution can occur at any time with potentially deadly effects.

Vaccination is one of the best ways to prevent the spread of pandemic influenza and reduce its severity. However, producing live attenuated and inactive vaccine seed viruses against a potential pandemic-causing avian influenza strain, and subsequently performing pre-clinical tests and clinical trials can take several months, if not longer. Unfortunately, it is not possible to predict which avian virus strains will cause the next influenza pandemic or when the pandemic will occur. Of great concern is the fact that once pandemic avian influenza surfaces, it will spread globally in no time at all because the world is connected via air travel.

The 2002 outbreak of severe acute respiratory syndrome (SARS) demonstrated that international air travel accelerated the global spread of an infectious disease [14]. This paper attempts to study the effects of air travel on the spread of avian influenza. Understanding the effects can help public health officials and policy-makers to select the appropriate disease control measures. Also, it can provide guidance to decision-makers about where to implement control measures while conserving precious resources.

This paper presents a mathematical model with spatial heterogeneity that is designed to better understand the emergence and the spread of pandemic avian influenza. Spatial effects regarding disease spread can be modeled by diffusion or dispersal models. In a diffusion model, the movements of infected individuals are instantaneous and the disease spreads immediately to neighboring areas. On the other hand, in a dispersal model, the movements of individuals are discrete and usually occur between so-called patches connected by dispersion. Dispersal models are more appropriate when considering travel over long distances. Thus, a two-city dispersal model is developed to predict the spread of avian influenza from Asia and Australia to major U. S. cities via air travel. Real air travel data is used to model the disease spread by individuals who are susceptible to or are infected with pandemic avian influenza. The two-city model helps identify the most effective intervention strategies at the origin and destination cities as well as help quantify the effectiveness of control measures that should be applied to reduce the morbidity and mortality of a pandemic. This can provide valuable guidance to public health officials and policy-makers as they decide how, where and when to target

pandemic influenza intervention strategies while efficiently using the available resources.

## 2. Mathematical methods

This section describes the mathematical model, and the data and model parameters.

### 2.1. Mathematical model

A two-city model is used to express the spread of avian influenza from its origin in an Asian or Australian city to major cities in the United States. A single-city model is first specified, which is subsequently generalized to a two-city model by considering the travel of susceptible and infected individuals with the new strain of avian influenza.

#### 2.1.1. Single-city model

Avian influenza, one of the most dangerous diseases that links humans and animals, is currently the foremost pandemic threat. Early mathematical models that investigate the impact of a hypothetical pandemic have focused only on humans [1,4,5,10,13]. At this time, the avian influenza virus can only be transmitted from birds to humans; it is not yet capable of sustained human-to-human transmission. Most of the human cases reported to the WHO were due to close contact between humans and domestic birds. Recent mathematical models capture the bird-to-human transmission pathway of avian influenza [6–9]. The simplest bird-to-human model was introduced by Iwami et al. [7]; this model is the starting point for the single-city model presented in this paper. The notation used in our model is different, but the two models are equivalent.

In our single-city model, the domestic bird population is divided into two non-intersecting classes: susceptible domestic birds denoted by  $S_d(t)$  and infected domestic birds denoted by  $I_d(t)$ . The natural birth rate of the bird population is expressed by  $\Lambda_d$ . Susceptible birds have a natural death rate  $\mu_d$  while infected birds die at the rate  $\mu_d + \nu_d$ , where the additional death rate  $\nu_d$  is induced by HPAI.

Susceptible humans are denoted by  $S(t)$  and infected humans by  $I(t)$ . The natural birth rate of the human population is denoted by  $\Lambda$ . Susceptible humans die at the rate  $\mu$  while infected humans die at the rate  $\mu + \nu$ , where  $\nu$  is the additional death rate due to avian influenza.

The single city model, which comprises the bird and human populations, is given by

$$\begin{aligned} \frac{dS_d}{dt} &= \Lambda_d - \beta_d I_d S_d - \mu_d S_d \\ \frac{dI_d}{dt} &= \beta_d I_d S_d - (\mu_d + \nu_d) I_d \\ \frac{dS}{dt} &= \Lambda - \beta I_d S - \beta_p P S - \mu S \\ \frac{dI}{dt} &= \beta I_d S - (\mu + \nu) I - m I \\ \frac{dP}{dt} &= \beta_p P S + m I - (\mu + \nu_p) P. \end{aligned} \quad (1)$$

The force of the infection in the domestic bird population is denoted by  $\beta_d I_d S_d$ , where  $\beta_d$  is the transmission rate at which a susceptible bird contracts avian influenza from an

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