Optimal allocation of pandemic influenza vaccine depends on age, risk and timing

Sido D. Mylius\textsuperscript{a,1}, Thomas J. Hagenaars\textsuperscript{a,2}, Anna K. Lugnér\textsuperscript{a,*}, Jacco Wallinga\textsuperscript{a, b}

\textsuperscript{a} National Institute for Public Health and the Environment (RIVM), Centre for Infectious Disease Control, Epidemiology and Surveillance Unit, P.O. Box 1, NL – 3720 BA Biltoven, The Netherlands
\textsuperscript{b} Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, P.O. Box 85500, 3508 GA Utrecht, The Netherlands

\textbf{ARTICLE INFO}

Article history:
Received 16 October 2007
Received in revised form 15 April 2008
Accepted 17 April 2008
Available online 7 May 2008

Keywords:
Mathematical modeling
Dynamic model
Interventions against pandemic

\textbf{ABSTRACT}

The limited production capacity for vaccines raises the question what the best strategy is for allocating the vaccine to mitigate an influenza pandemic. We developed an age-structured model for spread of an influenza pandemic and validated it against observations from the Asian flu pandemic. Two strategies were evaluated: vaccination can be implemented at the start of the influenza pandemic, or vaccination will be implemented near the peak of it. Our results suggest prioritizing individuals with a high-risk of complications if a vaccine becomes available during a pandemic. If available at the start, vaccinating school children might be considered since this results in slightly lower expected number of deaths.

\textsuperscript{*} Corresponding author. Tel.: +31 30 274 8540; fax: +31 30 274 4409. E-mail address: anna.lugner@rivm.nl (A.K. Lugnér).

\textsuperscript{1} Current address: Quantitative Veterinary Epidemiology, Division of Infectious Diseases, Animal Sciences Group, Wageningen University and Research Centre, P.O. Box 65, NL – 8200 AB Lelystad, The Netherlands.

\textsuperscript{2} Current address: National Institute for Public Health and the Environment (RIVM), Public Health and Health Services Division, Expertise Centre for Methodology and Information Services, P.O. Box 1, NL – 3720 BA Biltoven, The Netherlands.

1. Introduction

The current worldwide spread of avian influenza A, subtype H5N1, and the occasional, often fatal, cross-species transmission to humans have raised considerable concern about a possible human influenza pandemic. The most severe influenza pandemic known so far, the 1918–1919 ‘Spanish flu’ (A/H1N1) has probably caused between 40 and 50 million deaths worldwide\cite{1, 2}. The other two 20th century pandemics, the 1957–1958 ‘Asian flu’ (A/H2N2) and the 1968–1969 ‘Hong Kong flu’ (A/H3N2) were relatively mild with probably less than 1 million deaths\cite{2, 3}. Pandemic contingency planning is key to mounting an adequate response to the morbidity, mortality and the corresponding demand on healthcare, in case a new pandemic would occur\cite{4, 5}. Many countries are currently updating their pandemic contingency plans, and science and industry are developing better vaccines and faster production methods.

An effective vaccine would probably not be available in the early stages of a pandemic, due to limitations in development, production and delivery. It is expected that it will take several months from the isolation of a new pandemic virus to the start of mass vaccine production. If available, supply will most likely be limited and the authorities face an allocation problem: who should be vaccinated earlier, if at all? The goal of most current pandemic plans is to minimize morbidity and mortality and to prevent social disintegration. Apart from healthcare workers and others involved in the response to the pandemic, vaccine priority groups are generally those with the highest complication rates during past pandemics: mainly people with chronic respiratory diseases, the old and the very young\cite{6, 7}.

Several mathematical models, individual-based stochastic models\cite{8}, spatially structured models\cite{9, 10}, age-stratified mass action models\cite{11} and mass action models\cite{12} have been proposed to translate the individual-level effects of vaccines and antiviral drugs into effectiveness of control strategies. Some of these recent modeling studies indicate that including school children in the vaccination program could be an efficient approach to reduce community transmission and deaths\cite{13, 14}.

The aim of this study is to investigate how the effectiveness of vaccine allocation schemes aimed at different risk groups depends on both age-dependent transmission patterns and the timing of vaccination. We consider only the first pandemic wave, as the vaccine supply is expected to be limited during the first wave of a pandemic and the peak in health care demand is expected to be largest. For this purpose, we set up a transmission model based on estimated infectious contact patterns within and among age groups. We compared our model predictions on attack rates, incidence and the timing of incidence peak levels with observations from the well-studied 1957–1958 ‘Asian flu’. We calculated the effect of scenarios where a limited vaccine supply would have to
be allocated between different age groups or risk groups, to find the best strategy, defined as the allocation scheme that resulted in the smallest number of expected deaths. We repeated these calculations for variable timing of vaccination.

2. Methods

2.1. Transmission model

We developed a basic compartmental transmission model including age-specific transmission parameters [15]. By assuming a large number of infections we could ignore stochasticity and use a deterministic model of SEIR type [16,17], depicted in Fig. 1. The population was stratified into age groups and subsequently high-risk vs. low-risk groups for influenza-related complications. The top row in Fig. 1 represents disease progress for infected individuals in age group \( a \) and risk-group \( r \) (subscripts \( a, r \)). Individuals can be either susceptible (\( S \)), exposed (\( E \), i.e., latent), infectious (\( I \)), recovering (\( G \), i.e., not infectious any more but still suffering from the disease and requiring medical attention), or removed (\( R \), i.e., either recovered or dead). The \( G \) compartment is included solely to calculate the number of people in hospital; from the point of view of transmission the individuals in this compartment are equivalent to the individuals in the \( R \) compartment. The incidence of new infections acquired by susceptibles of a certain age/risk-group \( (a, r) \) from infectious individuals in the age/risk groups \( (a', r') \), \( \Lambda_{a,r} \), was assumed to be proportional to the product of the sizes of the susceptible and the infectious groups \( (S_{a,r} \) and \( I_{a',r'} \), respectively) and to the contact rate between members of these groups:

\[
\Lambda_{a,r} = qS_{a,r} \sum_{a'} C_{aa'} \sum_{r'} I_{a',r'}
\]

In this formula, \( c_{aa'} \) is a coefficient of the contact matrix \( \epsilon \) that describes the mixing pattern among individuals, denoting the frequency of contacts between \( (a, a') \) pairs of individuals. Parameter \( q \) measures the transmission probability between an infectious and a susceptible individual, given contact. We assumed \( q \) to be independent of the age/risk-group combination. The durations of exposed and infectious period are modelled by gamma distributions (or more precisely, Erlang distributions) that better describe observed variations in these periods than the exponential distribution used in the standard SIR model. All calculations refer to an outbreak in a population that is completely susceptible for the pandemic virus. The births of susceptible and influenza-unrelated deaths during the epidemic can be neglected because we are interested only in the first pandemic wave. For the same reason, we can also neglect possible changes in the contact rates \( c_{aa'} \) due to the mortality (i.e., reduction in total population size) caused by the virus. The complete transmission model is described in Appendix A.

The key parameter that describes the transmission potential is the basic reproduction number \( R_0 \), and this parameter is entirely determined by the number of individuals in the different age groups, the contact matrix \( \epsilon \), and the transmission probability \( q \). If an intervention brings \( R_0 \) below unity, containment is achieved: the transmission process will be unable to sustain itself within the population and new cases only arise from small, rapidly ceasing outbreaks, or by immigration of infected individuals [16].

2.2. Parameterization

We used the age distribution of the Dutch population in 2007 (16 million individuals [18]) and the same classification into low- vs. high-risk groups for influenza and associated complications as van Genugten et al. [19]. High-risk groups include immunocompromised individuals, people with chronic respiratory diseases, and all people over 65 years in nursing homes. The contact patterns for the transmission model were inferred from a study using social contact data to estimate age-dependent transmission parameters for respiratory-spread infectious diseases, validated against infection patterns of circulating mumps and pandemic influenza [15]. The resulting mixing matrix \( \epsilon \) is characterized by most intense mixing between school-age children, and most indiscriminate contact behavior occurring in the 20–39 years age group.

We chose the distributions of exposed and infectious periods such that the mean generation interval equals 2.85 days, as was observed in a household transmission study [20]. The disease-specific transmission probability parameter \( q \) was calibrated such that the basic reproduction number \( R_0 \) equals 1.73. This value was estimated from applying the mixing matrix to infection attack rates during the ‘Asian’ 1957–1958 influenza A/H2N2 pandemic [15], and is in line with other recent analyses of past pandemics [8,10,20,21]. Asymptomatic cases (40% of infections) were assumed to have the same probability to cause secondary infections as symptomatic cases.

We define the start of the epidemic by the introduction in our default parameter setting of 20 exposed individuals into an entirely susceptible population. This initial group of infected was distributed over the age classes in a way that would correspond to the stable distribution attained during an exponentially increasing outbreak. We calculated the predicted incidence of hospitalizations (and deaths, respectively) throughout the course of the pandemic by multiplying the number of newly infectious (removed) individuals with assumed group-specific hospitalization (mortality) rates ([19], cf. bottom row in Fig. 1). Appendix B contains details

![Flow diagram of the transmission model and healthcare demand.](image-url)
of values and references of the parameters for the transmission model as well as parameters describing the age- and risk-group dependent morbidity, mortality and associated healthcare demand.

2.3. Allocation schemes

We are considering a scenario in which, during the first phases of a pandemic, pharmaceutical companies are producing vaccines, sufficient to vaccinate a substantial proportion of the general population, but insufficient to achieve protection of the entire population through herd immunity. Such a scenario is obtained by assuming a 35% vaccine coverage. In our default parameter setting we assume that vaccine confers protection immediately after the second dose (separated by a period of 14 days), with an individual efficacy of 0.8 (0.56 for 65+ individuals, with efficacy defined as the reduction in probability, given exposure, that a vaccinated individual will develop influenza, as compared to an untreated individual). Note that in case of uniform vaccine allocation and random contacts (homogeneous mixing, Section 3.4), the critical vaccination threshold to prevent an outbreak would be $1 - 1/R_0$ divided by vaccine efficacy, or 55%. We analyzed two allocation schemes:

- Allocation Scheme 1: Vaccination of individuals with high-risk of complications; in this ‘high-complication risk’ scheme, first the high-risk groups are vaccinated in the order 65+, 0–4, 5–12, 40–64, 20–39, and 13–19 years, and then the low-risk groups in the same order. If the size of an age/risk-group is larger than the amount of vaccine units available, vaccine is allotted randomly to this group, and the lower priority groups remain unvaccinated.

- Allocation Scheme 2: Vaccination of individuals with high-risk of infection; in this ‘high-infection risk’ scheme, high-risk and low-risk groups are combined by age and vaccine is allocated to age groups, prioritized by their expected attack rates (see Fig. 2a), in the order 13–19, 20–39, 5–12, 40–64, 0–4, and 65+ years.

Allocating vaccine to 35% of the current Dutch population with the high-complication scheme means that all high-risk groups, all low-risk children up to 13 years old and low-risk 65+ individuals, and a small part of low-risk 40–64 years class are vaccinated, and everyone else remains unvaccinated. The high-infection scheme means in this case that every 13–19 and 20–39-year-old is vaccinated and 0.5% of the 5–12 years class, and the rest of the population is left unvaccinated.

For each of these two intervention scenarios we considered immunization at a different number of days before or after the peak of the uncontrolled pandemic. We use “days until peak of uncontrolled epidemic” as a measure of time, as it is more robust than “time since introduction” because it does not depend on the particular initial conditions. The time of vaccination is defined by the second dose. Individuals are immunized irrespective of whether they possibly have been infected already.

2.4. Sensitivity analyses

Some of the assumptions of our default parameter setting reflect uncertainty about the control measures that can be implemented, and some other assumptions reflect unknown characteristics of the infection. To highlight the impact of these uncertainties on the outcome we conduct a sensitivity analysis. We vary the following parameter values: the contact matrix, the amount of vaccine, vaccine efficacy, delay in vaccine protection, the length of the mean exposed and mean infectious periods, and the magnitude of the reproduction number $R_0$. We also investigate the sensitivity of the results to the introduction of infections from outside the Netherlands throughout the epidemic.

To elucidate the importance of the contact patterns that we incorporated in the transmission model, we consider a simplified version where the age-specific contact structure is removed entirely.
3. Results

3.1. Model validation

The model predicts an overall population attack rate of 63.4%. With 40% asymptomatic infections, this would correspond to an overall clinical attack rate of 38%. For the default parameters, more than 99% of all infections occur within a period of 60 days. Fig. 2a shows the age-group specific attack rates for the uncontrolled pandemic as predicted by the model, compared with influenza attack rates by age as measured by serologic tests during the Asian flu in Cleveland [22]. Clearly, teenagers are most severely hit by the pandemic. The relationship between age and attack rate of the model predictions is similar to the observations, with the exception of the adult age group(s). For adults the model predicts higher attack rates than observed in the Cleveland data but we note that the adults attack rate in the Asian flu study is likely to be subject to sampling bias [15]. The apparent discrepancy could be explained in part by pre-existing immunity that has been reported for adults [22,23].

The different contribution of infections over the different age groups causes them to reach their highest incidence at different points in time. This is shown in Fig. 2b, where we compare model predictions of the timing of peaks in hospitalizations for different age groups with observations on timing of mortality in the Netherlands during the 1957 'Asian' influenza pandemic [24]. Both model predictions and observations show that the teenager group takes the lead, and that the larger the age difference between this and the other groups, the longer the delay in peak incidence compared with the teenager group; the oldest groups are the last ones to reach maximum incidence. The model underestimates the delay for the older age groups, which could be due to less frequent contacts of older age groups with the younger age groups than described by the contact patterns in the model, or due to age-dependent differences in disease progress not taken into account here.

In Fig. 2c we compare the incidence of infections per person per week with observations on infections, confirmed by virus isolation from Cleveland. Because the sum of observations on the incidence of virus-isolated infections only accounts for 41% attack rate whereas the serologic attack rate in unvaccinated persons was measured to be 55% [22], we corrected the model predictions of infections by a factor 41/55. The model captures the qualitative shape of the epidemic curve in weeks 2–9 when the incidence is large enough to use a deterministic model, but underestimates the incidence in the rising and falling phase and overestimates the peak values. The difference between model and data can be due to a limited capacity for viral isolation around the peak of the pandemic.

3.2. Model predictions: effect of vaccination

We calculate the impact of the two vaccine allocation schemes when (the second) vaccination is implemented 20 days before the peak of an uncontrolled pandemic. Fig. 3 shows the cumulative numbers of patients with influenza-like illness (ILI), hospitalizations and deaths for the uncontrolled pandemic and the intervention strategies. In Fig. 3a we see that allocation Scheme 2, vaccinating individuals with a high-infection rate first, suppresses both morbidity and mortality better than allocation Scheme 1, where priority is given to individuals with high rate of complications. In Fig. 3b the sensitivity of this result to a range of parameter values is studied. We observe that the result of better performance of allocation Scheme 2 with respect to total deaths is very robust, as it is insensitive to all parameter changes considered in Fig. 3b. Amongst the parameter changes studied, a 15% increase in the reproduction number (rightmost small bars) has the largest impact. It much reduces the difference in total deaths between the schemes, and leads to a marginally better performance of Scheme 1 in terms of hospitalizations. As illustrated in Fig. 3b by the effect of a 15% reduction of $R_0$, a lowering of the reproduction number enhances the benefit of vaccination of individuals with a high-infection rate, thus improving the better performance of allocation Scheme 2. We note that this latter effect provides an indication to which extent our results may also apply to a second pandemic wave. If a lowering of the reproduction number due to induced immunity levels were the main effect of a preceding wave, this sensitivity analysis suggests that the relative performance of the two schemes carries over to the context of a second wave.
3.3. Time dependency of the optimum vaccine allocation scheme

We compare the two allocation schemes (allocation Scheme 1: vaccinating individuals with a high-risk of complications; allocation Scheme 2: vaccinating individuals with a high-risk of infection) for different moments of implementation. If one would vaccinate before the pandemic starts, the high-risk allocation scheme will result in a much larger reduction of both number of deaths and number of cases with ILI. The difference in impact of both allocation schemes on number of ILI cases becomes smaller if we start vaccinating later during the pandemic. The difference in impact of the two allocation schemes reverses if we vaccinate at a later moment. This means that, if one would control with the objective of maximizing the number of averted deaths, the best possible allocation depends crucially on timing of implementation: if supply of vaccine is available before the pandemic wave hits the population, one should vaccinate the groups with the highest risk of infection; if supply is only obtained during the pandemic wave and the implementation of a vaccination campaign not be realized much before uncontrolled incidence would reach its highest point, one should target the groups with the highest risk of developing complications (Fig. 4). We have found these results to be robust under assum-

3.4. Importance of age-structured mixing

In Fig. 5 we show that interventions not only have an effect on cumulative numbers but also on the progress in time of the outbreak. In Fig. 5a we show the results for the default parameter setting. In Fig. 5b we assumed homogeneous mixing and calibrated the overall transmission parameter $q$ such that the transmission model produces the same overall attack rate (63.4%) as our default model with age-specific contact rates (Fig. 3). We see that, although infection attack rates are the same for the uncontrolled outbreak, hospitalization is higher for the homogeneous mixing case. This is because the attack rate is now uniform over all age groups, whereas in the case with age-specific contact rates the older age-group with a higher proportion of high-risk individuals, have lower attack rates than the population average (Fig. 2a). Interventions in the homogeneous mixing case cause a slower, longer outbreak in which peak levels are relatively lower as well, which could help to unburden the healthcare system. The two vaccination schemes swap position in the homogeneous mixing case: the high-complication priority scheme outperforms the high-infection priority scheme when it comes to preventing hospitalizations.

4. Discussion

A time delay of several months is expected from the isolation of a new pandemic virus to the start of mass production of an effective vaccine. Such a vaccine, if development is successful, will most
likely become available in limited supply, such that the authorities will need to decide how to allocate the supply between different age groups or risk groups. We have shown that the optimum allocation of vaccine will not only depend on the objective and the constraints of the interventions, but also on the time at which interventions are carried out during progress of the outbreak.

Age-specific transmission plays an important role in the underlying mechanism. Here we have used age-specific social contact data to represent the relevant pattern of at-risk contact events for influenza transmission. In a previous study we have shown that this age-specific social contact data yielded a more parsimonious description of the age-specific infection attack rates during the Asian influenza pandemic than usual a priori assumptions about mixing patterns such as homogeneous mixing, proportionate mixing or who-acquired-infection-from-whom matrices [15]. In this paper, we have shown that the inclusion of this age-specific social contact data in a relatively simple transmission model for pandemic influenza yields a good fit to data on the time at which various age groups within the population suffer from the disease: the age-specific transmission pattern explains why teenagers experience their largest incidence in the beginning and older age groups in the last phase of a pandemic.

With respect to vaccination, recent studies suggest targeting schoolchildren and recommend morbidity-based (analogous to high-infection priority) or mortality-based (high-complication priority) strategies, depending on the assumed transmissibility of the virus [13,14]. With an insufficient supply of pre-pandemic vaccine, one option would be to use smaller doses, allowing more people to be vaccinated [25]. Another option is to target the limited amount to specific groups to maximize the impact.

Our results suggest that if a vaccine becomes available during the pandemic, when the number of new cases is close to its peak value, priority should be given to groups with a high-risk of developing complications. In case there is a vaccine available before the epidemic starts, vaccination of groups with a high-risk of infection can be considered. A vaccine allocation strategy should therefore optimally be flexible enough to take such considerations into account.

Acknowledgment

This work was supported by the EC project INFTRANS (contract FP6-513715).

Appendix A. Transmission model

The model equations are

\[
\begin{align*}
\frac{dS_{a,r}}{dt} &= -qS_{a,r} \sum_b C_{a,b} \sum_{i,s} E^{(i)}_{b,s} \\
\frac{dE_{a,r}}{dt}^{(0)} &= qS_{a,r} \sum_b C_{a,b} \sum_{i,s} (\hat{h}_{b,s} - \tilde{h}E_{a,r}) \\
\frac{dE_{a,r}}{dt}^{(i)} &= \tilde{h}E_{a,r} - \dot{\gamma}E_{a,r} \\
\frac{dI_{a,r}}{dt}^{(0)} &= \tilde{h}E_{a,r} - \dot{\gamma}I_{a,r} \\
\frac{dI_{a,r}}{dt}^{(i)} &= \gamma E_{a,r} - \gamma I_{a,r} \\
\frac{dR_{a,r}}{dt} &= \gamma G_{a,r} \\
\end{align*}
\]  

(A.1)

where parameters \(\eta, \nu\) and \(\gamma\) denote the removal rates from the exposed, the infectious and the recovering stages, respectively. The durations of exposed and infectious period follow Erlang distributions (i.e., a type of gamma distribution). This is accomplished by splitting up both exposed and infectious compartments in \(n_E\) and \(n_I\), respectively, consecutive stages, the superscripts \(i\) and \(j\) (\(i \in \{1, \ldots, n_E\}\) and \(j \in \{1, \ldots, n_I\}\)) denote the stage numbers. The overall transition rates between consecutive stages are given by \(\tilde{\eta} = n_E \eta\), and \(\tilde{\nu} = n_I \nu\), respectively.

The total population size \(N\) is then given by the following equation:

\[
N = \sum_{a,r} \left( S_{a,r} + \sum_i E^{(i)}_{a,r} + \sum_i I^{(i)}_{a,r} + G_{a,r} + R_{a,r} \right)
\]  

(A.2)

We assume infectiousness to be constant during the infectious period. The distribution of the generation time, \(P_c(t)\), can be expressed in terms of the distributions of the exposed and infectious periods, \(P_E(t)\) and \(P_I(t)\), respectively, by noting that the probability density \(P_c(t)\) is the probability density corresponding to the two conditions \(t > t_E\) and \(t < t_E + t_I\) being met simultaneously

\[
P_c(t) = \frac{\delta(t > t_E)\delta(t < t_E + t_I)}{\int_0^{\infty} \delta(t > t_E)\delta(t < t_E + t_I) \, dt}
\]

\[
\frac{\delta}{n_I} \int_0^t P_E(t_E) \int_{t-t_E}^{\infty} P_I(t_I) \, dt_I \, dt_E
\]

(A.3)

After substituting gamma-distributional forms for \(P_E(t)\) and \(P_I(t)\) the mean and variance of \(P_c(t)\) can analytically be expressed in terms of \(\eta, \nu, n_E\) and \(n_I\).

Appendix B. Parameter values

In Table B1 we list the age-specific contact rates for the Dutch population [15], redistributed over the age groups used here (from [19]), and normalized such that \(c_{11} = 1.0\). The infectivity parameter \(q\) was calculated as the multiplication factor of the next-generation matrix resulting from this contact pattern and model (A.1)–(A.2) that corresponds to a value for \(R_0\) of 1.73 ([15,20]). \(R_0\) was calculated as the dominant eigenvalue of the next-generation matrix.

Parameters that characterize the population composition and the transmission process are listed in Table B2. The generation interval was estimated from a Japanese household study [26]: exclusion of possible co-primary and tertiary infections yielded a mean value of 2.85 days and a standard deviation of 0.93 day [20]. The number of exposed and infectious stages, \(n_E\) and \(n_I\), respectively, were both set to 8. The corresponding values of the mean durations of exposed and infectious periods matching the required mean and standard deviation of the generation interval are 1/\(\eta = 1.95\) and 1/\(\nu = 1.6\), respectively. Table B3 lists the model parameters that characterize morbidity, mortality, the demand for healthcare, and the effects of vaccination, defining the intervention strategies considered in this paper.

<table>
<thead>
<tr>
<th>C</th>
<th>0–4</th>
<th>5–12</th>
<th>13–19</th>
<th>20–39</th>
<th>40–64</th>
<th>65+</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4</td>
<td>1.000</td>
<td>0.186</td>
<td>0.105</td>
<td>0.204</td>
<td>0.094</td>
<td>0.068</td>
</tr>
<tr>
<td>5–12</td>
<td>0.186</td>
<td>1.232</td>
<td>0.145</td>
<td>0.157</td>
<td>0.092</td>
<td>0.052</td>
</tr>
<tr>
<td>13–19</td>
<td>0.105</td>
<td>0.145</td>
<td>1.549</td>
<td>0.350</td>
<td>0.259</td>
<td>0.103</td>
</tr>
<tr>
<td>20–39</td>
<td>0.204</td>
<td>0.157</td>
<td>0.350</td>
<td>0.410</td>
<td>0.268</td>
<td>0.136</td>
</tr>
<tr>
<td>40–64</td>
<td>0.094</td>
<td>0.092</td>
<td>0.259</td>
<td>0.268</td>
<td>0.228</td>
<td>0.123</td>
</tr>
<tr>
<td>65+</td>
<td>0.068</td>
<td>0.052</td>
<td>0.103</td>
<td>0.136</td>
<td>0.123</td>
<td>0.349</td>
</tr>
</tbody>
</table>
Table B2
Default setting of the parameter values in the transmission model

<table>
<thead>
<tr>
<th>Description</th>
<th>Units</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population (N)</td>
<td>16,357,992</td>
<td>Person</td>
</tr>
<tr>
<td>Age groups</td>
<td>[0.5]; [5,13]; [13,20]; [20,40]; [40,65]; [65,∞]</td>
<td>Year</td>
</tr>
<tr>
<td>Risk groups</td>
<td>Low, high</td>
<td>–</td>
</tr>
<tr>
<td>Relative sizes (age/risk) groups in population</td>
<td>0.0577; 0.0951; 0.0835; 0.2478; 0.3278; 0.0942; 0.0014;</td>
<td>–</td>
</tr>
<tr>
<td>Mean exposed period (1/ν)</td>
<td>0.0023; 0.0020; 0.0162; 0.0215; 0.0506</td>
<td>Day</td>
</tr>
<tr>
<td>Mean infectious period (1/ι)</td>
<td>1.95</td>
<td>Day</td>
</tr>
<tr>
<td>Mean recovery period (1/γ)</td>
<td>7.0</td>
<td>Day</td>
</tr>
<tr>
<td>Number of exposed stages (nE)</td>
<td>8</td>
<td>–</td>
</tr>
<tr>
<td>Number of infectious stages (nI)</td>
<td>8</td>
<td>–</td>
</tr>
<tr>
<td>Number of recovery stages (nR)</td>
<td>2</td>
<td>–</td>
</tr>
</tbody>
</table>

Note: For explanation see the text and references.

Table B3
Probabilities of morbidity and mortality per infection

<table>
<thead>
<tr>
<th>Probability of</th>
<th>Age group</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza-like illness</td>
<td>0–4</td>
<td>0.60</td>
</tr>
<tr>
<td></td>
<td>5–13</td>
<td>0.60</td>
</tr>
<tr>
<td></td>
<td>14–19</td>
<td>0.60</td>
</tr>
<tr>
<td></td>
<td>20–39</td>
<td>0.60</td>
</tr>
<tr>
<td></td>
<td>40–64</td>
<td>0.60</td>
</tr>
<tr>
<td></td>
<td>65+</td>
<td>0.60</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>High-risk</td>
<td>8.70 × 10⁻¹</td>
</tr>
<tr>
<td></td>
<td>Low-risk</td>
<td>3.45 × 10⁻⁵</td>
</tr>
<tr>
<td>Death</td>
<td>High-risk</td>
<td>3.44 × 10⁻⁴</td>
</tr>
<tr>
<td></td>
<td>Low-risk</td>
<td>1.47 × 10⁻⁵</td>
</tr>
<tr>
<td>Relative susceptibility if vaccinated (vaccine efficacy)</td>
<td>0.80</td>
<td></td>
</tr>
</tbody>
</table>

Note: For explanation see the text and references.

References


