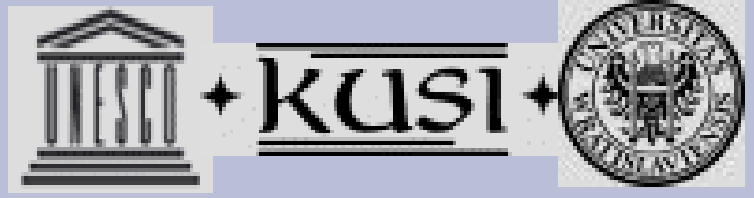

Contact networks and the spread of MRSA in hospitals

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27.11.2010, FENS, Warszawa

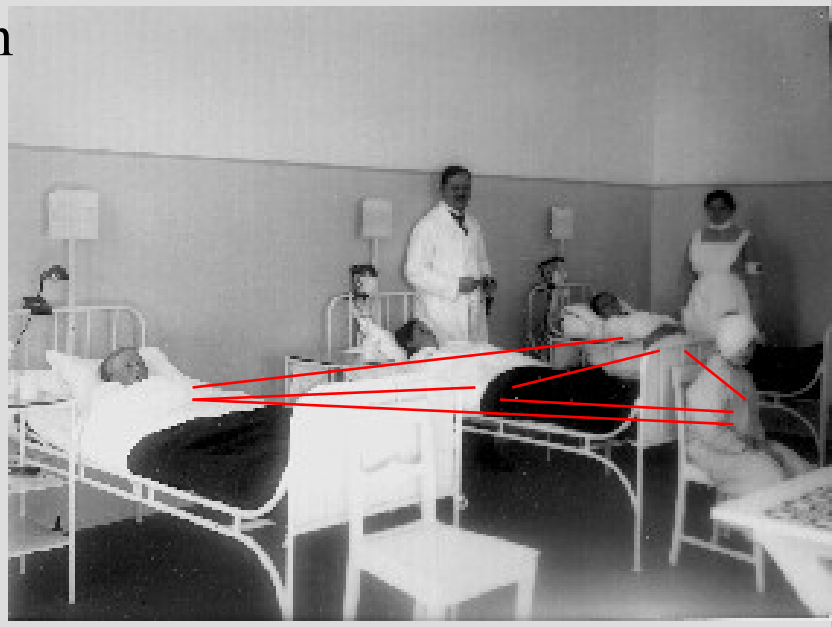
Outline

- The MRSA outbreak in Stockholm 1999-2005
- Statistical Analyze
- Stationary Case
- Dynamic Case (Results)

MRSA - Background and Social Network

The bacterium Meticillin Resistant *Staphylococcus Aureus* **(MRSA)** is resistant against more than half of all antibiotics and is known to alone be the largest care related the infection problem.

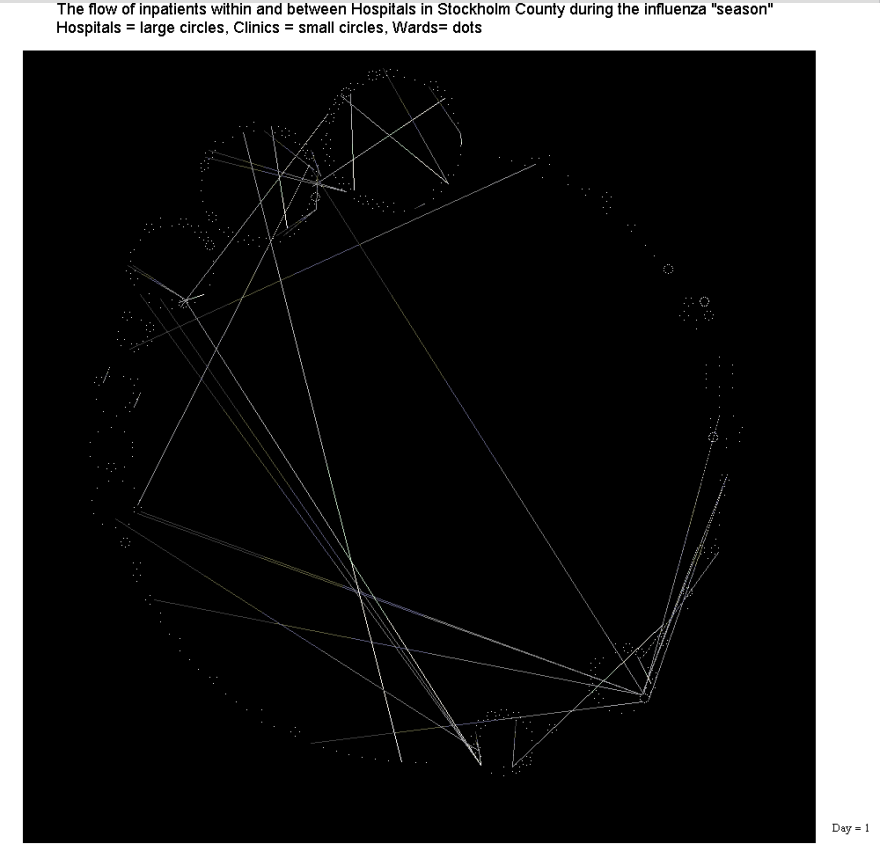
For such a infectious diseases, where a close contact is needed for a transmission to occur, the individual's position in the contact network is important for the person's risk to get infected. The awareness of the importance of contact network has brought methods from sociological studies of social networks into the area of preventive infectious disease protection work.



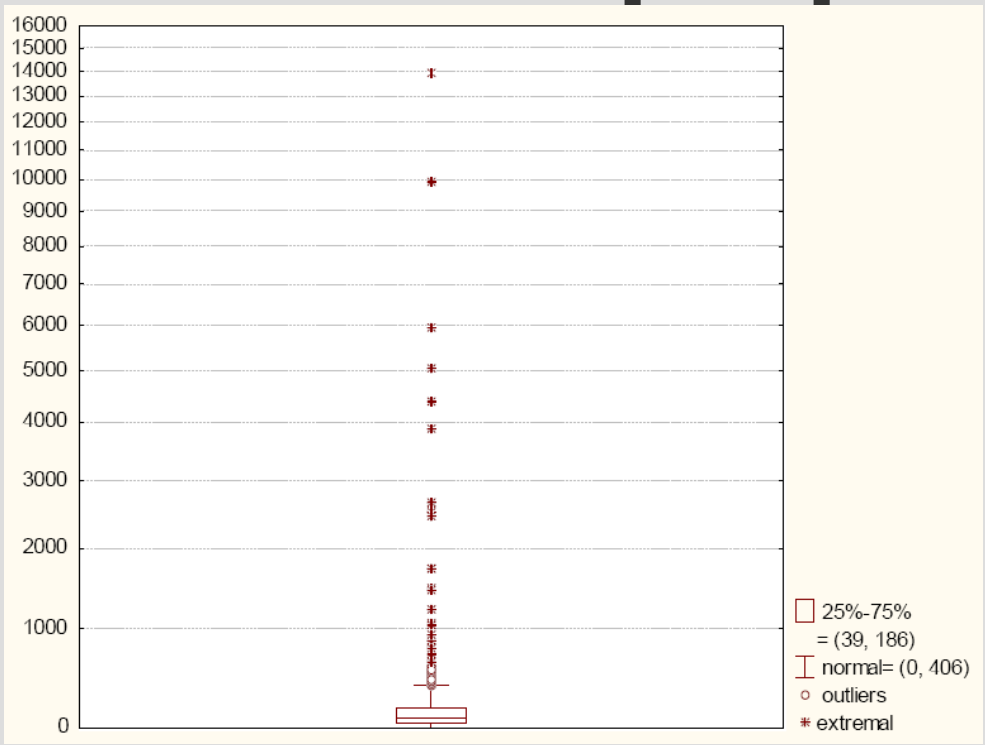
The MRSA outbreak in Stockholm 1999-2005

- 1337 Cases
- Population 2 314 517 Patients
- 210 different types of MRSA
- UK-E15 is the most frequent one
- The outbreak is now under control

Dataset contains information about all in- and outpatient visits within Stockholm County during the period outbreak and a registry over diagnosed MRSA cases.



MRSA – Some statistical properties



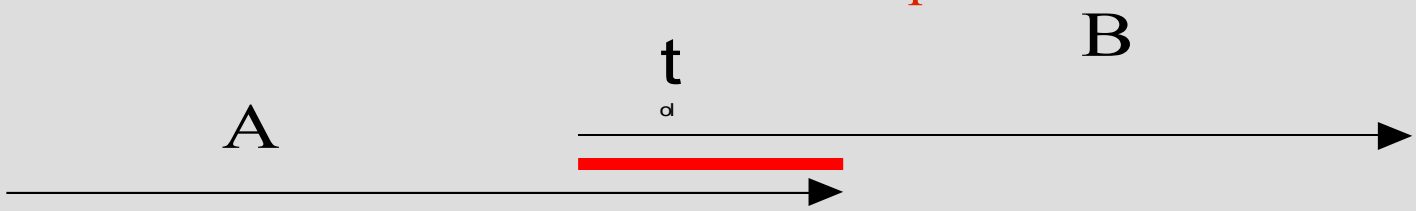
Scatter plot of number of contact ill persons with others. Most cases are between 39 and 186, but there are few outliers as well.

Efect	binomial test values(ill-1 or health-0)			
	Evaluation	standard error	Wald Stat.	p
free element	-4,01480	0,025059	25669,39	0,000000
days	-0,00027	0,000486	0,31	0,579326

A statistical hypothesis test is a method of making statistical decisions using experimental data and in our case is it logistic regression as a joining function with result taken from {0,1}. The null hypothesis was that the days spent with infected person have significant influence on being infected. P-Values is above 0.1 so there is no significant dependence between explaining and dependent variables.

MRSA – Method of realization

We study matrix of disease transition in hospitals population. This matrix **P** is our first goal. In rows are Infected and in Columns people, who could sent infection. Elements of matrix are probabilities, what Infection was sent by indicated person. Diagonal elements are probabilities of being infected by someone out of hospital, but they are in first approximation zeros. Unfortunately ¼ of all infected are patients, who had no contact with no other infected person.

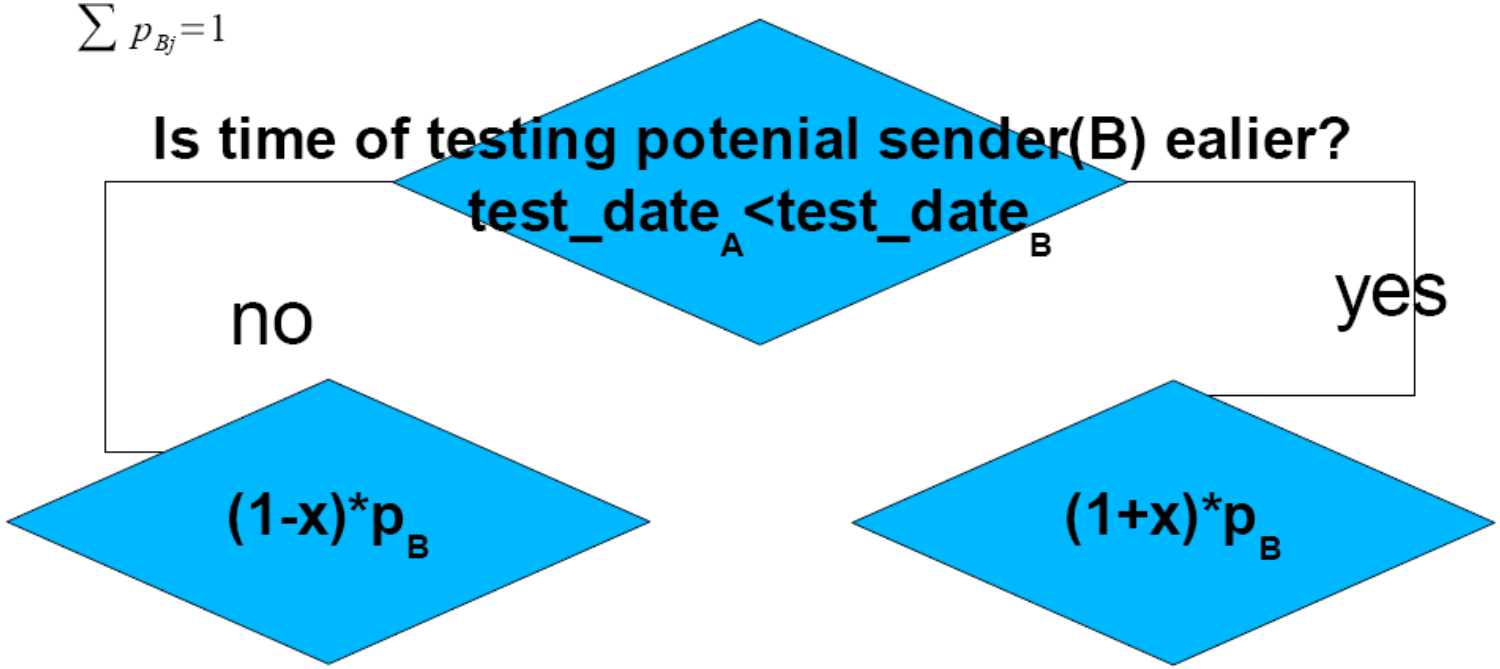


Probabilities calculation is based on time of contact (time of sharing the same ward)

MRSA – Improved matrix of p

A-individual infected
B-set of all infected
p_{B1} – *B1->A* example for one potential sender where *j*=1

$\sum p_{Bj}=1$



MRSA – Matrix of probabilities (*P*)

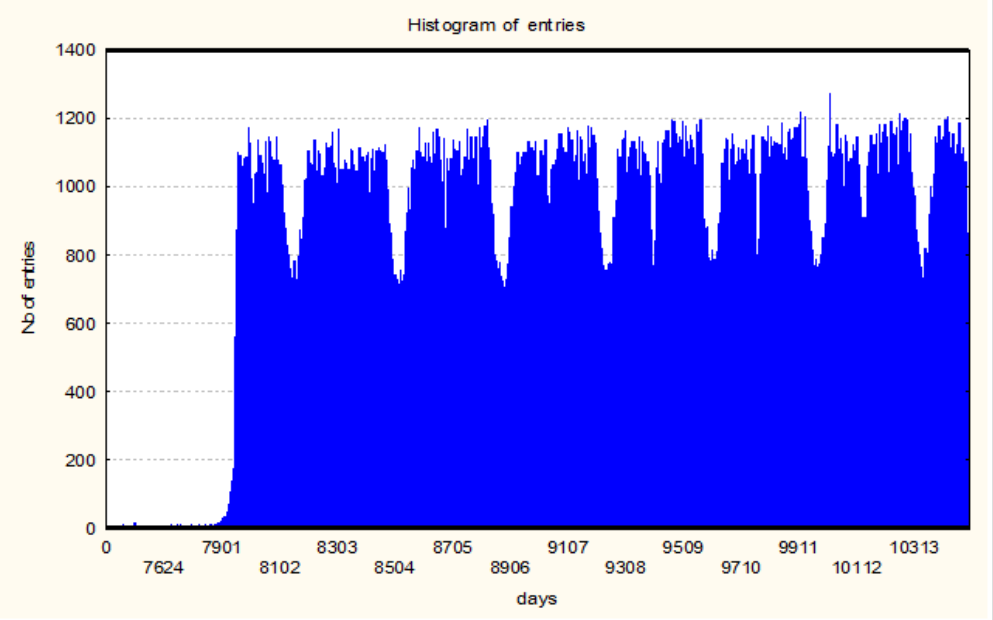
	1 Zmn1	2 Zmn2	3 Zmn3	4 Zmn4	5 Zmn5	6 Zmn6	7 Zmn7	8 Zmn8	9 Zmn9	10 Zmn10	11 Zmn11	12 Zmn12	13 Zmn13	14 Zmn14	15 Zmn15	16 Zmn16	17 Zmn17	18 Zmn18	19 Zmn19	Z
1	1																			
2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0,225	0,225	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0,4875	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0,495918	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8								1												
9									1											
10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0,108	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0	0,3375	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0,9	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0,18	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0,028125	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
25																				
26	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0,81	0
28	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Part of matrix for one type of MRSA (UK-E15). In rows are Infected (291) and in Columns people, who could sent infection (291 who also were infected).

MRSA –Dynamic case

Let build matrixes of contacts in smaller times intervals (*dt*). Let starts from time t_0 (1999) and matrix $\boldsymbol{P_0}$. That can divided The Stockholm Outbreak 1999-2005 into smaller periods, but last ***P*** will show situation during period (2005-*dt*). From that data we will also need matrix matrixes **P'** which will not be normalized and tell us some characteristics of numbers of contacts for patients in that time intervals (with contacts with all patients).

The best *dt* is whole year because of periodicity of visits to hospitals. That mean, that there will be 7 matrixes (both ***P*** and ***P'***), in which we are considering contact networks in that time interval.



MRSA – MCqMC simulation

We can look at how MRSA is spreading in time and tried to simulate similar scenarios using MCqMC Markov Chain quasi-Monte Carlo class of algorithms, which are based constructing a Markov chain that has the desired distribution as its equilibrium distribution.

- We assume that vector of our population (0-health, 1-ill) evaluate in time.
- We want to find mechanism of change.

0 0 ... 0 1 ... 0

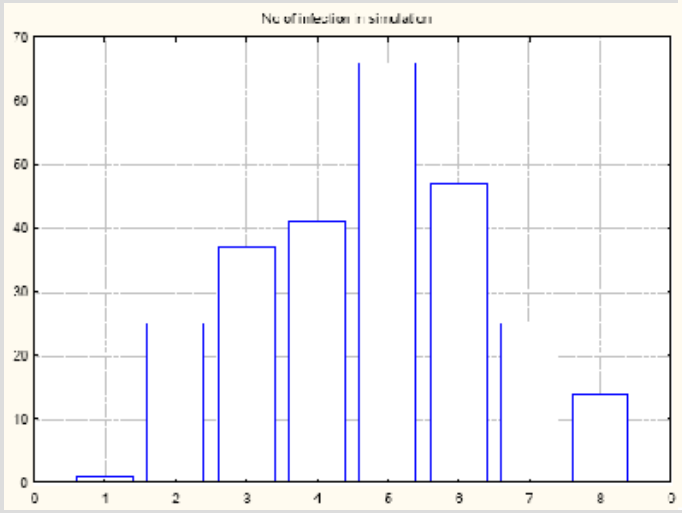
0 1 ... 0 1 ... 0 change after time interval

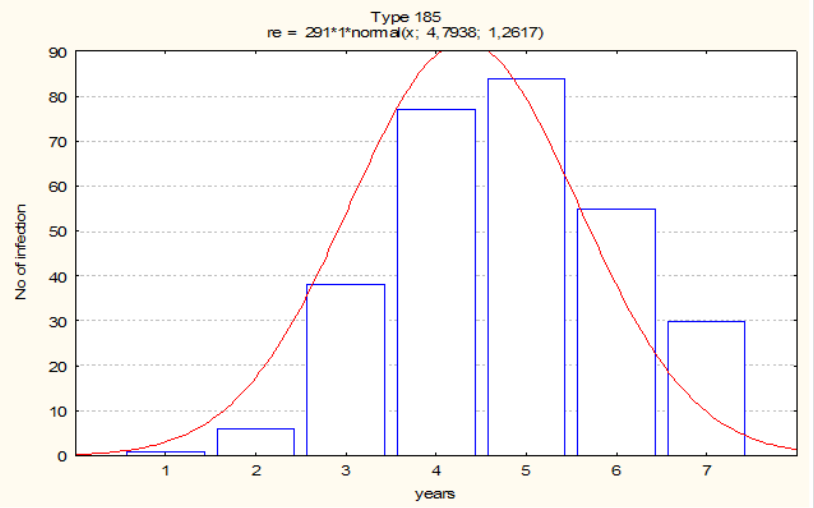
- All individuals can have specific p_t (probability transition). We can estimate that probabilities using historical data and try to run MCMC to predict future states.

MRSA – quasi-MCMC simulation

To get the most likely probabilities let use Metropolis Algorithm. One (tested positive) has more influence on the sending infection, whereas the second one (not tested) is also included influence. We studied, via computer simulations (like Ising model with Metropolis Monte Carlo algorithm), the interplay between states in depends on such factors as: fraction of contacted infected, and the possibility of contact between all patient. That model has it roots in the domain of magnetism, but the meaning of magnetic spins has been changed into health states (0-health or ill-1).

Right: observed
Left: simulated

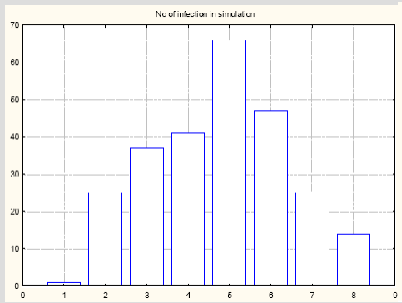


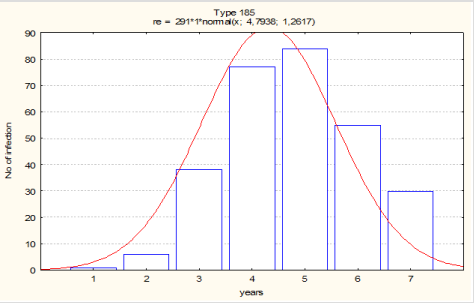


Metropolis Monte Carlo algorithm

In a first step we try to start with a vector of 291 patient, who have UK-E15. At beginning only one patient was ill (was tested positive during 1 year). So first state has 290-zeros and only one-1. Our goal is to get at the end of simulation also similar number of infected. We calculated matrixes **P** and vectors **P'** for each years, but there are not normalized.

We need 2 parameters:



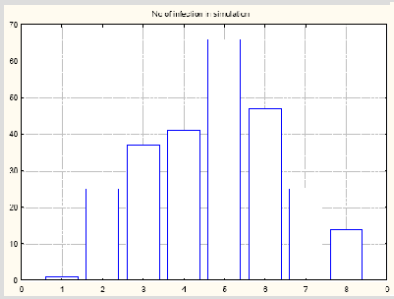


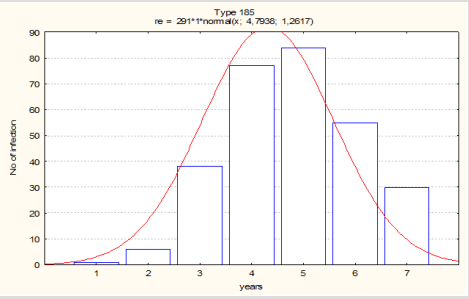
Metropolis Monte Carlo algorithm

We need 2 parameters:

- s- normalization on influence of contacts with infected (there is important to treat all of possible senders individually to find path of transition)
- m- normalization on influence of contacts with infected (there is no need to treat it individually, so the best measure is person*day)

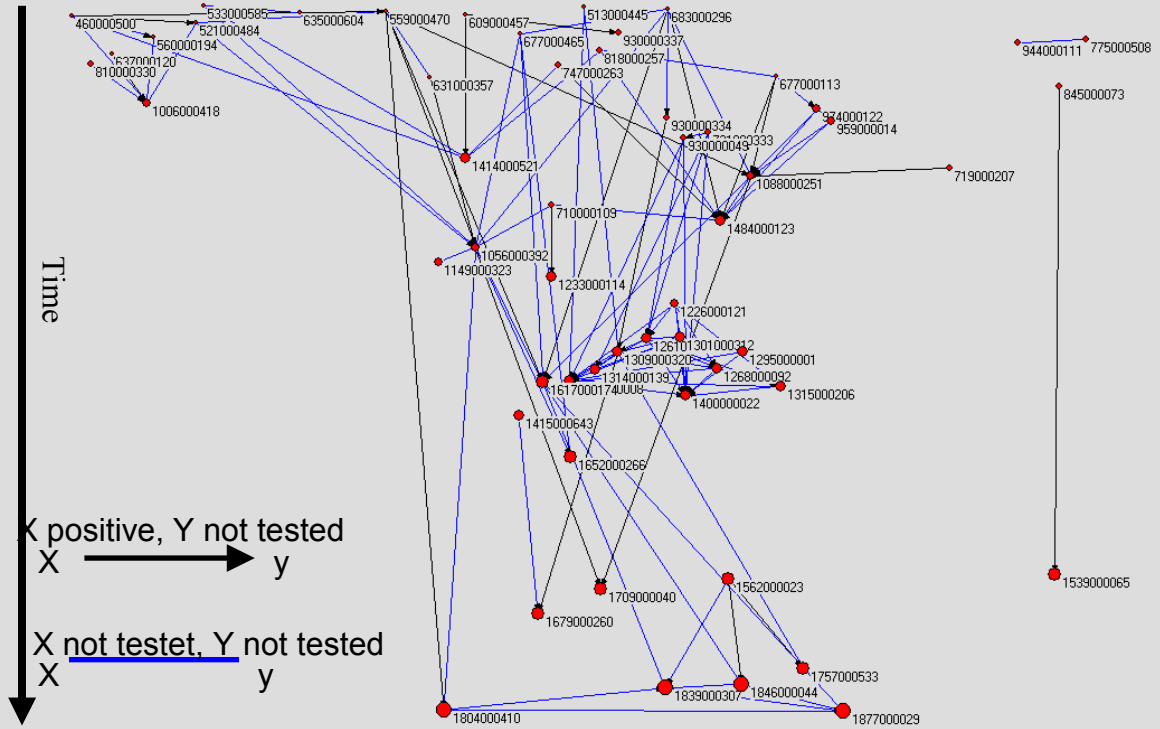
There is also third parameter n- as we showed before ¼ of all infections cannot be explain at all by a social network. We introduce it into a model respectively to time step (partly each year) to get rate of ¼ at the end of simulation.





Summary

- **Statistical properties (more in previous works of Liljeros)**
- **One step to get most likely path of transmission**



Limits of model

- R^2~70%, big error in first year of epidemic
- R^2~95%, with medical intervention (non-stationary factor)
- Maximal length of tree (6)
- Validation of model on controlled outbreak
- Problems of operational research

Acknowledgent

- Ph.D. **Lisa Brouwers** (Swedish Institute for Infectious Disease Control) for inviting me to DSV department in Stockholm;
- Ph.D. **Frederik Lilieros** and M.Sc. **Lu Xin** (Department of Sociology, University of Stockholm) for releasing unique dataset of MRSA patient and for giving sociological advises in coupling with that data.

Thank You for Your attention!

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