Cost-effectiveness of influenza control measures: a dynamic transmission model-based analysis

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SUMMARY

We investigated the cost-effectiveness of different influenza control strategies in a school setting in Taiwan. A susceptible-exposure-infected-recovery (SEIR) model was used to simulate influenza transmission and we used a basic reproduction number ($R_0$)-asymptomatic proportion ($\theta$) control scheme to develop a cost-effectiveness model. Based on our dynamic transmission model and economic evaluation, this study indicated that the optimal cost-effective strategy for all modelling scenarios was a combination of natural ventilation and respiratory masking. The estimated costs were US$10/year per person in winter for one kindergarten student. The cost for hand washing was estimated to be US$32/year per person, which was much lower than that of isolation (US$55/year per person) and vaccination (US$86/year per person) in containing seasonal influenza. Transmission model-based, cost-effectiveness analysis can be a useful tool for providing insight into the impacts of economic factors and health benefits on certain strategies for controlling seasonal influenza.

Key words: Cost-effectiveness analysis, influenza, modelling, control measures, basic reproduction number.

INTRODUCTION

The influenza virus causes widespread morbidity and mortality in various populations: an average of 250,000–500,000 deaths occur every year worldwide [1]. In subtropical regions like Taiwan, this impact is felt predominantly during the winter months, and the epidemics recur with a highly predictable seasonal pattern. Seasonal variation in disease transmission thus plays an important role in the transmission dynamics of influenza. Since schools are centres for the spread of influenza, the probability of disease transmission is considerably higher due to increased mixing level of people during school terms compared to school holidays [2].

Our previous studies [3–5] have focused on both the theoretical and empirical aspects of the transmission dynamics of indoor respiratory infections. These were aimed at both understanding observed epidemiological patterns and predicting the consequences of introduced public health interventions along with effective engineering control measures to contain infectious diseases.

A Wells-Riley mathematical model was employed for modelling indoor respiratory infection [3–5] to
estimate the exposure concentrations \((q)\) in indoor environments and to estimate the basic reproduction number \((R_0)\) in a shared indoor airspace. Riley et al. [6] developed a Wells–Riley mathematical equation to estimate the probability of airborne transmission of an infectious agent indoors. The key parameter is the quantum generation rate \((q)\) of infectious quanta by an infected person. The \(q\) value was defined by Wells [7] who conducted a series of experiments to estimate the response and reaction to inhaled infectious droplets, indicating that a quantum (or infectious dose) can infect 63.2% of susceptibles tested. Hence, exposure to one quantum of infection gives an average probability of 63% of becoming infected [7]. The \(R_0\) value is the key epidemiological determinant that characterizes the transmission potential of a disease, which is defined as the average number of successful secondary infection cases generated by a typical primary infected case in an entirely susceptible population [8]. \(R_0\) essentially determines the rate of spread of an epidemic and how intensive a policy will need to be to control the epidemic. \(R_0>1\) implies that the epidemic is spreading within a population and that incidence is increasing, whereas \(R_0<1\) means that the disease is dying out. An average \(R_0=1\) means the disease is in endemic equilibrium within the population.

We also adopted the competing-risks model [9–11] to understand the dynamics of the interplay in different enhanced engineering control measure strategies. The competing-risks model is a probabilistic model by which the dynamics of interplay in different enhanced engineering control-measure strategies can be described. The basic assumption of the probabilistic calculations on the competing-risks model was based on an underlying Poisson model, i.e. different control efficacies act independently of each other. The selected optimal control measures include environmental controls by ventilation and air filtration, as well as respiratory protection. The inclusion of competing risks in the model recognized the fact that an individual might gain substantial benefits in risk reduction of airborne infection from many different control measures including technological controls at the source (by surgical masking and treatment booths), environmental controls (by ventilation, air filtration and ultraviolet germicidal irradiation), and receptor controls (by respiratory protection via respirators) [12–14].

We linked the competing-risks model and Wells–Riley mathematical equation in order to estimate the reduction of the potential infectious force of \(R_0\). Finally, a susceptible-exposed-infected-recovery (SEIR) model was used for quantitatively explaining the dynamics of an epidemic. However, in our study, we ignored the control measure effectiveness variation and unit cost estimations.

The cost benefits of influenza vaccination were assessed for many countries; the methods of assessment and unit cost of control measures were different in each country [15, 16]. Published studies provide the cost analysis methods and consider the direct (hospitalization or vaccination) and indirect costs (parent work loss) of disease burden for comparison with different scenarios, such as the vaccinated coverage rate [17] and school closure policies of varying length [18]. However, in Taiwan, the major efforts act independently of each other. The selected optimal control measures include environmental controls by ventilation and air filtration, as well as respiratory protection. The inclusion of competing risks in the model recognized the fact that an individual might gain substantial benefits in risk reduction of airborne infection from many different control measures including technological controls at the source (by surgical masking and treatment booths), environmental controls (by ventilation, air filtration and ultraviolet germicidal irradiation), and receptor controls (by respiratory protection via respirators) [12–14].

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pertaining to seasonal influenza, in order to formulate tentative guidelines.

MATERIALS AND METHODS

Influenza epidemiology characteristics

Our study was conducted at Ming-Chuan Elementary School located in southern Taipei. A total of 494 students, including 60 kindergarten and 434 elementary students, were housed in four buildings. The school has two kindergarten classes and 19 elementary classes with grades ranging from 1 to 6. Within those classes, schoolchildren were classified into four age groups: kindergarten (aged 4–6 years) and elementary students (7–8, 9–10, 11–12 years). Teaching and administrative staff aged 25–45 years were also included. Detailed descriptions of the study population have been presented in Chen et al. [4]. We adopted the elementary school setting based on weekly seasonal influenza epidemiological data from the Taiwan Center for Disease Control (CDC) databank from 2003 to 2005 (http://www.cdc.gov.tw/en/index.asp). We pooled data into spring/winter and summer/autumn to reflect the seasonal average incidences (Fig. 1a).

Control measure modelling

Here we used a $R_0=\theta$ control curve to formulate the cost-effectiveness analysis, where $R_0$ represents the basic reproduction number and $\theta$ represents the asymptomatic proportion of infected persons. The $R_0=\theta$ control curve, denoted as $R_0=f(\theta)$, can be derived from an equation-based control model [5, 23]. Based on the $R_0=\theta$ control curve, if a given infectious agent localizes below the curve (area $A_1$), the outbreak is always controlled eventually; however, if an infectious agent localizes above the curve (area $A_2$), additional control measures would be required to control spread. The uncontrollable ratio ($f_{uc}$) used to examine the effectiveness of the control measure adopted can be determined from the $R_0=f(\theta)$ curve as (Fig. 2):

$$f_{uc} = \frac{A_2}{A_1 + A_2}, \quad (1)$$

where $A_1$ and $A_2$ are areas under (representing the controllable area) and above (representing the uncontrollable area) the $R_0=f(\theta)$ curve, respectively.

Table 1 summarizes the mathematical models used to calculate $R_0$ with and without control measures and $R_0=f(\theta)$ functions based on different public health interventions. The proposed control measures included engineering approaches such as natural ventilation (G), high-efficiency particulate air (HEPA, H) filtration, and ultraviolet germicidal irradiation (UVGI, U) and personal protection equipment such as utilization of respiratory protection masks (M). The public health interventions were isolation (I), vaccination (V), and hand washing (HW).

Parameter estimates for $\theta$ can be determined by the specific biological characteristics of the aetiological agents, where $\theta=(incubation\ period−latent\ period)/infectious\ period$. We calculated the distribution of $\theta$
Table 1. Mathematical expressions for basic reproduction number ($R_0$) without control measures, with engineering and personal protection control measures, and $R_0=f(\theta)$ functions with $i$ public health interventions and personal control measures

<table>
<thead>
<tr>
<th>$R_0$ without control measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R_0 = (n-1) \times \left{ 1 - \exp \left{ -\frac{qpt}{Q} \left[ 1 - V \left{ 1 - \exp \left( -\frac{Q}{V} \right) \right]\right]\right} \right}$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>$R_0$ with engineering and personal protection control measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R_{0E} = (n-1) \left{ 1 - \exp \left{ -\left( \frac{qpt(1-\eta_1)}{Q+\lambda V+Q_1 \eta_2} \right) \left{ 1 - \exp \left( -\left(ACH+\eta + ACH_1 \eta_1 \right) t \right) \right} \right}$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>$R_0=f(\theta)$ functions with $i$ public health intervention(s) and personal control measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>$i=1$ \hspace{1cm} $R_0 = \left[ 1 - r(1-\epsilon_1) + \epsilon_1 \theta \right]^{-1}$</td>
</tr>
<tr>
<td>$i=2$ \hspace{1cm} $R_0 = \left[ (1-\epsilon_1)(1-\epsilon_2) + \epsilon_1(1-\epsilon_2) \theta + \left( 1 - \epsilon_1 \right) \epsilon_2 \theta + \frac{\theta}{2-\theta} \eta_3 \right]^{-1}$</td>
</tr>
<tr>
<td>$i=3$ \hspace{1cm} $R_0 = \left[ (1-\epsilon_1)(1-\epsilon_2)(1-\epsilon_3) + \left( 1 - \epsilon_1 \right) \epsilon_2 \left( 1 - \epsilon_3 \right) \theta + \epsilon_3 \theta + \epsilon_3 \theta + \left( 1 - \epsilon_1 \right)(1-\epsilon_2) \frac{\theta}{2-\theta} + \left( \epsilon_1 \epsilon_2 \theta \epsilon_3 \left( 1 - \epsilon_1 \right) \frac{\theta}{2-\theta} + \epsilon_1 \epsilon_2 \theta \epsilon_3 \left( 3 - 2\theta \right) \right) \left( 2 - \theta \right) \right]^{-1}$</td>
</tr>
</tbody>
</table>

$n$ is the population size; $I$ is the number of infectors; $q$ is the quantum generation rate by an infected person (quanta/day); $p$ is the breathing rate per person ($m^3$/day); $t$ is the total exposure time (days); $Q$ is the fresh air supply rate ($m^3$/day); $V$ is the volume of the ventilated space ($m^3$); $Q_1$ is the air flow rate through a recirculation HEPA filter ($m^3$/h); $\eta_2$ is the efficiency of respiratory protection masking used by an infected person (dimensionless); $\eta_1$ is the single-pass removal efficiency for an infectious droplet nuclei passing through the recirculation HEPA filter (dimensionless); $ACH$ is the air change rate (h); $ACH_1$ is the air change rate through a recirculation HEPA filter (h); $\lambda$ is the inactivation rate of an infectious droplet nuclei due to UVGI (h); and $\epsilon_1$, $\epsilon_2$, and $\epsilon_3$ denote the efficacies of isolation, vaccination, and hand washing, respectively.

Fig. 2 [colour online]. Illustration of the $R_0-\theta$ criteria for outbreak control. The critical line represents the combination of $R_0$, $\theta$, and certain efficacies of control measures that can be shown in equations (T3)-(T5) (Table 1).

using the Monte Carlo simulation to quantify the uncertainty concerning $\theta$, which was attributable to the large variance of the incubation, latent, and infectious periods for a specific airborne infection. Utilizing previous work, we were able to obtain range values for the incubation, latent, and infectious periods as 1–4, 1–3, and 4–8 days, respectively, for influenza [8].

**Unit cost estimations**

Table 2 summarizes the unit cost per year for engineering control measures, personal protection, and public health interventions. The costs of outpatient treatment were estimated to be US$11.55 per person [22]. The costs of UVGI were separated into equipment (lamp) and consumption (UV) costs. The lifespan of one lamp was estimated to be around 8000–10000 hours; hence, the costs of UVGI per year were estimated to be US$182. The costs of HEPA filtration were also separated into equipment and consumption costs based on the available market price, resulting in a consumption cost estimated at US$137 per year.

The costs of isolation per year were reasonably assumed to be US$3040 based on expert opinion. The costs of inactivated influenza vaccination per year were estimated by the cost of one vaccine...
Table 2. Unit cost of control measures including engineering, personal protection, and public health interventions

<table>
<thead>
<tr>
<th>Control measure</th>
<th>Symbol</th>
<th>Cost factor (US$/person)</th>
<th>Estimated process</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatient treatment</td>
<td></td>
<td>11.55</td>
<td>380 NTS (outpatient treatment cost)/32.9</td>
</tr>
<tr>
<td>UVGI</td>
<td>U</td>
<td>182.37</td>
<td>6000 NTS (Cost per UV lamp)/32.9</td>
</tr>
<tr>
<td>HEPA</td>
<td>H</td>
<td>136.78</td>
<td>4500 NTS (HEPA expendable filter)/32.9</td>
</tr>
<tr>
<td>Isolation</td>
<td>I</td>
<td>3040</td>
<td>10000 NTS (administrative cost)/32.9</td>
</tr>
<tr>
<td>Vaccine</td>
<td>V</td>
<td>4875</td>
<td>18.75 (US$/per vaccine) × 260 (total number in Min-Chung Elementary School)</td>
</tr>
<tr>
<td>Respiratory masking</td>
<td>M</td>
<td>27.36</td>
<td>15 (NTS per surgical mask) × 60 (estimated number)/32.9</td>
</tr>
<tr>
<td>Hand washing</td>
<td>HW</td>
<td>1605</td>
<td>(6 (times of hand washing a day) × 1000 c.c./ml × (volume of hand washing per time) × 0.01 NTS (water cost per litre) × 180 (days per year) × 260 persons) + 50000 NTS (administrative cost)/32.9</td>
</tr>
</tbody>
</table>


(USS12.50) plus the administrative fee (US$6.25), resulting in a cost of US$18.75 per person [21]. The costs of respiratory masking (i.e., using surgical masks) were estimated to be US$27.36 per year based on the 60 masks used per year at Ming-Chung Elementary School. The costs of hand washing were calculated to be US$1605 per year, which was estimated based on the advertised cost of US$1520 plus the cost of water consumption. Detailed descriptions are listed in Table 2.

Cost-effectiveness analysis

Our proposed cost-effectiveness analyses involved four scenarios. Scenario 1 represented no control measures. Scenario 2 represented a combination of engineering approaches and personal protection equipment. Our costs only reflected the outpatient treatment costs due to a lack of information in the questionnaire and other related information such as the costs associated with work loss. Scenario 3 involved a combination of public health interventions and personal protection equipment. Scenario 4 represented several engineering approaches and public health interventions associated with personal protection. Detailed descriptions of the cost estimation for scenarios 1–4 are presented in Appendix 2. Finally, the cost-effectiveness analysis tended to quantify the unit cost per person per year. In other words, we used average cost burden per year divided by all populations (in units of US$/year per person) in order to evaluate the optimal control measures.

RESULTS

Estimates of basic reproduction number

A Wells–Riley mathematical model [equation (T1), Table 1] of indoor respiratory infection [3–5] was employed to estimate the exposure concentrations ($q$) in indoor environments and to estimate the basic reproduction number ($R_0$) in a shared indoor airspace. The exposure concentrations ($q$) were calculated with input parameters of $N = 50$, $V = 600 \text{ m}^3$, $t = 6 \text{ h}$, $\rho = 0.38 \text{ m}^3/\text{h}$, $f = 0.00119$, $I = 1$, $P = \text{LN} (0.0073, 1.22)$ and $\text{LN} (0.0048, 1.44)$ for winter and summer, respectively (Table 3). The Monte Carlo simulation results show the best fitted lognormal distributions of $q$ with geometric means of 33.92 and 51.62 and geometric standard deviations of 1.14 and 1.22 for summer and winter, respectively.

The box-and-whisker plots of the median basic reproduction numbers ($R_0$) were estimated to be 3.22, 2.14, 1.71, 2.15, 2.85 for summer and 7.32, 3.78, 4.30, 5.43, 5.98 for winter, respectively, for the five age groups at Ming-Chuan Elementary School (Fig. 3a, b). Figure 3(c, d) shows the median risks of infection ($P$) in the five age groups for summer and winter, respectively. Grades 5 and 6 gave the highest risk of infection for all seasons. Kindergarten had the highest $R_0$ estimates, implicating that the density of the population affects age group-specific $R_0$. 


Predicting the effects of engineering and personal protection

We used equation (T2) (Table 1) to calculate the basic reproduction number \( R_0E \) under multiple engineering and personal protection control measures. We inputted the inactivation rate of infectious droplets due to UVGI (\( \lambda = 12/h \)) [24], single-pass removal efficiency for infectious droplet nuclei passing through the recirculation HEPA filter (\( \eta_r = 99·97\% \)), and air change rate through a recirculation HEPA filter (\( Q_r = 3·499 \text{ m}^3/\text{h} \)) into equation (T2).

The effects of engineering and personal protection are shown in Figure 4. For one control measure (G, natural ventilation) in winter, the median \( R_0E \) estimates notably decreased from 7·32, 4·5, and 5·98 (Fig. 3b) to 1·35, 2·11, and 1·33 (Fig. 4b) for kindergarten, elementary, and staff and administrative staff, respectively. For two control measures, it produced an order of G+U > G+M > G+H. Finally, using combinations of G+M+H, G+M+U, and G+H+U produced an order of efficacy of G+M+U > G+H+U > G+M+H (Fig. 4).

Effectiveness of public health interventions and personal protection

Table 4 summarizes the available published effectiveness data for inactivated influenza vaccination (V), hand washing (HW), and isolation (I). We deduced that the average vaccination effectiveness estimates were 0·70, 0·62, and 0·50 with standard deviations of 0·06, 0·06, and 0·03 for children, adults, and the elderly, respectively, by using 10000 Monte Carlo simulations. On the other hand, the average effectiveness of hand washing and isolation were estimated to be 0·24 and 0·82 with standard deviations of 0·03 and 0·06, respectively.

The impact of the different combinations of public health interventions (V, HW, I) were assessed by \( R_0 - \theta \) control models [equations (T3)–(T5)] (Table 1). Parameter estimates for \( \theta \) of influenza were determined by the specific biological characteristics of the aetiological agents. The uniform distributions [represented as mean (min-max)] that best fit the incubation, latent, and infectious periods were estimated to be 2·5 (1·0–4·0), 2·0 (1·0–3·0), and 6·0 (4·0–8·0) days, respectively. In the uniform distribution, all values between the minimum and maximum occur with equal likelihood. Hence, we assumed the ranges were minimum and maximum and all values between the minimum and maximum occur with equal likelihood. The 95% confidence intervals (CIs) for the proportion of people with asymptomatic infection ranged from 0·19 to 0·44 by the definition of \( \theta \). Finally, Figure 5 shows that the effectiveness of public health intervention followed the order of I > V > HW and I+V > I+HW > V+HW across all age groups, indicating that isolation had the greatest effect on influenza control without considering the cost effects.
Cost-effectiveness analysis

Cost-effectiveness analysis for scenario 1 is presented in Figure 6(a, b). The box-and-whisker plots without any control measures in summer show that the average cost for a kindergarten student was US$2.64/year per person (95% CI 2.39–2.84), indicating that the costs are higher than those of elementary students (US$1.40/year per person; 95% CI 1.00–1.85) and teaching and administrative staff (US$2.32/year per person; 95% CI 2.23–2.40) (Fig. 6a). Similarly, the costs for kindergarten students in winter (US$4.5/year per person; 95% CI 4.23–4.77) were also higher than those of elementary students (US$3.4/yr per person; 95% CI 2.69–4.13) and teaching and administrative staff (US$4.13/year per person; 95% CI 4.01–4.27) (Fig. 6b). The costs in winter were 41% higher than in summer for the kindergarten age group.

Cost-effectiveness analysis for scenario 2 was estimated to be US$0.67 (G+M), US$3.23 (G+U), and US$3.92/year per person (G+H) for kindergarten students (Fig. 6c). Costs in winter were 68%, 10%, and 30% higher than those in summer for kindergarten students for the G+M, G+U, and G+H combinations, respectively (Fig. 6d). For cost-effectiveness analysis in scenario 3, the results showed that US$31.25/year per person for hand washing was the highest cost-effectiveness control measure compared to isolation (US$55.16/year per person) and vaccination (US$85.75/year per person) (Fig. 7).

DISCUSSION

This study attempted to examine the potential health outcomes and cost-effectiveness of different
combinations of influenza control strategies in a school setting. This information may be useful to maximize the health benefits per dollar spent and can be used as an aid to rational public health decision making.

We found a set of intervention strategies that gave the highest reduction in basic reproductive number. For multiple engineering approaches and personal control measures, G+M+H+U strategies were the most effective interventions with a corresponding $R_{0E}$ estimate of 0·22 (95% CI 0·15–0·33) for kindergarten students in winter. G+U and G+M+U strategies had an $R_{0E}$ estimation of 0·45 (95% CI 0·30–0·66) and 0·22 (95% CI 0·15–0·33), respectively (Fig. 4b). For multiple public health interventions, the $R_0$ estimates for kindergarten students in winter decreased to 6·88 (95% CI 5·98–8·12), 7·19 (95% CI 6·25–8·49), and 7·32 (95% CI 6·36–8·64) for I+V+HW, I+V, and I+HW, respectively [equations (T3)–(T5)].

Regarding our dynamic transmission model and economic evaluation, this study indicated that the optimal cost-effective strategy for all scenarios was the combination of natural ventilation and respiratory masking. The estimated costs were US$10/year per person in winter for one kindergarten student. The cost for hand washing was estimated to be US$32/year per person, which was much lower than isolation (US$55/year per person) and vaccination (US$86/year per person) costs in containing seasonal influenza.

The main strength of this study was that it provides a new perspective on methods to integrate the
maximum estimation for infected numbers of people, unit cost of outpatients, and cost estimations of control measures. We used the $R_0 = f(\theta)$ function to describe the control impact on the basic reproduction number ($R_0$) through the use of isolation, vaccination, and hand washing. This study also simulated engineering approaches (using HEPA filtration and UVGI) and respiratory protection masking in a school setting by use of a modified Wells–Riley equation. Most cost-effectiveness studies are focused on vaccination of high-risk populations, including the elderly [21, 25–27] and children [28, 29], because many countries have an established Medicare system, and hospital databases that can offer methods to evaluate (in)direct costs when influenza vaccination is adopted. Many of these studies did not consider the effects of engineering approaches or respiratory protection masking on cost-effectiveness analysis for influenza epidemics. For seasonal-specific analysis, results indicate that it was not possible to provide an exact prediction of cost-effectiveness because several model inputs were uncertain. For example, the frequency of hand washing in 1 day or the cost per 1 litre of water was variable. Other model inputs such as the replacement frequency of respiratory masks and the types of masks used were different. There are two limitations to our study. A potential weakness of the analysis was that it only considered the costs of outpatient treatment for people who became infected. The indirect costs for work and productivity loss, even the hospitalization costs that arise from illness, were not taken into account. Hence, the burden of disease could be underestimated in our study. In other words, the total costs for each scenario were largely derived from the costs of control measures and not the costs of outpatient treatment. The second potential weakness of our study is that engineering methods may not be feasible. Natural ventilation represents a cost-effective approach; however, the ventilation conditions were not easy to quantitate and adjust.

### Table 4. Published effectiveness (median with 95% confidence interval) of selected public health interventions of vaccination, hand washing, and isolation

<table>
<thead>
<tr>
<th>Population</th>
<th>Outcome studied</th>
<th>Effectiveness*</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inactivated influenza vaccination effectiveness</strong></td>
<td>Influenza-like illness</td>
<td>0.75 (0.61–0.84)</td>
<td>[31]</td>
</tr>
<tr>
<td>Children (3–14 yr)</td>
<td>Influenza A cases confirmed by PCR</td>
<td>0.88 (0.49–0.97)</td>
<td>[31]</td>
</tr>
<tr>
<td>Children (6 months–17 years)</td>
<td>Vaccine effectiveness in preventing influenza illness</td>
<td>0.69 (0.40–0.90)</td>
<td>[29]</td>
</tr>
<tr>
<td>Healthy adults</td>
<td>Culture positive</td>
<td>0.77 (0.37–0.92)</td>
<td>[32]</td>
</tr>
<tr>
<td></td>
<td>Real-time PCR positive</td>
<td>0.74 (0.37–0.89)</td>
<td>[32]</td>
</tr>
<tr>
<td></td>
<td>Culture or real-time PCR positive</td>
<td>0.75 (0.42–0.90)</td>
<td>[32]</td>
</tr>
<tr>
<td></td>
<td>Serological positive</td>
<td>0.78 (0.37–0.93)</td>
<td>[32]</td>
</tr>
<tr>
<td>Community-dwelling elderly</td>
<td>Hospitalizations (respiratory conditions)</td>
<td>0.32 (0.29–0.40)</td>
<td>[32]</td>
</tr>
<tr>
<td></td>
<td>Deaths from all cases</td>
<td>0.50 (0.45–0.56)</td>
<td>[32]</td>
</tr>
<tr>
<td>Elderly in nursing homes</td>
<td>Respiratory illness</td>
<td>0.56 (0.39–0.68)</td>
<td>[32]</td>
</tr>
<tr>
<td></td>
<td>Hospitalizations</td>
<td>0.48 (0.28–0.65)</td>
<td>[32]</td>
</tr>
<tr>
<td></td>
<td>Deaths</td>
<td>0.68 (0.56–0.76)</td>
<td>[32]</td>
</tr>
<tr>
<td><strong>Hand washing effectiveness</strong></td>
<td>Relative risk</td>
<td>0.27 (0.0–0.58)</td>
<td>[33]</td>
</tr>
<tr>
<td></td>
<td>1.37 (0.78–2.40)</td>
<td>0.20 (0–0.48)</td>
<td>[34]</td>
</tr>
<tr>
<td></td>
<td>1.25 (0.81–1.92)</td>
<td>0.06 (0–0.31)</td>
<td>[33]</td>
</tr>
<tr>
<td></td>
<td>1.06 (0.78–1.44)</td>
<td>0.32 (0.009–0.53)</td>
<td>[35]</td>
</tr>
<tr>
<td></td>
<td>1.47 (1.01–2.13)</td>
<td>0.11 (0.029–0.18)</td>
<td>[36]</td>
</tr>
<tr>
<td></td>
<td>1.80 (1.78–1.82)</td>
<td>0.45 (0.438–0.45)</td>
<td>[37]</td>
</tr>
<tr>
<td></td>
<td>1.34 (0.96–1.89)</td>
<td>0.25 (0–0.47)</td>
<td>[38]</td>
</tr>
<tr>
<td></td>
<td>1.25 (1.14–1.37)</td>
<td>0.20 (0.12–0.27)</td>
<td>[39]</td>
</tr>
<tr>
<td><strong>Isolation effectiveness</strong></td>
<td></td>
<td>0.88 (0.9–0.75)</td>
<td>[40]</td>
</tr>
</tbody>
</table>

PCR, Polymerase chain reaction.

* Effectiveness = $1 - (1/relative risks) \times 100\%$ [40].
In conclusion, this study provides important baseline information on the costs and effectiveness of control strategies that can be used to judge the overall impact of communicable disease on the health of the population. For seasonal-specific cost-effectiveness analysis, the cost in winter was slightly higher than in summer, implying that we need more efforts on school health promotion programmes in the winter.
season. Our study also demonstrates that model-based, cost-effectiveness analysis can be useful to explore infectious disease trends and health consequences of interventions in a population over time, providing insight into the impacts of economic factors and health benefits on certain prevention combinations against seasonal influenza transmission. In the future, cost-effectiveness analysis must be part of a comprehensive strategy that involves changing incentives at multiple levels.

APPENDIX 1. The SEIR model

The parameters $S$, $E$, $I$, and $R$ were used for the epidemiological classes. The SEIR model can provide a basic description of the transmission dynamics of pandemic influenza by using a simple parameterized set of ordinary differential equations:

\[
\begin{align*}
\frac{dS}{dt} &= \mu N - \beta IS - \mu S, \\
\frac{dE}{dt} &= \beta IS - \sigma E - \mu E, \\
\frac{dI}{dt} &= \sigma E - \upsilon I - \mu I, \\
\frac{dR}{dt} &= \upsilon I - \mu R,
\end{align*}
\]

where $N(t)$, $S(t)$, $E(t)$, $I(t)$, and $R(t)$ represent the number of total persons, susceptible, exposed, infected, and recovered at time $t$ for specific age groups, respectively. $\beta$ represents the transmission coefficient for the probability that an infected person will have contact with and successfully infect a susceptible person.

Fig. 6 [colour online]. (a, b) Cost-effectiveness analyses for scenario 1 (without any control measures) for the three age groups of kindergarten, elementary, and staff/administrative staff. (c, d) Cost-effectiveness analysis for scenario 2 (multiple engineering and personal protection control measures) are presented.

\[
\begin{align*}
\text{(A1)} & \quad \frac{dS}{dt} = \mu N - \beta IS - \mu S, \\
\text{(A2)} & \quad \frac{dE}{dt} = \beta IS - \sigma E - \mu E, \\
\text{(A3)} & \quad \frac{dI}{dt} = \sigma E - \upsilon I - \mu I, \\
\text{(A4)} & \quad \frac{dR}{dt} = \upsilon I - \mu R, \\
\text{(A5)} & \quad N(t) = S(t) + E(t) + I(t) + R(t),
\end{align*}
\]
person, which can be estimated by $R_0 = \frac{\beta}{\mu + \nu}$ [8]. $\sigma$ represents the rate at which an exposed individual becomes infectious per unit time, which is equal to 0·333/day [8]. $\nu$ represents the rate at which an infectious individual recovers per unit time (per day) and is equal to 0·143 (1/average infectiousness periods of 7 days). $\mu$ represents the birth rate and death rate, which is equal to 0·013/year (http://www.mio.gov.tw/stat/).

**APPENDIX 2. Cost estimations for scenarios 1–4**

The costs (in US$/year per person) for scenario 1 ($\text{cost}_{WC}$) and scenario 2 ($\text{cost}_{EC}$) are represented as:

\[
\text{cost}_{wc} = I_{max-WC} \times C_f, \quad (A6)
\]

\[
\text{cost}_{EC} = C_{EC} + (I_{max-EC} \times C_f), \quad (A7)
\]

where $I_{max-WC}$ and $I_{max-EC}$ represent the maximum infected number of people without intervention and with intervention (engineering and personal protection control), respectively. $C_f$ represents the unit cost per person of the outpatient treatment. $C_{EC}$ represents the cost associated with the combination of engineering and personal protection control strategies. The estimated basic reproduction numbers in scenarios 1 and 2 are respectively denoted as $R_0$ and $R_{0E}$. A classic SEIR model (see Appendix 1) can be used to estimate the maximum infected number in a population ($I_{max}$).

The costs in scenarios 3 and 4 are given as:

\[
\text{cost}_{PI} = C_{PI} + (I_{max-PI} \times C_f), \quad (A8)
\]

\[
\text{cost}_{PE} = C_{EC} + C_{PI} + (I_{max-PE} \times C_f), \quad (A9)
\]

where $I_{max-PI}$ is the maximum infected number of people with intervention (public health interventions and personal protection strategies). $C_{PI}$ represents the cost of specific public health interventions and personal protection in a population. For scenario 3, $R_0$ estimates can be obtained based on $R_0 = f(\theta)$ functions as varied with different public health interventions and personal protection as: $R_0 \times f_{ac}$. For scenario 4, the total costs of control measure combinations ($\text{cost}_{PE}$) are given in equation (A9). The $I_{max-PE}$ is the maximum infected number of people with intervention (public health interventions and the combination of engineering and personal protection controls). $R_0$ estimates can then be estimated from $R_{0E} \times f_{ac}$.

![Fig. 7](colour online) (a) Cost-effectiveness analysis for scenario 3 (multiple public health intervention and personal protection control measures) in summer and winter for the three age groups, respectively.
DECLARATION OF INTEREST

None.

REFERENCES


