Estimation of the Time-dependent Reproduction Number of Influenza A(H1N1)pdm2009 in South Korea

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Abstract

Background: The reproduction number is one of the most crucial parameters in determining disease dynamics, providing a summary measure of the transmission potential. However, estimating this value is particularly challenging owing to the characteristics of epidemic data, including non-reproducibility and incompleteness.

Methods: In this study, we propose mathematical models with different population structures; each of these models can produce data on the number of cases of the influenza A(H1N1)pdm09 epidemic in South Korea. These structured models incorporating the heterogeneity of age and region are used to estimate the time-dependent effective reproduction numbers. Subsequently, the age- and region-specific reproduction numbers are also computed to analyze the differences illustrated in the incidence data.

Results: The basic SIR fails to provide a reasonable estimation of the reproduction numbers. The estimated values demonstrate a large variation and remains outside of the feasible range for the influenza, regardless of the time period for data. Real-time estimation using age- and region-structured models demonstrated that the effective reproduction number rose sharply during mid-October when the number of patients increased dramatically. The reproduction number fell below unity at the end of October and stayed lower than unity indicating that the epidemic starts decreasing, which is consistent with the incidence data.

Conclusions: Numerical results reveal that the introduction of heterogeneity into the population to represent the general characteristics of dynamics is essential for the robust estimation of parameters.

Keywords: Influenza; Reproduction number; Antiviral agents
Background

The reproduction number is defined as the average number of secondary cases generated by a typical primary case. It is a measure of the transmission potential associated with the contact rate, duration of infectivity, and probability of transmission per contact. The maximum reproduction number is attained when an infectious person is introduced into a totally susceptible population and is called the basic reproduction number, $R_0$. Various approaches such as the exponential growth rate of infections during the early epidemic stage, model-based schemes, and maximum-likelihood estimations have been used to analyze this number [1–4].

When an infection spreads throughout a population, the time-dependent effective reproduction number, $R_t$, is often more useful for assessing the transmission potential throughout a pandemic, especially during the period with the highest level of activity. Real-time estimation continues to track the number of secondary infections caused by a single infective, providing a quantitative measure of the time evolution of the epidemic force. Cruz-Pacheco et al. demonstrated the manner in which sanitary measures reduce the prevalence of an infected population [1]. Estimates of the reproduction number were shown to decrease from 1.4-1.5 initially to 1.1-1.2 later in the summer, which was most likely because of the vacation period and the seasonality of influenza transmission [5]. In addition to capturing temporal dynamics, it is important to consider heterogeneous patterns of the transmission. It is well known that school-age children are disproportionately responsible for influenza transmissions. Estimates of the age-specific reproduction number help with our understanding of the role of each group in the transmission dynamics and with devising effective targeting mitigation strategies.

If all incident cases could be traced back to their index cases, estimating the reproduction number would simply be a matter of counting the number of secondary cases. However, with most epidemics, only the epidemic curve is observed, and there is no available information regarding who infected whom. To appropriately estimate the reproduction number from the influenza outbreak data, it is essential that the selected model capture the underlying dynamics embedded in the data. The objective of this study is to estimate the reproduction numbers based on the incidence data.
When the World Health Organization announced the emergence of influenza\(^1\) A(H1N1)pdm09 (pH1N1) in 2009 [6], the first probable patient in South Korea\(^2\) was identified on April 28. A total of 763,759 confirmed cases, of which 270 were\(^3\) fatal, were reported by the end of August 2010 [7]. During the initial epidemic\(^4\) phase, the main control measure was containment through quarantine and isolation. Surveillance programs in schools and medical facilities were implemented, and all confirmed cases were investigated. However, when community outbreaks were detected in June, the intervention policy switched from containment to mitigation, including vaccination and antiviral prescription. Vaccination was started on October 27, 2009, and 12.7 million people were vaccinated by the end of August 2010.\(^10\) Before August 20, antiviral agents were prescribed to patients with acute febrile respiratory illness (AFRI) and who had a history of travel abroad or contact with a confirmed patient. However, when the number of community-acquired cases increased, antiviral agents were prescribed to patients with AFRI symptoms.

According to the database, 3,087,788 courses of antiviral agents were prescribed from August 21, 2009 to April 30, 2010. The daily number of incident patients was estimated based on the amount of prescribed antiviral agents (Refer to [8] for details). Figure 1 shows the temporal incidence distribution of pH1N1 in South Korea. The amount of antiviral agents prescribed and the number of incident patients soared from mid-October, reached its peak at the end of October, and started declining in mid-November.

Demographic and regional characteristics are illustrated in Table 1 and Figure 2. The incidence rate is higher in children and students than in other age group individuals (Table 1). The rate is higher in urban areas than in rural areas and is the highest in the national capital and the south-eastern region (Figure 2).

In this paper, two different structured models are proposed to estimate reproduction numbers on the basis of the epidemic curve. We begin by introducing a basic SIR model to describe a single outbreak and build age- and region-structured models by incorporating population heterogeneity. Numerical simulations are conducted to analyze the impact of terminal time and the effect of heterogeneous structures on the estimation of parameters. Finally, the proposed models are applied to the 2009 incidence data of novel pH1N1 in South Korea to compute the age- and region-specific reproduction numbers.
Methods

Basic SIR model

We consider the standard SIR (Susceptible-Infected-Recovered) model to represent single-outbreak influenza dynamics. The model classifies individuals into three key compartments: susceptible, infected, and recovered. The nonlinear system of differential equations describing the dynamics is given by the following equation.

\[ S'(t) = -\beta S(t)I(t) \]

\[ I'(t) = \beta S(t)I(t) - \gamma I(t) \]

\[ R'(t) = \gamma I(t). \]

The state variables \( S(t) \), \( I(t) \), and \( R(t) \) denote the number of individuals who are susceptible, infected, and recovered, respectively, at time \( t \). The number of contact events sufficient for transmitting an infection during unit time per individual is \( \beta N \) based on the mass action incidence. Infective individuals leave the compartment at the recovery rate \( \gamma \), thereby acquiring immunity to the disease. We can drop the equation for \( R(t) \) as it has no effect on the dynamics of others and hence is determined once \( S(t) \) and \( I(t) \) are known. Based on the SIR model, we have the time-dependent net reproduction number \( R_t = \beta S(t)/\gamma \), which quantifies the level of transmission at time \( t \). Note that \( R_t \) is the per-infective rate at which new infections occur within the average duration of infection at time \( t \).

Age-structured model

An age-structured model is employed to estimate the reproduction number of pH1N1 because the transmission rate is higher in preschool and schoolchildren than in other age group individuals, in general. We consider a subgroup SIR model where the population is divided into \( n_a \) age groups with different transmission dynamics. We denote the number of susceptible and infected individuals within the \( i \)th age group by \( S_i \) and \( I_i \), respectively. Let \( \beta_{ij} \) refer to the transmission from the \( j \)th age group to the \( i \)th age group, and \( \beta = [\beta_{ij}] \) denote the transmission matrix, also...
known as Who-Acquires-Infection-From-Whom matrix. Putting these elements together, we have the following system of differential equations.

\[ S'_i(t) = - \sum_{j=1}^{n_a} \beta_{ij} S_i(t) I_j(t) \]

\[ I'_i(t) = \sum_{j=1}^{n_a} \beta_{ij} S_i(t) I_j(t) - \gamma_i I_i(t). \]

(1)

In a general structured model of the form (1) with \( n_a \) distinct classes, \( n_a^2 \) transmission terms are required. However, one transmission term is available at most for each class. The typical way to address this lack of specificity is to constrain the structure of the transmission matrix and/or to use prior knowledge of social mixing behavior. For an age-structured model, we assume that the transmission rates are proportional to the rates of social contact, which can be estimated from contact patterns. A large multi-country population-based survey conducted in Europe as a part of the POLYMOD [9] enables us to implement this approach. The transmission is modeled as the product of the contact rate in the survey and an age-specific proportionality factor to account for characteristics related to susceptibility and infectiousness, which are not captured by contact rates. This leads to

\[ \beta_{ij} = \begin{cases} q_i c_{ij} & i = j \\ \sigma c_{ij} & i \neq j \end{cases} \]

where \( c_{ij} \) is the contact rate and \( q_i \) and \( \sigma \) are proportionality factors.

Based on the age-structured SIR model (1), the reproduction number can be calculated by following Driessche and Watmough [10]. It is the spectral radius of the next generation matrix \( M \) where

\[ M_{ij} = \frac{\beta_{ij} S_i(t)}{\gamma_j}. \]

The details are given in Appendix.

Region-structured model

The second mechanism incorporates a heterogeneous population based on regions to account for the wave of the pH1N1 pandemic. We denote the number of susceptible
and infected individuals within the $i^{th}$ region by $S_i$ and $I_i$, respectively. Let $\beta_{ij}^1$ refer to the transmission from the $j^{th}$ subgroup to the $i^{th}$ subgroup and $\beta = [\beta_{ij}]^{2}$ denote the transmission matrix. In the same manner as the age-structured model, we have the following system of differential equations.

$$S_i'(t) = -\sum_{j=1}^{n_r} \beta_{ij} S_i(t) I_j(t)$$

$$I_i'(t) = \sum_{j=1}^{n_r} \beta_{ij} S_i(t) I_j(t) - \gamma_i I_i(t).$$

We assume that transmission rates between distinct regions in the region-structured model can be expressed as the frequency of transportations multiplied by a region-specific proportionality factor. The transportation information was extracted from the highway portal site and Kakao map for number of buses and highway traffic, respectively [11, 12]. Let the number of buses and highway traffic from region $j$ to region $i$ be denoted by $w_{i,j}$ and $W_{i,j}$, respectively. Note that $w$ is symmetric because the bus route is circular, although $W$ is not necessarily. The transmission rate can be written as

$$\beta_{ij} = \begin{cases} q_i & i = j \\ q_i \sigma_l w_{i,j} + q_i \sigma_g W_{i,j} & i \neq j \end{cases}$$

where $q_i$ is the proportionality factor, and $\sigma_l$ are $\sigma_g$ can be chosen such that they balance the weight between different types of transportations.

The same argument as that presented in the age-structured model gives the expression of the effective reproduction number $R_t$, which is the spectral radius of the following next generation matrix

$$\begin{bmatrix} \beta_{ij}S_i(t) \\ \gamma_i \end{bmatrix}.$$

Study subjects and parameter estimation

Study subjects were patients who were prescribed antiviral agents from the national stockpile from August 21, 2009 to April 30, 2010. Because of mandatory antiviral agent management program during study period, all patients who were prescribed...
antiviral agent were included in this study. The data employed to estimate the pa-
rameters are the daily number of incident patients in figure 1. It was estimated
based on the aggregation of prescribed antiviral agents from deidentified database.
This study was approved by the Institutional Review Board (IRB) of Yonsei Uni-
versity Health System. Since this study used retrospective data and the study subjects
were anonymized, the IRB waived the requirement for written consent from the
patients.

Our goal is to estimate the optimal parameters that provide the states that are
best fit to the given data. This section briefly reviews the parameter estimation
technique of the least squares method. In general, parameter estimation is conducted
by minimizing the cost function, which measures the difference between the model
prediction and observation. Let \( \theta \) be the parameter set and \( y_j \) be the measurement
data at time \( t_j \). We recast the mathematical model as

\[
x'(t) = g(t, x(t), \theta),
\]

and assume a statistical model for measurement of the form

\[
y_j = f(t_j; \theta) + \varepsilon_j, \quad j = 1, \cdots, N
\]

where \( f(t_j; \theta) \) is the model prediction at time \( t_j \) with parameter \( \theta \) and the mea-
surement error \( \varepsilon_j \sim \mathcal{N}(0, a^2) \). The least squares estimator can be obtained by
minimizing the following cost function over the given parameter space \( \Omega_\theta \) [13]:

\[
\sum_{j=1}^{N} [y_j - f(t_j; \theta)]^T [y_j - f(t_j; \theta)]
\]

The parameter sets to be estimated for the basic SIR model, age-structured model,
and region-structured model, are

\[
\theta_{\text{basic}} = \{\beta, \gamma\},
\]

\[
\theta_{\text{age}} = \{q_i, \sigma_i, \gamma_i \text{ for } i = 1, 2, \cdots, n_a\},
\]

\[
\theta_{\text{region}} = \{q_i, \sigma_i, \sigma_g, \gamma_i \text{ for } i = 1, 2, \cdots, n_r\}
\]

where \( n_a \) and \( n_r \) denote the number of age groups and regions, respectively.
Results

Time-dependent reproduction number

We illustrate the proposed methodology and investigate its performance by applying it to 2009 incidence data of pH1N1 in South Korea. This section presents the results of the estimation obtained by applying the least squares method to basic SIR, age- and region-structured models. In each experiment, data with different time periods by varying the terminal time are tested to determine the earliest stage of the epidemic sufficient to provide a reasonable estimation. Figure 3 displays the predicted incidence based on the basic SIR model compared with the observed data. Predictions using data only during the initial growth phase cannot effectively exhibit the dynamics and substantially overestimate the spread of the infection. The results of simulation improved after the peak of the epidemic, and the wave is roughly generated at a later stage. However, the simple SIR model does not provide a reasonable estimation of the reproduction numbers. The estimated values demonstrate a large variation and remains outside of the feasible range for the influenza, regardless of the time period for data. The plausible reason for this involves the model assumptions that are too simple to capture the underlying mechanisms.

For the age-structured SIR model (1), the total population is split into 14 subgroups of 5-year age bands and one with 70 years and older (i.e., 0-4, 5-9, ..., 65-69, 70+). This incorporates a heterogeneous population into the model in order to reflect different transmission rates in each age group. In figure 4, the outbreaks are simulated using data during various time periods in the same manner as mentioned above. Results of both the models show similar trends as long as the terminal time is earlier than mid-November when the gentle growth begins during the decline stage. Additionally, as the growth begins to decline, the age-structured SIR model fits the incidence data better than the basic SIR model. The reproduction number starts increasing in early October, peaks at 2.5 on October 17, and then decreases to unity at the end of October. Real-time estimation demonstrated that the effective reproduction number rose sharply during mid-October when the number of patients increased dramatically. The reproduction number fell below unity at the end of October and stayed lower than unity indicating that the epidemic starts decreasing, which is consistent with the incidence data. Incorporation of the age
structure allows for robust estimation of reproduction numbers, as observed on the bottom of figure 4.

The general characteristics of regional difference led us to consider a second type of heterogeneity in the model. The nation is split into 252 in the region-structured model (2), where the transmission rates are implemented based on transportation patterns. Figure 5 compares the predicted cases based on the region-structured SIR model with the observed data over the course of the epidemic. As it was discussed in the previous experiment, it is not earlier than the epidemic peak for estimation to start adjusting to outbreak data. Since this outbreak, the incidence data is well described in the form of the characteristic exponential rise, turnover, and decline pattern predicted by the process model. The estimated time-dependent effective reproduction numbers are illustrated in figure 5, which demonstrates a pattern similar to that obtained using the age-structured SIR model in figure 4.

Age-specific and region-specific reproduction numbers

It is widely known that the transmission is considerably different among various age groups. We also observe from the pH1N1 epidemic data that the incidence rate is higher in children and students than in other age groups (Table 1). Estimates of the age-specific reproduction number help in clarifying the role of each age group in the transmission dynamics and in suggesting guidelines for effective targeting intervention strategies. The estimated age-specific reproduction numbers are displayed in figure 6. The result is closely related to the cumulative incidence for each age group because it is often the contact rate within the same age group is higher than with other groups.

The incidence rate is higher in urban areas than in rural areas, and the highest in the national capital and the south-eastern region, as shown in figure 2. We estimated the region-specific reproduction number and observed that it is more than two in some areas and less than one in the others (Figure 7). This is consistent with regions having larger cumulative incidence with a similar argument regarding contact patterns to age-specific cases.

Discussion

An estimation of reproduction numbers is crucial because it provides a measure of the transmission potential when an infection is spreading throughout a population.
The reproductive numbers in the early phase of the pandemic have been estimated in several countries with different settings, yielding median 1.46 and range 1.0–3.6[14]. Many of these studies focused on cases confirmed in the early stage of the pandemic. Because laboratory tests focused on severe cases and there are possible changes in laboratory testing and notification rates, the number of confirmed cases does not necessarily represent the underlying epidemic. It also does not reflect the dynamics during the period of the highest level of activity, which is the winter in temperate climates. Some studies used the number of cases from sentinel surveillance that is much less than the actual number of influenza patients. It is necessary to estimate the reproductive number using the number of all the patients throughout a pandemic, including the period with the highest level of activity. In this study, the reproductive number of was estimated based on the national data of incidence deduced from antiviral agent prescription in South Korea during the pandemic.

We discussed parameter estimation methodologies based on deterministic SIR models incorporating population heterogeneity. Age-structured and region-structured models were employed to describe the underlying epidemic process. The proposed mechanisms were applied to influenza A(H1N1)pdm09 in South Korea to compute the time-dependent effective reproduction numbers. We found that the introduction of heterogeneity into the population and sufficient data to represent general characteristics of dynamics are essential to the robust estimation of parameters. Real-time estimation showed that the reproduction number started increasing in early October, peaked at 2.5 on October 17, and then decreased to unity at the end of October. The effective number rose sharply during the mid-October when the number of patients increased dramatically. The reproduction number fell below unity at the end of October and remained lower that unity, indicating that the epidemic starts decreasing, which is consistent with the incidence data.

Subsequently, age-specific and region-specific basic reproduction numbers were estimated to account for the differences of incidence. We observe from the pH1N1 epidemic data that the incidence rate is higher in children and students than in other age groups. The estimated age-specific reproduction numbers agree with the cumulative incidence for each age group because the mixing is assortative. The incidence rate is higher in urban areas than in rural areas, highest in the national capital and in the south-eastern region. We estimated the region-specific reproduction number.
whose trend is similar to the number of cases in each region. Estimates of the age-specific and region-specific reproduction number help to predict the transmission dynamics, and to suggest guidelines for effective targeting intervention strategies.

This study has both limitations and strengths. The first limitation is that the number of cases is estimated from the amount of prescribed antiviral agents assuming the time lag between symptom onset and antiviral agent prescription, the proportion of prescription and the proportion of pH1N1 confirmation among AFRI patients. Another limitation is that vaccination is not considered in the model. However, the effect of vaccination on the transmission of pH1N1 may have been insignificant because the vaccination for general group was initiated in January 2010. On the contrary, the present research has its strengths compared to previous studies. The reproduction number was estimated based on the national level antiviral agent prescription data in South Korea throughout the pandemic including the period of the highest level of activity. The real-time estimation incorporating population structures can be used to predict the disease dynamics, thereby providing guidelines for the optimal implementation of preventive measures, such as school closing and distribution of antiviral agents.

Conclusions

In this study, we proposed age- and region-structured SIR models to estimate the time-dependent reproduction number of Influenza A(H1N1)pdm2009 in South Korea. The basic SIR fails to provide a reasonable estimation of the effective reproduction numbers, possibly due to the model assumptions that are too simple to capture the underlying mechanisms. Numerical results reveal that the introduction of heterogeneity into the population to represent the general characteristics of dynamics is essential for the robust estimation of parameters.

Appendix

The reproduction number for the age-structured SIR model (1), can be calculated following the approach of Driessche and Watmough [10]. Let $F_i$ be the new infections and $V_i$ be the transitions of $i^{th}$ compartment, then

$$F_i = S_i \left( q_i c_{ii} I_i + \sum_{j \neq i} \sigma c_{ij} I_j \right)$$ (1)
and
\[ V_i = \gamma I_i. \] (2)
for \( i = 1, \ldots, n_a. \)

Subsequently, the derivatives of \( \mathcal{F} = [\mathcal{F}_i] \) and \( \mathcal{V} = [\mathcal{V}_i] \) are
\[
\frac{d}{dt} \mathcal{F} = \begin{bmatrix}
S_1 q_1 c_{11} & S_1 \sigma c_{12} & \cdots & S_1 \sigma c_{1n_a}

S_2 \sigma c_{21} & S_2 q_2 c_{22} & \cdots & S_2 \sigma c_{2n_a}

\vdots & \vdots & \ddots & \vdots

S_{n_a} \sigma c_{n_a1} & S_{n_a} \sigma c_{n_a2} & \cdots & S_{n_a} q_{n_a} c_{n_an_a}
\end{bmatrix}
\]
\[ \frac{d}{dt} \mathcal{V} = \begin{bmatrix}
\gamma & 0 & \cdots & 0

0 & \gamma & \cdots & 0

\vdots & \vdots & \ddots & \vdots

0 & 0 & \cdots & \gamma
\end{bmatrix}, \]
respectively, and the next generation matrix is
\[
\mathcal{FV}^{-1} = \frac{1}{\gamma} \begin{bmatrix}
S_1 q_1 c_{11} & S_1 \sigma c_{12} & \cdots & S_1 \sigma c_{1n_a}

S_2 \sigma c_{21} & S_2 q_2 c_{22} & \cdots & S_2 \sigma c_{2n_a}

\vdots & \vdots & \ddots & \vdots

S_{n_a} \sigma c_{n_a1} & S_{n_a} \sigma c_{n_a2} & \cdots & S_{n_a} q_{n_a} c_{n_an_a}
\end{bmatrix}, \] (3)

Thus, the reproduction number is the spectral radius of \( \mathcal{FV}^{-1} \) and the age-specific reproduction number is the column sum of \( \mathcal{FV}^{-1} \) corresponding to the age of interest.

Abbreviations

- \( R_0 \): Basic reproduction number; \( R_t \): Time-dependent effective reproduction number; pH1N1: Influenza A(H1N1)pdm09; AFRI: Acute febrile respiratory illness; SIR: Susceptible-Infected-Recovered; IRB: Institutional Review Board; LSM: Least squares method

Declarations

Ethics approval and consent to participate
This study was approved by the Institutional Review Board (IRB) of Yonsei University Health System.

Consent for publication
Not applicable.

Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests
The authors declare that they have no competing interests.
The work of Jeehyun Lee was supported by NRF-2015R1A5A1009350 and NRF-2016R1A2B4014178. The funders had a major role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Authors’ contributions
Conceived and designed the experiments: DHL JL. Analyzed the data: DHL CK. Performed the experiments: YL HDK. Wrote the paper: YL DHL JL. Interpreted the data: YL DHL HDK. Contributed to draft and revised the manuscript for content: All. Read and approved the manuscript: All.

Acknowledgements
Not applicable.

Authors’ information
Not applicable.

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Figure Legends

**Figure 1** Daily antiviral agent prescription and incident patients from September 1, 2009 to March 30, 2010 [8]. The adjusted antiviral agent prescription (dotted line) is obtained by tuning the discrepancy in the amount of prescribed antiviral agents between weekdays and weekends using cubic splines. The estimated number of incident patients (solid line) is approximated by reflecting the time lag between symptom onset and antiviral agent prescription, proportion of antiviral agent prescription, number of pH1N1 confirmations among AFRI patients, and number of asymptomatic cases.

**Figure 2** Cumulative incidence by region.

**Figure 3** Comparison of pH1N1 incidence data with predictions of least squares method (LSM) using the basic SIR model (top and bottom left): The red dots show the number of new cases per day and the blue line presents the predicted number of cases. Terminal time of data used for estimation is displayed by a black dotted vertical bar. In each figure, the end of time period was set at October 24, 2009, November 14, 2009, and March 30, 2010. Estimation of the time-dependent effective reproduction number using the basic SIR model (bottom right): The black dots show the estimated value using data during the time period at different terminal times.

**Figure 4** Comparison of pH1N1 incidence data with predictions of least squares method (LSM) using age-structured SIR model (top and bottom left): The red dots show the number of new cases per day, and the blue line presents the predicted number of cases. Terminal time of data used for estimation is displayed by a black dotted vertical bar. In each figure, the end of time period was set at October 24, 2009, November 14, 2009, and March 30, 2010. Estimation of the time-dependent effective reproduction number using the age-structured SIR model (bottom right): The black dots show the estimated values at different terminal times.

**Figure 5** Comparison of pH1N1 incidence data with the predictions of least squares method (LSM) obtained using the region-structured SIR model (top and bottom left): The red dots show the number of new cases per day, and the blue line presents the predicted number of cases. The terminal time of data used for estimation is displayed by a black dotted vertical bar. In each figure, the end of time period was set at October 24, 2009, November 14, 2009, and March 30, 2010. The estimation of the time-dependent effective reproduction number using the region-structured SIR model (bottom right): The black dots show the estimated value at different terminal times.
Figure 6  Age-specific reproduction number (left) and cumulative incidence for each age group (right).

Figure 7  Region-specific reproduction number (left) and cumulative incidence for each region (right).

Table 1  Cumulative incidence by age.

| Age  | Population size | Total number of cases | Incidence rate(%) |
|------|-----------------|-----------------------|-------------------|
| 0-4  | 2273634         | 917793                | 40                |
| 5-9  | 2671496         | 1084094               | 41                |
| 10-14| 3284134         | 920937                | 28                |
| 15-19| 3368818         | 781238                | 23                |
| 20-24| 3153001         | 305403                | 10                |
| 25-29| 4001090         | 341940                | 9                 |
| 30-34| 3856438         | 290354                | 8                 |
| 35-39| 4466962         | 303670                | 7                 |
| 40-44| 4244225         | 220743                | 5                 |
| 45-49| 4321262         | 164735                | 4                 |
| 50-54| 3761143         | 149067                | 4                 |
| 55-59| 2611705         | 97571                 | 4                 |
| 60-64| 2117041         | 73540                 | 3                 |
| 65-69| 1870279         | 66033                 | 4                 |
| 70+  | 3306607         | 100728                | 3                 |