Economic consequences to society of pandemic H1N1 influenza 2009 – preliminary results for Sweden

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Experiments using a microsimulation platform show that vaccination against pandemic H1N1 influenza is highly cost-effective. Swedish society may reduce the costs of pandemic by about SEK 2.5 billion (approximately EUR 250 million) if at least 60 per cent of the population is vaccinated, even if costs related to death cases are excluded. The cost reduction primarily results from reduced absenteeism. These results are preliminary and based on comprehensive assumptions about the infectiousness and morbidity of the pandemic, which are uncertain in the current situation.

Introduction

In cooperation with the epidemiological unit at the Swedish National Board of Health and Welfare, researchers at the Swedish Institute for Infectious Disease Control and the Royal Institute of Technology micro-modelled the effects of a possible future scenario of an outbreak of pandemic H1N1 influenza in Sweden, projected for the autumn of 2009. An executable simulation model [1] was used together with registry data from Statistics Sweden (Statistiska centralbyrån, SCB) [2] to link the entire Swedish population together in a large spatially explicit social network. The overall aim of developing the model has been to allow for the simulation of the spread of infection in a population in a realistic manner, and examine the effects of applying different policy strategies. Individuals in the stochastic model go to kindergarten, schools, work, healthcare facilities, and travel to places where they may be exposed to the risk of infection. Since all places have explicit coordinates, the geographical spread can be studied.

Method

The simulations were run with the following assumptions (see detailed description in the Annex at the end of the article): The outbreak of pandemic influenza in Sweden starts on 1 September 2009, and is mild. The infection rate produces an R0-value of approximately 1.4, but here only cases from the first waves of the epidemic (first 180 days) and not from the whole outbreak are reported. Children and adolescents are assumed to be more susceptible and more infectious than adults. For all ages, the following allocation of morbidity holds: 16% are asymptomatically ill (i.e. show no symptoms), 34% are mildly ill, 40% display a typical illness, while 10% have a severe form of illness. The latter category includes patients referred to specialised care at a hospital, which does not necessarily entail hospitalisation. One adult in the household stays home from work for as many days as a child younger than 12 years is sick.

The 90% coverage scenario amounts to mass vaccination, since 10% of the population are assumed to be impossible to vaccinate. Each simulation covered 180 days and began with 50 randomly selected individuals infected on day 0. Each scenario was simulated five (or ten for the most likely scenarios of 50%, 60%, or 70% vaccination coverage) times with different random seeds to obtain

Table

Distribution of the level of immunity. Simulation of pandemic H1N1 influenza in Sweden.

Level of immunity after dose 1	Proportion of vaccinated	Proportion of individuals with 40% immunity after dose 2	Proportion of individuals with 60% immunity after dose 2	Proportion of individuals with 80% immunity after dose 2	Proportion of individuals with 100% immunity after dose 2
100%	15%				100%
80%	20%			40%	60%
60%	25%		40%	40%	20%
40%	20%	10%	40%	35%	15%
30%	15%	40%	35%	25%	0%
10%	5%	40%	35%	25%	0%

robust results and to examine variability. Vaccination started after 30 days (on 1 October). The doses were delivered weekly at a rate that gave all people time to be vaccinated with two doses over 14 weeks. For immunity, the following assumptions were made: Dose 1 gives partial immunity, which is then increased through the second dose (Table 1). For example, an individual who after the first dose gained 40% immunity (i.e. risk of getting the infection reduced by 40%) will after the second dose stand a 10% chance of staying at the same level, a 40% chance of increasing the immunity to 60%, a 35% chance of reaching 80% immunity, and finally a 15% chance of obtaining full immunity (i.e. being no longer susceptible). If a vaccinated individual is infected, the disease will be milder and the infectivity lower than that of an unvaccinated individual.

To compare the societal costs of the six scenarios, the following cost estimations — obtained from health economists at the Swedish Ministry of Health and Social Affairs — were used:

- Cost of one-day absence from work per employee: SEK 2,000 (this includes average daily salary of SEK 1,500 and secondary costs (taxes, overhead) of SEK 500).
- Cost of treatment by a doctor in primary care: SEK 2,000.
- Cost of one-day inpatient care: SEK 8,000.
- Cost of vaccine and administration of vaccination per person: SEK 300.

For all scenarios, the SEK 300 vaccine costs are based on the assumption that the entire population is vaccinated (a total of 18 million doses), split evenly between vaccine cost and vaccine administration. This means that no savings on vaccine administration are attributed to a lower number of vaccinated than 90%. The model presupposes absent workers to take care of sick children, and thus the event of sick children does not produce the SEK 2,000 cost in a family where a parent is already ill. The inpatient care does not include expensive specialist care, but is based on the average cost of one day in inpatient care (SEK 8,119, according to figures from 2007, obtained from: http://sjvdata.skl.se).

Direct costs related to death cases are considered, using the figure of SEK 22 million per deceased (as employed by the Swedish Institute for Transport and Communications Analysis), but the case fatality rate (CFR) is hard to assess. Since the CFR for pandemic H1N1 influenza is still unknown [3], one way to proceed is to use a best estimate. Three scenarios were used for the present analysis, motivated by the early figures from New Zealand: 0.005%, 0.010%, and 0.050%. The first of these is considered the most likely scenario [4]. A similar cost assessment could be made regarding those suffering permanent health damages from the disease, but this is not reported here. Finally, neither deaths resulting from vaccination, nor import infections (i.e. cases of infected individuals travelling to Sweden from abroad) have been included in the model.

Results

For the scenario in which no policy interventions are made, the outbreak reaches its peak in weeks 16-20 in the five simulations run, each with over 100,000 newly infected in that peak week (Figure 1). More than a third of the individuals were infected at home (Figure 2). The neighbourhood is an aggregate of all contacts in geographical and social proximity, outside the home. That schools play a relatively important role in spreading a new infection is in

Figure 1

The number of infected persons per week during five simulations of the scenario without intervention. Estimation of costs of pandemic H1N1 influenza 2009 for Sweden.

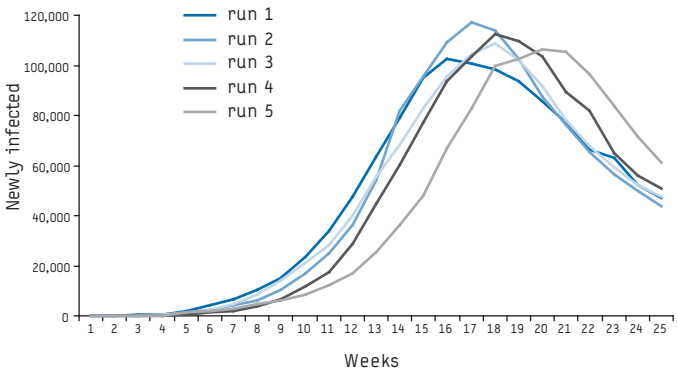
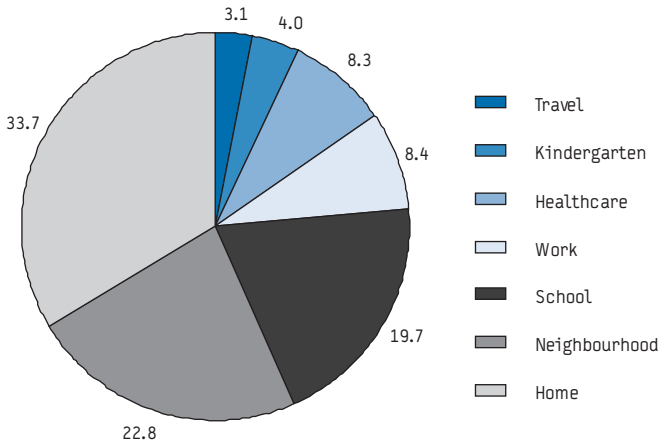


Figure 2

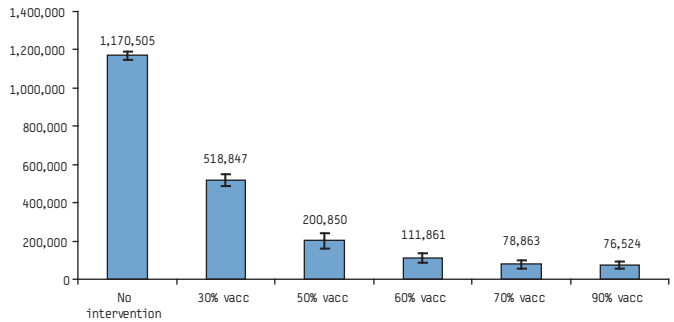
The place distribution of infected individuals, for the scenario without intervention. Estimation of costs of pandemic H1N1 influenza 2009 for Sweden.



Note: Numbers denote percentages, averaged over the five runs of this particular scenario.

Figure 3

The total number of infected individuals (y axis), for all runs. The error bars indicate one standard deviation of uncertainty. Estimation of costs of pandemic H1N1 influenza 2009 for Sweden.



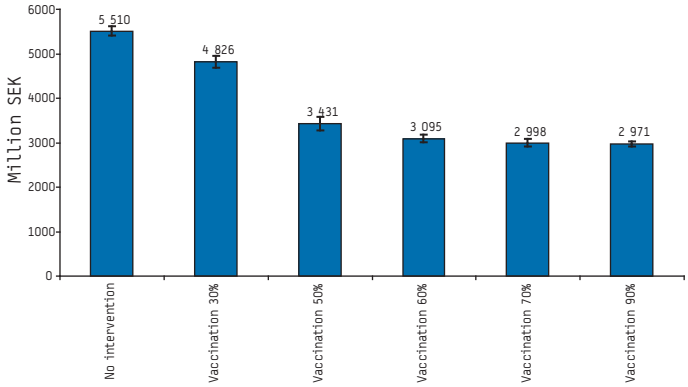
part a result of the assumption of increased infectiousness in the young population.

In Figure 3, the total numbers of infected individuals are presented, for all runs. The age distribution is not presented here, but is largely consistent with reports from actual spread, with an overrepresentation of the youngest and an underrepresentation of the oldest individuals.

The societal costs have been computed for four levels of CFR, including a baseline zero risk scenario depicted in Figure 4 (total costs) and Figure 5 (costs broken down into five categories). The two figures do not include the vaccine cost for the baseline scenario, even though it should be noted that Sweden has already ordered 18 million doses, putting the baseline scenario out of step with the actual fact. This fact notwithstanding, the scenario without interventions proves the most costly, and Figure 5 makes it evident that the mounting costs related to sick leave is the dominating factor. Including costs related to death cases provides even more evidence for the preliminary result that a vaccination level of at least 60% should be recommended (Figure 6). Figure 7 provides a simple sensitivity analysis, where the cost related to the deceased become the major cost as the most plausible CFR (0.005% of infected individuals) is increased by a factor of ten.

FIGURE 4

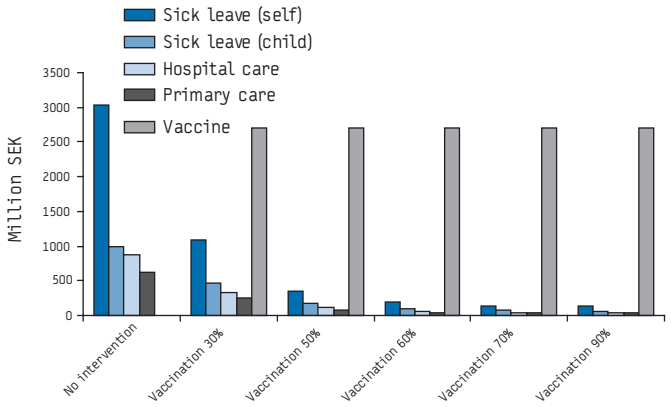
Total costs for the six scenarios, averaged over all runs. Estimation of costs of pandemic H1N1 influenza 2009 for Sweden.



Note: Case fatality rate is here set to zero. The "no intervention" scenario acts as a base line with zero cost for vaccination, while the other five scenarios all have actual cost for vaccination (SEK 2.7 billion). Error bars denote the standard error of the mean.

FIGURE 5

Detailed costs for the six scenarios. Estimation of costs of pandemic H1N1 influenza 2009 for Sweden.



Note: Case fatality rate is set to zero.

Discussion

There are many reasons to be careful when interpreting the results of these simulation experiments, since the assumptions made might not reflect the actual characteristics of the current pandemic. However, as the effects of the pandemic are being assessed,,new assumptions and new sensitivity analyses can relatively easily be made, following the same methodology as described here. And, we believe, that the overall conclusion stands, namely that given an outbreak of pandemic H1N1 influenza of the size contemplated here, vaccinating at least 60% of the Swedish population is recommended, from an economic perspective. When the actual doses arrive in Sweden, they will be distributed among the counties based on county population: the more people, the more doses. In Sweden, vaccination will be voluntary, but for the purpose of these simulation experiments it was assumed, somewhat unrealistically [5], that everyone offered vaccination will accept it. A recent survey, conducted on behalf of the National Board of Health and Welfare, on attitudes towards vaccination in Sweden, found a 72% willingness-to-vaccinate. The survey was conducted between July 27 and August 23, and consisted of 2,000 interviews.

The time to reach the peak of an outbreak in these simulation experiments was more than two weeks longer than what has been reported for the actual outbreaks in the southern hemisphere. This is likely to favour immunisation. Our hypothesis is that the relatively rapid, especially in view of the R0 values reported, peaks in Australia and New Zealand could be explained by the earliest cases going unrecognised, and a constant influx of new cases from abroad. In the model presented here, all cases are recognised, including the earliest asymptomatic cases, pushing back the start date of the epidemic. The fact that cases from abroad were not included can to some extent be justified by the relatively small number of people travelling to Sweden in the early fall.

A recent study [6] suggests that vaccinating school children and their parents leads to a reduction of spread, in large part thanks to herd immunity [7]. The MicroSim model is highly suitable for investigating the efficiency of such policies, since the social network allows for identifying the parents, and a replication study is under way.

Acknowledgements

Model assumptions have been scrutinised by both The Swedish National Board of Health and Welfare (SoS), and by the panel of experts employed in the project which includes Anders Tegnell, Annika Linde, Åke Örtqvist, and Fredrik Elgh. Information on supplies and effectiveness of vaccines is based on information from GlaxoSmithKline AB, Hillar Kangro. Simulation model developed at SMI, by Lisa Brouwers, Martin Camitz, Baki Cakici, and Kalle Mäkilä. The programming of interventions was done mainly by Baki Cakici. Analysis and reporting is the responsibility of Lisa Brouwers, with technical assistance from Magnus Boman.

Figure 6

Detailed costs for the six scenarios, including the costs related to the deceased, where the CFR is set to 0.005%. Estimation of costs of pandemic H1N1 influenza 2009 for Sweden.

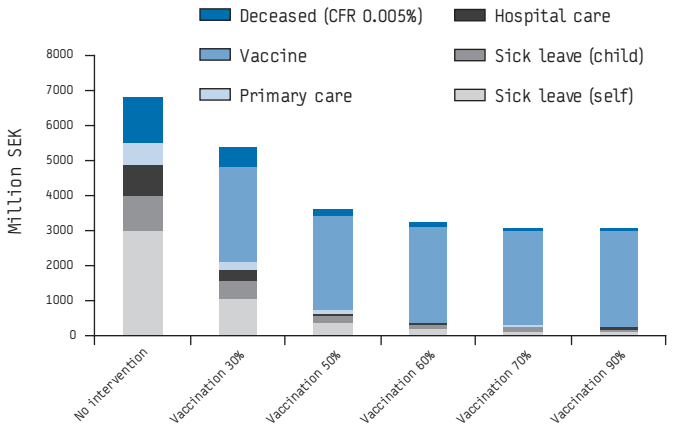
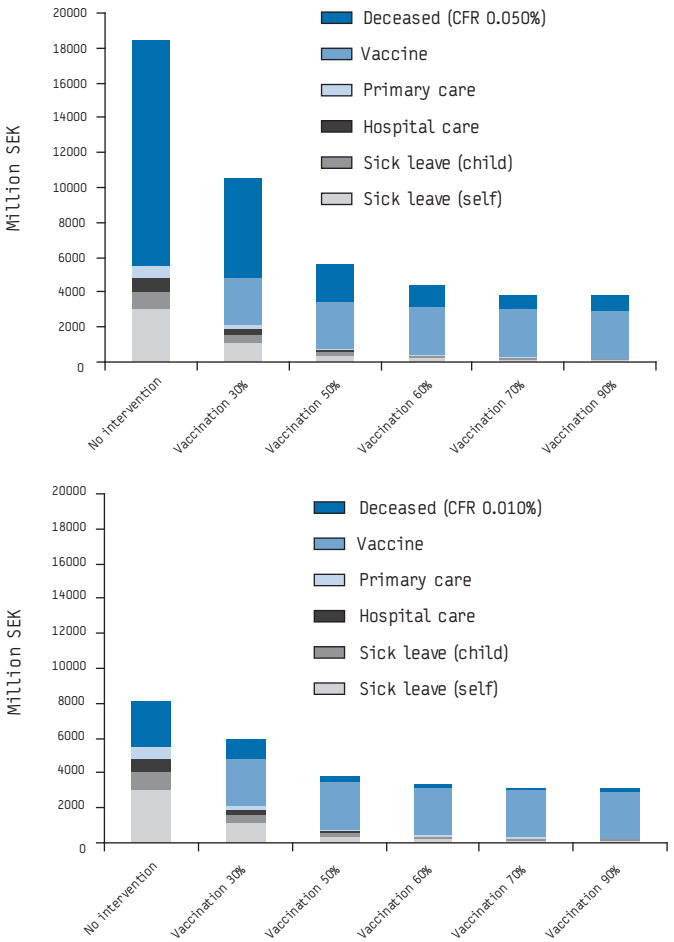


Figure 7

Detailed costs for the six scenarios, including the costs related to the deceased, where the CFR is set to 0.050% (top) and 0.010% (bottom). Estimation of costs of pandemic H1N1 influenza 2009 for Sweden.



References

1. Brouwers L, Camitz M, Cakici B, Mäkilä K, Saretok P. MicroSim: modeling the Swedish population. arXiv:0902.0901. Available from: http://arxiv.org/abs/0902.0901
2. Statistics Sweden (Statistiska centralbyrån, SCB). Homepage on the internet: http://www.scb.se
3. Garske T, Legrand J, Donnelly CA, Ward H, Cauchemez S, Fraser C, et al. Assessing the severity of the novel influenza A/H1N1 pandemic. BMJ. 2009;339:b2840.
4. Baker MG, Wilson N, Huang QS, Paine S, Lopez L, Bandaranayake D, et al. Pandemic influenza A(H1N1)v in New Zealand: the experience from April to August 2009. Euro Surveill. 2009;14(34):pii=19319. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19319
5. Chor JS, Ngai KL, Goggins WB, Wong MC, Wong SY, Lee N, et al. Willingness of Hong Kong healthcare workers to accept pre-pandemic influenza vaccination at different WHO alert levels: two questionnaire surveys. BMJ. 2009 Aug 25;339:b3391.
6. Medlock J, Galvani A P. Optimizing influenza vaccine distribution. Science. 2009 Aug 20. [Epub ahead of print].
7. Fine PE. Herd immunity: history, theory, practice. Epidemiol Rev. 1993;15(2):265-302.
8. Carrat F, Luong J, Lao H, Sallé AV, Lajaunie C, Wackernagel H. A 'small-world-like' model for comparing interventions aimed at preventing and controlling influenza pandemics. BMC Med. 2006;4:26.
9. Ferguson NM, Cummings DA, Cauchemez S, Fraser C, Riley S, Meeyai A, et al. Strategies for containing an emerging influenza pandemic in Southeast Asia. Nature. 2005;437(7056):209-14.
10. Moser MR, Bender TR, Margolis HS, Noble GR, Kendal AP, Ritter DG. An outbreak of influenza aboard a commercial airliner. Am J Epidemiol. 1979;110(1):1-6.
11. Swedish Association of Local Authorities and Regions (SALAR). Sjukvårdsdata i focus [Healthcare data in focus]. 2006. Available from: http://sjvdata.skl.se/sif/start/
12. Swedish Social Insurance Agency (Försäkringskassan). Homepage on the internet: http://www.forsakringskassan.se
13. Swedish Institute for Transport and Communications Analysis (Statens Institut för Kommunikationsanalys SIKA). RES 2001. Den nationella reseundersökningen [National Travel Survey]. Stockholm: Birger Gustafsson AB; 2002. Available from: http://www.sika-institute.se/Doclib/Import/100/ss2002_2.pdf

Annex: Assumptions prior to the experiment

1. Introduction of infection

On the first day of simulation, 50 individuals are randomly selected to be the initially infected.

$$R_0 = \frac{-\ln\left(\frac{A}{B}\right)}{1-\frac{A}{B}}$$

2. R0 value

R0 is defined as the average number of individuals a typical person infects under his/her full infectious period, in a fully susceptible population. Here parameter values were used that, on average, cause outbreaks with R0-value 1.4. This value was calculated using the following formula:

B: Total number of susceptible individuals before the outbreak
A: Total number of susceptible individuals after the outbreak

Note that 7,978,105 out of 8,861,388 individuals in Sweden belong to the giant component, that is to say, they are connected to the social contact network. We use this lower value instead of the total population for the "susceptible before" value in the calibrations in order to avoid overestimating the infectiousness.

To reach the required R0-value, we adjusted the amplitude of the epidemic profiles. We used a factor 0.997 as the escape probability to obtain the required R0-value (4,000,080 infections).

3. Infectiousness profiles

We use different infectiousness profiles for different disease severities. Additionally, we assume that children are both more infectious and more susceptible. The infectiousness is the risk of transmission through personal contact, i.e. when an infectious and a susceptible person meet (during a period of eight hours). See Annex Figures 1 through 4 below for the corresponding profile graphs.

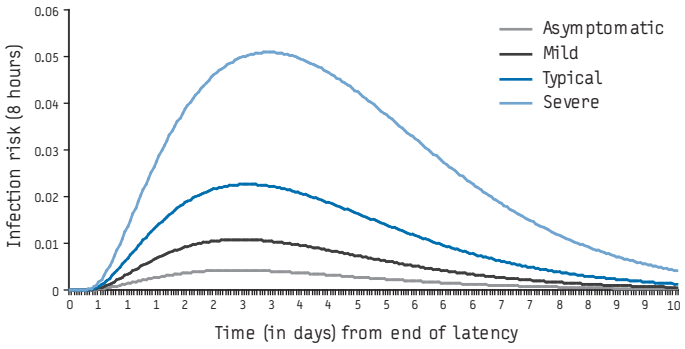
The infectiousness profiles are adapted from Carrat et al. [8], where a static latency period is included. We chose to remove this latency period from the Carrat profiles and instead introduced a varying latency period (12 to 60 hours), generated from a Weibull distribution with scale parameters 1.1 and 2.21 [9,10].

4. Disease profiles

In the experiments, all infected individuals are assigned a certain disease profile with the following proportion: asymptomatic (16%), mild (34%), typical (40%) and serious (10%). The infected individuals display different levels of illness depending on their disease profile (Annex Figure 5).

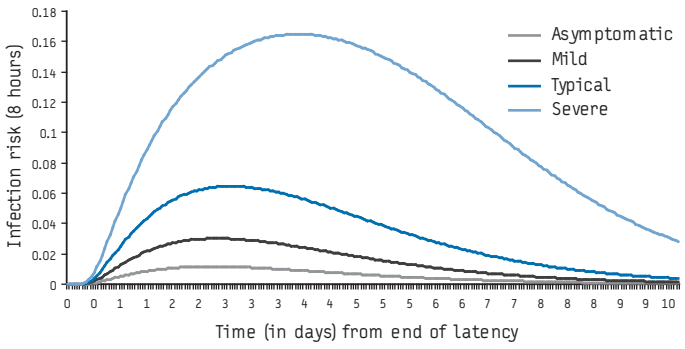
Annex: Figure 1

Infectiousness profiles adult -> adult



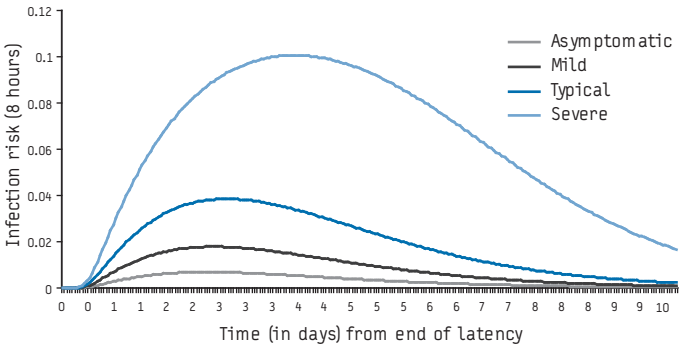
Annex: Figure 2

Infectiousness profiles child -> child



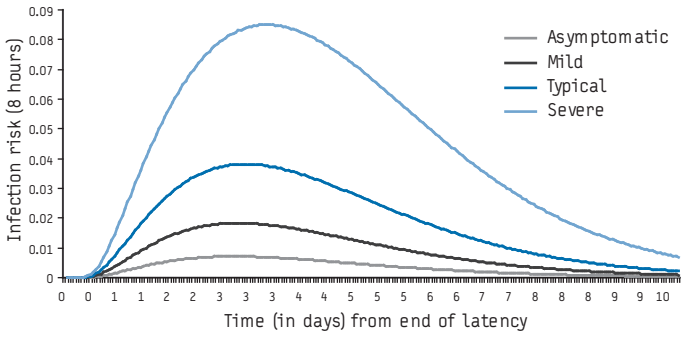
Annex: Figure 3

Infectiousness profiles child -> adult



Annex: Figure 4

Infectiousness profiles adult -> child



The number of deaths was calculated externally, after the simulations, due to the uncertainty of case fatality rates. We multiplied the number of infected individuals by the CFR 0.005% estimated in another study [4].

5. Choice of place according to disease level

Depending on their disease level, the individuals spend their day in different settings (Annex Figure 6). The choice of place is determined randomly. Persons with the same disease level can spend the day in different settings: one stays at home from work, another is at work, and a third person visits the emergency room. Disease level 0 represents all individuals who are not infected, as well as those infected without symptoms.

Settings in the model extracted from register data

By using different SCB (Statistics Sweden) register data [2] individuals have been linked to their workplaces and their residences. Individuals are also linked together in their families.

In the model, each person object contains the family identifier, birth year, gender, coordinates for the family residence (indicated at the level of 100 x 100 meter squares), and workplace identifier. Workplace representations include the workplace identifier, county, and coordinates of the workplace. The workplace identification number is used to connect the person and the workplace. Place objects include a list of members; for residences this list contains the family members and for workplaces it contains employed individuals.

Unit size

We have decided on a maximum number of persons, x, to belong to any one unit. This means that an individual is in close contact with a maximum of x other individuals at his/her workplace, school, nursery centre, etc.

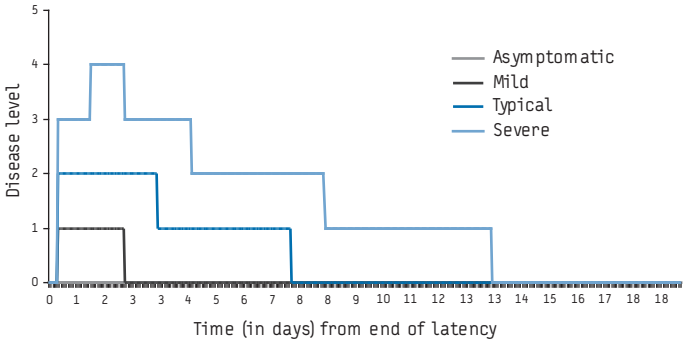
At large places, it is also possible to transmit infection between units.

Since the individuals in the model lack memory, it is possible for them to visit primary care one day, go to work the next day and visit primary care again on the third day. To avoid this issue, we created a place choice rule to limit emergency room visits to one.

The number of visits to emergency rooms and primary treatment are based on information gathered by the Swedish Association of Local Authorities and Regions (SALAR) in 2006 [11]. This database is also the source of the costs for 24 hours of inpatient care, as noted in the paper.

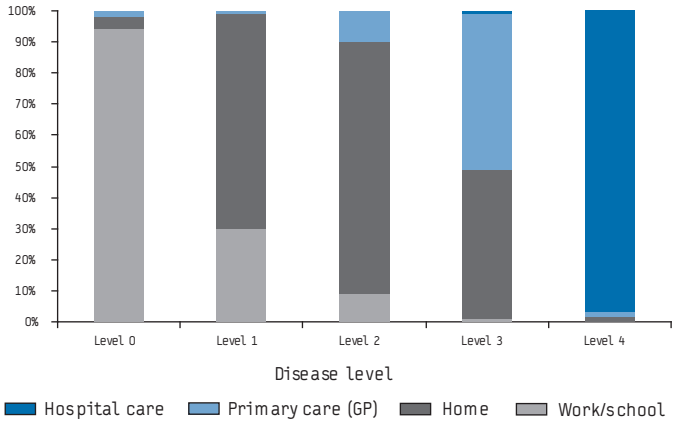
Annex: Figure 5

Disease levels



Annex: Figure 6

Place distribution by disease level



Annex: Table 1

Maximum size of places

Type of place	Maximum size of unit/group
Kindergarten	no unit division
School	25
Office	25
Emergency room	no unit division
Infectious diseases clinic	no unit division

Annex: Table 2

Number of outpatient visits

Visits to general practitioners (excluding antenatal and paediatric care)	25,238,500
All other visits (including day care treatment)	34,131,400
Total:	59,369,900
Per day:	162,657

Annex: Table 3

Number of infected individuals

Scenario	Number of infected	Standard deviation	Number of runs
No interventions	1,170,505	45,345	5
Vaccination coverage 30%	518,847	63,742	5
Vaccination coverage 50%	200,850	40,653	10
Vaccination coverage 60%	111,861	52,219	10
Vaccination coverage 70%	78,863	45,586	10
Vaccination coverage 90%	76,524	37,307	5

In the model, the daily risk of visiting primary care (for an individual with disease level 0) has been determined to be 0.0184 (162,657/8,860,000).

The estimates of daily probability of staying home from work due to illness or for other reasons at disease level 0 are based on data from SCB [2] and the Swedish Social Insurance Agency [12]. The absence, as indicated in the data, varies over time depending on changes in compensation levels and regulations. We use 4%, a relatively low level, for the current model.

6. Ad hoc contacts

In addition to contacts within the social network, we include two additional place types to represent ad hoc contacts: neighbourhood and travel. Neighbourhood infections are used to represent infections in an individual's geographical vicinity, while travel indicates infectious spread between Sweden's 81 regions.

Neighbourhood

Infection transmission in the neighbourhood occurs in two steps for each region:

1) Calculate the total number of new infections for each region:

N = Current number of infected in region

C = Number of contacts (=10, for the current model)

R = Risk of infection: the mean value of the four disease profiles

$$I = N \times C \times R$$

The number of individuals infected in the neighbourhood decreases over time, as described by multiplying the right-hand side of the above equation by the fraction S/T, where S is the number of susceptible individuals and T is the total number of individuals.

2) Choose the individuals to be infected

We pick an infectious person at random from the list of infectious individuals in the region, and search for a susceptible person within a radius of 15km to infect. If no susceptible individuals are found, we increase the radius and try again.

Travel

The daily number of travellers from one region to another has been estimated using statistics about travel [13]. This number is used to calculate the new infections that will occur as a result of infected individuals travelling within the country.

7. Vaccine availability

We assume that 346 boxes of vaccine arrive in Sweden every week. Each box contains eight cases, and each case contains 500 doses. Vaccination can be initiated three days after the boxes' arrival. One to two days are needed to administer 346x8x500 doses of vaccine. After 14 weeks we will have received 19 million doses, which is enough to vaccinate the entire population using two doses for each individual.

8. Total number of infected individuals

The table below presents the total number of infected individuals, averaged over all 180 day runs, for the six scenarios, with their standard deviations (Figure 3 in the article above).