



ORIGINAL ARTICLE

# Assessment of Intensive Vaccination and Antiviral Treatment in 2009 Influenza Pandemic in Korea

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**Abstract**

**Objectives:** We characterized and assessed public health measures, including intensive vaccination and antiviral treatment, implemented during the 2009 influenza pandemic in the Republic of Korea.

**Methods:** A mathematical model for the 2009 influenza pandemic is formulated. The transmission rate, the vaccination rate, the antiviral treatment rate, and the hospitalized rate are estimated using the least-squares method for the 2009 data of the incidence curves of the infected, vaccinated, treated, and hospitalized.

**Results:** The cumulative number of infected cases has reduced significantly following the implementation of the intensive vaccination and antiviral treatment. In particular, the intensive vaccination was the most critical factor that prevented severe outbreak.

**Conclusion:** We have found that the total infected proportion would increase by approximately six times under the half of vaccination rates.

## 1. Introduction

The worldwide influenza A/H1N1 pandemic in 2009–2010 had a huge impact on the public health system in Korea. The Korean scientists traced the pathogenesis and chronological localization of influenza A/H1N1 [1], and also evaluated and identified strains with antiviral resistance in Korea [2]. Surveillance data on influenza-like illness (ILI) were used to estimate the number of patients with influenza in Korea [3]. Mathematical models were formulated to evaluate the parameters of the existing preparedness plans in Korea [4].

Many pharmaceutical and nonpharmaceutical measures were implemented during an epidemic to delay the peak of the epidemic curve and reduce the casualties [5]. A previous study had demonstrated the effectiveness of nonpharmaceutical measures under certain situations [6], but the timely intervention with pharmaceutical measures using vaccines and antiviral treatment is known to effectively contain or mitigate the impact of an outbreak [7–9]. Public health experts have closely monitored the preventive strategies implemented for recurrent or future epidemics. Recently, many more realistic, tailored mathematical transmission models

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have been developed to answer specific public health questions on an epidemic and their empirical validity have been tested [8,9]. This study aims to investigate how the onset time and the levels of control measures are associated with the effectiveness of intensive vaccination and antiviral treatment. In this study, results from models with full-control measures and models with partial control measures were compared, highlighting the significant differences in model outcomes.

## 2. Materials and methods

A mathematical influenza transmission model was proposed to investigate the characteristic of the 2009

$$\left\{ \begin{array}{l} \dot{S}(t) = -\beta S(t)[\{bA(t) + I(t)\}/N(t) - u(t)S(t)] \\ \dot{V}(t) = u(t)S(t) - (1 - \sigma)\beta V(t)(\{bA(t) + I(t)\}/N(t)) \\ \dot{E}(t) = \{S(t) + (1 - \sigma)V(t)\}\beta[\{bA(t) + I(t)\}/N(t)] - kE(t) \\ \dot{I}(t) = kpE(t) - (\alpha + \gamma + f)I(t) \\ \dot{A}(t) = k(1 - p)E(t) - \gamma A(t) \\ \dot{H}(t) = \alpha I(t) - (\theta + \delta)H(t) \\ \dot{R}(t) = \gamma[A(t) + I(t)] + fI(t) + \theta H(t) \\ \dot{D}(t) = \delta H(t) \end{array} \right.$$

influenza pandemic and to evaluate the impact of intensive vaccination and antiviral treatment methods implemented in the Republic of Korea. A standard compartment model was used to divide the population into eight compartments with different epidemiological status. The Korean population is integrated to the influenza transmission model, based on data from the 2009 census. Our model classifies individuals as susceptible ( $S$ ), vaccinated ( $V$ ), exposed ( $E$ ), clinically ill and infectious ( $I$ ), asymptomatic but still infectious ( $A$ ), hospitalized ( $H$ ), recovered ( $R$ ), and dead ( $D$ ). It is assumed that susceptible individuals become infected at rate:

$$\beta \frac{bA(t) + I(t)}{N(t)}$$

where the total population size is given as follows:

$$N(t) = S(t) + V(t) + E(t) + I(t) + A(t) + H(t) + R(t)$$

Vaccination is administered to susceptible individuals with a vaccination rate  $u(t)$ . We assumed that the vaccine provides only partial immunity so that vaccinated individuals are less susceptible than unvaccinated individuals, which is modeled by vaccine efficacy ( $\sigma$ ). Latently infected individuals proceed to become infectious with a latent period,  $1/k$  and a proportion ( $p$ ) of infected individuals become

symptomatic. We define  $b$  as relative infectiousness of asymptomatic cases compared with symptomatic cases. Both symptomatic and asymptomatic individuals recover at the rate  $\gamma$ . Infectious individuals are treated with an antiviral drug at the rate  $f$ . Infectious individuals are hospitalized at the rate  $\alpha$  and recover at the rate  $\gamma$ . Hospitalized individuals either recover at the rate  $\theta$  or die from influenza at the rate  $\delta$ . Recovered individuals are assumed to remain protected for the duration of the epidemic. The baseline values of epidemiological parameters are presented in Table 1. The population is assumed to be completely susceptible at the beginning of the epidemic. The system of differential equations that describes our influenza transmission model is given as follows:

Moreover, the basic reproductive number for the aforementioned system is written as:

$$R_0 = \beta \left[ \frac{p}{\gamma} + \frac{(1-p)b}{\gamma} \right]$$

## 3. Results

Simulation results are generated by numerically solving the given influenza dynamical system. Parameter estimations were carried out using the incidence data of clinically infected, vaccinated, treated, and hospitalized patients during the 2009 influenza pandemic in the Republic of Korea. First, the transmission rate, the vaccination rate, the antiviral treatment rate, and the hospitalized rate were estimated using the least-squares method for the 2009 influenza data, respectively. The estimated range  $R_0$  for the 2009 influenza pandemic is approximately 1.5 using the transmission rate  $\beta$  in Table 1, and the expression for the basic reproductive number  $R_0$  is presented earlier. The estimated vaccination, antiviral treatment, and hospitalized rates are presented in Table 1 and shown in Figure 1E. Next, we explored a baseline pandemic scenario in the context of the 2009 A/H1N1 outbreak in

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