



Eidgenössische Technische Hochschule Zürich
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Lecture with Computer Exercises: Modelling and Simulating Social Systems

Project Report

**Pertussis resurgence in societies
with high vaccination coverage**

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1 Abstract

The first objective of this paper is to model find which level of immunisation is required to eradicate Pertussis in a society. We simulated the effects of various initial vaccination rates and draw a comparison to theoretical models, and observe the stability of our results. The second objective is to find out under which circumstances Pertussis outbreaks occur, in particular in societies with high vaccination coverage. We find that a lack of

2 Individual contributions

3 Introduction and Motivations

Vaccines are without doubt one of the greatest advances in medicine, whose widespread use has led to the eradication or restriction of some of the deadliest diseases, including smallpox, polio and measles. Every vaccination carries a small risk of side effects. According to the WHO, severe adverse events are extremely rare for most vaccines (for the Hepatitis B vaccine only one in a million is affected) or not yet clinically proven like in the case of Hepatitis A.¹ However, contested medical papers and rumours have led to a reluctance to vaccinate in parts of the society.

We modelled the specific case of Pertussis or Whooping cough, as there have been several incidents where a rising number of infections have been observed despite relatively high vaccination rates. One of these cases is the Netherlands, where, despite a coverage rate of 95% several cases of Pertussis have been registered. One of the reasons is waning immunisation and the lack of people getting vaccinated. Even though these cases might be few, the survival of the disease means that the coverage rate should remain high.

This paper tries to answer the question of how people take decisions on whether to get vaccinated or not, and how the dynamics of the disease changes.

Figures 1 and 2 show interesting data from two countries with good vaccination coverage, the UK and Germany. In the second the basic immunisation (having had the two first pertussis shots) of children by age-group.²

¹WHO (2018-10-06), [http : //www.who.int/vaccine_safety/initiative/tools/vaccine_sheets/en/](http://www.who.int/vaccine_safety/initiative/tools/vaccine_sheets/en/)

²Robert-Koch-Institut und BZgA: Zur Gesundheit von Kindern und Jugendlichen in Deutschland

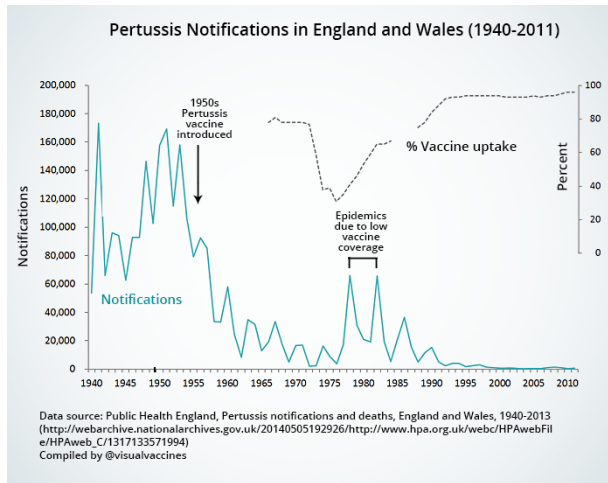


Figure 1: Pertussis Notifications in England and Wales 1940-2011

Abbildung 5.2.2.5
Vollständige Grundimmunisierung gegen Keuchhusten nach Alter

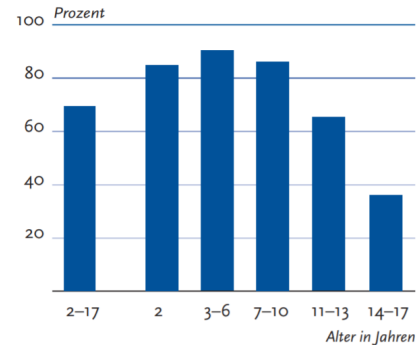


Figure 2: Basic immunisation against Pertussis by age-groups

4 Description of the Model

4.1 SIR Model

We used an SIR model for the simulation of the spreading of Pertussis. Pertussis is transmitted by respiratory droplets human-to-human with an incubation period ranging from 9 to 14 days, while symptoms can last up to 6 weeks. ³

```
#probability of infection from outside sources
prob_for_diseases = 0.001
prob_for_contact_infection = 0.5
```

This estimation is taken from a simulation which assesses the susceptibility of family members. We assume that a person has frequent contact with close family members and modulate the outcome with another variable that uses the probability that you meet with someone from your network on a given day to depict a realistic depiction of the society. ⁴

Markus

³Torres Codeço, C; Mendes Luz, P; Is pertussis actually reemerging? Insights from an individual-based model, Cad. Saúde Pública vol.17 no.3 Rio de Janeiro May/June 2001

⁴Estimation of Household Transmission Rates of Pertussis and the Effect of Cocooning Vaccination Strategies on Infant Pertussis Epidemiology 23(6):852-860, November 2012

In our model individuals have the choice of vaccinating or not. They do that based on the current benefits of each option. The main parameters influencing their decision are the perceived risk of side effects of the vaccination r_v and perceived risk to get harmed by the disease r_i . These two parameters do not just have to be caused by one specific reason but can be composed of a number of factors. Certainly the actual risks play a part, but equally the perceived risk, which will rise for example when individuals in the neighborhood are infected. But also financial consideration may play a part. We will elaborate on the possible influences in Chapter. . . . Furthermore we will assume that the disease can only be transmitted by humans. Childhood diseases like pertussis or measles are of that kind. Diseases like Cholera or Malaria can also infect someone if nobody else is infected. This sort of diseases will not be looked at in our initial model. We will however incorporate that possibility later. The probability to get infected PI_i is primarily determined by the proportion of people that are currently infected li and the proportion of people that are vaccinated lc

4.1.1 Modelling immunisation

We assume that the vaccination provides 100% safety, equal to having recovered from the disease. However, as recent research has shown that the protection considerably decreases about 10 years after the initial protection. To simplify the length of the protection acquired either by being vaccinated or by having recovered from Pertussis, we give people the option to vaccinate again after 8 years. The average duration of protection is 12 years with a standard deviation of 2 years, which is on the conservative side, given that only 10% of those vaccinated are still protected 12 years after the vaccination. There is less data available to assess the immunity after having recovered from the disease, but it can be assumed to be similar to the immunity acquired by vaccination. In addition we analyse a society with a high rate of coverage, so that the majority will have acquired their immunity by vaccination.⁵ As this dynamics of waning immunity already provides us with a constant population, we do not model births and deaths, as Pertussis is not a disease that frequently causes death.

4.2 Network

The main model of our project uses a complex network representing the contacts of each person. The vertices are the individuals in the simulation and each edge is a contact between the two people. We worked with undirected networks in all our simulations. The transmission of a disease, at least in the case of pertussis, occurs if

⁵Wendelboe, Van, Salmaso, Englund: Duration of immunity against pertussis after natural infection or vaccination. S58–S61

and only if the two individuals have direct contact. Meaning if Person A has contact to Person B, then Person B has automatically also contact to Person A. That context is better represented by an undirected network. However, our simulation works for directed networks as well. All networks we used were also connected, which means that there is a path between each two vertices. All social networks nowadays are that way, in particular small sized systems like in our simulation. Moreover, unconnected individuals do not play a role as the disease can only be transmitted by human contact.

As studied by Barabasi,⁶ randomly generated graphs are not a good representation of real human networks as some people will have contact to many more people than average, while most will have contact to far fewer individuals. That is because people with a large number of contacts are more likely to connect with even more people. That means real human networks exhibit so called scale-free behavior, meaning that the degree distribution falls by some polynomial rather than being constant like in a completely random network. The Barabasi-Albert-Network reaches that by sequentially adding single nodes each with two new edges connecting randomly, but with a preference to nodes with a higher degree, to the already existing nodes. Using that process, a degree distribution of k^{-3} is reached. We did create our own generator which builds a network after the Barabasi-Albert-Model. However, due to considerable runtime length we used the Barabasi-Albert-Generator from the Python Module Networkx for most of our simulation, especially for those with a high number of vertices.

4.3 Vaccination Decision

We assume that every person is a rational decision maker, who decides whether or not to get vaccinated based on the perceived costs of getting vaccination vs risking getting sick.⁷

has an initial inclination to vaccinate themselves, which we initialise before the simulation.

Cost functions To evaluate the probability of a person to get vaccinated, we use a static model in which each individual assesses their personal cost of getting vaccinated versus getting infected.

⁶INSERT REFERENCE BARABASI

⁷INSERT RESEACH ABOUT 12 YEARS HERE

4.3.1 Perceived vaccination cost

As we consider the ratio of the perceived cost of vaccination and the perceived cost of infection (i.e. getting sick) and not the absolute values, we set the perceived cost of vaccination arbitrarily to 1 at the start. This number does not only include the monetary cost, but also the risk of side effects and other factors, which we do not consider separately. For finding the perceived cost of infection, we go back to our initial assumption that a voluntary vaccination policy is in place. That means that the initial perceived cost of infection is related to the initial coverage level in our system. If initially 97% of the people are vaccinated, we set the perceived vaccination cost in such a way that the expected gain due to vaccination is slightly negative for every person exceeding the 97% coverage level.

$$E(P, p) = -rP + (1 - P) * i \quad (1)$$

expected_gain = - perceived risk of vaccination + infection cost *(infection level * (1 - coverage level)* risk of infection)

4.3.2 Perceived infection cost

The perceived vaccination cost of a person changes in two scenarios:

1. When someone in the immediate surroundings is infected, the perceived infection cost rises by a factor of 1.2 (after recovery of the contact it decreases by 0.9).
2. When the global level of

4.4 One person among N people

To illustrate this, let us have a look how a person A takes the decision to vaccinate: We initialise each person with a value for perceived vaccination cost and perceived infection cost (which are the same for everyone at the beginning. If a person B in the network of A falls ill, A's perceived infection cost rises by a factor of 1.2. If another person C in A's network were to fall ill, A's perceived infection cost would rise by a factor of 1.2 again. After person B recovers, A's perceived infection cost are multiplied by a factor of 0.9, the same is true when person C recovers, leaving person A with a perceived risk of infection of 1.1664 compared to 1 at the beginning, accounting for the fact that the person is more aware of the cost of the disease because B and C in their network have been affected.

4.5 Equilibria for N people

In addition to the "local" information of the nodes in the network of the person, there is also information on the general coverage and infection level in society available to the individual, as well as an additional factor that we call

4.6 Important Parameters

First we look at the dynamics of the disease. Pertussis is highly contagious, and is transmitted via the respiratory organs. Sneezing, coughing or even speaking can release enough infected particles to cause the disease, making crowded spaces such as public transport and educational institutions ideal for transmission. We therefore initialised everyone in the network to have 40 connections, of which he or she meets 40% every day, which seems realistic given that even a short encounter on a train station might cause the disease.

```
#Random probability (per day and person) to become sick  
#without being infected by someone else  
prob_for_diseases = 0.000001
```

```
#probability to infect someone when there is contact  
prob_for_contact_infection = 0.5
```

```
#incubation time (in days)  
incubation_time = 12
```

```
#days from infection , after this time a person is recovered  
time_to_get_healthy = 42
```

5 Implementation

The model was implemented using Python. First, we wrote the basic SIR model with infection and recovery. Then we added the "vaccination function" which returns whether a person is getting vaccinated or not.

5.1 General Principle of the Simulation

The programme has an object-oriented approach, meaning that the main program is executed by objects of a class Person in vacc.py. Each Person is one individual in

our model. There are two derived classes, each corresponding to a way of simulating the interactions between those individuals:

Grid_Person: Places people on a two-dimensional plane, where each pixel stands for one Person. Not a very realistic model, but it allows for nice graphical representations and animations.

Network_Person: More realistic and thus the one used for the whole analysis. Every Network_Person has an adjacency list of all its contacts and can only interact with those.

Each timestep (one day) several member functions are called to refresh the status of each Person.

Next_day(): Checks, whether immunisation or infection is still active or refreshes the corresponding variables if this is not the case

Get_vaccinated(): Every day, each person decides whether to get vaccinated today, depending on the expected gain for themselves. The details of that can be found in 4.3.

Start_infection(probability_to_meet): An infected person starts being contagious 7 days after being infected until the end of incubation time, as we expect that sick people do not mingle anymore and are only attended by those who have been vaccinated.⁸ The probability_to_meet represents the probability of two people meeting each other, with the probability of being infected is prob_for_contact_infection.

5.2 Initialisation for long time analysis

The main goal of the long-term analysis is to investigate if and when the disease can reemerge. To model this, a few new functions and parameters are needed. Following the assumptions about waning immunisation (**explained in 4.1.1**), we approximate the length of immunity of an individual by a gaussian with a mean of 12 years and a standard deviation of two years. The individuals obviously do not know, whether they are still immune, but can vaccinate again after 8 years, consistent with recommendations from health organisations.

Another parameter that we introduce is a random probability to be infected. Pertussis is only transmitted by other humans. However, that random probability is needed as the disease would die out quickly due to the small size of our system,

⁸Bundeszentrale für Gesundheitliche Aufklärung Germany, Keuchhusten www.infektionsschutz.de/erregersteckbriefe/keuchhusten/#c3580, accessed 30.11.2018

and represents contact with others outside the system (e.g. travellers) that would otherwise not be accounted for.

The last but arguably most important parameters are the perceived cost of vaccination and infection. As the literature on this topic is very theoretical in nature, we took and adjusted a simple game-theory based model by Heal⁹ and fit it to our model. **(Read more in 4.3.1 and 4.3.2).** The first problem is that no one vaccinates if nobody is infected. That is evidently false, so we set the infection level to a minimum of 0.1 percent, corresponding to the probability of getting infected by an outside person.

Letting this model run yields no results, as it operates in an equilibrium. As soon as one person's immunisation becomes inactive they will immediately vaccinate again, resulting in a constant coverage level. This is also consistent with the real situation. If 97% of the people have decided to vaccinate and the opinion of everybody remains the same, they will immediately vaccinate again upon losing immunisation.

5.2.1 Vaccination scares

That means we have to introduce a parameter to vary their opinion, which we call vaccination scares. At different times we change the perceived cost of vaccination of some proportion of the population just like a anti-vaccine newspaper article or television documentary for example would. If there has not been a noticeable outbreak, the perceived vaccination percent of 30% of the population (selected randomly) is increased by a factor of 1.5, this happens all 500 days at maximum. Since these dynamics are hard to model, we decided to implement it this way. However, if you were to implement this mechanism in a different way, you would get similar results, the main difference being the time intervals at which those events occur. Since we are not trying to predict when an outbreak will occur, we are indifferent to the exact timing and instead observe the reaction of the system to such a vaccination scare.

6 Simulation Results and Discussion

6.1 Initial breakout

In our first test, we ran our model with different levels of initial coverage level, analogous to the study by Hein on Herd Immunity.¹⁰ As predicted by other models,

⁹HEAL

¹⁰Fine, Paul, Ken Eames, and David L. Heymann. "Herd immunity": a rough guide." *Clinical infectious diseases* 52.7 (2011): 911-916.

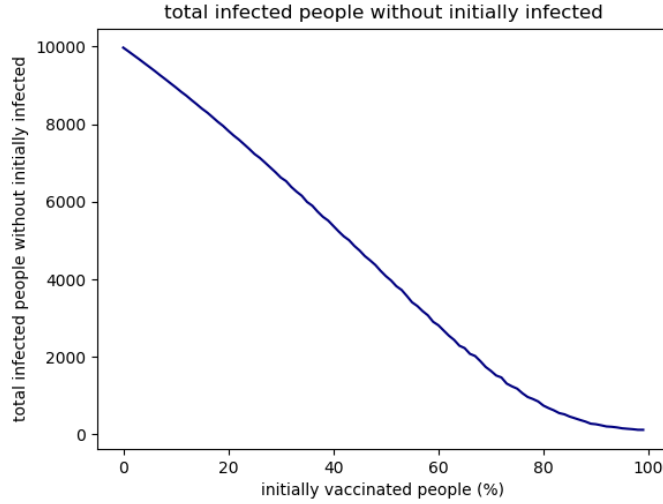


Figure 3: caption

our results indicate that there is a threshold of vaccination coverage, which is needed to keep the number of infections low. On the x-Axis we have the percentage of initially vaccinated people (we do not take into account waning immunity as we only run the programme for a period of 500 days), on the y-Axis the absolute number of people who get infected at some point during this time period, excluding the persons who are infected at the start of the simulation (just one person in our case).

This also coincides with the Vaccination coverage V_c and the Basic Reproduction Number R_c of Pertussis, that we have set to the value of xxxxxxxxxxxxxxx¹¹ for the purpose of our study. (This is based on the standard SIR model, which in our case was slightly modified).

$$V_c = 1 - \frac{1}{R_0} \quad (2)$$

total infected people without initially infected

6.2 Long-term study

As explained in 5.2.1, we introduced vaccination scares in our long-term model, which results in a system that is a lot more unstable than the initial model without such

¹¹INSERT BASIC REP NO

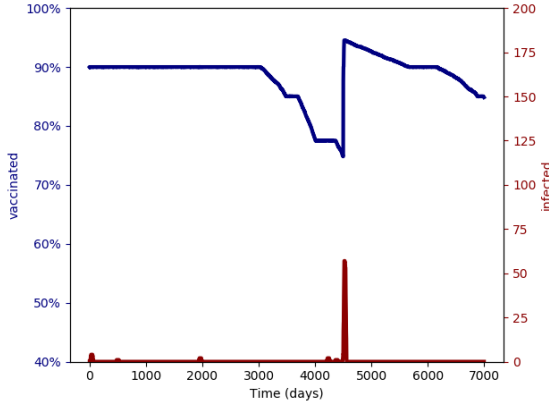


Figure 4: graph 1

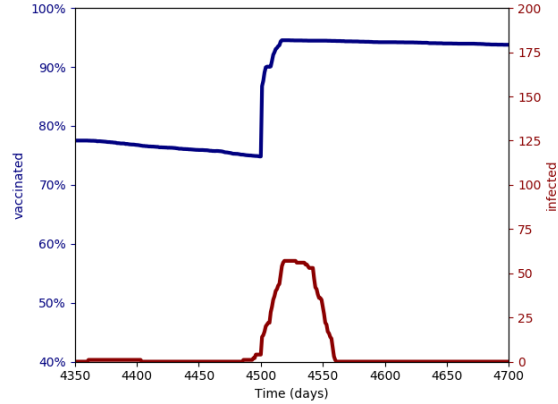


Figure 5: graph 2

supplement. Not only is this expected, it is also realistic to assume that outbreaks happen randomly and are not 'scheduled'.

6.3 Limitations

As with any model, this model has a range of limitations that result from the simplifying assumption that were taken.

The short term analysis has the same limitations as a standard stochastic SIR model. All the parameters of the disease like incubation time or the probability of transmission are the same for every person. However, having the stochastic SIR on the network approximates the transmission of the disease already much better than a deterministic SIR.

In the long term analysis people decide if they should get vaccinated based on perfect information of infections of other people. That is the same as Bauch did it in his deterministic model. In contrast to that, our model has two dynamic variables, perceived infection cost and perceived vaccination cost. As perceived vaccination cost is dependent on the contacts, our model has a "cluster effect". This means that people who are closely connected are prone to doing the same thing as their connections, which is something we can observe in society, where those who criticise/favour vaccinations often influence their friends' decisions. Additionally we introduced vaccination scares that change the long term properties of the system. Both effects are very hard to quantify, as they are complicated and unpredictable processes. Therefore, our model simplifies these effects; this could be extended to account for more variance in reactions than we were able to account for. However, for the purpose of showing the phenomenon of declining coverage and the resurgence of diseases it is

well suited.

6.4 Algorithm Performance

As we have a stochastic model on a network performance, a fast runtime is important for scaling and running the test multiple times. For each day in our simulation we need to iterate through all people to update their status. The only operations possibly taking more than constant time are the interactions of the people. That depends on the network. If the highest number of edges for one vertice is not constant, it will prolong the runtime drastically. However, this effect was minor for all networks we tested. So for the length of the simulation d , the number of people n , and the number of edges m , the simulation has a time complexity of $O(d*n*m)$. Therefore, we expect a linear dependence of people and the other way around for a constant number of days (assuming m is constant in n). The graphs show exactly that dependence.¹²

7 Summary and Outlook

We found the critical coverage level which needs to be reached or surpassed in order to prevent an outbreak, with several

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¹²INSERT TIMO’S GRAPH HERE

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[https : //www.gapminder.org/data/](https://www.gapminder.org/data/) search for 'vaccine'

Immunization coverage, system indicators and schedule, and disease incidence *www.who.int/immunization/monitoring_surveillance/data/en*