Socio-economic Impacts of Pandemic Influenza Mitigation Scenarios in Slovakia

Pavol BRUNOVSKÝ – Daniel ŠEVCÔVIČ – Ján SOMORČÍK* – Dagmar HRONCOVÁ** – Kateřina POSPÍŠILOVÁ***

Abstract

The aim of this paper is to assess the expected socio-economic impacts of various scenarios of pandemic influenza mitigation on the economy and mortality for Slovakia. Compared to similar past studies (e.g. Van Genugten et al. (2003)), our approach bears a significant difference. Whereas those studies work from the very beginning with the expected values of the data, we have treated the data as well as the model parameters as random variables. Results in the form of probability distributions and their characteristics (expected values and tolerance intervals) were obtained by stochastic Monte Carlo simulations of random impacts on 5,400,000 inhabitants of Slovakia. Six scenarios of pandemic mitigation have been analyzed. Total costs of medical treatment, the number of casualties as well as social costs with casualties included were compared.

Keywords: pandemic, influenza, Monte Carlo, mitigation

JEL Classification: I18, C15

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Introduction

Influenza pandemics can occur when a novel strain of flu virus causes epidemics that spreads very fast worldwide and affects high proportion of the world population. There have been 31 influenza pandemics recorded since 1580 (Lazzari and Stöhr, 2004). Reliable epidemiological data are sparse until the pandemics in 1889 – 1992. Most knowledge about the epidemiology of pandemic influenza can be obtained from the three well-documented pandemics of the 20th century in 1918 – 1919, 1957 – 1958 and 1968 – 1969 (Beran and Havlík, 2005). They represent the main source of evidence on the potential human toll of the next pandemic. The intervals between the consecutive pandemics of the 20th century ranged from 11 to 40 years. It has now been 40 years since the occurrence of the last pandemic in 1968. In 1997, the avian influenza virus H5N1 was shown to infect humans directly. As of 10 September 2008, 387 human cases of avian flu have been reported by WHO (World Health Organisation), 245 of which were fatal. Case fatality has reached over 60% (WHO, 2008a). At present, WHO confirmed few cases of human-to-human transmission of H5N1 (WHO, 2008b).

Increased awareness on influenza pandemics has led to discussions held by WHO, public health authorities, regulatory authorities, pharmaceutical industry on what our society can do and also should do to be prepared for the next pandemic. In a number of countries pandemic influenza plans have been drafted with several alternatives of mitigation scenarios that should decrease the health impacts including severe mortality and death and to minimize the social and economical impact of the next pandemic. Reports on the expected outcomes of such scenarios can be found e.g. in recent papers by Van Genugten et al. (2003), German et al. (2006), Fraser et al. (2004), Longini et al. (2005), Ferguson et al. (2006).

The present paper represents an analysis of the impacts of several mitigation scenarios for the country of Slovakia. However, while the papers cited above work merely with expected values, we take into account entire probability distributions of the variables. A similar approach has been employed by Meltzer et al. (1999) as well as Doyle et al. (2006). However, whereas in the cited papers uncertainty is restricted to the mitigation variable, we admit all probability parameters to be of stochastic nature. Further, instead of triangular or uniform distributions we work with more adequate beta ones (see below).

This approach is much more computationally involved but also more informative: in addition to the expected values of the outcomes it yields their entire probabilistic distributions and, hence, e.g. the value of risk coming from uncertainty of their predictions.
1. The Simulation Model and its Parameters

1.1. Input Parameters and Scenarios

The data in the Table 1 below have been taken from accessible literature. They have been consulted with specialists from pharmaceutical and health insurance companies.

### Table 1

**Parameters of the Influenza Mitigation Model for the Case of Slovakia**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of inhabitants</td>
<td>5,400,000</td>
</tr>
<tr>
<td>Influenza clinical attack rate</td>
<td>30%</td>
</tr>
<tr>
<td>Influenza mortality</td>
<td>2.5%</td>
</tr>
<tr>
<td>Percentage of infected medically treated</td>
<td>50%</td>
</tr>
<tr>
<td>Clinical complications rate of medically treated</td>
<td>25%</td>
</tr>
<tr>
<td>Percentage of infected hospitalized</td>
<td>8%</td>
</tr>
<tr>
<td>Percentage of infected hospitalized at ICU</td>
<td>2%</td>
</tr>
<tr>
<td>Antivirotics price</td>
<td>26.55 Euro</td>
</tr>
<tr>
<td>Price of complications treatment drugs</td>
<td>6.63 Euro</td>
</tr>
<tr>
<td>Standard hospitalization costs</td>
<td>464.7 Euro</td>
</tr>
<tr>
<td>ICU hospitalization costs</td>
<td>995.8 Euro</td>
</tr>
<tr>
<td>Pandemic vaccine price</td>
<td>7.83 Euro</td>
</tr>
<tr>
<td>Pre-pandemic vaccine price</td>
<td>7.83 Euro</td>
</tr>
</tbody>
</table>

*Note: ICU abbreviates the Intensive Care Unit.*  

We have simulated six different scenarios of influenza mitigation:

1. No vaccination (so-called control).
2. Whole population pre-vaccination (i.e. 2x pre-pandemic vaccination + 1x pandemic).
3. 2x pandemic vaccination of 50% population.
4. 2x pre-pandemic vaccination of whole population.
5. Pre-vaccination of 35% population + 2x pandemic vaccination of 32.5% population.
6. 1x pre-pandemic + 1x pandemic vaccination of the entire population.

The expected vaccine efficacy could be found in Table 2.

### Table 2

**Vaccination Efficacy (in %)**

<table>
<thead>
<tr>
<th>Type of Vaccination</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-vaccination</td>
<td>70</td>
</tr>
<tr>
<td>2x pandemic</td>
<td>80</td>
</tr>
<tr>
<td>2x pre-pandemic</td>
<td>60</td>
</tr>
<tr>
<td>1x pre-pandemic + 1x pandemic</td>
<td>65</td>
</tr>
</tbody>
</table>

*Sources: WHO (2008b) – line 1, authors’ estimates – lines 2 – 4.*

The figures 1 – 8 represent the decrease of the influenza clinical attack rate due to type of vaccination.
1.2. Simulation principle

To simulate particular scenarios the computer “infected” each individual of the population of 5,400,000 with the probability corresponding to the scenario, hence the distribution of infected individuals was binomial:

\[ \text{number of infected people} \sim \text{Bin}(n, p_{\text{car}}) \]
\[ n = 5,400,000 \quad p_{\text{car}} = \text{specific clinical attack rate} \]

where

specific clinical attack rate = clinical attack rate \times (1 - \text{vaccination efficacy}).

Recall that a discrete random variable \( X \) has a binomial (or Bernoulli) distribution \( \text{Bin}(n, p) \) with parameters \( n \in \mathbb{N} \) and \( p \in [0,1] \), if the probability \( \text{Prob}(X = k) \) satisfies

\[
\text{Prob}(X = k) = \binom{n}{k} p^k (1 - p)^{n-k}
\]

The binomial distribution is the discrete probability distribution of the number of successes in a sequence of \( n \) independent random yes/no experiments, each of which is successful with probability \( p \) between 0 and 1.

In case of Scenarios 3 and 5 the population has been partitioned into vaccinated/non-vaccinated and “infection” was carried out in each group separately. Then, for each infected person the computer generated (randomly with corresponding probability) whether she/he has been medically treated or not: thus, the number of treated individuals had a binomial distribution:

\[ \text{number of treated people} \sim \text{Bin}(n_{\text{inf}}, p_{\text{mt}}) \]
\[ n_{\text{inf}} = \text{number of infected people, } p_{\text{mt}} = \text{probability of medical treatment.} \]

We have assumed that each treated person has received antiviriotics and in case of complications (the computer generated their occurrence) other drugs as well. The distribution of the number of complications has been taken as binomial as well:

\[ \text{number of complications} \sim \text{Bin}(n_{\text{inf}}, p_{\text{ccr}}) \]
\[ n_{\text{inf}} = \text{number of infected people, } p_{\text{ccr}} = \text{clinical complications rate}. \]

For an infected individual the computer has generated whether he/she would has been subject to (standard or ICU) hospitalization or not:

\[ \text{number of hospitalizations} \sim \text{Bin}(n_{\text{inf}}, p_{\text{sh}}) \]
\[ n_{\text{inf}} = \text{number of infected people, } p_{\text{sh}} = \text{probability of standard hospitalization; } \]
number of ICU hospitalizations $\sim \text{Bin}(n_{\text{inf}}, p_{\text{icu}})$

$n_{\text{inf}} = \text{number of infected people}, \ p_{\text{icu}} = \text{probability of the ICU hospitalization.}$

Eventually, for each infected person the computer generated whether she/he has survived the infection or not:

number of deaths $\sim \text{Bin}(n_{\text{inf}}, p_d)$

$n_{\text{inf}} = \text{number of infected people}, \ p_d = \text{probability of death}$

To summarize we have confronted the numbers of infected, medically treated, hospitalized (hospitalized in ICUs, in particular) and dead individuals. The costs of vaccination, drugs and hospitalization have been calculated as follows:

vaccination costs = (number of prepandemic vaccines) $\times$ (prepandemic vaccine price)

$+ (number\ of\ pandemic\ vaccines) \times (pandemic\ vaccine\ price);$

drug costs = (number of treated people) $\times$ (antiviriotics price)

$+ (\text{number of complications}) \times (\text{cost of drugs for complications});$

hospitalization costs =

$= (\text{number of standard hospitalizations}) \times (\text{standard hospitalization cost})$

$+ (\text{number of hospitalized in ICU}) \times (\text{price of ICU hospitalization}).$

The total costs are obtained by summing up all the above costs:

$\text{total costs} = (\text{vaccination costs}) + (\text{drug costs}) + (\text{hospitalization costs}).$

The procedure described above (i.e. an individual simulation of pandemic influenza) has been repeated 10,000 times for each of the 6 scenarios. This has given us an interval in which, for a given scenario, one could expect particular outcomes (i.e. numbers of infected, dead, heights of costs of particular type, etc.) and which values would be the most probable ones. Notice that random data simulations we carried out for each individual lead to a time consuming computational procedure. Approximation of the binomial distribution by a normal one would not result in a noteworthy decrease of the time complexity of our Monte Carlo simulations.

1.3. Randomization of Input Parameters

The results of the simulations depend significantly on parameters of the input probabilities (represented by the percentage data in the Tables 1 and 2), the values of which are based on estimates of medical specialists. Therefore, we have considered these parameters as random ones: for each of the 10,000 Monte Carlo simulations of a particular scenario they have been generated by the computer from the Beta distribution having its probability density distribution function $f$ defined as:
\[ f(x) = \begin{cases} x^{\alpha - 1}(1-x)^{\beta - 1} / B(\alpha, \beta), & \text{if } x \in (0,1) \\ 0, & \text{otherwise} \end{cases} \]

where \( B(\alpha, \beta) = \int_0^1 x^{\alpha - 1}(1-x)^{\beta - 1} \, dx \) is the Euler Beta function.

Recall that for an integer value of the parameter \( \alpha \) the cumulative probability of the Beta distribution from 0 to \( x \) is the probability that at least \( \alpha \) of the random variables are less than \( x \), a probability is given by summing over the binomial distribution. We have therefore chosen the Beta distribution because of its relation to the Binomial distribution and because of its flexibility from the point of view of approximation of a wide class of distributions.

**Figure 1**

**Model Parameters as Random Variables Generated by Beta Distributions**

- **a)** Influenza Clinical Attack Rate
  - Beta (6, 14)

- **b)** Influenza Mortality
  - Beta (25/20, 975/20)

- **c)** % of Infected Medically Treated
  - Beta (20, 20)

- **d)** Clinical Mortality Rate of Medically Treated
  - Beta (25, 75)

- **e)** % of Infected Hospitalized
  - Beta (8, 92)

*Note:* The dashed vertical line represents the mean value taken from Table 1.

*Source:* Own results.
The particular Beta distribution has been chosen with expected value equal to the value in Table 1 or 2. The shape of the density of the particular Beta distribution reflects our subjective confidence in the values of the parameters of Table 1 and 2: in case we have chosen a wide peak Beta density, the computer generated values of the respective parameter with a large dispersion around the value in Table 1 or 2. This means that we do not trust much the value in Table 1 or 2 and admit deviations from it. On the other hand, a narrow Beta distribution density means that the generated values of parameter do not deviate significantly from the value in Table 1 or 2; this reflects our higher trust in the values of Table 1 and 2. Particular choices of the Beta distribution are depicted in Figure 1.

2. Results

2.1. Total Costs

In Figure 2 total costs of the six scenarios are compared. The graphs represent estimated densities of the costs of particular scenarios, vertical lines being their statistical frequencies.

Figure 2
Total Costs

Note: 1: no vaccination (so-called control); 2: whole population pre-vaccination (i.e. 2x pre-pandemic vaccination plus 1x pandemic); 3: 2x pandemic vaccination of 50% population; 4: 2x pre-pandemic vaccination of whole population; 5: pre-vaccination of 35% population plus 2x pandemic vaccination of 32.5% population; 6: 1x pre-pandemic plus 1x pandemic vaccination of whole population.
Source: Own results.

The location of the peak indicates where one can approximately expect total costs of a particular scenario. We see that the peaks of scenarios 2 to 6 are located to the right of the peak of scenario 1. This means that the expected value of scenario 1 is lower than the ones of any of remaining scenarios.
The height of the graph in a certain interval indicates how likely the costs in this interval are for a particular scenario. For example, under scenario 1 we see that costs in the interval 66 to 133 millions of Euro are much more likely than costs between 133 and 200 millions of Euro because the graph is much higher over the interval 66 to 133 millions than the corresponding graph over the interval 133 to 200 millions of Euro.

Important information is carried by the width of the peak. It informs about the dispersion of the expected costs: the wider the peak, the higher the uncertainty of the expected costs of the particular scenario. The width of the peak allows us to compare e.g. the scenarios 1 and 3 (Figure 2). From the point of view of mean expected values the scenarios are practically equivalent. However, the peak of the density of scenario 3 is considerably narrower which means that the costs of scenario 3 are much more predictable than those of scenario 1. The width of the peak can be characterized by the 95% tolerance interval that is, by definition, the interval including with 95% probability the total costs of the particular scenario. The results are summarized in Table 3. For the reader’s convenience, let us recall the numbering of the scenarios:

1. No vaccination (so-called control).
2. Whole population pre-vaccination (i.e. 2x pre-pandemic vaccination + 1x pandemic).
3. 2x pandemic vaccination of 50% population.
4. 2x pre-pandemic vaccination of whole population.
5. Pre-vaccination of 35% population + 2x pandemic vaccination of 32.5% population.
6. 1x pre-pandemic + 1x pandemic vaccination of whole population.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Mean Value</th>
<th>Median</th>
<th>Tolerance Interval</th>
<th>Interval Width</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>86.3</td>
<td>79.6</td>
<td>from 30 to 169.3</td>
<td>139.4</td>
</tr>
<tr>
<td>2</td>
<td>152.7</td>
<td>146.0</td>
<td>from 129.5 to 205.8</td>
<td>76.3</td>
</tr>
<tr>
<td>3</td>
<td>92.9</td>
<td>89.6</td>
<td>from 59.7 to 146</td>
<td>86.3</td>
</tr>
<tr>
<td>4</td>
<td>119.5</td>
<td>112.8</td>
<td>from 89.6 to 179.2</td>
<td>89.6</td>
</tr>
<tr>
<td>5</td>
<td>112.9</td>
<td>109.5</td>
<td>from 86.3 to 159.3</td>
<td>73.0</td>
</tr>
<tr>
<td>6</td>
<td>112.9</td>
<td>109.5</td>
<td>from 86.3 to 169.3</td>
<td>83.0</td>
</tr>
</tbody>
</table>

Note: Mean value, median, 95% tolerance interval and interval width in millions of Euro.
Source: Own results.

One can see that lowest mean costs can be expected under scenario 1 (i.e. without intervention) whereas the highest mean costs can be expected under scenario 2 (i.e. pre-vaccination of the total population). Scenario 2, on the other hand, is the best from the point of view of the expected dispersion: its estimated density in Figure 2 has the narrowest peak, and therefore the smallest tolerance interval. The reason is that by the expensive pre-vaccination (which is primarily responsible
for the high total costs) the unpredictability of the course of infection of the population is lowered. As a result of pre-vaccination the vulnerability to infection of the population drops considerably and so do the random costs of medical treatment and hospitalization that are exclusively responsible for the dispersion.

However, the lowest costs of scenario 1 are misleading. Undoubtedly, this scenario has the widest peak of the estimated costs and the widest tolerance interval. This means that the total costs of scenario 1 may deviate considerably from their mean value. So, the lowest mean of scenario 1 is outweighed by a significant uncertainty due to uncertainty of the costs.

2.2. Mortality

An analysis similar to the one of total costs has been carried out for mortality. Figure 3 compares scenarios 2 to 6 with the non-interventional scenario 1.

Figure 3
Mortality

Note: 1: no vaccination (so-called control); 2: whole population pre-vaccination (i.e. 2x pre-pandemic vaccination plus 1x pandemic); 3: 2x pandemic vaccination of 50% population; 4: 2x pre-pandemic vaccination of whole population; 5: pre-vaccination of 35% population plus 2x pandemic vaccination of 32.5% population; 6: 1x pre-pandemic plus 1x pandemic vaccination of whole population.

Source: Own results.

The graphical plots in Figure 3 are statistically summarized in Table 4. It can be seen that scenario 2 appears as optimal. The average number of deaths as well as its dispersion appears to be the lowest (i.e. the peak of the distribution density is the lowest and the tolerance interval are the narrowest ones). The opposite extreme is represented by the non-interventional scenario 1: it has the highest average number of deaths and, more importantly, an extremely large dispersion, which means significant planning uncertainty (of e.g. medical care costs).
Table 4

Number of Deaths

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Mean</th>
<th>Median</th>
<th>Tolerance Interval</th>
<th>Interval Width</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40.9</td>
<td>28.7</td>
<td>from 1.7 to 153.3</td>
<td>151.6</td>
</tr>
<tr>
<td>2</td>
<td>12.3</td>
<td>6.7</td>
<td>from 0.2 to 57.6</td>
<td>57.4</td>
</tr>
<tr>
<td>3</td>
<td>24.3</td>
<td>16.7</td>
<td>from 1.0 to 89.7</td>
<td>88.7</td>
</tr>
<tr>
<td>4</td>
<td>16.4</td>
<td>9.7</td>
<td>from 0.4 to 71.9</td>
<td>71.5</td>
</tr>
<tr>
<td>5</td>
<td>19.8</td>
<td>13.7</td>
<td>from 0.9 to 74.2</td>
<td>73.2</td>
</tr>
<tr>
<td>6</td>
<td>14.4</td>
<td>8.2</td>
<td>from 0.3 to 64.4</td>
<td>64.1</td>
</tr>
</tbody>
</table>

Note: Mean, median, 95% tolerance interval and interval width in thousands.
Source: Own results.

2.3. The Impact of Parameter Uncertainty

The widths of the peaks of the total costs and the number of deaths are determined by our trust in the input parameters. None of the values of the parameters we have considered is certain. This is why we have modelled them by a Beta distribution around the reference value. The dispersion of the Beta distribution reflected our trust in the reference value (smaller dispersion reflects more trust). The decrease of the uncertainty of the input parameter (i.e. decrease of dispersion of the corresponding Beta distribution) would decrease the dispersion of the output parameters (e.g. total costs, number of death, etc.).

Figure 4
Total Costs under Random/Fixed Pre-vaccination Efficacy

Source: Own results.

As an example we consider “pre-vaccination efficacy” and the impact of its dispersion on the dispersion of the total costs of scenario 2 (i.e. pre-vaccination of the total population). Normally, the pre-vaccination efficacy has been generated from the Beta (35,15) distribution (cf. Figure 1), the mean of which is 70%, the
reference value from Table 2. We have carried out additional simulations of the pandemic impacts under scenario 2: the pre-vaccination efficacy has been set to exactly 70%. That is, we have trusted to this value absolutely, its dispersion having been zero. Figure 4 and Table 5 show a decrease of the dispersion of total costs that can be considered as an advantage.

Table 5

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>Mean</th>
<th>Median</th>
<th>Tolerance Interval</th>
<th>Interval Width</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random</td>
<td>152.7</td>
<td>146</td>
<td>from 129.5 to 205.8</td>
<td>76.3</td>
</tr>
<tr>
<td>Fixed</td>
<td>152.7</td>
<td>149.4</td>
<td>from 136 to 175.9</td>
<td>39.8</td>
</tr>
</tbody>
</table>

Note: Mean value, median, 95% tolerance interval and interval width in millions of Euro.
Source: Own results.

We see that a decrease of the parameter dispersion yields improved (i.e. less dispersed) information about the values of the output parameters (e.g. the tolerance interval narrowed almost by 1/2).

A decrease of the parameter dispersion (i.e. improvement of information) can be achieved either by better understanding of the pandemic mechanisms or by improved observation. The costs due to uncertainty can be considered as a measure of the value of additional information. This issue will be pursued in the future.

2.4. Variable Percentage of Vaccinated

Scenarios 1 to 2 represent the two opposite extremes of total costs, the number of deaths and their dispersions. This is due to the fact that under scenario 1 there is no vaccination whereas under scenario 2 all the population is pre-vaccinated, a vaccine being applied 3 times. To tie these extreme cases we have simulated scenarios that are compromises between scenarios 1 to 2 with pre-vaccinations of 20%, 40%, 60% or 80% of the population. The results are depicted in Figures 5 and 6 and summarized in Tables 6 and 7.

Table 6

<table>
<thead>
<tr>
<th>% of Pre-vaccinated</th>
<th>Mean</th>
<th>Median</th>
<th>Tolerance Interval</th>
<th>Interval Width</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>86.3</td>
<td>79.7</td>
<td>from 29.9 to 169.3</td>
<td>139.4</td>
</tr>
<tr>
<td>20</td>
<td>96.3</td>
<td>92.9</td>
<td>from 53.1 to 169.3</td>
<td>116.2</td>
</tr>
<tr>
<td>40</td>
<td>112.9</td>
<td>106.2</td>
<td>from 73 to 175.9</td>
<td>102.9</td>
</tr>
<tr>
<td>60</td>
<td>126.1</td>
<td>119.5</td>
<td>from 92.9 to 179.2</td>
<td>86.3</td>
</tr>
<tr>
<td>80</td>
<td>139.4</td>
<td>132.8</td>
<td>from 112.9 to 192.5</td>
<td>79.7</td>
</tr>
<tr>
<td>100</td>
<td>152.7</td>
<td>146.0</td>
<td>from 129.5 to 205.8</td>
<td>76.3</td>
</tr>
</tbody>
</table>

Note: Mean value, median, 95% tolerance interval and interval width in millions of Euro.
Source: Own results.
Figure 5
Total Costs under Varying Percentages of Vaccinated

Source: Own results.

Figure 6
Number of Deaths for Various Parameter Values

Source: Own results.

Table 7
Numbers of Deaths under Varying Percentages of Pre-vaccinated

<table>
<thead>
<tr>
<th>% of Pre-vaccinated</th>
<th>Mean</th>
<th>Median</th>
<th>Tolerance Interval</th>
<th>Interval Width</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>40.9</td>
<td>28.7</td>
<td>from 1.7 to 153.3</td>
<td>151.6</td>
</tr>
<tr>
<td>20</td>
<td>34.3</td>
<td>24.3</td>
<td>from 1.5 to 123.5</td>
<td>122.0</td>
</tr>
<tr>
<td>40</td>
<td>28.8</td>
<td>20.1</td>
<td>from 1.2 to 103.4</td>
<td>102.2</td>
</tr>
<tr>
<td>60</td>
<td>23.5</td>
<td>16.3</td>
<td>from 1.0 to 85.1</td>
<td>84.1</td>
</tr>
<tr>
<td>80</td>
<td>17.8</td>
<td>11.6</td>
<td>from 0.6 to 69.7</td>
<td>69.1</td>
</tr>
<tr>
<td>100</td>
<td>12.3</td>
<td>6.7</td>
<td>from 0.2 to 57.6</td>
<td>57.4</td>
</tr>
</tbody>
</table>

Note: Mean value, median, 95% tolerance interval and interval width in thousands.

Source: Own results.
The graph labelled “0%” represents the non-intervention scenario 1. We see that an increase of the percentage of pre-vaccinated leads to an increase of total costs and a decrease of the number of deaths until the values of “100%”, i.e., scenario 2 are reached. It is worth noting that an increase of the pre-vaccination percentage decreases the width of the estimated peaks, i.e. the dispersion of total costs and the number of deaths. As already mentioned, this is caused by the fact that by an increase of the percentage of pre-vaccinated individuals the probability of infection is decreased. This eliminates uncertainty of the costs and the number of deaths implied by the uncertainty of the number of infected.

2.5. Total Loss

Until now we have assessed the scenarios by the values of total costs and the number of deaths separately. These two criteria appear to be in conflict since by more vaccination total costs (consisting primarily from the vaccination costs) increase, while the number of deaths is considerably lower.

Now, we attempt to summarize these two indicators into one number to be called total loss consisting of total costs plus the number of deaths multiplied by the value of one life. The value of life is an extremely sensitive and questionable parameter. For illustration we have chosen the value 33,200 Euro (1,000,000 SKK). The estimated densities of total loss under particular scenarios are depicted in Figure 7 and summarized in Table 8.

Figure 7
Total Loss (= costs + loss due to lost lives)

Note: 1: no vaccination (so-called control); 2: whole population pre-vaccination (i.e. 2x pre-pandemic vaccination plus 1x pandemic); 3: 2x pandemic vaccination of 50% population; 4: 2x pre-pandemic vaccination of whole population; 5: pre-vaccination of 35% population plus 2x pandemic vaccination of 32.5% population; 6: 1x pre-pandemic plus 1x pandemic vaccination of whole population.

Source: Own results.
Table 8
Total Loss (= costs + value of lost lives).

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Mean</th>
<th>Median</th>
<th>Tolerance Interval</th>
<th>Interval Width</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1,427.3</td>
<td>1,035.6</td>
<td>from 126.1 to 5198</td>
<td>5,072</td>
</tr>
<tr>
<td>2</td>
<td>561.0</td>
<td>371.8</td>
<td>from 142.7 to 2091</td>
<td>1,849</td>
</tr>
<tr>
<td>3</td>
<td>899.6</td>
<td>647.3</td>
<td>from 116.2 to 3090</td>
<td>2,974</td>
</tr>
<tr>
<td>4</td>
<td>663.9</td>
<td>441.5</td>
<td>from 112.9 to 2532</td>
<td>2,420</td>
</tr>
<tr>
<td>5</td>
<td>770.1</td>
<td>567.6</td>
<td>from 132.8 to 2589</td>
<td>2,390</td>
</tr>
<tr>
<td>6</td>
<td>594.2</td>
<td>385.0</td>
<td>from 103 to 2300</td>
<td>2,197</td>
</tr>
</tbody>
</table>

Note: Mean value, median, 95% tolerance interval and interval width in millions of Euro.

Source: Own results.

It appears that scenario 2 is best and scenario 1 worst. It should be noted, though, that this result is considerably affected by the parameter value of life. Should we choose a lower value of life, the optimal scenario could be different. In order to carry out an adequate optimization analysis it is unavoidable to make a more adequate estimate of vaccination costs including profit margins, taxes, costs of storing and carrying out vaccination. The vaccination cost then become a nonlinear function of its extent (i.e. the unit cost increases with vaccination extent) and includes an element of randomness due to the uncertainty of storing and acquirement.

2.6. The Costs per Life Saved and the Index of Effectiveness

The assessment of the vaccination scenarios by the total loss depends strongly on the subjectively chosen value of life. Alternatively, we can include mortality into consideration by the “costs per life saved” (see e.g. Gold et al., 1996). However, because the number of casualties is small compared to the size of the population, a certain normalization is needed. This is why we introduce an index of effectiveness. It relates the scenario under consideration to the non-interventional (control) scenario 1 by considering the increase of total costs and relative decrease of the number of deaths:

\[
\frac{tc_i / tc_1}{(d_1 - d_i) / d_1}
\]

Here \(tc_i\) and \(d_i\) stand for the total costs and number of deaths under the \(i\)-th scenario respectively. In order to compute the index we have carried out each of the 10 000 Monte Carlo simulation runs simultaneously for scenario \(i\) \((i = 2, ..., 6)\) with the same random statistical parameters. Fitted densities of the simulated indices of effectiveness are depicted on Figure 8 and summarized in Table 9.

It is obvious that a decrease of the numerator and an increase of the denominator increases effectiveness. Hence, the smaller is the index of effectiveness, the more effective is the scenario. As one can see from Figure 8 and Table 9,
scenario 6 (1x pre-pandemic plus 1x pandemic vaccination of whole population) appears to be the most effective one. It is rather surprising because this scenario did not appear to be optimal from the point of view of total costs including mortality.

**Figure 8**
**Index of Effectiveness**

![Index of Effectiveness](image)

**Note:** 2: whole population pre-vaccination (i.e. 2x pre-pandemic vaccination plus 1x pandemic); 3: 2x pandemic vaccination of 50% population; 4: 2x pre-pandemic vaccination of whole population; 5: pre-vaccination of 35% population plus 2x pandemic vaccination of 32.5% population; 6: 1x pre-pandemic plus 1x pandemic vaccination of whole population.

**Source:** Own results.

**Table 9**
**Index of Effectiveness**

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Mean</th>
<th>Median</th>
<th>Tolerance Interval</th>
<th>Interval Width</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>3.5</td>
<td>2.8</td>
<td>from 1.1 to 10.2</td>
<td>9.1</td>
</tr>
<tr>
<td>3</td>
<td>3.2</td>
<td>2.8</td>
<td>from 1.7 to 6.8</td>
<td>5.1</td>
</tr>
<tr>
<td>4</td>
<td>3.5</td>
<td>2.6</td>
<td>from 0.9 to 11.9</td>
<td>11.0</td>
</tr>
<tr>
<td>5</td>
<td>3.1</td>
<td>2.8</td>
<td>from 1.5 to 6.6</td>
<td>5.1</td>
</tr>
<tr>
<td>6</td>
<td>2.9</td>
<td>2.2</td>
<td>from 0.8 to 9.1</td>
<td>8.3</td>
</tr>
</tbody>
</table>

**Source:** Own results.

**Conclusions**

By random Monte Carlo simulations of pandemic influenza effects on the 5,400,000 inhabitants of Slovakia under several mitigation scenarios we have assessed their national impacts including economic costs and mortality losses. Simulation of individual cases allowed us to obtain the entire probabilistic distribution of the outcome variables. In particular, we have been able to obtain not only their expected values but also their dispersions.
We show that, although preventive measures mean extra social expenses, this is outweighed by the reduction of losses due to mortality. A direct assessment of the mortality losses involves a subjective element — the value of life. In order to remedy this difficulty we introduce an index measuring the costs of lives saved by a particular intervention measure. Rather unexpectedly, this index indicates the scenario of one pre-pandemic and one pandemic vaccination as the most effective.

It is worthwhile to observe that dispersions representing uncertainty are the lowest under the most expensive scenario of twice pre-pandemic and once pandemic vaccination of the total population. Since uncertainty represents additional costs, the dispersions should be taken into account when comparing different mitigation scenarios as well. Expressing this circumstance in economic terms needs an assessment of the uncertainty costs which is an interesting challenge for further research.

References

Erratum

Figure 8 on page 177 is a copy of figure 7 on page 175. It should be replaced by the following figure:

Figure 8
Index of Effectiveness

Note: 2: whole population pre-vaccination (i.e. 2x pre-pandemic vaccination plus 1x pandemic); 3: 2x pandemic vaccination of 50% population; 4: 2x pre-pandemic vaccination of whole population; 5: pre-vaccination of 35% population plus 2x pandemic vaccination of 32.5% population; 6: 1x pre-pandemic plus 1x pandemic vaccination of whole population.

We apologize for this misprint.