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Research article

Separable mixing: The general formulation and a particular example focusing on mask efficiency

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Abstract: The aim of this short note is twofold. First, we formulate the general Kermack-McKendrick epidemic model incorporating static heterogeneity and show how it simplifies to a scalar Renewal Equation (RE) when separable mixing is assumed. A key general feature is that all information about the heterogeneity is encoded in one nonlinear real valued function of a real variable. Next, we specialize the model ingredients so that we can study the efficiency of mask wearing as a non-pharmaceutical intervention to reduce the spread of an infectious disease. Our main result affirms that the best way to protect the population as a whole is to protect yourself. This qualitative insight was recently derived in the context of an SIR network model. Here, we extend the conclusion to proportionate mixing models incorporating a general function describing expected infectiousness as a function of time since infection.

Keywords: Kermack-McKendrick; epidemic model; heterogeneity; separable mixing; mask efficiency

1. Introduction

The work described below was triggered when the third author of the present paper attended the lecture of R. Pastor-Satorras during the 'Workshop on Epidemic Modelling: Current Challenges' in Girona, 19-21 June 2023. This lecture reported on the models, methods and results of the paper [1] and culminated in a powerful qualitative insight: masks that protect the wearer against infection are,

also in public health perspective, more efficient than masks that, if the wearer is infectious, protect its contacts against infection. This conclusion is derived in the context of network models.

Already, for quite a while, the present authors are working on the manuscript [2], which aims to provide a general survey of various effects of (mainly static) heterogeneity. A natural question arises: is it possible to sustain the qualitative insight by rederiving it in the context of homogeneous mixing models? As we show below, the methodology developed in our manuscript in preparation allows us to easily provide an affirmative answer.

2. Formulation of a comprehensive model for epidemic outbreaks in heterogeneous host populations

By using the word 'outbreak', we imply that demographic turnover is ignored and that infection leads to permanent immunity. Host individuals are characterized by a trait x taking values in a set Ω. We assume that Ω is a measurable space, meaning that it comes equipped with a σ-algebra. We introduce a positive measure Φ on Ω to describe the distribution of the trait in the host population. We normalize $\Phi(\Omega) = 1$ and denote the host population size by N. For a concrete example, see Section 4.

A major restriction is that the trait of an individual does not change during the outbreak. Thus, if the trait corresponds to age, the assumption is that the duration of the outbreak is so short, that we can ignore that individuals are becoming older while it lasts. Let $s(t, x)$, with $s(-\infty, x) = 1$, denote the probability that an individual with trait x is susceptible at time t. When the NUMBER of infected individuals is small, demographic stochasticity has a large impact and cannot be ignored. Our description starts when a small FRACTION of the very large host population is infected. With an informal appeal to the Law of Large Numbers, we then also interpret $s(t, x)$ as the FRACTION of individuals with trait x that is susceptible at time t, see e.g. [3]. It follows that

$$s(t, x) = \exp\left(-\int_{-\infty}^{t} F(\tau, x)d\tau\right), \tag{2.1}$$

with F the force of infection as a function of time and trait. In the spirit of [4] (for a reformulation in modern language see [5]) we introduce as the key modelling ingredient

$$\begin{aligned} A(\tau, x, \xi) = {} & \text{the expected contribution to the force of infection on an individual with trait } x \\ & \text{by an individual with trait } \xi \text{ that became infected } \tau \text{ units of time ago.} \end{aligned} \tag{2.2}$$

A is a measurable non-negative function mapping $\mathbb{R}_+ \times \Omega \times \Omega$ into $\mathbb{R}_+$ and A is integrable with respect to (τ, ξ) over $\mathbb{R}_+ \times \Omega$. We shall call τ 'infection age' or 'age of infection', since it is the time on a clock that starts at the moment at which the individual becomes infected.

The formula

$$F(t, x) = N \int_0^\infty \int_\Omega A(\tau, x, \xi)F(t - \tau, \xi)s(t - \tau, \xi)\Phi(d\xi)d\tau, \tag{2.3}$$

expresses the force of infection as a sum of contributions of individuals that were infected time τ ago while having trait ξ. By integrating (2.3) over time, interchanging the integrals, using the differentiated version of (2.1), i.e.,

$$\frac{\partial s}{\partial t}(t,x) = -F(t,x)s(t,x), \tag{2.4}$$

to evaluate and inserting the result at the rhs of (2.1), we arrive at the nonlinear abstract Renewal Equation (RE)

$$s(t,x) = \exp\left(-N\int_0^\infty \int_\Omega A(\tau,x,\xi)[1-s(t-\tau,\xi)]\Phi(d\xi)d\tau\right). \tag{2.5}$$

(In this paper we do not discuss the initial value problem, corresponding to prescribing the history of s on a time interval extending back to $-\infty$, nor the dynamical systems point of view, corresponding to shifting in time along the function s obtained by extending the given history. Instead, we refer to [6], [7] and [8] for an exposition of the relevant ideas.)

Equation (2.5) provides a concise representation of a rather general class of models (see, e.g., [3, 9] for a general introduction to epidemic models and [10,11] for recently developed methodology for computing the basic reproduction number for structured populations). For quantitative work, the discrete time variant introduced in [12] might be more suitable, especially when Ω is (or can be approximated, in some sense, by) a finite set, see [13–15] for steps in this direction.

As we show next, an alternative way to increase the tractability is to assume separable mixing.

3. Separable mixing

The function A has arguments τ and ξ pertaining to the infectious individual and argument x pertaining to the susceptible individual. The contact process can be assortative (individuals with similar traits are more likely to meet) or disassortative (individuals with dissimilar traits are more likely to meet) or proportional.

'Proportionality' means that, given that an individual with trait ξ makes a contact, the probability distribution of the trait of the other individual involved in the contact does not depend on ξ. This probability distribution is then obtained by first multiplying the probability distribution of trait x in the population with the function describing how active individuals with trait x participate in the contact process and next applying a normalization to obtain that the integral equals one.

In terms of A, proportionality manifests itself by A being separable, i.e., being a product of a function of x and a function of τ and ξ. We call this *separable mixing*. The τ dependence in A captures how the infectiousness (as manifested in the probability of transmission, given a contact and, possibly, in a reduction or, for instance in case of rabies, enhancement of participation in the contact process) depends on infection age. If this dependence on τ is not itself depending on the trait ξ, A is the product of three non-negative functions of one variable, say

$$A(\tau,x,\xi) = a(x)b(\tau)c(\xi). \tag{3.1}$$

Here, b should be integrable over $[0,\infty)$ and c should be integrable over Ω with respect to Φ. Often, the form (3.1) for A is called proportionate (or proportional) mixing, in particular when c equals a (note that a and c are only unique up to a multiplicative constant and that such a constant can be incorporated in the factor b). It follows straight away from (3.1) and (2.3) that the force of infection factorizes as a product of $a(x)$ and an unknown function of time. The same holds for the cumulative force of infection $\int_{-\infty}^t F(\tau,x)d\tau$ and accordingly we put

$$s(t,x) = e^{-a(x)w(t)}, \tag{3.2}$$

and find that w should satisfy the scalar nonlinear RE

$$w(t) = \int_0^\infty b(\tau)\Psi(w(t-\tau))d\tau, \tag{3.3}$$

where $\Psi : \mathbb{R} \to \mathbb{R}$ is defined by

$$\Psi(w) := N \int_\Omega c(\eta)(1 - e^{-a(\eta)w})\Phi(d\eta). \tag{3.4}$$

In the 'trivial' case that both c and a are identically equal to one, all individuals have identical susceptibility as well as expected infectiousness, so, after all, there is no heterogeneity. In this case,

$$\Psi(w) = N(1 - e^{-w}), \tag{3.5}$$

and (3.3) is the standard Kermack-McKendrick RE as, for instance, presented in [5]. So (3.3) tells us how, in the separable mixing case, the various components of heterogeneity, viz., susceptibility a, infectiousness c and distribution Ψ, affect the nonlinearity in the RE. Incidentally, in [16], it is shown how to efficiently derive compartmental models that incorporate heterogeneity, by choosing in (3.3) functions b that are a matrix exponential sandwiched between two vectors.

To investigate the initial phase of an outbreak, we linearize at the disease-free steady state $w = 0$, which amounts to replacing $\Psi(w)$ by $\Psi'(0)w$. Inserting the trial solution $w(t) = e^{\lambda t}$, we obtain the Euler-Lotka equation

$$1 = \Psi'(0) \int_0^\infty b(\tau)e^{-\lambda\tau}d\tau, \tag{3.6}$$

which has a unique positive solution $\lambda = r$ whenever the Basic Reproduction Number R_0 [10, 11, 17], given by

$$R_0 = \Psi'(0) \int_0^\infty b(\tau)d\tau, \tag{3.7}$$

exceeds one. The non-negativity of b guarantees that in the complex plane r is the right most root of (3.6); for $R_0 < 1$ there exists a solution $r < 0$ provided the rhs of (3.6) assumes, on the real axis, values greater than one; a sufficient condition for this to happen is that b has compact support. Note that

$$\Psi'(0) = N \int_\Omega c(\eta)a(\eta)\Phi(d\eta). \tag{3.8}$$

The Herd Immunity Threshold (HIT) is, by definition, reached when w assumes the value $\bar{w}$ such that the reproduction number corresponding to the situation in which $\Psi'(0)$ is replaced by $\Psi'(\bar{w})$ equals one (note that after reaching the HIT there might still be a high incidence, simply because the reservoir of already infected individuals generates a considerable force of infection; but the contents of the reservoir will gradually diminish once the HIT is reached). The HIT itself is defined as $\bar{s}$, where $\bar{s}$ is the fraction of the population that is still susceptible when w assumes the value $\bar{w}$. Hence,

$$\bar{s} = \int_\Omega e^{-a(x)\bar{w}}\Phi(dx), \tag{3.9}$$

with $\bar{w}$ the unique (since $\Psi''(w) < 0$) solution of

$$1 = \Psi'(\bar{w}) \int_0^\infty b(\tau)d\tau. \tag{3.10}$$

For $t \to \infty$, w tends to $w(\infty)$ characterized by

$$w(\infty) = \Psi(w(\infty)) \int_0^\infty b(\tau)d\tau = \frac{\Psi(w(\infty))}{\Psi'(0)} R_0 \tag{3.11}$$

and the fraction of the population that escapes is accordingly given by

$$\tilde{s} = \int_\Omega e^{-a(x)w(\infty)} \Phi(dx). \tag{3.12}$$

Note that (3.11) implies that $\Psi'(w(\infty)) < \frac{\Psi'(0)}{R_0}$ (since $\Psi(y) > y\Psi'(y)$ for $y > 0$) and hence that $w(\infty) > \bar{w}$ and $\tilde{s} < \bar{s}$. The quantity $1 - \tilde{s}$ is called the final size of the outbreak, since it is the fraction that got infected during the outbreak.

In the next section we shall specialize the model ingredients Ω, Φ, a and c such that they reflect a situation in which a fraction f of the population wears (all the time) a mask and that wearing a mask reduces, potentially, both the susceptibility and the infectiousness.

4. Efficiency of masks

For a more general and quantitative study of mask wearing as a non-pharmaceutical intervention we refer to [18] and [19]. Here, we focus on one particular aspect.

Consider a population in which a fraction f of the individuals wears a mask (whenever they are in a situation where they can come into contact with other individuals) while the complementary fraction $1 - f$ never wears a mask. To describe this distinction, we let Ω consist of two points, indicated by 1 and 2. We label the individuals that do not wear a mask 1 and those who do, we label 2. We specify:

$$\Phi(1) = 1 - f \quad \text{and} \quad \Phi(2) = f. \tag{4.1}$$

We assume that wearing a mask is not correlated with any property that has influence on the contact process (in principle one could imagine that the contact process is assortative, in the sense that mask wearers meet disproportionately often with other mask wearers; but by this assumption we explicitly exclude such effects). Accordingly, we adopt (3.1). Recalling that this decomposition provides the freedom of incorporating multiplicative constants into the factor b, we normalize a and c by choosing:

$$a(1) = 1 \quad \text{and} \quad c(1) = 1. \tag{4.2}$$

The values of $a(2)$ and $c(2)$ then describe the relative susceptibility and infectiousness of those who wear a mask. The idea that a mask offers protection is reflected in our assumption that these values lie in the interval $[0, 1]$. The aim of our analysis is to investigate the influence of these values on the epidemic outbreak. Therefore we introduce parameters ϵ_1 and ϵ_2 and put:

$$a(2) = \epsilon_1 \quad \text{and} \quad c(2) = \epsilon_2. \tag{4.3}$$

It follows that:

$$\Psi(w) = N\left[(1-f)(1-e^{-w}) + f\epsilon_2(1-e^{-\epsilon_1 w})\right], \tag{4.4}$$

and

$$\Psi'(w) = N\left[(1-f)e^{-w} + f\epsilon_1\epsilon_2 e^{-\epsilon_1 w}\right]. \tag{4.5}$$

In succession, we now consider the initial phase, the HIT and the final size, focusing on the (a)symmetry of the impact of the two parameters ϵ_1 and ϵ_2. As (3.6) and (3.7) show, the crucial quantities for the initial phase are $b(\tau)$ and $\Psi'(0)$. From (4.5) we deduce:

$$\Psi'(0) = N\left[1 - f + f\epsilon_1\epsilon_2\right]. \tag{4.6}$$

It follows that in the initial phase of an outbreak the two protection factors carry equal weight, in the sense that both the reproduction number R_0 and the Malthusian parameter r depend only on their product. Motivated by this observation, we shall keep the product constant, say

$$\epsilon_1\epsilon_2 = \epsilon, \tag{4.7}$$

when investigating the HIT and the final size.

Theorem 4.1: Assume (4.7) with $\epsilon \in (0,1)$. The HIT $\bar{s}$, defined in (3.9), is a decreasing function of ϵ_1.

Proof. Define:

$$G(w,\epsilon_1) = (1-f)e^{-w} + \epsilon f e^{-\epsilon_1 w}, \tag{4.8}$$

then (3.10) can be rewritten as:

$$G(\bar{w},\epsilon_1) = \left(N\int_0^\infty b(\tau)d\tau\right)^{-1}. \tag{4.9}$$

Since

$$\mathrm{D}_1 G(w,\epsilon_1) = -(1-f)e^{-w} - \epsilon_1\epsilon f e^{-\epsilon_1 w} < 0 \tag{4.10}$$

$$\mathrm{D}_2 G(w, \epsilon_1) = -w\epsilon f e^{-\epsilon_1 w} < 0, \tag{4.11}$$

we have by differentiation of $G(\bar{w}(\epsilon_1), \epsilon_1) = 0$ with respect to ϵ_1 (implicit function theorem) that

$$\frac{d\bar{w}}{d\epsilon_1}(\epsilon_1) = -\left(\mathrm{D}_1 G(\bar{w}, \epsilon_1)\right)^{-1} \mathrm{D}_2 G(\bar{w}, \epsilon_1) < 0. \tag{4.12}$$

Next observe that the expressions for $\bar{s}$ and for $G(\bar{w}, \epsilon_1)$ differ only by a factor ϵ in the last term. To exploit this, we rewrite $\mathrm{D}_1 G \frac{d\bar{w}}{d\epsilon_1} + \mathrm{D}_2 G = 0$ as

$$-\epsilon_1 f e^{-\epsilon_1 \bar{w}} \frac{d\bar{w}}{d\epsilon_1}(\epsilon_1) - \bar{w} f e^{-\epsilon_1 \bar{w}} = \frac{1}{\epsilon}(1-f) e^{-\bar{w}} \frac{d\bar{w}}{d\epsilon_1}(\epsilon_1). \tag{4.13}$$

Because

$$\frac{d\bar{s}}{d\epsilon_1}(\epsilon_1) = -(1-f) e^{-\bar{w}} \frac{d\bar{w}}{d\epsilon_1}(\epsilon_1) - \epsilon_1 f e^{-\epsilon_1 \bar{w}} \frac{d\bar{w}}{d\epsilon_1}(\epsilon_1) - \bar{w} f e^{-\epsilon_1 \bar{w}} \tag{4.14}$$

we find

$$\frac{d\bar{s}}{d\epsilon_1}(\epsilon_1) = \left(\frac{1}{\epsilon} - 1\right)(1-f) e^{-\bar{w}} \frac{d\bar{w}}{d\epsilon_1}(\epsilon_1) < 0, \tag{4.15}$$

since $0 < \epsilon < 1$. □

We conclude that we should minimize ϵ_1 to maximize the susceptible fraction upon reaching the HIT or, in other words, we should maximize self protection.

Theorem 4.2: Assume (4.7) with $\epsilon \in (0, 1)$. The fraction $\tilde{s}$ that is still susceptible after the outbreak, defined in (3.12), is a decreasing function of ϵ_1.

Sketch of the proof: Define

$$H(w, \epsilon_1) = (1-f)\frac{1 - e^{-w}}{w} + \epsilon f \frac{1 - e^{-\epsilon_1 w}}{\epsilon_1 w}, \tag{4.16}$$

then (3.11) can be rewritten as the equation

$$H(w(\infty), \epsilon_1) = \left(N \int_0^\infty b(\tau) d\tau\right)^{-1}. \tag{4.17}$$

Using that $\frac{d}{dx}\frac{1-e^{-x}}{x} < 0$ for $x > 0$ one can copy the reasoning in the proof of Theorem 4.1 and derive that both $w(\infty)$ and $\tilde{s}$ are decreasing functions of ϵ_1.

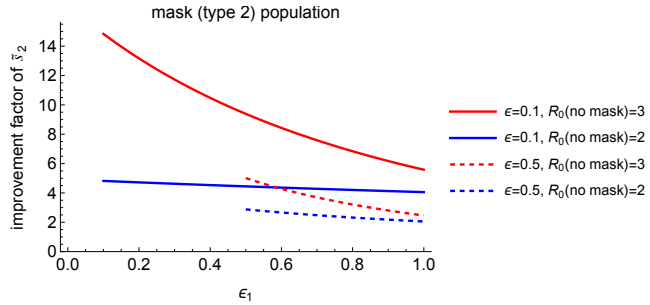
From (3.12) we have

$$\tilde{s} = (1 - f)e^{-w(\infty)} + fe^{-\epsilon_1 w(\infty)}. \tag{4.18}$$

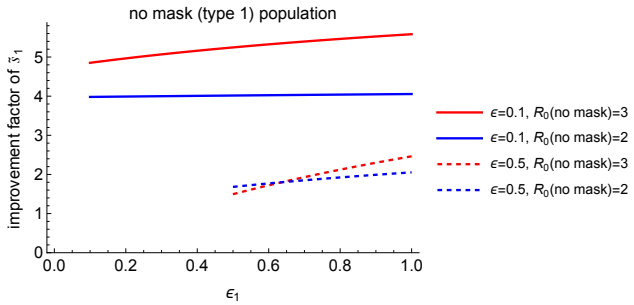
Since $w(\infty)$ is a decreasing function of ϵ_1 the escape probability for those who do NOT wear a mask, represented by $e^{-w(\infty)}$, increases with ϵ_1. From Theorem 4.2 it follows then that the escape probability of those who DO wear a mask, represented by $e^{-\epsilon_1 w(\infty)}$, decreases strongly enough to make the overall per capita escape probability $\tilde{s}$ decreasing as well.

Stated otherwise, maximizing self protection by those who wear a face mask improves the escape probability for themselves (Figure 1a) and the population as a whole (Figure 2), but reduces the escape probability for those who do not wear a mask (Figure 1b).

The intuitive 'explanation' of the overall positive effect is that when infection of an individual is prevented, automatically the secondary infections that potentially are caused by this individual are prevented. In other words, self protection occurs one step earlier in a chain of potential transmissions.



(a) Higher self protection by those who wear a face mask (lower ϵ_1) leads to a higher escape probability for those who wear a mask

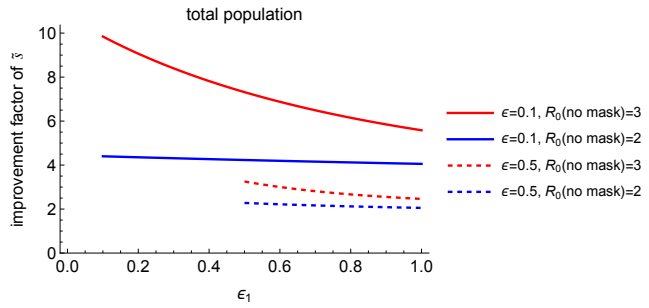


(b) Higher self protection by those who wear a face mask (lower ϵ_1) leads to a lower escape probability for those who never wear a mask

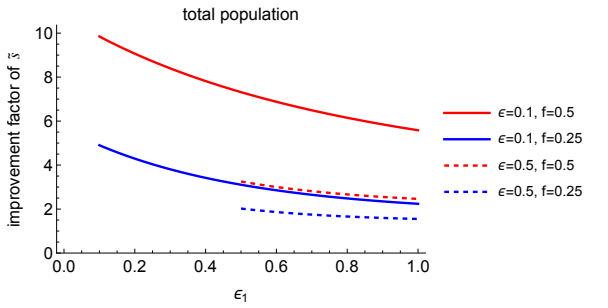
Figure 1. Improvement factor of escape probability for type 2 individuals who always wear a mask and for type 1 individuals who never wear a mask. Recall that a higher self protection by those who wear a face mask corresponds to a lower ϵ_1. We find the respective escape probabilities of type 1 and type 2 individuals, $\tilde{s}_1 = e^{-w(\infty)}$ and $\tilde{s}_2 = e^{-\epsilon_1 w(\infty)}$, by numerically solving equation (3.11) with Ψ given by (4.4) and with, in this particular numerical example, $f = 0.5$. Next we compute the improvement factor of the escape probability by dividing the calculated escape probability by the escape probability in a maskless population. We refer to $N\int_0^\infty b(\tau)d\tau$ as 'R_0(no mask)' since R_0 in a maskless population equals $N\int_0^\infty b(\tau)d\tau$ (see (3.7)). Please note that equation (3.11) depends on ϵ_1, ϵ_2, f and the compound parameter R_0(no mask) but not at all on the shape of the graph of the function b. Curves are shown for two choices of R_0(no mask) and two choices of mask protection level ϵ. Note that the self protection parameter ϵ_2 is related to ϵ and ϵ_1 by $\epsilon_2 = \epsilon/\epsilon_1$ as assumed in (4.7).

5. Concluding remarks

In a top down approach to the mathematical epidemiology of infectious diseases [3, 9], one starts general and abstract in order to create a theoretical framework that, hopefully, facilitates the investiga-



(a) Higher self protection by those who wear a face mask (lower ϵ_1) leads to a higher escape probability for the population as a whole. We show the effect of different levels of mask protection ϵ and R_0(no mask).



(b) Higher self protection by those who wear a face mask (lower ϵ_1) leads to a higher escape probability for the population as a whole. We show the effect of different levels of mask protection ϵ and sizes of the masked population f.

Figure 2. Improvement factor of escape probability for the population as a whole. Recall that a higher self protection by those who wear a face mask corresponds to a lower ϵ_1. We find the escape probability $\tilde{s}$ for the population as a whole by first numerically solving equation (3.11) and inserting the outcome in (3.12)/(4.18). Then we compute the improvement factor of the escape probability by dividing the calculated escape probability by the escape probability in a maskless population. We refer to $N\int_0^\infty b(\tau)d\tau$ as 'R_0(no mask)' since R_0 in a maskless population equals $N\int_0^\infty b(\tau)d\tau$ (see (3.7)). Please note that equation (3.11) depends on ϵ_1, ϵ_2, f and the compound parameter R_0(no mask) but not at all on the shape of the graph of the function b. In Figure 2a we choose $f = 0.5$ (recall $\tilde{s} = (1-f)\tilde{s}_1 + f\tilde{s}_2$) and in Figure 2b we choose R_0(no mask) $= 3$. Note that the self protection parameter ϵ_2 is related to ϵ and ϵ_1 by $\epsilon_2 = \epsilon/\epsilon_1$ as assumed in (4.7).

tion of concrete questions that arise in the context of specific diseases. In exactly that spirit, we introduce in [2] a variant of the general Kermack-McKendrick model that incorporates static heterogeneity and next focus on the impact of heterogeneity on various characteristics of an outbreak, such as the Herd Immunity Threshold and the Final Size. In the first half of the present paper, we briefly described this general model and we showed how the assumption of separable mixing leads to a relatively simple scalar renewal equation in which the influence of heterogeneity is captured by one nonlinear function. In the second half of the paper, we turned to a concrete question concerning the non-pharmaceutical intervention of wearing face masks to reduce the spread of a disease like Covid-19. Here, the heterogeneity is simply that some individuals wear a mask, while others do not. Additionally, if the contact process is 'proportional', cf. beginning of Section 3, we do have separable mixing. Thus, we can use the scalar renewal equation and consequently have a simple characterization of the herd immunity threshold and of the final size. This allowed us to show that obstructing incoming virus is more efficient for reducing the herd immunity threshold and the final size than obstructing outgoing virus. Thus, we confirmed for a very large class of models the conclusion recently obtained in [1] in the context of an SIR model for disease spread over a configuration network.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

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Conflict of interest

The authors declare there is no conflict of interest.

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