感染症に対するワクチン接種戦略の有効性と人の接触ネットワーク

Effectiveness of vaccination strategies for infectious diseases according to human contact networks

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We discuss the validity of various vaccination strategies on containing the spread of infectious diseases referring to the structure of human contact networks.

INTRODUCTION

A ‘contact network’ can model contacts that are capable of transmitting an infection between nodes (or individuals). Here, the magnitude of the spreading of infection is destined not solely by the infectiousness of the pathogen but also by the structure of the contact network. In particular, a major factor is the distribution in each node’s ‘degree,’ the number of neighboring nodes in contact. If all nodes have the same degree and the contacts between nodes are random, there exists a threshold value in ‘transmissibility,’ the probability that an infected node transmits the infection to a susceptible node in contact, under which an outbreak extinguishes as an endemic (*1*). On the contrary, if there are significant number of high-degree nodes, or hubs, such nodes can become super-spreaders, and cause an epidemic even under weak transmissibility. In fact, a series of scale-free networks, which only have a power decrease in the number of high-degree nodes, allow epidemic for pathogens of infinitely small transmissibility, which are typically observed as computer virus infections in the internet (*2*).

Vulnerability to infection attributable to the inhomogeneous degree distribution can also happen in contact networks of infectious diseases, thus becomes an important issue for public health. Although our knowledge on the contact network of infectious diseases is still limited, there are networks between individuals which can give some insight. As for the degree distribution, sexual contacts are known to follow the scale-free degree distribution (*3*), and besides, encounters in urban society is suggested to take place in contact locations whose degree distribution is scale-free (*4*). On the other hand, as for the overall magnitude of degree, we can guess that aerial infection would be the largest followed by spray infection and then physical contact infection. Studies on such infections and their containment are important both for existing diseases such as AIDS or SARS or for those introduced deliberately by bioterrorism.

The primary measure for containing infection is vaccination, either preventive or post-outbreak. The epidemic in scale-free networks cannot be stopped by preventive mass vaccination of randomly selected nodes even of a large proportion, but can be halted by prioritized vaccination of hub nodes (*5, 6*). However, for the implementation of vaccination in case of infectious diseases in human, the latter hub vaccination is much difficult than the former random mass vaccination, because the contact network is not apparent and potential hubs are not evidently identified. On the other hand, among post-outbreak vaccination strategies, the one important in practice is the ring vaccination, in which the susceptible individuals in contact with an infected individual are vaccinated. However, to date, there has been no study evaluating the effectiveness of ring vaccination or its combination with random mass vaccination, the two applicable containment strategies, on infections on contact networks potentially causing epidemic by inhomogeneous degree distribution.

Thus, we here studied how the effectiveness of mass preventive and ring post-outbreak vaccination changes for contact networks of various degree distributions. The study is by simulation on random networks, but with realistic number of nodes, and could derive quantitative conclusions applicable in real situations.

MATERIAL AND METHODS

Generating contact networks

We generated random contact networks of 100,000 nodes with average degree either m=10 or 100 for three types of degree distributions. For the scale-free degree distribution, the proportion of degree k nodes was set to be $(m^2\ k^{-3})/2$ with the minimum degree $m/2$. For the exponential degree distribution, the proportion was $(2e\ \exp(-2k/m))/m$ again with the minimum degree $m/2$. For the constant degree case, all nodes had degree m. For each case, a contact network was generated by first listing nodes with various degree according to the distribution, and then connecting the nodes randomly. The scale-free case had the largest number of high-degree nodes, the exponential case was in the medium, and the constant case had no such hubs. The mean squared degree $\langle k^2 \rangle$ of the generated scale-free network was 336.9 for m=10 and 33,701.2 for m=100, that of the exponential network was 125.1 for m=10 and 12,499.2 for m=100, and that of the constant network was 100 for m=10 and 10,000 for m=100.

SIRV model

The nodes in our simulation had four possible status: Susceptible (*S*), Infected (*I*), Removed (*R*) or Vaccinated (*V*). The simulation proceeds stepwise. In each step, if an *S* node is vaccinated, it changes to a *V* node. Then, an *I* node in contact with an *S* node can change it to an *I* node (in the next step) with probability *T*. Meanwhile, any *I* node changes to an *R* node in the next step. Thus, *R* nodes and *V* nodes do not change further.

Transmissibility and basic reproductive number

A fundamental measure for the strength of infection other than the transmissibility is the basic reproductive number R_0, the expected number of secondary infections for nodes in contact with a primary infected node. Whereas the transmissibility *T* basically defines the biological strength of transmission of the pathogen, $R_0 = (\langle k^2 \rangle / m - 1)T$ is proportional to *T* but depends on the degree distribution of the network (*7*) . In particular, the value of R_0 becomes larger even for a constant *T*, when there are denser contacts between the nodes. In practice, since the contact network is invisible, *T* is difficult to measure. On the contrary, R_0 is easier to survey after an infection event, and has been utilized more commonly. The parameters used for our simulation was R_0 = 0.5, 1, 2, ..., 64, and the corresponding values for *T*. (The values of R_0 differ widely according to diseases: influenza has 1.7, SARS has 1.2-3.6, smallpox has 4-10, and measles have 17 (*1*).)

Simulation of infection and vaccination

For contact networks and values of transmissibility discussed above, we performed simulations parameterized by the implemented rate of mass preventive vaccination and ring post-outbreak vaccinations. In the first step, 0.25, 0.5 or 0.75 of the population was randomly selected as *V* nodes (mass vaccination), one node among the remaining was randomly selected to become an *I* node, and all of the remaining nodes were set as *S* nodes. In each of the following step, all of the *S* nodes in contact with an *I* node were listed, and either 0.25, 0.5 or 0.75 of them were vaccinated (ring vaccination). The simulation becomes stable when the *I* nodes are extinct. Each set of simulation was repeated five times, and the mean number of the resulting nodes of each status was computed.

Evaluation of maximum containable transmissibility

For each scenario determined by a contact network and the parameters of vaccination, we evaluated the maximum containable transmissibility. Firstly, for each simulated value of transmissibility, the final ratio $(R+V)/(S+R+V)$ was computed. This ratio becomes close to the preventive mass vaccination rate for small values of *T*, and increases in accordance with *T*. Under an epidemic, the ratio approaches to one. When the maximum ratio became larger than 0.9, the maximum containable value of *T* was defined as the value (interpolated in log scale) attaining the average of the minimum and the maximum of this ratio. Otherwise, the maximum ratio under the strongest transmissibility *T*=1 still remains close to the preventive vaccination rate. In such case, there is no epidemic in the scenario, and the maximum containable transmissibility was not defined.

RESULTS

Despite the difference in degree distribution among the scale-free, exponential and constant networks, the maximum containable transmissibility of infection showed remarkable consistence. This indicates that ring vaccination, regardless of its implemented rate from 0.25 to 0.75, could cancel the super-spreading by the hubs in the scale-free or exponential networks. When the implemented ratio of ring vaccination was set to 0.75, none of the case caused epidemic, although there were medium sized endemics for the mass vaccination rate of 0.25 and *T*=1: 13,769 were removed and 66,300 were vaccinated in the exponential case, and 14,506 were removed and 68,517 were vaccinated in the constant case.

DISCUSSION

Although contact networks including high-degree nodes have been shown to be vulnerable for infection by causing epidemic even from pathogens of weak infectiousness (*2*), we have demonstrated that ring vaccination, even of low implementation ratio, could prevent such effect. This indicates the effectiveness of ring vaccination, especially in case of heterogeneous degree distribution. In practice, higher implementation rate of ring vaccination can be achieved for diseases of longer latent time, for example tuberculosis compared to influenza, which allow more time for vaccination. In addition, the consistence in maximum containable infectiousness measured in transmissibility *T* among the three types of networks under ring vaccination indicated the appropriateness of the evaluation of infectiousness by *T* rather than by basic reproductive number R_0. The appropriateness of *T* because of its independence to the structure of contact network was also shown by Meyers and colleagues from a different perspective (*7*).

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