SIMULATING THE EFFECTS OF SCHOOL CLOSING INTERVENTIONS AGAINST PANDEMIC INFLUENZA

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Abstract

InfluSim is a deterministic, compartmental model of pandemic influenza. A basic SEIR model has been adapted for Influenza and extended such that the effects of interventions can be investigated. The model subdivides the population into age- and risk groups and implements interventions like antiviral treatment, prophylaxis and social distancing. This results in a system of more than 3000 differential equations. In this paper the model has been used to address the question whether and under which time schedule day care centers and schools should be closed during a pandemic influenza. The effect of school closing is modeled by reducing contacts within the child age groups and by partially redistributing these contacts to child-adult and child-elderly contacts. It is shown that these changes to the contact matrix do not necessarily contribute to containing the pandemic and it is therefore necessary to look at the effects of the intervention to each age group of the population. A similar argument applies to the optimal scheduling of the school closing intervention: A given schedule can be beneficial for some age groups while disadvantageous for others.

Keywords: Deterministic Simulation, Epidemiology, Pandemic Influenza, Intervention Planning, Social Distancing.

Presenting Author's biography

Markus Schwehm studied mathematics and computer science in Karlsruhe & Munich, presented a doctoral thesis on parallel optimization algorithms in Erlangen, worked as a postdoc on parallel databases in Cupertino, USA and on mobile agents in Stuttgart. Then he worked as research assistant in bioinformatics and systems biology in Tübingen, and is currently working in the medical biometry department on the simulation of the spread of infections for optimal intervention planning.

1 Introduction

Influenza pandemics have taken place three times in the last hundred years. There is not much knowledge about the dynamics of previous influenza pandemics, let alone the possible properties of a future pandemic with the unknown properties of a not yet existing virus. Nevertheless health care agencies around the world have to prepare for a possible influenza pandemic now while only very few simulation tools are available.

School closing has been recently discussed as possible intervention against pandemic influenza. It is well established that school closure can have an effect on the spread of seasonal influenza, see e.g. [1] and [2] for a discussion of data where school holidays or a teacher strike at the beginning of the influenza season in some regions of a country have locally mitigated the spread of seasonal influenza. But pandemic influenza is different from seasonal influenza. While seasonal influenza preferably reaches children who have not yet built up immunity against a recurring virus, a pandemic influenza hits all age groups of a population because no immunity could possibly have built up against its newly emerged virus. While school closure might reduce contacts between children, the number of contacts between children and adult and elderly are increased, with unknown consequences on the dynamic of the pandemic. Current investigations on the effect of school closure on pandemic influenza range from 'very effective' [3, 4] over moderate or mixed results [5, 6] to 'not substantial' [7].

In this paper we use the pandemic influenza simulator InfluSim to simulate the effect of school closing during an influenza pandemic. Section 2 gives a brief overview over the model architecture of InfluSim. Section 3 describes how the school closing intervention was integrated into the model. In Sections 4 and 5 the simulator is used for some simulation studies to investigate parameter sensitivity and to find an optimal pandemic influenza school closing policy.

2 The InfluSim Simulator

InfluSim is a deterministic compartmental model based on the standard SEIR model of epidemiology. In the SEIR model, the population is subdivided into susceptible (S), exposed (E), infectious (I) and removed (R) individuals. Gamma distributed sojourn times for exposed and infectious states were obtained by splitting compartments into sequences of stages.

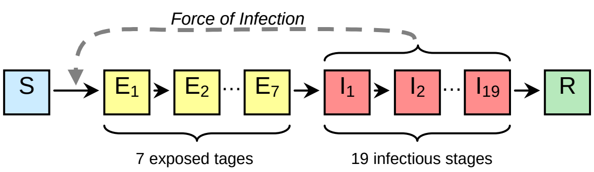

Fig. 1 The SEIR model with stages

This basic model has been extended to better model the natural history of influenza. The infectious individuals are further subdivided into asymptomatic (A), moderately sick (M), very sick (V) and extremely sick (X) cases. The particular course of disease is dependent of age and risk group. A realistic time schedule for people seeking medical help by visiting a doctor (W) or a hospital (H) and receiving or not receiving medical treatment is implemented. The removed individuals are subdivided into dead (D), convalescent (C) and recovered and immune (R) cases.

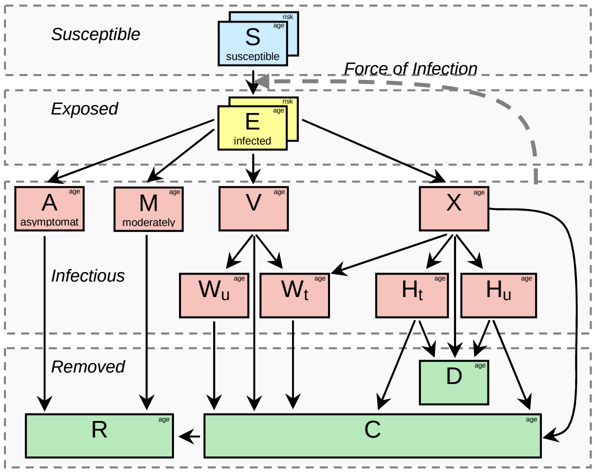

Fig. 2 The pandemic influenza compartment model

Further interventions include social distancing of cases and the general population and the prophylaxis of health care workers and essential services workers. Health care planning is supported with output graphs for the number of outpatients, the number of occupied hospital beds or the number of antiviral treatments used. Finally the model distinguishes six age groups of individuals and the force of infection between groups is controlled by a contact matrix given by [8], resulting in a system of 3140 differential equations.

The InfluSim software is implemented in Java using the Eclipse Rich Client Platform. InfluSim is available on the Internet under an open source license [9-11].

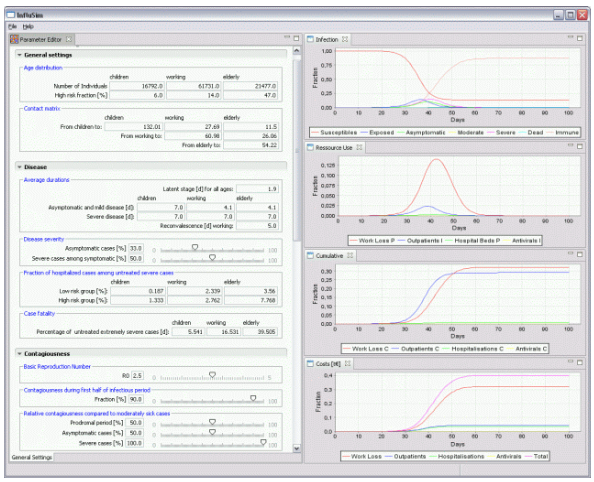

Fig. 3 The InfluSim user interface

3 Modeling School Closing

In order to implement school closing, the number of age groups was extended to include three children age groups ranging from age 0-5, 6-12 and 13-19, two adult age groups from age 20-39 and 40-59 and one elderly age group of age 60 and above. Closing of day care centers and schools can now be modeled by changing the contact matrix. Contacts within the same child age group are reduced by reducing the corresponding diagonal elements of the contact matrix (red boxes in Fig. 2). A redistribution of some of these contacts is modeled by increasing the contacts between children and adult/elderly (green boxes in Fig. 2).

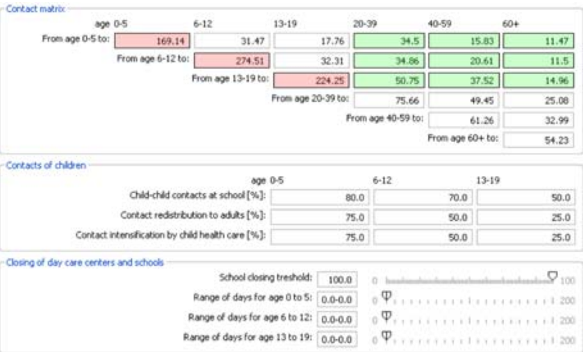

Fig. 2 School closing parameters

The fraction of child-child contacts at school and the redistribution factors (Fig. 2) and the school closing schedule can be set independently for each age group.

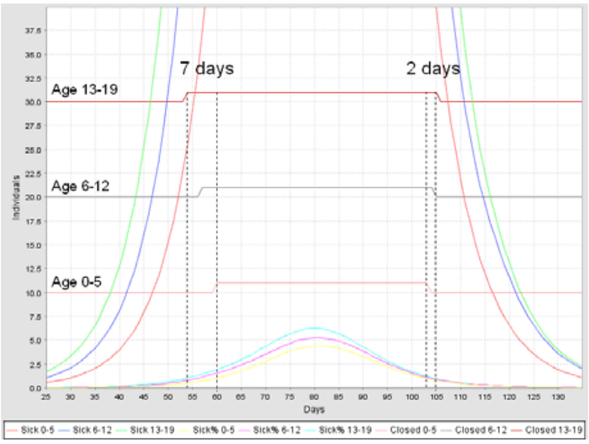

Fig. 3 School closing graph view

In Fig.3 an absenteeism threshold of 1% is used for the closing of day care centers and schools. It can be observed that according to this policy the schools for older children (age 13-19) are closed one week earlier than the day care centers (age 0-5), while the institutions are reopened again within two days.

4 Redistribution Study

In the redistribution study we have used a full intervention baseline scenario (without school closing) to compare with. The baseline scenario includes 100% treatment of severe and extremely sick cases with unlimited resource of antivirals. Schools are closed with a 1% absenteeism threshold, i.e. when more than 1% of children are absent due to pandemic influenza. The three children age groups have 80%, 70% and 50% of their child-child contacts at school. The redistribution factors are varied between 50% and 100% for ages 0-5, between 25% and 75% forages 6-12 and between 0% and 50% for ages 13-19. This parameter variation resulted in 2850 independent simulation runs. The output includes the cumulative incidence of cases per age group, the peak prevalence of severe cases, the peak day and the cumulative number of deaths. Figures 4 to 6 show the relative difference (in %) between the full intervention scenario with school closing subtracted by the and the baseline scenario without school closing .

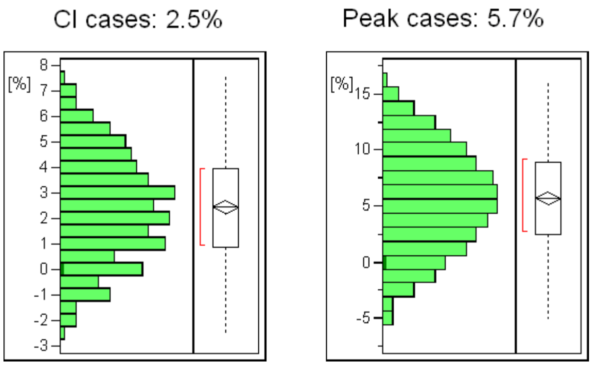

Fig. 4 Relative effects of school closing on the cumulative incidence of cases (left) and the peak prevalence of severe cases (right).

Fig.4 shows that school closing can decrease the cumulative incidence of cases by 2.5% and even further decrease the peak prevalence of cases by 5.7%. Fig 5 shows that the school closing intervention has only a small effect on the peak day of the pandemic, since the intervention is centered on the peak of the pandemic rather than starting right from the beginning of the pandemic. Contrary to the so far positive results, the cumulative incidence of deaths is slightly increased by 0.3%.

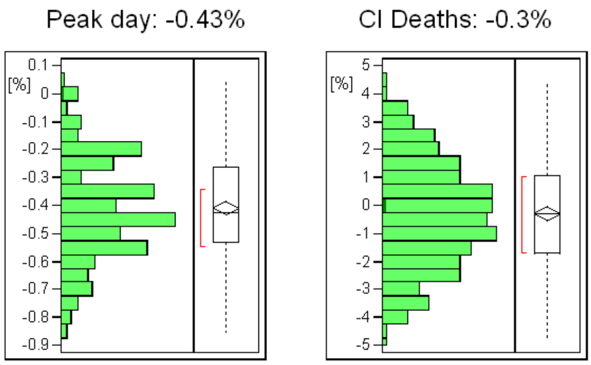

Fig. 5 Relative effects of school closing on the day of the peak prevalence of severe cases (left) and the cumulative incidence of deaths (right).

In order to understand these contradictory results, it is necessary to look at the results with respect to the different age groups. Fig. 6 reveals that the children age groups benefit from school closing by 3.9% for ages 0-5, by 15.2% for ages 6-12 and by 12.1% for ages 13-19. On the other hand the adult and elderly age groups have slight disadvantages with an increase of cases between 0.19% and 0.43%. The large advantage for the children applies to only 22% of the population is balanced by a slight disadvantage for the 78% of adult and elderly population. Since elderly people have a higher risk of dying from influenza, the cumulative number of deaths can be increased by 0.3%, (see Fig. 5 at right), while the cumulative incidence of cases in the whole population is decreased (see Fig. 4 at left).

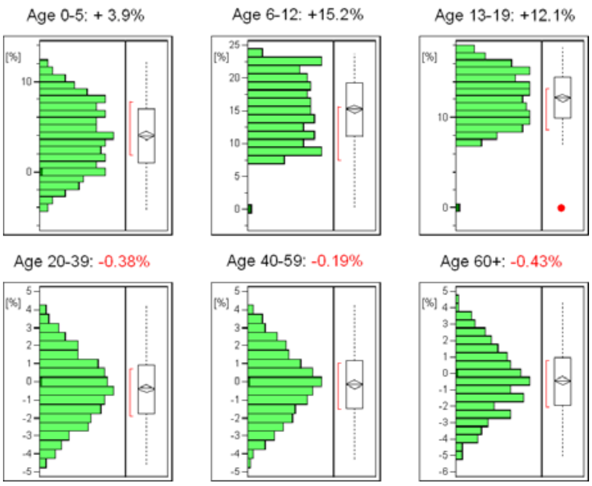

Fig. 6 Relative effects of school closing on the cumulative incidence of cases for different age groups.

Fig. 7 shows that the redistribution factor has a major effect on the cumulative incidence of cases (CIC). While the older children age groups (6-12 and 13-19) always benefit from school closing, the younger children (age 0-5) only benefit from school closing if the redistribution factor for their age class is small enough, i.e. if only a small fraction of their child-child contacts is redistributed to child-adult or child-elderly contacts.

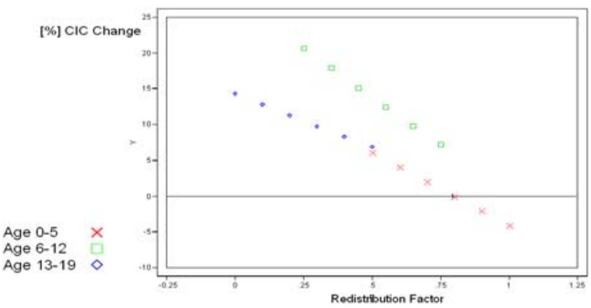

Fig. 7 Relative effect of school closing on the cumulative incidence of cases by redistribution factor

5 Optimal Synchronous Timing Study

In the optimal timing study we have again compared full intervention scenario with school closing against a baseline scenario with full intervention but without school closing. As above the full intervention includes 100% antiviral treatment of severe cases and with unlimited resources of antivirals, 10%, 20% and 30% of partial isolation of mild, severe and extremely sick cases and a 15% general contact reduction in the healthy population over the whole simulation period.

The school closing parameters are set to 80%, 70% and 50% child-child contacts at school and 75%, 50% and 25% redistribution factor for the three children age groups 0-5, 6-12 and 13-19 respectively as displayed in Fig 2. The school closing schedule is set to a range between day 0 and day 150 of the pandemic with a step size of 2 days. All 2850 possible day ranges were simulated and the output included the cumulative incidence of cases per age group, the peak and peak day of severe cases prevalence and the cumulative incidence of deaths. Fig. 8 shows the relative effect of school closing on the cumulative incidence of cases. The green tail indicates maximum effect of school closing by closing the schools as long as possible. The simulation from the previous section using a 1% absentee threshold is marked by a green arrow. The blue arrow shows a simulation using a 2.5% absentee threshold and shorter duration of the intervention.

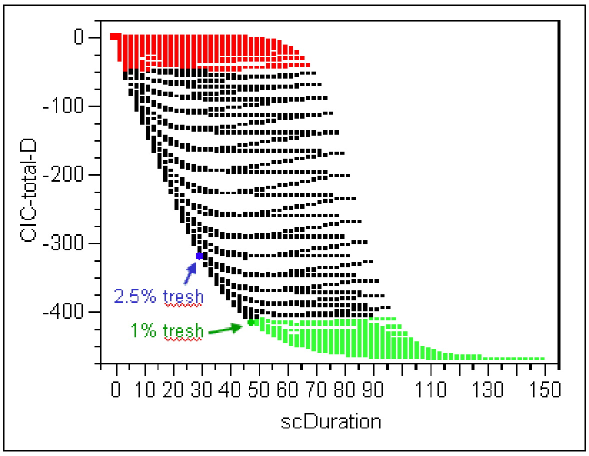

Fig. 8 Relative effect of school closing duration on the cumulative incidence of cases

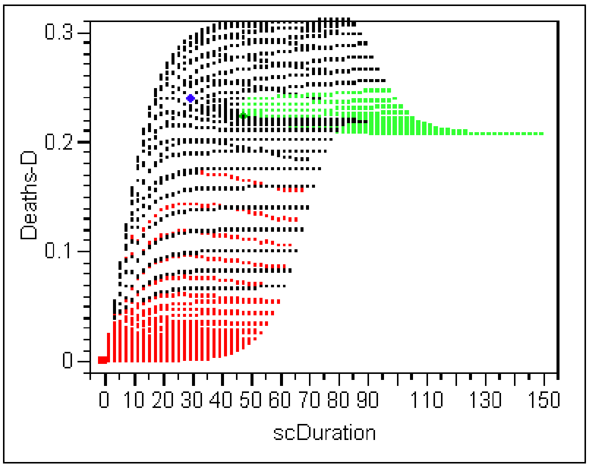

Fig. 9 Relative effect of school closing duration on the cumulative incidence of deaths

Fig. 9 shows the corresponding figure for the cumulative incidence of deaths. Since deaths are slightly increased by the intervention, the red tail indicates minimum increase of deaths by closing the school as short as possible. The blue 2.5% absentee threshold schedule that looked like a compromise between long and short school closing intervention in Fig. 8 does not have this property in Fig. 9; it increases deaths more than a long school closing indicated by the green tail.

Again it is necessary to look at the effects of school closing for each age group in Fig. 10. Children benefit from long school closing while adult and elderly benefit from no or very short school closing.

A satisfactory compromise between the two contradictory objectives of reduction of the cumulative incidence of cases and the cumulative incidence of deaths is not possible as long as day care centers and schools are closed synchronously.

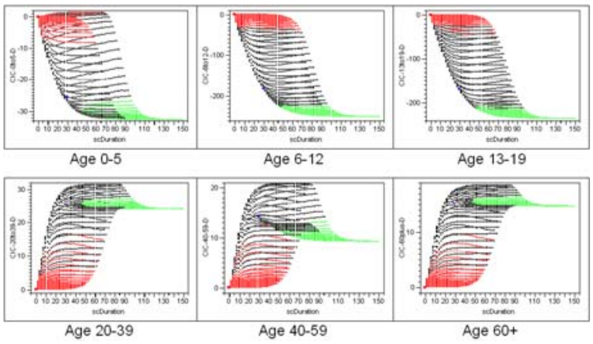

Fig. 10 Relative effect of school closing duration on cumulative incidence of cases of different age groups

6 Optimal Asynchronous Timing Study

The study in section 5 used synchronous closing ranges, i.e. all daycare centers and schools were closed during the same day range. The following study investigated the effect of independent closing ranges for the three children age groups.

Table 1 summarizes some results from the large set of closing schedules executed in this study. Each row lists the optimal effect and the optimal closing schedule for the given age group. The second column lists absolute and relative effects on the number of cases. Columns 3 to 5 list the closing day ranges for daycare centers (age 0 – 5) children schools (age 6 – 12) and teenager schools (age 13 – 19). Most of the closing day ranges can be classified into "never closed" or "always closed" policies except for the optimal closing schedule for daycare centers which should be "closed after the peak" for an optimal result for very young children of age 0 – 5.

This unexpected closing schedule can be explained by the observation that children of age 0-5 get infected and reach their peak later than other age groups. For example in Figure 3 the 1% threshold is reached by age group 0-5 one week later than for age group 13-

Table 1 Relative effect of school closing duration on the cumulative incidence of deaths

	Absolute (relative) minimum effect	Closing days for daycare centers	Closing days for children schools	Closing days for teenager schools
age 0-5	-40.0 (-5.0%)	80 – 120 **closed after peak**	10 – 120 always closed	0 – 120 always closed
age 6-12	-257.3 (-17.3%)	0 – 30 never closed	0 – 120 always closed	30 – 120 always closed
age 13-19	-243.6 (-13.8%)	0 – 30 never closed	20 – 120 always closed	10 – 120 always closed
age 20-39	-78.8 (-1.4%)	0 – 10 never closed	0 – 0 never closed	10 – 120 always closed
age 40-59	-78.0 (-1.5%)	0 – 10 never closed	0 – 0 never closed	10 – 120 always closed
age 60+	-43.0 (-1.5%)	0 – 10 never closed	0 – 0 never closed	10 – 120 always closed
total	-646.2 (-3.7%)	0 – 20 never closed	0 – 120 always closed	20 – 120 always closed

ISBN 978-3-901608-32-2

19. Before the peak, very young children of age 0-5 benefit from being in day care centers and thus being isolated from the infection dynamics in the rest of the population. The situation changes when the other age groups are already after their peak while age group 0-5 is still before its peak. Now this age group would benefit from the closing of day care centers because they get isolated from the still rising infection dynamics within their own age group and increase their contacts with the already declining infection dynamics in the adult and elderly age groups.

The age-dependent assumptions about the fraction of child-child contacts at school and the age-dependent redistribution of prevented contacts to child-adult/elderly contacts lead to age dependent closing schedules. The best overall effect is obtained by closing schools for ages 6-12 and 13-19 as long as possible, but leaving day care centers (age 0-5) open.

7 Conclusion

Modeling emerging infectious diseases like a pandemic influenza is a difficult task. The properties of a virus that might emerge in the future cannot be known in advance. Even for previous outbreaks of pandemic influenza most of the relevant parameters are not known and large ranges for these parameters are discussed in the literature. Even if we could calibrate our model against the sparse data available from previous pandemics, this would not necessarily give a better model for the emerging next pandemic.

But health care decision makers around the world have to prepare *now* for a possible pandemic. They cannot wait until after the pandemic when all unknown parameters could be extracted from collected data. They have to write preparedness plans and to decide beforehand which interventions and which resources shall be applied during a pandemic. How can modeling help health care decision makers to find good containment policies? In this paper we have demonstrated two approaches how modeling and simulation can help in the preparedness planning process.

First we have used a deterministic simulator to scan the parameter space. We did not know how much of the child-child contacts within the same age group take place at school and we did not know how many of these contacts would be redistributed to contacts between children and adult during a school closure. After discussion with health care agencies we have estimated some ranges for these parameters and used a deterministic simulator to scan the parameter space systematically. In this way we have turned parameter input ranges into simulation output ranges, allowing to analyze best-case and worst-case scenarios.

Secondly, we have exploited the fact that health care planners are not only interested in the absolute size of a pandemic, but they also need to know relative sizes of the pandemic under alternative intervention policies. We have run thousands of simulations scanning simultaneously the space of unknown parameters and a set of alternative intervention strategies. This allowed us to evaluate whether one intervention was preferable than another intervention and even allowed to optimize the timing schedule for the closing of schools without knowing or predicting the absolute size of the pandemic.

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