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Discrete stochastic metapopulation model with arbitrarily distributed infectious period



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ABSTRACT

In this study, a stochastic discrete-time model is developed to study the spread of an infectious disease in an *n*-patch environment. The model includes an arbitrary distribution of the (random) infectious period *T*, and the results are used to investigate how the distribution of *T* may influence the model outcomes. General results are applied to specific distributions including Geometric, Negative Binomial, Poisson and Uniform. The model outcomes are contrasted both numerically and analytically by comparing the corresponding basic reproduction numbers \mathcal{R}_0 and probability of a minor epidemic (or probability of disease extinction) \mathbb{P}_0 . It is shown analytically that for n = 2 the reproduction numbers corresponding to different distributions of *T* can be ordered based on the probability generating function ϕ_T of *T*. In addition, numerical simulations are carried out to examine the final epidemic size \mathcal{F} and duration of the epidemic \mathcal{D} of a two-patch model.

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1. Introduction

Deterministic and stochastic epidemic models have commonly assumed that the disease stages, particularly the infectious period (IP), follow an exponential distribution (continuous-time) or a Geometric distribution (discrete-time). The very property of these distributions that makes these models tractable, the memoryless property, is biologically unrealistic for most infectious diseases. It has been shown that models with these simplifying assumptions may generate misleading assessments on disease control strategies [1,2].

One of the more realistic alternatives to the exponential (Geometric) distribution for the IP that has been considered is the Gamma (Negative Binomial) distribution, which is a natural generalization due to its relationship with the exponential (Geometric) distribution. When a Gamma distribution is considered, the so called "linear chain trick" can be used to reduce the system of integro-differential equations to a system of ordinary differential equations (see, for example, [1,3-5]). The key idea in this approach is to introduce multiple substages for the IP, each of which follows an exponential distribution. A similar idea is applied in stochastic models to allow the use of Gamma distribution for the IP, while still preserving the Markov property of the process. Such models were first developed and studied in [6,7] and more recently in [8,9].

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Stochastic models with an arbitrary distribution for the IP were first considered in [10-12], but Sellke's construction [13] helped derive stronger results such as those in [14,15]. Some recent studies have focused on understanding the effect of disease stage distributions on the model outcomes (see, for instance, [16-19]).

In [20], a patch model is used to study the spread of an epidemic through a population divided into *n* sub-populations (patches), in which individuals move between the patches according to the law of a continuous Markov chain (dynamic population epidemic model). In this framework, infected individuals make contacts with members currently in the same patch. In a more recent study on a continuous-time patch model [21], an expression for the basic reproduction number \mathcal{R}_0 and the extinction probability of the epidemic are derived in terms of the IP distribution. It was shown that for a two patch model \mathcal{R}_0 is maximized by an IP with constant length. For three or more patches, however, it is very difficult to draw general conclusions about the effects of IP distribution on \mathcal{R}_0 or the extinction probability. In the current study, we extend some of the results in [21] to an analogous discrete-time model.

Most epidemic models are in the continuous-time setting, studies on discrete models have been very limited. Mathematical formulations of continuous-time models are in general complicated when an arbitrarily distributed IP is included, particularly when the models also include control measures such as quarantine and isolation (e.g., [1]). This may make it challenging for modelers to communicate with biologists and public health policymakers. Analogous discrete-time models can be formulated in a way that is much easier to understand for non-mathematicians (see, for example, [2,22,23]). Another major advantage of discrete-time models is their capability of incorporating distributions directly from empirical data, whereas for continuoustime models one usually needs to estimate the parameters for a standard distribution via data fitting.

In Section 2, the general model with *n* patches and Markov displacement (with transition matrix D) is described. For an infected individual, the infectious period (T) is assumed to be a discrete random variable with an arbitrary distribution. We derive a formula for the basic reproduction number \mathcal{R}_0 , which is given by the spectral radius of the mean offspring matrix, a matrix that depends on D and the probability generating function (pgf) of T. An equation for the probability of minor epidemic (extinction probability) \mathbb{P}_0 is also derived for this *n*-patch model.

In Section 3, these general results are then applied to the case n = 2 patches. For the two-patch model, in addition to an exact formula, lower and upper bounds for \mathcal{R}_0 are also identified. To examine the effect that the distribution of *T* has on \mathcal{R}_0 , we consider three specific distributions: shifted Geometric, shifted Negative Binomial, and shifted Poisson. The reproduction numbers corresponding to these distributions have a specific order relation. Numerical simulations for the two-patch model are carried out to explore the influence of the T distribution on the final epidemic size (\mathcal{F}), duration of epidemic (\mathcal{D}), as well as the probability of disease extinction (\mathbb{P}_0).

2. General model

We adopt the approaches used in [20,21] for continuous models to develop a discrete stochastic SIR metapopulation model, in a closed population, for an epidemic outbreak with an arbitrarily distribution for the infectious period (IP). The main objective of this study is to investigate how the distribution of IP may affect the model outcomes, particularly the basic reproduction number \mathcal{R}_0 and the probability of major epidemic $(1 - \mathbb{P}_0)$.

Consider a metapopulation with n sub-populations (patches). Let $N_i(t)$ denote the size of population *i* at time *t* for i = 1, 2, ..., n. Assume that the total population size $N = \sum_{i=1}^{n} N_i(t)$ remains constant for all time. Individuals can move between any two patches, this movement is determined by a **discrete** time Markov chain U, which is described by the transition matrix $D = (\sigma_{ii})$. The entry σ_{ii} represents the probability of moving from population *i* to population *j* at each time step.

Effective contacts by individual in population *i*, per unit of time, is modeled by a Poisson random variable with parameter β_i . In the early stages of the epidemic most effective contacts will produce an infection because most individuals are susceptible. The disease transmission dynamics within each sub-population is governed by an SIR model. It is assumed that individuals become immune after recovery. Let *T* denote the random variable for the IP (the time until recovery), which is assumed to be the same for all sub-populations. Here, we place no restriction on the *T* distribution, other than *T* is discrete, non negative and has a finite mean. All variables and parameters are listed in Table 2. Fig. 1 provides a graphical representation of the model described above.

New infections are produced between time steps in the interval (t, t + 1), while recovery and geographical displacement (governed by the discrete random variables T and U) occur at integer time points. This simplification assumption accompanies discrete models and not their continuous counterpart. However, the assumption is biologically reasonable for different situations, including (i) commuters traveling at peak hours from city to city or (ii) domestic animals who are transported from farm to farm at night.

Assume that, at time t = 0, $N_i(0) \approx N\pi_i$ (i = 1, 2, ..., n), where $\pi = (\pi_i)_{i=1}^n$ is the stationary probability (i.e. $\pi D = \pi$). Thus, although random, the subpopulation $N_i(t)$ will remain close to its initial value throughout time. Some of the properties of the model are described in the following sections.

2.1. Computation of \mathcal{R}_0

In this section, we follow the approach of [21]. The early stages of an epidemic is approximated by a properly defined multi-type branching process. The "convergence" of the epidemic model to its associated branching process has been established previously (see [12,24,25]). A less formal but more practical exposition can be found in [9,23,26,27]. To compute the basic reproduction number \mathcal{R}_0 , we introduce the notation:

- ζ_{ii} = random time spent in patch *j* (before recovery) by an infectious individual from patch *i*;
- m_{ii} = average number of "offspring" (i.e., secondary infections) that an individual, from patch *i*, can produce in patch *j* during the entire "life span" (i.e. the random infectious period modeled by T);
- $M = (m_{ii})$, the mean offspring matrix.

m(4)

 \mathcal{R}_0 is given by the spectral radius of the matrix *M*, which entries m_{ii} can be written as

$$m_{ij} = \beta_j \mathbb{E}(\zeta_{ij}). \tag{1}$$

By conditional expectation $\mathbb{E}(\zeta_{ij}) = \sum_{t=0}^{\infty} \mathbb{E}(\zeta_{ij}|T=t)\mathbb{P}(T=t)$ and

$$\mathbb{E}(\zeta_{ij}|T=t) = \mathbb{E}\left(\sum_{k=0}^{t-1} \mathbb{I}_{U_i(k)=j}\right) = \sum_{k=0}^{t-1} \mathbb{P}(U_i(k)=j) = \sum_{k=0}^{t-1} \sigma_{ij}^{(k)},$$

where $\sigma_{ii}^{(k)}$ denotes the *ij*th entry of the matrix D^k , $U_i(k)$ the state of the Markov chain at time *k* given that $U_i(0) = i$, and $\mathbb{I}_{U_i(k)=j}$ the indicator function of the event $U_i(k) = j$. Notice that new infections at time t are generated by infective individuals at time t - 1, which is why the sum above has been taken from 0 to t - 1. Combining the last two equations we obtain the matrix of expectations of ζ_{ij}

$$\begin{bmatrix} \mathbb{E}(\zeta_{11}) & \cdots & \mathbb{E}(\zeta_{1n}) \\ \vdots & \ddots & \vdots \\ \mathbb{E}(\zeta_{n1}) & \cdots & \mathbb{E}(\zeta_{nn}) \end{bmatrix} = \sum_{t=1}^{\infty} \mathbb{P}(T=t) \sum_{k=0}^{t-1} D^k = \mathbb{E}\left(\sum_{k=0}^{T-1} D^k\right).$$
(2)

Let $\lambda_1, \ldots, \lambda_n$ be the eigenvalues of the stochastic matrix $D = (\sigma_{ij})$. Since *D* is a Markov matrix, $\lambda_i = 1$ for some *i* and $|\lambda_i| \le 1 \forall i$. If *D* is



Fig. 1. (a) Individuals move from patch to patch at time $t \in \mathbb{N}$ according to the Markov chain U. (b) Once the infection process has started in one patch, the disease can spread to other patches. Contacts by an infected individual, per unit of time in patch *i*, is described by Poisson(β_i).

(3)

diagonalizable, then there exists a nonsingular matrix Λ such that $D^k = \Lambda \operatorname{diag}(1, \lambda_2^k, \dots, \lambda_n^k) \Lambda^{-1}$, so that

$$\sum_{k=0}^{t-1} D^k = \Lambda \operatorname{diag}\left(t, \sum_{k=0}^{t-1} \lambda_2^k, \dots, \sum_{k=0}^{t-1} \lambda_n^k\right) \Lambda^{-1}.$$

Substitution of (3) into (2) yields

$$\begin{bmatrix} \mathbb{E}(\zeta_{11}) & \cdots & \mathbb{E}(\zeta_{1n}) \\ \vdots & \ddots & \vdots \\ \mathbb{E}(\zeta_{n1}) & \cdots & \mathbb{E}(\zeta_{nn}) \end{bmatrix}$$
$$= \Lambda \left[\sum_{t=1}^{\infty} \mathbb{P}(T=t) \operatorname{diag}\left(t, \sum_{k=0}^{t-1} \lambda_{2}^{k}, \dots, \sum_{k=0}^{t-1} \lambda_{n}^{k}\right) \right] \Lambda^{-1}$$
$$= \Lambda \operatorname{diag}(\varphi(1), \varphi(\lambda_{2}), \dots, \varphi(\lambda_{n})) \Lambda^{-1}, \qquad (4)$$

where φ is the function defined by

$$\varphi(s) = \sum_{t=1}^{\infty} \mathbb{P}(T=t) \sum_{k=0}^{t-1} s^k = \begin{cases} \mathbb{E}(T) & \text{if } s = 1, \\ \mathbb{E}\left(\frac{1-s^T}{1-s}\right) & \text{if } s \neq 1. \end{cases}$$
(5)

The following lemma, a discrete equivalent of a result presented in [21], is obtained using equalities (1) and (4).

Lemma 1. \mathcal{R}_0 is given by the spectral radius of M, $\varrho(M)$, where

 $M = \mathbb{E}(1 + D + \dots + D^{T-1})\operatorname{diag}(\beta_1, \dots, \beta_n).$

Moreover, if the Markov matrix D is diagonalizable then

 $M = \Lambda \operatorname{diag}(\varphi(1), \varphi(\lambda_2), \dots, \varphi(\lambda_n)) \blacksquare^{-1} \operatorname{diag}(\beta_1, \dots, \beta_n).$

Remark. Notice that the trivial case T = 0 yields M = 0 and $\mathcal{R}_0 = 0$. For this reason $T \neq 0$ is assumed from now on.

This result can also be expressed using the probability generating function (pgf) of *T*, which we denote by $\phi(s)$, i.e.,

 $\phi(s) = \mathbb{E}(s^T). \tag{6}$

For $s \neq 1$ (see (5)),

$$\varphi(s) = \frac{1 - \phi(s)}{1 - s}.\tag{7}$$

The series $\phi(s) = \sum_{t=1}^{\infty} s^t \mathbb{P}(T = t)$ is absolutely convergent in $|s| \le 1$, and so is $\varphi(s)$. An explicit formula for the pgf is usually available for most commonly used discrete distributions. In addition, it is easily verified that $0 \le \varphi(s) \le \mathbb{E}(T) \forall s \in [-1, 1]$.

Applications of Lemma 1 are illustrated later when specific distributions for *T* are considered in the model with n = 2 patches (see Section 3.1). This result also allows us to compare the reproduction numbers \mathcal{R}_0 corresponding to different distributions of *T* (see Section 3.2).

2.2. Probability of minor and major epidemics

As presented in [21] for continuous models, in addition to \mathcal{R}_0 , one can analyze the probability of extinction of the branching process, which is also known as the probability of a minor epidemic [9,12, 14,26]. In this section, we derive an analogous result for our discrete model.

The probability of extinction of a branching process can be determined using the probability generating function (pgf) of the offspring distribution, denoted by *G*. To obtain an expression for *G*, let η_{ij} be the number of offsprings (secondary infections) generated in population *j* by an individual from population *i*. Since the sum of independent Poisson random variable is still Poisson we have that $\eta_{ij}|\zeta_{ij} = \text{Poisson}(\beta_j\zeta_{ij})$. Let $\vec{s} = (s_1, \dots, s_n)$. Then the function $G : [0, 1]^n \to [0, 1]^n$ can be expressed as

$$G_{i}(\vec{s}) = \mathbb{E}\left(\prod_{j=1}^{n} s_{j}^{\eta_{ij}}\right) = \mathbb{E}\left(\mathbb{E}\left(\prod_{j=1}^{n} s_{j}^{\eta_{ij}} \middle| \zeta_{i1}, \dots, \zeta_{in}\right)\right)$$
$$= \mathbb{E}\left(\prod_{j=1}^{n} \mathbb{E}(s_{j}^{\eta_{ij}} \middle| \zeta_{i1}, \dots, \zeta_{in})\right) = \mathbb{E}(e^{-\sum_{j=1}^{n} \beta_{j} \zeta_{ij}(1-s_{j})}).$$
(8)

Define $\zeta_{ij}(t)$ to be the time spent in group *j* by an individual from group *i* up to time *t*, and

$$X_i(t) = \sum_{j=1}^n \beta_j \zeta_{ij}(t)(1-s_j)$$

Using the conditional expectation formula, Eq. (8) becomes

$$G_{i}(\vec{s}) = \mathbb{E}\left(e^{-\sum_{j=1}^{n}\beta_{j}\zeta_{ij}(1-s_{j})}\right) = \sum_{t=1}^{\infty}\mathbb{E}\left(e^{-\sum_{j=1}^{n}\beta_{j}\zeta_{ij}(1-s_{j})}\Big|T=t\right)\mathbb{P}(T=t)$$
$$= \sum_{t=1}^{\infty}\mathbb{E}(e^{-X_{i}(t)})\mathbb{P}(T=t)$$
(9)

A recursive formula for $e^{-X_i(t)}$ is provided in the Appendix A. Using this expression in Eq. (9), an explicit formula for *G* can be found.

Lemma 2. Let $A(\vec{s})$ be the $n \times n$ matrix given by $A(\vec{s})_{ij} = e^{-\theta_i}\sigma_{ij}$. Let $E(\vec{s})$ be the $n \times 1$ matrix given by $E(\vec{s})_i = e^{-\theta_i}$, where $\theta_j = \beta_j(1 - s_j)$. Then $G : [0, 1]^n \to [0, 1]^n$ is given by

$$G(\vec{s})^{tr} = (G_1(\vec{s}), \dots, G_n(\vec{s}))^{tr} = \sum_{t=1}^{\infty} A(\vec{s})^{t-1} E(\vec{s}) \mathbb{P}(T=t)$$

The proof of Lemma 2 is included in the Appendix A.

The extinction probability (or probability of minor epidemic) is determined by the equation $G(\vec{s}) = \vec{s}$. This is a well known fact from the theory of branching process [28]. If $\mathcal{R}_0 < 1$, the only fixed point of $G(\vec{s})$ is (1, 1, ..., 1). If $\mathcal{R}_0 > 1$, the equation $G(\vec{s}) = \vec{s}$ has a nontrivial solution $\vec{z} = (z_1, ..., z_n) \in (0, 1)^n$. Each value z_i represents the extinction probability given the initial condition $I_i(0) = 1$ and $I_j(0) = 0 \forall j \neq i$. Thus, if there are m_i initial infective individuals in population i at t = 0, then the extinction probability \mathbb{P}_0 (probability of minor epidemic) is

$$\mathbb{P}_0 = \prod_{i=1}^n z_i^{m_i}.$$
(10)

Naturally, the probability that a major epidemic occurs is $1 - \mathbb{P}_0$.

Lemma 2 is valid for any distribution of *T* and any number *n* of subpopulations. When a specific distribution of *T* is used, the formula may simplify and (10) can be determined numerically. Examples with n = 2 patches are presented in Section 3.3.

3. Two-patch model

When *n* is large, an explicit expression for the spectral radius of the matrix *M* can be difficult to obtain. However, for n = 2 patches, most formulas can be dramatically simplified, especially when specific distributions of *T* are used. In Section 3.1, explicit formulas for \mathcal{R}_0 (see Lemma 1) and the pgf of offspring distribution $G(\vec{s})$ (see (9)) are derived for n = 2 subpopulations. In Section 3.2, we analyze the effect of the distribution of *T* on \mathcal{R}_0 . Section 3.3 includes some simulation results and Section 3.4 presents a more detailed formula for *G*, which is used to compute the probabilities of major and minor epidemics.

3.1. Computation of \mathcal{R}_0

Without loss of generality, assume that the transmission parameters β_i satisfy $\beta_1 \ge \beta_2$. To simplify the notation, let $a = \sigma_{11}$ and

 $b = \sigma_{22}$. Then, the transition matrix of the Markov chain becomes

$$D = \begin{bmatrix} a & 1-a \\ 1-b & b \end{bmatrix}.$$
 (11)

To avoid extreme cases, let $a, b \in (0, 1)$. The eigenvalues of D are 1 and

$$\lambda = a + b - 1. \tag{12}$$

Let π denote the stationary probability distribution of the Markov chain described by D (i.e. $\pi D = \pi$). It is easy to verify that $\pi = [\pi_1, \pi_2]$ with

$$\pi_1 = \frac{1-b}{2-a-b} \in (0,1), \quad \pi_2 = \frac{1-a}{2-a-b} \in (0,1).$$

The matrix *D* can be diagonalized and rewritten as

$$D = \Lambda \begin{bmatrix} 1 & 0 \\ 0 & \lambda \end{bmatrix} \Lambda^{-1}, \quad \text{where} \quad \Lambda = \begin{bmatrix} 1 & 1-a \\ 1 & -(1-b) \end{bmatrix}. \tag{13}$$

From Lemma 1, the mean offspring matrix is given by

Remark. If $\beta = \beta_1 = \beta_2$ (i.e., identical transmission in both subpopulations), formula (15) reduces to $\mathcal{R}_0 = \mathcal{R}_{0i} = \overline{\mathcal{R}}_0 = \beta \mathbb{E}(T)$, which is consistent with the standard simple SIR model with a single population. In the following sections we assume that $\beta_1 > \beta_2$ to avoid this trivial case.

3.2. Effect of the distribution of T on \mathcal{R}_0

To investigate how the choice of the IP distribution may affect \mathcal{R}_0 , we examine our model under several distributions for *T* and compare the corresponding \mathcal{R}_0 values. We consider two models to be *comparable* if they have the same values for β_1 , β_2 , π , and mean infectious period $\mathbb{E}(T)$.

The following four distributions will be considered: **A.** shifted Geometric (sGeom); **B.** shifted Negative Binomial (sNegBinom); **C.** shifted Poisson (sPoisson); and **D.** discrete with finitely many points (for example the empirical distribution obtained from data). In all cases the support of *T* lies in \mathbb{N} .

Distribution	Parameter	$\mathbb{P}(T=t)$	$\phi_g(\lambda)$
A. $T \sim sGeom(\gamma)$ $\mathbb{E}(T) = \frac{1}{\gamma}$	$0 < \gamma < 1$	$\gamma (1-\gamma)^{t-1}$	$\mathbb{E}(\lambda^{T}) = \frac{\gamma\lambda}{1-\lambda(1-\gamma)}$ $= \frac{\lambda}{\mathbb{E}(T)-\lambda[\mathbb{E}(T)-1]}$
B. $T \sim sNegBinom(k, \eta)$	$k \in \mathbb{N}$		$\mathbb{E}(\lambda^T) = \lambda \left(\frac{\eta}{1 - \lambda(1 - \eta)}\right)^k$
$\mathbb{E}(T) = (1 - \eta)k/\eta + 1$ If $k = 1, T \sim sGeom(\gamma)$	$\eta = \frac{k}{\mathbb{E}^{(T)+k-1}}$	$\binom{t+k-2}{t-1}\eta^k(1-\eta)^{t-1}$	$= \lambda \left(\frac{k}{\mathbb{E}(T) - \lambda [\mathbb{E}(T) - 1] - 1 + k} \right)^k$
C. $T \sim sPoisson(\kappa)$ $\mathbb{E}(T) = \kappa + 1$	$\kappa > 0$	$e^{-\kappa} \frac{\kappa^{t-1}}{(t-1)!}$	$\mathbb{E}(\lambda^T) = \lambda e^{-\kappa(1-\lambda)}$ $= \lambda e^{-[\mathbb{E}(T)-1](1-\lambda)}$
D. $T \sim$ discrete with support on $\{1, 2,, m\}$ $\mathbb{E}(T) = \sum_{k=1}^{m} k p_k$	$p_i = 1, \ldots, m$	$\mathbb{P}(T=t_i)=p_i$	$\mathbb{E}(\lambda^T) = \sum_{k=1}^m p_k \lambda^k$

$$M = \Lambda \begin{bmatrix} \mathbb{E}(T) & \mathbf{0} \\ \mathbf{0} & \varphi(\lambda) \end{bmatrix} \Lambda^{-1} \begin{bmatrix} \beta_1 & \mathbf{0} \\ \mathbf{0} & \beta_2 \end{bmatrix}$$
$$= \begin{bmatrix} \beta_1[\pi_1 \mathbb{E}(T) + \pi_2 \varphi(\lambda)] & \beta_2 \pi_2[\mathbb{E}(T) - \varphi(\lambda)] \\ \beta_1 \pi_1[\mathbb{E}(T) - \varphi(\lambda)] & \beta_2[\pi_2 \mathbb{E}(T) + \pi_1 \varphi(\lambda)] \end{bmatrix}.$$

Recall from (5) that $\varphi(1) = \mathbb{E}(T)$ is the mean infectious period and $\varphi(\lambda) = \mathbb{E}(\frac{1-\lambda^T}{1-\lambda})$. For ease of notation, let

$$\mathcal{R}_{0i} = \beta_i \mathbb{E}(T), \quad \overline{\mathcal{R}}_0 = \pi_1 \mathcal{R}_{01} + \pi_2 \mathcal{R}_{02}. \tag{14}$$

 $\overline{\mathcal{R}}_0$ can be interpreted as the weighted average of \mathcal{R}_{01} and \mathcal{R}_{02} , the intuitive patch reproduction numbers. Finally, by analyzing M we can find not only the exact value of \mathcal{R}_0 but also other important properties that are listed in the next lemma.

Lemma 3. Let $z = \varphi(\lambda)$ and $\phi(\lambda)$, $\varphi(\lambda)$, λ , $\overline{\mathcal{R}}_0$, \mathcal{R}_{01} be defined as in (6), (7), (12), (14). For n = 2 patches,

(i) An explicit expression for \mathcal{R}_0 is

$$\mathcal{R}_{0} = \frac{\overline{\mathcal{R}}_{0} + z(\beta_{1}\pi_{2} + \beta_{2}\pi_{1}) + \sqrt{[\overline{\mathcal{R}}_{0} + z(\beta_{1}\pi_{2} + \beta_{2}\pi_{1})]^{2} - 4\beta_{1}\beta_{2}\mathbb{E}(T)z}}{2};$$
(15)

(ii) \mathcal{R}_0 has the following upper and lower bounds:

 $\overline{\mathcal{R}}_0 \leq \mathcal{R}_0 \leq \mathcal{R}_{01};$

(iii) \mathcal{R}_0 is decreasing with respect to $\phi(\lambda)$ and increasing with respect to z.

The proof of Lemma 3 can be found in the Appendix A.

Plots of the pgf $\phi(\lambda)$ for the distributions **A–C** are shown in Fig. 2. We observed that the order of the pgfs can be very different depending on the sign of λ , the smallest eigenvalue of the transition matrix D(12). By Lemma 3, $\phi(\lambda)$ can be used to compare the \mathcal{R}_0 values associated with these specific distributions. Denote the reproduction numbers corresponding to distributions **A–C** by \mathcal{R}_0^g , \mathcal{R}_0^{nb} , and \mathcal{R}_0^p , respectively. Fig. 2 suggests that these numbers follow a certain order based on the corresponding distributions. This finding is described in the following result.

Lemma 4. Let $\lambda = a + b - 1$ be the smaller eigenvalue of the Markov matrix *D*. Let $T \neq 0$. The reproduction numbers corresponding to the distributions *A*–*C* can be ordered as follows:

$$\begin{aligned} \mathcal{R}_{0}^{g} &\leq \mathcal{R}_{0}^{nb_{k}} \leq \mathcal{R}_{0}^{nb_{k+1}} \leq \mathcal{R}_{0}^{p} \quad \text{if } \lambda \in [0, 1), \\ \mathcal{R}_{0}^{p} &\leq \mathcal{R}_{0}^{nb_{k+1}} \leq \mathcal{R}_{0}^{nb_{k}} \leq \mathcal{R}_{0}^{g} \quad \text{if } \lambda \in (-1, 0]. \end{aligned}$$

$$Moreover,$$

$$(16)$$

nb n

$$\mathcal{R}_0^{\mathrm{nb}_k} \to \mathcal{R}_0^{\mathrm{p}} \text{ as } k \to \infty.$$

Equality is attained only if $\lambda = 0$ or k = 1.

The proof of Lemma 4 can be found in the Appendix A.

Remark. Lemma 4 clearly shows that the effect of the IP distribution on \mathcal{R}_0 depends on the sign of λ . This phenomenon is not observed in the continuous-time models, for which the value of \mathcal{R}_0 is (i) smaller for Exponential than for Gamma distribution (with shape parameter larger 1); and (ii) maximized with fixed duration for the IP [21]. The similarity between continuous and discrete models exists for $\lambda > 0$ because the pgf can be expressed in terms of the mgf

$$\phi(\lambda) = \mathbb{E}(\lambda^T) = \mathbb{E}(e^{T\log\lambda}).$$
(17)



Fig. 2. Plots of the pgf $\phi(\lambda) = \mathbb{E}(\lambda^T)$ for sGeom, sNegBinom and sPoisson distributions for $\lambda \in (-1, 0)$ (left) and $\lambda \in (0, 1)$ (right). In all cases, the mean infectious period is $\mathbb{E}(T) = 10.5.$

On the other hand, the above equality is no longer valid for $\lambda < 0$. A possible biological reason for this discrepancy between continuous and discrete models has not been identified. In practice, most models would assume that individuals are more likely to stay in their patch than to migrate to the other patch. This implies $a, b \ge 0.5$, and therefore $\lambda = a + b - 1 \ge 0$.

If $\lambda > 0$, sharper bounds than those given in Lemma 3 can be obtained for \mathcal{R}_0 , regardless of the distribution of *T*.

Lemma 5. Let $\lambda > 0$.

(i) An upper bound for \mathcal{R}_0 is given by

$$\begin{split} &\frac{1}{2} \left\{ \, \overline{\mathcal{R}}_0 + \frac{1 - \lambda^{\mathbb{E}^{(T)}}}{1 - \lambda} (\beta_1 \pi_2 + \beta_2 \pi_1) \right. \\ &+ \sqrt{\left[\overline{\mathcal{R}}_0 + \frac{1 - \lambda^{\mathbb{E}^{(T)}}}{1 - \lambda} (\beta_1 \pi_2 + \beta_2 \pi_1) \right]^2 - 4\beta_1 \beta_2 \mathbb{E}^{(T)} \frac{1 - \lambda^{\mathbb{E}^{(T)}}}{1 - \lambda}} \right] \end{split}$$

This value is attained when T has a constant distribution with fixed duration $\mathbb{E}(T)$.

(ii) If $Var(T) \leq \sigma^2$, a lower bound for \mathcal{R}_0 is given by

$$\frac{1}{2} [\overline{\mathcal{R}}_0 + \underline{z}(\beta_1 \pi_2 + \beta_2 \pi_1) + \sqrt{[\overline{\mathcal{R}}_0 + \underline{z}(\beta_1 \pi_2 + \beta_2 \pi_1)]^2 - 4\beta_1 \beta_2 \mathbb{E}(T)\underline{z}]},$$
where

where

$$\underline{z} = \frac{\mathbb{E}(T)^2 \left(1 - \lambda^{\frac{\mathbb{E}(T)^2 + \sigma^2}{\mathbb{E}(T)}}\right)}{\left[\mathbb{E}(T)^2 + \sigma^2\right](1 - \lambda)}.$$

This value is attained if T is the two point distribution

$$\underline{T} = \begin{cases} 0 & \text{with probability} \quad \frac{\sigma^2}{\mathbb{E}(T)^2 + \sigma^2} \\ \frac{\mathbb{E}(T)^2 + \sigma^2}{\mathbb{E}(T)} & \text{with probability} \quad \frac{\mathbb{E}(T)^2}{\mathbb{E}(T)^2 + \sigma^2} \end{cases}$$

The proof of Lemma 5 is included in the Appendix A.

Remark. Since our model is discrete, we consider random variable with support on the set $\{0, 1, ...\}$, thus if $\mathbb{E}(T)$ or $\frac{\mathbb{E}(T)^2 + \sigma^2}{\mathbb{E}(T)} \notin \mathbb{N}_0$ are not integers, then the upper and lower bound might not be attained.

3.3. Numerical results

Numerical simulations of the model with n = 2 subpopulations have been conducted. Let $S_i(t)$, $I_i(t)$, $R_i(t)$ denote the numbers of susceptible, infective, and recovered individuals, respectively, of the population *i* at time t ($i = 1, 2, t \in \mathbb{N}$). Initial populations $N_1(0)$ and $N_2(0)$

are chosen near the Markov equilibrium, i.e., $N_1(0) \approx \pi_1 N$, $N_2(0) \approx$ $\pi_2 N$. Recall that the total population size $N = N_1(t) + N_2(t)$ remains constant for all time. Assume $I_i(0) > 0$ for at least one sub-population *i*. To determine the number of individuals in each epidemiological classes at time t, we first run the epidemic process (updating the number of susceptible, infected, recovered), and then shuffle the population from one patch to the other according to the Markov matrix D(13). The epidemiological process is simulated using a similar approach as in [23]. Since the number of effective contacts per person in population *i* is $Poisson(\beta_i)$, the number of secondary infections is determined by $x(t) \sim \text{Poiss}(\beta_i I_i(t-1) \frac{S_i(t-1)}{N_i(t-1)}).$

If $T \sim sGeom(\gamma)$ (see distribution **A** in Section 3.2), then the probability that an infected individual recovers at time t is equal to γ . Let $x_i(t)$ and $v_i(t)$ denote the newly infected and newly recovered individuals at time t, respectively, in population i. Note that $y_i(t)$ is distributed as Binomial($I_i(t-1), \gamma$). Then

$$S_i(t_-) = S(t-1) - x(t), \quad I_i(t_-) = I_i(t-1) + x(t) - y(t),$$

$$R_i(t_-) = R_i(t-1) + y(t)$$

The notation t_{-} is used because of the following consideration. To obtain $S_i(t)$, $I_i(t)$, and $R_i(t)$ we must simulate the movement from patch *i* to patch *j*. Let $s_{i \rightarrow i}$ denote the number of susceptible individuals staying in patch i (i = 1, 2). Then, the number of susceptible individuals staying in patch 1, $s_{1\rightarrow 1}$, is distributed as Binomial($S_1(t_-), a$). Similarly $s_{2\rightarrow 2} \sim \text{Binomial}(S_2(t_-), b)$. Define $s_{1\rightarrow 2} = S_1(t_-) - s_{1\rightarrow 1}$ and $s_{2\to 1} = S_2(t_-) - s_{2\to 2}$. Note that

 $S_1(t) = s_{1 \to 1} + s_{2 \to 1}$ and $S_2(t) = s_{2 \to 2} + s_{1 \to 2}$.

In the same fashion $i_{i \rightarrow j}$ and $r_{i \rightarrow j}$ are defined. Then,

$$I_1(t) = i_{1 \to 1} + i_{2 \to 1}, \quad I_2(t) = i_{2 \to 2} + i_{1 \to 2},$$

 $R_1(t) = r_{1 \to 1} + r_{2 \to 1}, \quad R_2(t) = r_{2 \to 2} + r_{1 \to 2}.$

Based on these rules, numerical simulations have been conducted. A sample path of the simulated epidemic with sGeometric distribution is illustrated in Fig. 3. The set of parameter values used in this figure are $N_1(0) = 340$, $N_2(0) = 660$, $I_1(0) = I_2(0) = 1$, a = 0.8, b = 0.9 $\beta_1 = 0.27, \beta_2 = 0.15$ and $\mathbb{E}(T) = 10$, which produce $\mathcal{R}_0^{\text{geom}} \approx 1.96$. In this realization, the epidemic ended at around t = 250.

Taking advantage of the fact that a Negative Binomial random variable with parameters (k, η) (see **B** in Section 3.2) can be written as the sum of *k* Geometric random variable with parameter η , the infectious class I_i has been artificially subdivide into k = 5 subclasses. The above ideas were then used to generate an epidemic with this distribution for T.



Fig. 3. Sample path of an epidemic with $T \sim$ sGeom. Parameter values, $N_1(0) = 340$, $N_2(0) = 660$, $I_1(0) = I_2(0) = 1$, a = 0.8, b = 0.9, $\beta_1 = 0.27$, $\beta_2 = 0.15$ and $\mathbb{E}(T) = 10$, produce $\mathcal{R}_2^{\text{geom}} = 1.964408$.



Fig. 4. Probability mass function $\mathbb{P}(T = t)$ of three comparable distributions: sGeom $(\gamma = \frac{1}{10})$; sNegBinom $(k = 5, \eta = \frac{5}{14})$ and Uniform in $\{5, ..., 15\}$. All three distributions have mean equal to 10.

To complement the numeric results, the case $T \sim \text{Unif}(\{5, 6, ..., 15\})$ was considered (i.e. $\mathbb{P}(T = i) = \frac{1}{11}$ for $i \in \{5, 6, ..., 15\}$). This distribution was chosen to emphasize the fact that *any* distribution for *T* is allowed by our model. $T \sim \text{Unif}$ represents the absolutely lack of a priori information, other than recovery takes place 5–10 days after acquiring the disease. Fig. 4 shows the three *comparable* distributions for which simulations were performed.

The influence of the distribution of *T* on the final size \mathcal{F} and the duration of an epidemic \mathcal{D} can also be examined by comparing results from multiple paths. Figs. 5 and 6 show simulations of 50,000 observations for the models with $T \sim$ sGeom (i.e., the Geometric Distribution Model or GDM); $T \sim$ sNegBinom with shape parameter k = 5 (i.e., the Negative Binomial Distribution Model or NBDM); and $T \sim$ Unif {5, ..., 15} (i.e., the Uniform Distribution Model or UDM). Parameter values for these figures are the same as in Fig. 3. The corresponding basic reproduction numbers can be computed using (15) and the pgf

formulas provided in Section 3.2:

$$\mathcal{R}_0^{Geom} = 1.964408 < \mathcal{R}_0^{NegBin} = 1.977059 < \mathcal{R}_0^{Unif} = 1.98091. \tag{18}$$

In Fig. 5, the histograms show the overall distribution of \mathcal{F} . The large bin near zero (representing lower \mathcal{F} values) collect observations that can be cataloged as minor epidemics, whereas all other bins collect major epidemics. The average of \mathcal{F} , from smaller to larger is given by Geometric, NegBinomial and Uniform distribution. This confirms (18), which indicates that the Geom distribution is likely to predict a less severe epidemic than the predicted by NegBinom and Uniform. In particular, a much lower level of final epidemic size was predicted.

Fig. 6 shows the result of 50,000 simulations for the duration of the epidemic \mathcal{D} . The Geometric (left), Negative Binomial (middle) and Uniform (right) models are compared. Our observations confirm the fact that $\mathcal{R}_0^{\text{Geom}} < \mathcal{R}_0^{\text{nb}} < \mathcal{R}_0^{\text{unif}}$, indicating that epidemics with $T \sim$ Geom tend to be milder but longer than those with $T \sim$ NegBinom and $T \sim$ Unif.

3.4. Probability of minor and major epidemics

Recall that the Markov matrix *D* for n = 2 patches is given in (11). From Lemma 2

$$A(s_1, s_2) = \begin{bmatrix} e^{-\theta_1}a & e^{-\theta_1}(1-a) \\ e^{-\theta_2}(1-b) & e^{-\theta_2}b \end{bmatrix},$$

$$E(s_1, s_2) = \begin{bmatrix} e^{-\theta_1} \\ e^{-\theta_2} \end{bmatrix}, \quad \begin{array}{l} \theta_1 = \beta_1(1-s_1) \\ \theta_2 = \beta_2(1-s_2) \end{bmatrix},$$

$$G(s_1, s_2)^{tr} = \frac{G_1(s_1, s_2)}{G_1(s_1, s_2)} = \sum_{t=1}^{\infty} A(s_1, s_2)^{t-1} E(s_1, s_2) \mathbb{P}(T=t)$$



Fig. 5. Distribution of the final size \mathcal{F} obtained from 50,000 simulations from the GDM (left), the NBDM (middle) and UDM (right). $\mathcal{R}_{0}^{\text{Geom}} \approx 1.96$, $\mathcal{R}_{0}^{\text{NeBin}} \approx 1.97$ and $\mathcal{R}_{0}^{\text{Unif}} \approx 1.98$.



Fig. 6. Distribution of the epidemic duration $\mathcal D$ obtained from 50,000 observations for the GDM (left), the NBDM (middle) and UDM (right).

Table 1

Comparison of the probabilities of minor epidemic (extinction probability \mathbb{P}_0) and simulation results for different initial values $I_1(0)$ and $I_2(0)$. A sample path for which the final size is less than 10 was considered to be a minor epidemic.

	Initial value $(I_1(0), I_2(0))$	\mathbb{P}_0	Proportion from simulations	Error
	(1,0)	0.4426690	0.43962	0.003048985
Geometric	(0,1)	0.5324051	0.52236	0.010045121
	(1,1)	0.2356792	0.22546	0.010219235
	(1,0)	0.2815446	0.28798	-0.006435354
NegBinom	(0,1)	0.3728444	0.37072	0.002124375
	(1,1)	0.1049723	0.10308	0.001892338
	(1,0)	0.18068085	0.2353	-0.05461915
Uniform	(0,1)	0.25198173	0.31478	-0.06279827
	(1,1)	0.04552827	0.07218	-0.02665173

Although it is difficult to find an analytic expression for the solution of $G(s_1, s_2) = (s_1, s_2)$, numerical solutions can be obtained for a given distribution of *T* by substituting appropriate expressions for $\mathbb{P}(T = t)$ in the above equations. For example, for the three models GDM, NBDM and UDM (see Figs. 5 and 6), the extinction probabilities \mathbb{P}_0 (or probability of a minor epidemic) are obtained numerically using the fixed point approach. Results are listed in Table 1. These probabilities are given by $\mathbb{P}_0 = z_1^{I_1(0)} z_2^{I_2(0)}$, as defined in Eqs. (9) and (10). For each model, three pairs of initial conditions ($I_1(0), I_2(0)$) are considered.

To examine how good these approximations are, listed in Table 1 are the "empirical" probabilities of minor epidemic. These quantities have been determined by the proportion of observations that have total infections ≤ 10 (see Fig. 5). The last (Error) column shows the difference between the analytic value \mathbb{P}_0 and the value from model simulations. Our simulations suggest that \mathbb{P}_0 provides a very good approximation.

4. Discussion

In this paper, discrete-time stochastic epidemic models in a metapopulation setting were studied. Although some of the ideas and methods are adopted from [21], which deals with an analogous continuous-time model, we obtained new findings and results that are not present in continuous models. A particular new behavior that is absent in continuous models is that, in the two patch model, the effect of distributions of *T* on \mathcal{R}_0 depends critically on the sign of λ (the smaller eigenvalue of the Markov matrix *D*, which describes the movement between patches). The consideration of arbitrarily distributed infectious period *T* (random) in the discrete model is also a new feature that has not been studied previously. The results obtained for the general distribution also make it easier to compare model outcomes under different assumptions on the distribution of *T* on

model predictions regarding the final epidemic size, duration of an epidemic, and probability of major or minor epidemic (probability of disease extinction).

For the model with *n* populations and an arbitrary infectious period *T*, we derived the expression for \mathcal{R}_0 (Lemma 1) and the equation for the probability of disease extinction \mathbb{P}_0 (see (9) and (10)). These general results are applied to the case of n = 2 populations, from which an explicit formula for \mathcal{R}_0 was derived in terms of the pgf ϕ of *T*. More importantly, it was proved that \mathcal{R}_0 is a decreasing function of ϕ , which allows us to obtain an order relation among the \mathcal{R}_0 that is dependent on the distributions of T (including sGeometric; sNegative Binomial; sPoisson; and a discrete distribution with finite support, representing the case of empirical data). It was shown that, when $\lambda > 0$ the Geometric distribution gives the smallest reproduction number (\mathcal{R}_0^g) while the Poisson distribution gives the largest (\mathcal{R}_0^p) . However, when $\lambda < 0$, the order is reversed (see Lemma 3). In addition, upper and lower bounds for \mathcal{R}_0 were provided for the case $\lambda > 0$. Notice that, if individuals in population *i* are more likely to stay than to move to the other population, i.e., a, b > 0.5, then $\lambda > 0$ will be a more likely scenario.

Because our model includes several random factors, e.g., the infectious period *T* and the number of effective contacts β_i , some of the results are obtained by carrying out a large number of numerical simulations for the model with n = 2 populations. From these simulation results we can obtain insights into the effect of distributions of *T* on the final epidemic size \mathcal{F} , duration of an epidemic \mathcal{D} and probability of minor epidemic \mathbb{P}_0 (e.g., see Figs. 5 and 6). Traditionally, models with Geometric infectious period are preferred due to its tractability. However, our findings suggest that when the model with $T \sim$ Geom is compared with the model with $T \sim$ NegBinom and $T \sim$ Uniform, the GDM predicts a **milder** epidemic (when $\lambda > 0$). This is supported by our analytical (see (16) and (18)) and numerical results (see Figs. 5 and 6). From the numerical simulations we also observe that the GDM and UDM.

We have also derived a formula for the probability of disease extinction \mathbb{P}_0 based on the approximations by a branching process. Comparisons of the \mathbb{P}_0 value with the proportion of minor epidemics from simulations of the three models (GDM, NBDM and UDM) suggest that the formula for \mathbb{P}_0 provides very good approximations (see Table 1). From the results shown in Table 1 we also observe that the Geometric model predicts a higher (smaller) probability of minor (major) epidemic.

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Appendix A

This appendix includes the proofs of Lemmas 2–5.

Proof of Lemma 2. To simplify notation, let $\theta_j = \beta_j (1 - s_j)$. Then

$$X_i(t) = \theta_1 \zeta_{i1}(t) + \theta_2 \zeta_{i2}(t) + \dots + \theta_n \zeta_{in}(t).$$

Alternatively, $X_i(t) = \theta_i + \theta_{U_i(1)} + \dots + \theta_{U_i(t-1)}$. Thus, by conditional expectation

$$\begin{split} \mathbb{E}(e^{-X_{i}(t+1)}) &= \mathbb{E}[\mathbb{E}(e^{-X_{i}(t+1)}|U_{i}(1))] \\ &= \sum_{j=1}^{n} \mathbb{E}(e^{-X_{i}(t+1)}|U_{i}(1) = k)\mathbb{P}(U_{i}(1) = k) \\ &= \sum_{j=1}^{n} \mathbb{E}(e^{\theta_{i}+\theta_{k}+\dots+\theta_{U_{i}(t)}}|U_{i}(1) = k)\sigma_{ik} \\ &= \sum_{j=1}^{n} e^{\theta_{i}}\mathbb{E}(e^{-X_{k}(t)})\sigma_{ik} \end{split}$$

The last equality makes use of the stationary property of the Markov chain U_i .

For ease of notation, let *A* and *E* represent the matrices $A(\vec{s})$ and $E(\vec{s})$ in Lemma 2, this is

$$A = \begin{bmatrix} e^{-\theta_{1}}\sigma_{11} & e^{-\theta_{1}}\sigma_{12} & \cdots & e^{-\theta_{1}}\sigma_{1n} \\ e^{-\theta_{2}}\sigma_{21} & e^{-\theta_{2}}\sigma_{22} & \cdots & e^{-\theta_{2}}\sigma_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ e^{-\theta_{n}}\sigma_{n1} & e^{-\theta_{n}}\sigma_{n2} & \cdots & e^{-\theta_{n}}\sigma_{nn} \end{bmatrix}, \quad E = \begin{bmatrix} e^{-\theta_{1}} \\ e^{-\theta_{2}} \\ \vdots \\ e^{-\theta_{n}} \end{bmatrix}$$

It is easy to prove by induction that $(\mathbb{E}(e^{-X_1(t)}), \dots, \mathbb{E}(e^{-X_n(t)}))^{tr} = A^{t-1}E$. Clearly, for t = 1, $\mathbb{E}(e^{-X_i(1)}) = e^{-\theta_i}$ and $A^0E = E$. Now, assume the statement is true for t and prove for t + 1:

$$A^{t}E = A(A^{t-1}E) = A\begin{bmatrix} \mathbb{E}(e^{-X_{1}(t)}) \\ \mathbb{E}(e^{-X_{2}(t)}) \\ \vdots \\ \mathbb{E}(e^{-X_{n}(t)}) \end{bmatrix}$$
$$= \begin{bmatrix} \sum_{k=1}^{n} e^{-\theta_{1}} \sigma_{1k} \mathbb{E}(e^{-X_{k}(t)}) \\ \sum_{k=1}^{n} e^{-\theta_{2}} \sigma_{2k} \mathbb{E}(e^{-X_{k}(t)}) \\ \vdots \\ \sum_{k=1}^{n} e^{-\theta_{n}} \sigma_{nk} \mathbb{E}(e^{-X_{k}(t)}) \end{bmatrix} = \begin{bmatrix} \mathbb{E}(e^{-X_{1}(t+1)}) \\ \mathbb{E}(e^{-X_{2}(t+1)}) \\ \vdots \\ \mathbb{E}(e^{-X_{n}(t+1)}) \end{bmatrix}$$

From Eq. (9), the *i*th component of *G* is given by

$$G_i(\vec{s}) = \sum_{t=1}^{\infty} \mathbb{E}(e^{-X_i(t)})\mathbb{P}(T=t).$$

Thus, using the above equality, we obtain

$$G(\vec{s}) = (G_1(\vec{s}), \dots, G_n(\vec{s})) = \sum_{t=1}^{\infty} A^{t-1} E \mathbb{P}(T=t)$$

This completes the proof of Lemma 2.



Fig. 7. Plot of the characteristic polynomial $f_{Z_1}(x)$.

Proof of Lemma 3. The proof follows a similar approach presented in [21]. Let $z = \varphi(\lambda)$, and denote by

$$f_{z}(x) = [\mathcal{R}_{01}\pi_{1} + z\beta_{1}\pi_{2} - x][\mathcal{R}_{02}\pi_{2} + z\beta_{2}\pi_{1} - x] - (\mathbb{E}(T) - z)^{2}\beta_{1}\beta_{2}\pi_{1}\pi_{2}$$

the characteristic polynomial of M. Straightforward calculations yield

$$f_z(0) > 0, \quad f_z(\mathcal{R}_{02}) \le 0, \quad f_z(\mathcal{R}_0) \le 0, \quad \text{and} \quad f_z(\mathcal{R}_{01}) \ge 0$$

Therefore, $f_z(x)$ has two real roots and \mathcal{R}_0 , the dominant eigenvalue of M, is in the interval [$\overline{\mathcal{R}}_0, \mathcal{R}_{01}$], as illustrated in Fig. 7. To analyze the connection between the distribution of T and \mathcal{R}_0 , consider two random variables with different distributions but the same mean, i.e., $\mathbb{E}(T_1) = \mathbb{E}(T_2)$ (so that the two distributions are "comparable"). Let $z_i = \varphi(\lambda, T_i) = \frac{1-\mathbb{E}(\lambda^{T_i})}{1-\lambda}$. Through z_i , the two distributions may yield different reproduction numbers, which we denote by $\mathcal{R}_0^{T_1}$ and $\mathcal{R}_0^{T_2}$. Notice that $\mathcal{R}_{01}, \mathcal{R}_{02}$ and $\overline{\mathcal{R}}_0$ do not depend on z_i (see (14)). Assume that $z_1 \leq z_2$, then it can be verified that

$$\begin{split} f_{z_1}(\mathcal{R}_0^{T_2}) &= \frac{z_2 - z_1}{\mathbb{E}(T_1)} [\big(\mathcal{R}_{01} - \mathcal{R}_0^{T_2} \big) \big(\mathcal{R}_0^{T_2} - \mathcal{R}_{02} \big) + \mathcal{R}_0^{T_2} \big(\mathcal{R}_0^{T_2} - \overline{\mathcal{R}}_0 \big)] \\ &\geq 0. \end{split}$$

Thus, $f_{z_1}(\mathcal{R}_0^{T_2}) \ge f_{z_1}(\mathcal{R}_0^{T_1}) = 0$. Since $\overline{\mathcal{R}}_0 \le \mathcal{R}_0^{T_i} \le \mathcal{R}_{01}$ (i = 1, 2) and f is an increasing function on $(\overline{\mathcal{R}}_0, \mathcal{R}_{01})$, it follows that $\mathcal{R}_0^{T_1} \le \mathcal{R}_0^{T_2}$. A graphical representation of this argument is provided in Fig. 7. Finally, since $z_1 \le z_2$ if and only if $\mathbb{E}(\lambda^{T_2}) \le \mathbb{E}(\lambda^{T_1})$, we conclude that \mathcal{R}_0 is a decreasing (increasing) function of $\phi(\lambda)$ $(\varphi(\lambda))$. This completes the proof of Lemma 3.

Proof of Lemma 4. Let $-1 < \lambda < 1$. From the Binomial Theorem

$$\left(1 + \frac{\mathbb{E}(T) - \lambda[\mathbb{E}(T) - 1] - 1}{k}\right)^{k} \ge \mathbb{E}(T) - \lambda[\mathbb{E}(T) - 1]$$

This, combined with the fact that $\mathbb{E}(T) - \lambda[\mathbb{E}(T) - 1] \ge 1$ yield

$$\frac{1}{\mathbb{E}(T) - \lambda[\mathbb{E}(T) - 1]} \ge \left(\frac{k}{k + \mathbb{E}(T) - \lambda[\mathbb{E}(T) - 1] - 1}\right)^{k}$$

Since

$$\begin{pmatrix} \frac{k}{k + \mathbb{E}(T) - \lambda[\mathbb{E}(T) - 1] - 1} \end{pmatrix}^{k}$$

= $\left(1 + \frac{(1 - \lambda)[\mathbb{E}(T) - 1]}{k} \right)^{-k} \searrow e^{-(1 - \lambda)[\mathbb{E}(T) - 1]}$

as $k \to \infty$, we can conclude that $\phi_g(\lambda) \ge \phi_{nb_k}(\lambda) \ge \phi_{nb_{k+1}}(\lambda) \ge \phi_p(\lambda)$ if $\lambda \in [0, 1)$, and $\phi_g(\lambda) \le \phi_{nb_k}(\lambda) \le \phi_{nb_{k+1}}(\lambda) \le \phi_p(\lambda)$ if $\lambda \in (-1, 0]$.

Proof of Lemma 5. For the upper bound, by Jensen's inequality $\mathbb{E}(e^{T\log \lambda}) \ge e^{\mathbb{E}(T)\log \lambda}$. Therefore, for all comparable *T*, $\phi(\lambda) > \lambda^{\mathbb{E}(T)}$. Substitution of this value in (15) leads to the upper bound expression.

Table 2

De	fi	ni	iti	io	n	0	fs	V	m	b	ol	S	fr	e	າເ	ıe	n	tl	v	u	S	ec	t	in	tl	he	2	m	00	le	l a	na	alv	IS	is	and	t	si	mu	lat	io	ns	
								~																																			

Symbol	Definition
t	= 1, 2,, discrete time
п	Number of sub-populations or patches
N_i, N	Sizes of population <i>i</i> , $N = \sum_{i=1}^{n} N_i$
Т	Random variable for the infectious period
β_i	Number of effective contacts per unit of time in population <i>i</i> (Poisson)
σ_{ij}	Probability of moving from population <i>i</i> to population <i>j</i> per unit of time
D	$= (\sigma_{ij})$, Markov matrix of transitions between sub-populations
π_i	Stationary probability that an individual is in population <i>i</i> , $\pi_i N = N_i$
m _{ij}	Average number of offsprings (secondary infections) generated in population <i>j</i> by an individual originally from population <i>i</i> during the lifetime (entire IP)
Μ	$=(m_{ij})$, mean offspring matrix
\mathcal{R}_0	$= \rho(M)$, the basic reproduction number (spectral radius of M)
η_{ij}	Random number of offsprings (secondary infections) generated in population <i>j</i> by an individual originally from population <i>i</i>
$G(\vec{s})$	$= \mathbb{E}(\prod_{j=1}^{n} s_{j}^{\eta_{j}}), \vec{s} = (s_{1}, \dots, s_{n}), \text{pgf of the offspring distribution}$
$\phi(s)$	$= \mathbb{E}(s^T)$, pgf of the IP distribution T
$\varphi(s)$	$= (1 - \phi(s))/(1 - s)$
GDM	Geometric Distribution Model, the model with $T \sim \text{Geom}(\gamma)$
PDM	Poisson Distribution Model, the model with $T \sim \text{Poisson}(\kappa)$
NBDM	Negative Binomial Distribution Model, the model with $T \sim$ NegBinom(k , η)
${\mathcal F}$	Final epidemic size
\mathcal{D}	Duration of an epidemic
\mathbb{P}_0	Extinction probability of an epidemic or probability of a minor epidemic
For the mod	the left with $n = 2$ populations
а	$= \sigma_{11}$, probability of staying in population 1 per time unit
b	$= \sigma_{22}$, probability of staying in population 2 per time unit
π_1, π_2	Stationary probability of being in population 1, 2,
	$\pi_2 = (1-a)/(2-a-b)$
λ	= a + b - 1, the smaller eigenvalue of D
\mathcal{R}_{0i}	$= \beta_i \mathbb{E}(T)$, the basic reproduction number for population $i = 1, 2$
$\overline{\mathcal{R}}_0$	$=\pi_1 \mathcal{R}_{01} + \pi_2 \mathcal{R}_{02}$, weighted average of \mathcal{R}_{01} and \mathcal{R}_{02}

For the lower bound, let $\phi(\lambda) = \mathbb{E}(\lambda^{\underline{T}})$ then it is easy to check that

$$\operatorname{Var}(\underline{T}) = \frac{\mathbb{E}(T)^2 \sigma^2}{\mathbb{E}(T)^2 + \sigma^2} + \left[\frac{\mathbb{E}(T)^2 + \sigma^2}{\mathbb{E}(T)} - \mathbb{E}(T)\right]^2 \frac{\mathbb{E}(T)^2}{\mathbb{E}(T)^2 + \sigma^2} = \sigma^2,$$

$$\underline{\phi}(\lambda) = \mathbb{E}\left(\lambda^{\underline{T}}\right) = \frac{\sigma^2}{\mathbb{E}(T)^2 + \sigma^2} + \frac{\mathbb{E}(T)^2}{\mathbb{E}(T)^2 + \sigma^2} \lambda^{\frac{\mathbb{E}(T)^2 + \sigma^2}{\mathbb{E}(T)}}.$$

It is known that the mgf of a non-negative random variable with variance σ^2 is maximized by <u>*T*</u> (see Theorem 1 in [29]). From (17) <u>*T*</u> also maximizes the pgf of all comparable infectious periods *T*. Moreover,

$$g(\sigma) = \frac{\sigma^2}{\mathbb{E}(T)^2 + \sigma^2} + \frac{\mathbb{E}(T)^2}{\mathbb{E}(T)^2 + \sigma^2} \lambda^{\frac{\mathbb{E}(T)^2 + \sigma^2}{\mathbb{E}(T)}}$$

is an increasing function of σ . Consider g as a function of $z = \sigma^2$. Then

$$g(z) = \frac{z + \mathbb{E}(T)^2 \lambda^{\frac{\mathbb{E}(T)^2 + z}{\mathbb{E}(T)}}}{\mathbb{E}(T)^2 + z} \quad \text{and} \quad g'(z) = \frac{\mathbb{E}(T)g_1(t)}{(\mathbb{E}(T)^2 + z)^2},$$

where $g_1(z) = \mathbb{E}(T) + [\log(\lambda)\mathbb{E}(T)^2 + \log(\lambda)z - \mathbb{E}(T)]\lambda^{\frac{\mathbb{E}(T)^2 + z}{\mathbb{E}(T)}}$. Clearly, the sign of g'(z) is determined by $g_1(z)$. Since $e^{-\mathbb{E}(T)\log(\lambda)} \ge -\mathbb{E}(T)\log(\lambda) + 1$, then

$$1 \ge [-\mathbb{E}(T)\log(\lambda) + 1]\lambda^{\mathbb{E}(T)} \quad \Rightarrow \quad 1 + [\mathbb{E}(T)\log(\lambda) - 1]\lambda^{\mathbb{E}(T)} \ge 0.$$

Therefore $g_1(0) = \mathbb{E}(T)[1 + [\log(\lambda)\mathbb{E}(T) - 1]\lambda^{\mathbb{E}(T)}] \ge 0$. Since

$$g_{1}'(z) = [\log(\lambda)\mathbb{E}(T)^{2} + \log(\lambda)z - \mathbb{E}(T)] \\ \times \frac{\log(\lambda)}{\mathbb{E}(T)}\lambda^{\frac{\mathbb{E}(T)^{2}+z}{\mathbb{E}(T)}} + \log(\lambda)\lambda^{\frac{\mathbb{E}(T)^{2}+z}{\mathbb{E}(T)}} \\ = \left[\log(\lambda)^{2}\mathbb{E}(T) + \frac{z\log(\lambda)^{2}}{\mathbb{E}(T)}\right]\lambda^{\frac{\mathbb{E}(T)^{2}+z}{\mathbb{E}(T)}} \ge 0$$

it follows that $g_1(z)$ is an increasing function of z. Thus, $g_1(z) \ge g_1(0) \ge 0 \quad \forall z \ge 0$; and, $g'(z) \ge 0 \quad \forall z \ge 0$. Therefore, conclude $g(\sigma_1) \le g(\sigma_2) \quad \forall \sigma_1 \le \sigma_2$. This implies that, if T satisfies $\operatorname{Var}(T) \le \sigma^2$, then its pgf is no greater than ϕ for any $\lambda \in [0, 1]$. Since \mathcal{R}_0 is a decreasing function with respect to the pgf ϕ , we conclude that \mathcal{R}_0 is minimized when $T = \underline{T}$. Finally, substituting the expression $\underline{z} = \underline{\varphi}(\lambda) = \frac{1 - \underline{\phi}(\lambda)}{1 - \lambda}$ for z in (15) we obtain the expression for the lower bound.

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