Effectiveness of realistic vaccination strategies for contact networks of various degree distributions

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Abstract

A “contact network” that models infection transmission comprises nodes (or individuals) that are linked when they are in contact and can potentially transmit an infection. Through analysis and simulation, we studied the influence of the distribution of the number of contacts per node, defined as degree, on infection spreading and its control by vaccination. Three random contact networks of various degree distributions were examined. In a scale-free network, the frequency of high-degree nodes decreases as the power of the degree (the case of the third power is studied here); the decrease is exponential in an exponential network, whereas all nodes have the same degree in a constant network. Aiming for containment at a very early stage of an epidemic, we measured the sustainability of a specific network under a vaccination strategy by employing the critical transmissibility larger than which the epidemic would occur. We examined three vaccination strategies: mass, ring, and acquaintance. Irrespective of the networks, mass preventive vaccination increased the critical transmissibility inversely proportional to the unvaccinated rate of the population. Ring post-outbreak vaccination increased the critical transmissibility inversely proportional to the unvaccinated rate, which is the rate confined to the targeted ring comprising the neighbors of an infected node; however, the total number of vaccinated nodes could mostly be fewer than 100 nodes at the critical transmissibility. In combination, mass and ring vaccinations decreased the pathogen’s “effective” transmissibility each by the factor of the unvaccinated rate. The amount of vaccination used in acquaintance preventive vaccination was lesser than the mass vaccination, particularly under a highly heterogeneous degree distribution; however, it was not as less as that used in ring vaccination. Consequently, our results yielded a quantitative assessment of the amount of vaccination necessary for infection containment, which is universally applicable to contact networks of various degree distributions.

Keywords: Contact network; Infection transmission; Vaccination; Degree distribution; Basic reproductive number

1. Introduction

A “contact network” that models infection transmission comprises nodes (or individuals) that are linked when they are in contact and thus can potentially transmit an infection. Here, the magnitude of infection spreading is determined by not only the infectiousness of the pathogen but also the structure of the contact network. The most influential factor is the distribution of each node’s “degree,” which is the number of nodes linked to it. If all the nodes have the same degree and the links are random, there exists a threshold value of the “transmissibility,” which is defined as the probability that an infected node transmits the infection to a susceptible node linked to it, below which an outbreak immediately vanishes (Anderson and May, 1991). On the contrary, if there are a significant number of high-degree nodes, or hubs, few nodes remain infected under the SIS model (where nodes transit between the “susceptible” and “infected” statuses) even under weak transmissibility (Pastor-Satorras and Vespignani, 2001). Similarly, under the more realistic SIR model (where nodes transit from the “susceptible” status to “infected,” and then to “removed”), it is shown that certain nodes become infected even under weak transmissibility; however, when the network size is finite, there does exist a transmissibility...
threshold below which an outbreak immediately diminishes (May and Lloyd, 2001). In order to cope with the vulnerability of degree-heterogeneous networks to infection, we studied the effectiveness of vaccination analytically and by simulation. Our simulations employ a realistic size of 100,000 nodes, and their agreement with the analytical evaluation and the finite-size effect were studied.

Studies on such infections and their containment are important from the viewpoint of both existing diseases, such as AIDS and SARS, and those deliberately introduced by bioterrorism such as smallpox; the vulnerability to infection attributable to a heterogeneous degree is a public health concern (Galvani and May, 2005). Although our knowledge on contact networks with regard to infectious diseases is limited, social networks can provide some insights. Sexual contact tends to follow a scale-free degree distribution (Liljeros et al., 2001), which exhibits a power decrease in the number of high-degree nodes and must yield the largest degree heterogeneity, whereas friendship networks tend to follow Gaussian degree distribution (Amaral et al., 2000) that include a considerably smaller number of hubs. In order to investigate the various possibilities, we studied a wide range of degree distributions and observed their effects on infection dynamics.

The primary measure for containing infection is vaccination—either preventive or post-outbreak. The above-mentioned epidemic for scale-free networks with large degree heterogeneity can be halted by preventive vaccination prioritizing the hub nodes, while preventive mass vaccination of randomly selected nodes is not very effective for this purpose (Pastor-Satorras and Vespignani, 2002). However, in the case of infectious human diseases, hub vaccination is difficult to implement because the entire shape of the contact network is not apparent and potential hubs are not evident. Acquaintance vaccination, on the other hand, accomplishes this task by vaccinating random neighbors of random nodes; thus, it utilizes only the local information of the network (Cohen et al., 2003). Among the post-outbreak vaccination strategies, the one that is important for practical purposes is ring vaccination. In this strategy, susceptible individuals in contact with an infected individual are vaccinated. As before, this method requires only the local information of the network. Thus, we can say that the mass and acquaintance vaccination strategies are feasible for preventive measures, while ring vaccination is feasible for post-outbreak measures. Nevertheless, no study has evaluated the effectiveness of ring vaccination or its combination with preventive mass vaccination from the viewpoint of degree distributions. Here, we evaluate the efficiency of these strategies and compare them with acquaintance vaccination.

2. Contact networks

We generated random contact networks of either \( n = 10,000 \) or 100,000 nodes with an average degree of either \( \langle k \rangle = m = 10 \) or 100 for three types of degree distributions in order to adjust the number of hub nodes. In the scale-free degree distribution, the number of high-degree nodes decreased only by a power (the case of third power studied here): the proportion of degree \( k \) nodes among all the nodes was set as \( p_k = (m^2 k^{-3})/2 \) for \( k \geq m/2 \), and \( p_k = 0 \) otherwise. In the exponential degree distribution, the high-degree nodes decreased exponentially: \( p_k = (2e \exp(-2k/m))/m \) for \( k \geq m/2 \), and \( p_k = 0 \) otherwise. As for the other extreme, we tested a constant degree case, where all the nodes had a degree \( m \) without any hubs (Fig. 1). According to each degree distribution, five random networks were generated for distinct simulations. Each network was generated by randomly connecting the links: first, nodes with various degrees were listed according to distribution; then, “stub links” emanating from each node were generated based on the number of its degree; and finally, the “stub links” were connected randomly.

Real-world contact networks and those generated in our simulation have a finite size. If the size of the network is sufficiently large, its average degree converges to the value calculated from the degree distribution for the infinite case. However, the mean squared degree \( \langle k^2 \rangle \) needs adjustment in order to demonstrate the finite-size effect. For a scale-free degree distribution with the maximum degree \( k_{max} \),

\[
\langle k^2 \rangle = \int_{m/2}^{k_{max}} \frac{m^2}{2k} \, dk \\
= \left[ \frac{m^2}{2} \log k \right]_{m/2}^{k_{max}} \\
= \frac{m^2}{2} \log \frac{2k_{max}}{m}.
\]

Thus, \( \langle k^2 \rangle \) increases with \( k_{max} \), which in turn increases with the network size. The largest degree \( k_{max} \) of a network with \( n \) nodes is estimated using the following expression:

\[
\frac{1}{2n} = \int_{k_{max}}^{\infty} \frac{m^2}{2k^3} \, dk \\
= \frac{m^2}{4k_{max}}.
\]

Thus, \( k_{max} = m\sqrt{n/2} \), which leads to

\[
\langle k^2 \rangle = \frac{m^2}{4} \log 2n.
\]

In fact, \( \langle k^2 \rangle \) of the generated scale-free network was 279.5 for \( n = 10,000 \) and \( m = 10 \), 336.9 for \( n = 100,000 \) and \( m = 10 \), and 33,701.1 for \( n = 100,000 \) and \( m = 100 \). On the other hand, \( \langle k^2 \rangle \) for the exponential degree distribution with the maximum degree \( k_{max} \geq m \) becomes

\[
\langle k^2 \rangle = \int_{m/2}^{k_{max}} \frac{2}{m} k^2 e^{-(2k/m)+1} \, dk \\
= \left[ -\left( k^2 + mk + \frac{m^2}{2} \right) e^{-(2k/m)+1} \right]_{m/2}^{k_{max}} \\
\approx \frac{5m^2}{4}.
\]
Thus, \( \langle k^2 \rangle \), which is independent of the network size, was 125.0 for \( n = 10,000 \) and \( m = 10 \), 125.1 for \( n = 100,000 \) and \( m = 10 \), and 12,499.1 for \( n = 100,000 \) and \( m = 100 \). The \( \langle k^2 \rangle \) of the constant network was 100 for \( m = 10 \) and 10,000 for \( m = 100 \).

3. SIRV model and transmissibility

The nodes in our simulation exhibit one of four possible statuses: susceptible, infected, removed (by death or acquired immunity), and vaccinated. The simulation proceeds in a stepwise manner. In each step, some of the “susceptible” nodes that are vaccinated change to “vaccinated.” Further, each “infected” node transmits the infection to a “susceptible” node in contact by converting its status to “infected” (in the next step) with a probability \( T \), i.e. the transmissibility. Meanwhile, all “infected” nodes are changed to “removed” in the next step. Thus, the “removed” and “vaccinated” nodes do not change their statuses further. The simulation becomes stable and terminates when there are no more nodes with the “infected” status. We assume that the population is fixed; in other words, we deal with infectious diseases that have an incubation or recovery time that is considerably smaller than the human lifespan, for example, influenza or SARS.

4. Mass and ring vaccination

For various contact networks and values of transmissibility, we performed simulations parameterized by the implemented rate of mass preventive and ring post-outbreak vaccinations. In the first step, with a predefined probability \( u = 0, 0.05, 0.1, 0.15, 0.2, 0.25, 0.5, \) or \( 0.75 \) each node of the population was randomly assigned the “vaccinated” status (mass vaccination); from the remaining nodes, either one node was randomly selected (random initial infection) or the highest-degree node was selected (hub initial infection) to become an “infected” node, and the status of the remaining nodes was set as “susceptible.” In each of the following steps, all the “susceptible” nodes in contact with each “infected” node were listed, and each of the nodes was assigned the “vaccinated” status with a predefined probability \( v = 0, 0.05, 0.1, 0.15, 0.2, 0.25, 0.5, \) or \( 0.75 \) (ring vaccination). Our formulation of ring vaccination assumes immediate detection of an infected individual and immediate vaccination of its neighbors. The predefined rate for ring vaccination differs from the total fraction of the population vaccinated by employing this strategy. Particularly in the case of early containment, the vaccination can be administered in fractions considerably smaller than the predefined rate.

5. Critical transmissibility

In the next two sections, we derive the critical transmissibility at which epidemics begin to emerge, and
compute the probability of epidemics for a transmissibility larger than this value. We expand the generating functions introduced by Newman (2002) and incorporate the effect of mass and ring vaccinations. For a sequence of numbers $a_0, a_1, \ldots, a_k, \ldots$, the corresponding generating function has $a_k$ as the coefficient of $x^k$; it becomes $\sum_{k=0}^{\infty} a_k x^k$.

We first define $G_0(x; u, v, T)$ as the generating function whose $k$th coefficient is the probability that $k$ secondary infections are caused when a randomly selected node is infected in a totally susceptible population. Here, we take the expected value under all possibilities of mass vaccination. Thus, the random node has a degree $k$ with probability $p_k$. In case the random node has a degree $k$, for each of its neighboring nodes, the probability that the neighbor is neither mass vaccinated nor ring vaccinated and becomes infected is $(1-u)(1-v)T$. Thus the probability that the infection is transmitted to $l$ neighbors is

$$\binom{k}{l} [(1-u)(1-v)T]^l [1-(1-u)(1-v)T]^{k-l}.$$ 

Hence, the overall contribution of a degree $k$ node to the generating function becomes

$$\sum_T \binom{k}{l} [(1-u)(1-v)T]^l [1-(1-u)(1-v)T]^{k-l} x^l$$

$$= (1-(1-u)(1-v)T + (1-u)(1-v)Tx)^k$$

$$= (1+(1-u)(1-v)T(x-1))^k.$$ 

Thus, we obtain

$$G_0(x; u, v, T) = \sum_k p_k (1+(1-u)(1-v)T(x-1))^k$$

$$= G_0(x; 0,0,(1-u)(1-v)T).$$ 

The second equality indicates that the number of secondary infections caused by a random infected node is the same when no vaccination is applied and instead the transmissibility is $(1-u)(1-v)T$.

Next, we compute the generating function $G_1(x; u, v, T)$ whose $k$th coefficient is the probability that $k$ secondary infections result from an initial infection via a randomly selected link in a totally susceptible population. As before, we take the expected number over all possibilities of mass vaccination. Thus, the probability that the node at the end of the random link has a degree $k$ is proportional to $kp_k$ and becomes $kp_x/\langle k \rangle$ (instead of $p_k$ as shown above). The number of as-yet-uninfected nodes among its $k$ neighbors is $k-1$ (instead of $k$ as shown above). Otherwise, with the same discussion as above, we obtain

$$G_1(x; u, v, T) = \sum_k \frac{kp_k}{\langle k \rangle} (1+(1-u)(1-v)T(x-1))^{k-1}$$

$$= G_1(x; 0,0,(1-u)(1-v)T).$$ (5.1)

In this case also, the number of secondary infections caused by a random infected link is the same as that in the case without vaccination and under transmissibility $(1-u)(1-v)T$.

The basic reproductive number $R_0$ is defined as the expected number of secondary infections caused by transmission via a random link in a totally susceptible population:

$$R_0 = G'_1(1; u, v, T)$$

$$= \left( \frac{\langle k^2 \rangle}{\langle k \rangle} - 1 \right) (1-u)(1-v)T,$$

where $G'_1(x; u, v, T)$ is the derivative of $G_1(x; u, v, T)$ with respect to $x$. (The formula not incorporating vaccination appears in Meyers et al. (2005).) An outbreak becomes an epidemic when $R_0 > 1$ and is extinguished when $R_0 < 1$. Whereas the transmissibility $T$ basically defines the biological strength of the transmission of the pathogen, $R_0$ indicates the strength of spreading in a specific contact network, which reflects the degree distribution of the network. In particular, $R_0$ can attain a large value even for a small $T$ when the degree distribution is heterogeneous and $(k^2)/\langle k \rangle$ is large. In order to measure the vulnerability to infection of networks under vaccination strategies, we adopted a value of critical transmissibility $T_c$ that achieves $R_0 = 1$; therefore,

$$\frac{1}{T_c} = \left( \frac{\langle k^2 \rangle}{\langle k \rangle} - 1 \right) (1-u)(1-v).$$

For a scale-free network of size $n$, this relation becomes

$$\frac{1}{T_c} = \left( -1 + \frac{m}{4} \log 2n \right) (1-u)(1-v),$$

for an exponential network

$$\frac{1}{T_c} = \left( \frac{5m}{4} - 1 \right) (1-u)(1-v),$$

and for the constant case

$$\frac{1}{T_c} = (m-1)(1-u)(1-v).$$

For a scale-free network, $T_c$ depends on both $m$ and $n$; thus, it exhibits the finite-size effect. The formulae for exponential and constant cases involve only $m$.

Originally, $R_0$ was defined as the expected number of secondary infected nodes caused by one primary infected node in a totally susceptible population (Anderson and May, 1991). Studies that mainly deal with sexually transmitted diseases, where individuals are classified according to the degree and random mixing among them is assumed, are along similar lines. Assuming that all nodes—susceptible, infected, or removed—die and are reborn as susceptible nodes at a rate $\gamma$, when the three populations are in equilibrium, it is shown that $R_0 = \langle k^2 \rangle T / (\langle k \rangle \gamma)$ (Anderson and May, 1991), which indicates that the effect of degree heterogeneity on $R_0$ almost coincides with the formulation for contact networks.
6. Probability of epidemics

Next, we derive generating functions that capture the probability of an epidemic when \( T > T_c \). First, we introduce \( H_1(x; u, v, T) \) as the generating function whose \( k \)th coefficient is the probability that \( k \) nodes are infected and the outbreak is “not epidemic” (defined here as the absence of a transmission to an already infected node during the infection spreading) when the infection begins from a randomly selected node. It is defined as the generating function that satisfies the following first equation:

\[
H_1(x; u, v, T) = xG_1(H_1(x; u, v, T); u, v, T) = xG_1(H_1(x; u, v, T); 0, 0, (1 - u)(1 - v)T) = H_1(x; 0, 0, (1 - u)(1 - v)T).
\]

The second equation follows from (5.1) and the third from the definition of \( H_1(x; u, v, T) \). Since \( H_1(1; u, v, T) \) is the total probability of a non-epidemic outbreak, the probability of an epidemic becomes

\[
1 - H_1(1; u, v, T) = 1 - H_1(1; 0, 0, (1 - u)(1 - v)T).
\]

It is evident that this probability is identical to the probability for the case without vaccination and instead under transmissibility \( (1 - u)(1 - v)T \).

Likewise, we define \( H_0(x; u, v, T) \) as the generating function whose \( k \)th coefficient is the probability of a size \( k \) non-epidemic outbreak when the infection begins from a randomly selected node:

\[
H_0(x; u, v, T) = xG_0(H_0(x; u, v, T); u, v, T) = xG_0(H_0(x; u, v, T); 0, 0, (1 - u)(1 - v)T) = xG_0(H_0(x; 0, 0, (1 - u)(1 - v)T); 0, 0, (1 - u)(1 - v)T) = H_0(x; 0, 0, (1 - u)(1 - v)T).
\]

Our goal here is to determine the probability of an epidemic for outbreaks initiating from a random node, which becomes

\[
1 - H_0(1; u, v, T) = 1 - H_0(1; 0, 0, (1 - u)(1 - v)T).
\]

Here, as before, this probability becomes equal to that of the case without vaccination under transmissibility \( (1 - u)(1 - v)T \).

In conclusion, we showed that \( R_0 \) and the probability of an epidemic under a mass vaccination of rate \( u \), ring vaccination of rate \( v \), and transmissibility \( T \) becomes equal to the values for the case without vaccination but under transmissibility \( (1 - u)(1 - v)T \). In other words, the vaccination decreases the pathogen’s “effective” transmissibility from \( T \) down to \( (1 - u)(1 - v)T \). This property holds regardless of the degree heterogeneity of the contact network.

7. Acquaintance vaccination

In acquaintance immunization, a random neighbor of a random node is repeatedly selected for vaccination (Cohen et al., 2003). This strategy tends to result in the vaccination of higher-degree nodes when the node degree is heterogeneous. The critical value of transmissibility \( T_c \) when a portion \( u \) of the nodes is vaccinated becomes the solution for the following simultaneous equation with variables \( T_c \) and \( q \)

\[
\frac{1}{1-e^{-T_c}} = \sum_k p_k k(k - 1) v(q)^{k-2} e^{-2q/k},
\]

\[
u(q) = \sum_k p_k q^k \left(1 - \frac{1}{nk}\right)^q
\]

as derived in Cohen et al. (2003).

8. Simulations of infection spreading

In our software implementation, for each of the five copies of generated networks and each vaccination composition under various transmissibilities, we performed 1000 simulations, for a total of 5000 simulations in each setting. We measured the sustainability of a specific network (under a specific vaccination strategy) by simulating the infection transmission for pathogens with various transmissibilities. Aiming for the containment of infectious diseases in a very early stage of spreading, we investigated the critical transmissibility (Section 5), which was defined as the minimum transmissibility at which an infectious disease epidemic begins to emerge. For practical applicability, we simulated a population of 100,000 nodes and defined an outbreak as an epidemic if a minimum of 100 nodes were infected. For the simulation, the critical transmissibility was defined as the transmissibility (interpolated in log scale with respect to transmissibility) at which the probability of such an epidemic was 1%.

The simulated probability of an epidemic was in accordance with the analytical results (Fig. 2, see Section 6). As indicated by the shift of the curve to the right according to vaccination, the “effective” transmissibility measured by the epidemic probability was confirmed to decrease by a factor of \( 1 - u \) under a mass vaccination of rate \( u \) or \( 1 - v \) under a ring vaccination of rate \( v \). The epidemic probability becomes positive at the critical transmissibility. The analytical value of this transmissibility under no vaccination is indicated by an arrow, and the scale-free network that exhibits the largest degree heterogeneity allowed epidemic emergence even for \( T = 0.031 \), followed by \( T = 0.087 \) for the lesser heterogeneous exponential network and \( T = 0.11 \) for the homogeneous constant network. This demonstrates the vulnerability of degree-heterogeneous contact networks to infection. In the exponential and constant degree distributions, the simulated values were larger than the analytical ones around the epidemic transmissibility because non-epidemic (by the analytical
criterion in Section 6) outbreaks with sizes larger than 100 were also regarded as epidemics in our simulation.

The critical transmissibilities under various vaccinations are depicted in Fig. 3. The trend of the simulated data was in accordance with the analytical line. This was consistent for all vaccination rates and networks. Their divergence was due to our definition of the approximate critical transmissibility for the simulation (see the beginning of this section). For the scale-free degree distribution, the epidemic probability was small (and smaller than 1%) around the analytical critical transmissibility; thus, the analytical critical transmissibility became smaller than the simulated value. The divergence in the exponential and constant cases was due to the > 100 size non-epidemics as explained above.

Ring vaccination was parameterized by the vaccination rate $v$ for the neighboring nodes in a ring; however, the
The actual number of vaccinated nodes becomes considerably smaller than this rate in the case of early containment. In fact, as observed from the square points in Fig. 3, ring vaccination was effective in reducing the required amount of immunization mostly to less than 100 nodes at the critical transmissibility for each of the three degree distributions; more than 100 nodes became vaccinated in a few percent of the simulation trials for \( v \leq 0.2 \) and at most 15% for \( 0.25 \leq v \leq 0.75 \).

As shown previously (Cohen et al., 2003), in the degree-heterogeneous scale-free and exponential cases, acquaintance vaccination was able to achieve the same level of containment as mass vaccination with a lesser number of vaccinated nodes (Fig. 3). However, acquaintance vaccination was not as efficient as ring vaccination.

Furthermore, in accordance with the analytical result, the combination of mass and ring vaccinations was confirmed to increase the critical transmissibility by a factor of \( \frac{1}{\left[(1-u) \cdot (1-v)\right]} \), as compared to the case without vaccination (Fig. 4). The fact that the critical transmissibility could be factored as a simple product of independent formulae for the mass and ring vaccinations is indicated by the shape of the grids connecting the data points being parallelograms.

Alternatively, we could apply mass vaccination for a randomly selected portion \( u \) of the population, or ring vaccination for a randomly selected portion \( v \) of the neighbors of each infected node. However, we did not adopt this formulation because the analytical treatment becomes more complicated. Yet, the alternative formulation does not change the critical transmissibility. Although the epidemic probability is the same for the case of mass vaccination, it approaches to one as \( T \) approaches to one when \( (\langle k^2 \rangle / \langle k \rangle - 1)(1-v) > 1 \) for the ring vaccination of portion \( v \). (Data not shown. We reiterate that the epidemic probability remained smaller than one even for \( T = 1 \), for the case \( v = 0.75 \) in Fig. 2.)

The above trends were consistent for cases with \( n = 10,000 \) or \( \langle k \rangle = 100 \) and thus were irrespective of the number of nodes or the average degree (data not shown). We also evaluated the manner in which the choice of an initially infected node affects an epidemic. An infection is transmitted faster when a high-degree node is initially infected (e.g. by a hub-targeted attack). However, even in the extreme case where the largest-degree node was infected initially, the critical transmissibility decreased by a factor of only 0.4 for the scale-free network and 0.9 for the exponential network, as compared to the case where an initially infected node was randomly selected (data not shown).

Fig. 3. Change in the critical transmissibility \( T_c \) according to the rate of vaccination for networks of various degree distributions. The horizontal axis represents the rate of vaccination, and the vertical axis represents the reciprocal of critical transmissibility. The analytical critical transmissibility that achieves \( R_0 = 1 \) is represented as a solid line. The value obtained by simulation (such that 100 nodes are infected with probability 1%) under mass vaccination is indicated by diamonds, the value under ring vaccination according to the vaccinated rate in a ring is indicated by stars, and the same value but according to the resultant total fraction of the vaccinated population is indicated by squares. Error bars show 95% confidence interval. For acquaintance vaccination, the critical transmissibility according to the vaccinated population is indicated by a dashed line. The plots are for three networks: (a) scale-free, (b) exponential, and (c) constant.
The emergence of an epidemic showed limited dependence on the choice of the initial infection. It is known that the probability of an epidemic varies, e.g., from 20% to 100%, according to the degree of the initially infected node, which was demonstrated by using a simulation of an urban network (Meyers et al., 2005). In our simulation, the transmissibility was regarded as critical when the epidemic probability was 1%. Thus, the critical transmissibility in our analysis would have been limitedly dependent on the selection of the initial node whether the largest-degree node or randomly selected, because even the lower-degree nodes would mostly cause an epidemic with a probability higher than 1%. Yet, when the largest-degree node is initially infected, the probability of epidemics quickly approaches to one even for transmissibility slightly larger than the critical value.

9. Discussion

We examined three feasible vaccination strategies for infectious diseases: mass, ring, and acquaintance. Mass preventive vaccination exhibited an inversely proportional effect for disease containment, irrespective of the degree distribution (Fig. 3). When the nodes were vaccinated, the critical transmissibility determined by simulation increased in an inverse proportion to the unvaccinated rate of the population, and the value was in accordance with the analytical value achieving $R_0 = 1$. In other words, the basic reproductive number $R_0$ (Anderson and May, 1991; Meyers et al., 2005), which is calculated solely on the basis of the mean degree, mean squared degree, and transmissibility, was confirmed to function as a reliable indicator of epidemic emergence.

When the node degree was highly heterogeneous, we could substantiate the efficiency of acquaintance vaccination (Cohen et al., 2003), which exploits this property and requires a considerably smaller number of nodes to be immunized than mass vaccination (Fig. 3). In fact, a 20% acquaintance vaccination for the scale-free network caused a five-fold increase in the critical transmissibility (i.e., a reduction of 80%), thereby confirming the 20/80 rule for the vaccination of heterogeneous networks (Anderson and May, 1991; Woolhouse et al., 1997; Galvani and May, 2005). Here, we measured the efficiency by counting the number of vaccinated nodes necessary for achieving containment.

The efficiency of the post-outbreak ring vaccination was better than that of the mass and acquaintance preventive vaccinations. Similar to mass vaccination, ring vaccination exhibited an inversely proportional effect to the rate of non-vaccination; the rate was confined to the targeted neighbors of a newly infected node. Meanwhile, the overall number of vaccinated nodes could be reduced to a considerably smaller number as compared to the preventive strategies (Fig. 3). In our formulation of ring vaccination, we assumed that the detection of an infected node and vaccination of the neighboring nodes could be performed
immediately; this requires that the disease be diagnosed before it begins to spread to the neighbors. This assumption might be applicable only for a limited number of diseases; however, even in the case of a time lag (provided it is not very large) enlarging the diameter of the ring vaccination (e.g. vaccinating not only the neighbors of the infected individual but also the neighbors of his/her neighbors) would accomplish epidemic prevention at the cost of a greater number of immunized nodes. The efficiency of such a ring vaccination was demonstrated in simulations on respiratory pathogens for an urban network of Vancouver (Pourbohloul et al., 2005). On the contrary, if the detection shows a time lag after the initiation of spreading and the diameter of the ring is not adequately large, the frontier of the infection escapes the vaccinated area and leads to the failure of ring vaccination, as simulated for the foot-and-mouth disease using a farm-based model (Keeling et al., 2003).

Our simulations confirm the following theorem for the amount of necessary vaccination used in epidemiology (Anderson and May, 1991 [Section 11.2.2, Eq. (12.23), and Section 12.3]): for heterogeneous contact networks, a hub-weighted vaccination requires a considerably lower amount of immunization than mass vaccination, and the quantity necessary for a homogeneous network with the same mean degree and for the same pathogen becomes intermediate. For example, for a pathogen with a transmissibility of 0.2 (i.e. $1/T = 5$), a scale-free network with a mean degree of 10 requires an acquaintance vaccination rate of 0.3 and a mass vaccination rate of 0.8 (Fig. 3a), and a constant network would require a vaccination rate of 0.4 (Fig. 3c).

The degree distribution of contact networks for real infectious diseases would appear somewhere between the constant and scale-free cases. In all these cases, our results showed that $R_0$ assuming no vaccination accurately indicates the necessary rate of vaccination, i.e. a mass vaccination of rate $u$ and ring vaccination of rate $v$ such that $R_0(1-u)(1-v) = 1$. The consistency across different degree distributions is due to the fact that $R_0$ accounts for the degree heterogeneity (Anderson and May, 1991). Although networks with higher degree heterogeneity are more vulnerable to infection, the factor of vaccination effectiveness is independent of the heterogeneity. We assumed random link connection for the contact network, and further study is necessary to judge if our results hold for clustered networks (e.g. when two friends of one individual are more likely to be friends than two unrelated subjects). Our quantitative assessments for the amount of vaccination indicated that a combination of mass preventive and ring post-outbreak vaccination would independently increase the critical transmissibility. Thus, a possible strategy for vaccination would be to evaluate the effectiveness of an implementable ring vaccination in advance and, if necessary, preventively implement acquaintance or mass vaccination for the deficient amount.

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