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DISCRETE EPIDEMIC MODELS

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Dedicated to Horst R. Thieme on the Occasion of his 60th Birthday

Abstract. The mathematical theory of single outbreak epidemic models really began with the work of Kermack and Mackendrick about 8 decades ago. This gave a simple answer to the long-standing question of why epidemics woould appear suddenly and then disappear just as suddenly without having infected an entire population. Therefore it seemed natural to expect that theoreticians would immediately proceed to expand this mathematical framework both because the need to handle recurrent single infectious disease outbreaks has always been a priority for public health officials and because theoreticians often try to push the limits of exiting theories. However, the expansion of the theory via the inclusion of refined epidemiological classifications or through the incorporation of categories that are essential for the evaluation of intervention strategies, in the context of ongoing epidemic outbreaks, did not materialize. It was the global threat posed by SARS in 2003 that caused theoreticians to expand the Kermack-McKendrick single-outbreak framework. Most recently, efforts to connect theoretical work to data have exploded as attempts to deal with the threat of emergent and re-emergent diseases including the most recent H1N1 influenza pandemic, have marched to the forefront of our global priorities. Since data are collected and/or reported over discrete units of time, developing single outbreak models that fit collected data naturally is relevant. In this note, we introduce a discrete-epidemic framework and highlight, through our analyses, the similarities between single-outbreak comparable classical continuous-time epidemic models and the discrete-time models introduced in this note. The emphasis is on comparisons driven by expressions for the final epidemic size.

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1. **Introduction.** The study of compartmental epidemic models, in the context of single-epidemic outbreaks, began with the work of Kermack and McKendrick [23]. Traditionally, mathematical epidemiology has been driven by a continuous-time perspective in deterministic or stochastic settings [2, 5, 7, 10, 20]. Kermack and McKendrick formulated their single-outbreak epidemic model in terms of age of infection, and established a final size relation. Applications or generalizations of Kermack and McKendrick's work were not carried out systematically for decades. Efforts to understand, manage and predict the impact of the 2003 SARS epidemic [14, 19, 28] also generated additional theoretical work on single epidemic outbreak models [9]. The analytical emphasis, as in the original work of Kermack and McKendrick, has been on the computation of expressions for the final epidemic size. Computation of a general expression for the final size relation, in the context of multiple modeling frameworks, requires computation of the basic reproduction number. Some aids for this computation can be found in [9, 15, 27, 29].

Most of the models studied have been continuous in part because these are more tractable mathematically. A good reason for studying discrete models is that data are collected at discrete times and hence it may be easier to compare data with the output of a discrete model. Furthermore, the numerical exploration of discrete-time epidemic models is rather straightforward and therefore can be easily implemented by non-mathematicians, an advantage in the public health world. There has been some study of discrete disease transmission models with births and natural deaths [1, 3, 4, 11, 12, 13, 24], but to our knowledge the only discrete epidemic study is [30]. The overall goal of this note is to contrast in setting of epidemiological interest the methods and approaches used to compute the final epidemic relation in continuous and discrete-time settings. The age of infection approach does not lend itself to discrete models but it is possible to give discrete versions of staged progression and differential infectivity epidemic models as well. Hence, the specific purpose of this note is twofold, namely, to extend the calculation of the basic reproduction number and the final size of an epidemic to general continuous staged progression and differential infectivity models for both discrete and continuous time models [21, 22]. We develop this theory, showing how to calculate the basic reproduction number and the final size of an epidemic. We assume throughout that there are no disease, deaths, so that the total population size remains constant.When disease deaths are significant then the final size relation is given by an inequality, that is, we can not be calculate the final size of an epidemic exactly. However, if the disease death rate is small, the final size relation is an approximate equality, and may be used to obtain good estimates of the final size.

The rest of this paper is organized as follows: Section 2 focuses on the study of continuous staged-progression, single outbreak, epidemic models, with the primary result being the computation of the final size relationship; the impact of treatment, at multiple levels, in the context of the model of Section 2 is explored and a final size relation is computed in terms of the control reproductive number in Section 3; Section 4 introduces a discrete-time epidemic model, that includes discrete stage progression, and computes the final epidemic size relation as a function of the basic reproductive number; Section 5 focuses on treatment and the computation of a final size relationship as a function of the control reproductive number; In Section 6, we collect some observations and conclusions.

2. **The continuous staged progression epidemic.** We consider an epidemic with progression from S through k infected stages $I_1, I_2, \cdots, I_k$. We assume that in stage i the relative infectivity is ε_i, the distribution of stay in the stage is given by P_i with $P_i(0) = 1, \int_0^\infty P(t)dt < \infty$, and P_i monotone non-decreasing. There are no disease deaths and the total population size N is constant. We assume initial conditions

$$S(0) = 0, \quad I_1(0) = I_0, \quad I_2(0) = I_3(0) = \cdots = I_k(0) = 0.$$

The total infectivity is given by

$$\varphi(t) = \sum_{i=1}^{k} \varepsilon_i I_i(t),$$

and

$$S'(t) = -\beta S(t)\varphi(t). \tag{1}$$

We let $B_i(t)$ denote the input to stage i at time t, so that

$$I_i(t) = \int_0^t B_i(s)P_i(t-s)ds, \quad i = 2, 3, \cdots, k. \tag{2}$$

Then

$$I_i'(t) = B_i(t) + \int_0^t B_i(s)P_i'(t-s)ds,$$

and this implies

$$B_{i+1}(t) = -\int_0^t B_i(s)P_i'(t-s)ds,$$

from which we calculate

$$\begin{aligned}
\int_0^\infty B_{i+1}(t)dt &= -\int_0^\infty \int_0^t B_i(s)P_i'(t-s)dsdt \\
&= \int_0^\infty B_i(s) \int_s^\infty B_i(s)P_i'(t-s)dtds \\
&= \int_0^\infty B_i(s)ds, \quad i = 2, 3, \cdots, k.
\end{aligned}$$

Next,

$$I_1(t) = I_0P_1(t) + \int_0^t [-S'(s)]P_1(t-s)ds. \tag{3}$$

The epidemic model consists of the equations (1), (2), and (3).

Differentiation of (3) gives

$$I_1'(t) = I_0P_1'(t) - S'(t) + \int_0^t [-S'(s)]P_1'(t-s)ds,$$

and the input $B_2(t)$ to stage 2 is

$$-I_0P_1'(t) - \int_0^t [-S'(s)]P_1'(t-s)ds.$$

Thus

$$\begin{aligned}\int_0^\infty B_2(t)dt &= I_0 - \int_0^\infty \int_0^t [-S'(s)]p_1'(t-s)dsdt \\ &= I_0 - \int_0^\infty [-S'(s)] \int_s^\infty P_1'(t-s)dtds \\ &= I_0 + S_0 - S_\infty = N - S_\infty.\end{aligned}$$

We now see that

$$\int_0^\infty B_i(s)ds = N - S_\infty, \quad i = 2, 3, \cdots, k.$$

Integration of (2) gives

$$\begin{aligned}\int_0^\infty I_i(t)dt &= \int_0^\infty \int_0^t B_i(s)P_i(t-s)dsdt \\ &= \int_0^\infty B_i(s) \int_s^\infty P_i(t-s)dtds \\ &= (N - S_\infty) \int_0^\infty P_i(u)du.\end{aligned} \tag{4}$$

Integration of (3) gives

$$\begin{aligned}\int_0^\infty I_1(t) &= I_0 \int_0^\infty P_1(t)dt + \int_0^\infty \int_0^t [-S'(s)]P_1(t-s)dsdt \\ &= I_0 \int_0^\infty P_1(t)dt + [S_0 - S_\infty] \int_0^\infty P_1(t)dt \\ &= [N - S_\infty] \int_0^\infty P_1(t)dt.\end{aligned} \tag{5}$$

Combining (2) and (3) we have

$$\int_0^\infty I_i(t)dt = [N - S_\infty] \int_0^\infty P_i(t)dt, \quad i = 1, 2, \cdots, k.$$

Integration of (1) gives

$$\begin{aligned}\ln \frac{S_0}{S_\infty} &= \beta \int_0^\infty \varphi(t)dt \\ &= \beta \sum_{i=1}^n \varepsilon_i \int_0^\infty I_i(t)dt \\ &= \beta[N - S_\infty] \sum_{i=1}^k \varepsilon_i \int_0^\infty P_i(t)dt.\end{aligned}$$

Since

$$\mathcal{R}_0 = \beta N \sum_{i=1}^k \varepsilon_i \int_0^\infty P_i(t)dt,$$

this takes the familiar final size relation form

$$\ln \frac{S_0}{S_\infty} = \mathcal{R}_0 \left[1 - \frac{S_\infty}{N}\right]. \tag{6}$$

3. **Treatment models.** We consider two alternatives for treatment. The first is treatment at the beginning of a stage, with a specified fraction of individuals entering the stage being selected for treatment and moving to a treatment compartment. The second is treatment throughout a stage, with a rate of transfer from the untreated compartment to a treatment compartment.

3.1. **Treatment at the beginning of a stage.** To the model given by (1), (2), (3) we add treatment at the beginning of each stage. By this, we mean that a fraction p_1 of members of S who are infected go to a treatment compartment T_1 while the remaining fraction q_1 of newly infected members go to I_1. There is a sequence $T_1, T_2, \cdots, T_n$ of treated compartments with relative infectivity δ_i and period distribution Q_i in T_i. Treated members continue through the treatment stages. In addition, of the members leaving an infected stage I_i, a fraction p_i enters treatment in T_{i+1} while the remaining fraction q_i continues to I_{i+1}. We let m_i denote the fraction of infected members who go through the stage I_i and n_i the fraction of infected members who go through the stage T_i. Then

$$\begin{aligned} m_1 &= q_1, m_2 = q_1 q_2, \cdots, m_k = q_1 q_2 \cdots q_k \\ n_1 &= p_1, p_2 = p_1 + q_1 p_2, \cdots, n_k = p_1 + q_1 p_2 + \cdots + q_1 q_2 \cdots q_{k-1} p_k. \end{aligned} \tag{7}$$

The total infectivity is now

$$\varphi(t) = \sum_{i=1}^{k} [\varepsilon_i I_i(t) + \delta_1 T_i(t)],$$

and we have

$$\begin{aligned} \int_0^\infty I_i(t)dt &= m_i(N - S_\infty) \int_0^\infty P_i(u)du \\ \int_0^\infty T_i(t)dt &= n_i(N - S_\infty) \int_0^\infty Q_i(u)du, \end{aligned} \tag{8}$$

so that

$$\mathcal{R}_c = \beta N \sum_{i=1}^{k} [m_i \varepsilon_i \int_0^\infty P_i(t)dt + n_i \delta_i \int_0^\infty Q_i(t)dt].$$

We use $\mathcal{R}_c$ in place of $\mathcal{R}_0$ to indicate that this is a control reproduction number. The final size relation takes the expected form

$$\ln \frac{S_0}{S_\infty} = \mathcal{R}_c \left[1 - \frac{S_\infty}{N}\right]. \tag{9}$$

The calculation of the control reproduction number takes a simpler form if treatment takes place in only one stage, say at the beginning of stage j. Then $p_1 = 0$ if $i \neq j$, and

$$\begin{aligned} m_i &= 1, \quad (i < j), \quad m_i = 1 - p_j, \quad (i \geq j) \\ n_i &= 0, \quad (i < j), \quad n_i = q_{j-1} p_j, \quad (i \geq j). \end{aligned}$$

It would be more realistic to consider a model in which members are moved from an infective class I_i to a treated class T_i rather than being designated for treatment at the beginning of the stageI_i. However, the mathematical analysis of this situation is more complicated.

3.2. **Treatment throughout a stage.** We now model treatment by moving members from I_i at proportional rate γ_i to a treatment compartment T_i with relative infectivity δ_i and duration distribution Q_i. We let $C_i(s)$ denote the input to the treatment stage T_i at time s; this input includes output from the previous treatment stage T_{i-1} if $i > 1$ as well as the input from I_i. Thus, we replace the model (1), (2), (3) by a new model containing S, I_i, T_i. The total infectivity is now given by

$$\varphi(t) = \sum_{i=1}^{k} [\varepsilon_i I_i(t) + \delta_i T_i(t)].$$

The equation (1) is unchanged, but now

$$I_1(t) = I_0 P_1 e^{-\gamma_1 t)} + \int_0^t [-S'(s)] P_1(t-s) e^{-\gamma_1 (t-s)} ds. \tag{10}$$

Differentiation of (10) gives

$$I_1'(t) = I_0 P_1'(t) e^{-\gamma_1 t} - S'(t) - \gamma_1 I_1(t) + \int_0^t [-S'(s)] P_1'(t-s) e^{-\gamma_1 (t-s)} ds,$$

and the input $B_2(t)$ to stage 2 is

$$-I_0 P_1'(t) e^{-\gamma_1 t} - \int_0^t [-S'(s)] P_1'(t-s) e^{-\gamma_1 (t-s)} ds.$$

With the aid of integration by parts, we see that

$$\begin{aligned} \int_0^\infty B_2(t) dt &= I_0[1 - \gamma_1 \int_0^\infty P_1(t) e^{-\gamma_1 t} dt] + (S_0 - S_\infty)[1 - \gamma_1 \int_0^\infty P_1(t) e^{-\gamma_1 t} dt] \\ &= [N - S_\infty][1 - \gamma_1 \int_0^\infty P_1(t) e^{-\gamma_1 t} dt]. \end{aligned} \tag{11}$$

In place of (2) we now have

$$I_i(t) = \int_0^t B_i(s) P_i(t-s) e^{-\gamma_i (t-s)} ds, \quad i = 2, 3, \cdots, k. \tag{12}$$

Then

$$I_i'(t) = B_i(t) - \gamma_i I_i(t) + \int_0^t B_i(s) P_i'(t-s) e^{-\gamma_i (t-s)} ds,$$

and this implies

$$B_{i+1}(t) = -\int_0^t B_i(s) P_i'(t-s) e^{-\gamma_i (t-s)} ds,$$

from which we calculate

$$\begin{aligned} \int_0^\infty B_{i+1}(t) dt &= -\int_0^\infty \int_0^t B_i(s) P_i'(t-s) e^{-\gamma_i (t-s)} ds dt \\ &= \int_0^\infty B_i(s) \int_s^\infty B_i(s) P_i'(t-s) e^{-\gamma_i (t-s)} dt ds \\ &= \int_0^\infty B_i(s) ds \int_0^\infty P_i'(u) e^{-\gamma_i u} du \\ &= \int_0^\infty B_i(s) ds [1 - \gamma_i \int_0^\infty P_i(u) e^{-\gamma_i u} du], \quad i = 2, 3, \cdots, k. \end{aligned}$$

Integration by parts gives

$$-\int_0^\infty P_i'(u)e^{-\gamma_i u}du = 1-\gamma_i\int_0^\infty P_i(u)e^{-\gamma_i u}du,$$

and we define

$$\Gamma_i = 1-\gamma_i\int_0^\infty P_i(u)e^{-\gamma_i u}du,$$

so that

$$\int_0^\infty B_{i+1}(t)dt = \Gamma_i\int_0^\infty B_i(s)ds.$$

Using (11) we see by induction that

$$\int_0^\infty B_i(t)dt = \Gamma_{i-1}\Gamma_{i-2}\cdots\Gamma_1(N-S_\infty). \tag{13}$$

The equation

$$I_1(t) = I_0e^{-\gamma_1 t}P_1(t) + \int_0^t [-S'(s)]P_1(t-s)e^{-\gamma_1(t-s)}ds$$

leads to

$$\int_0^\infty I_1(t)dt = [N-S_\infty]\int_0^\infty P_1(t)e^{-\gamma_1 t}dt.$$

A similar calculation leads to

$$\int_0^\infty I_i(t)dt = \int_0^\infty B_i(t)dt\int_0^\infty e^{-\gamma_i t}P_i(t)dt, \quad (i\geq 2).$$

Because of (13) we have

$$\int_0^\infty I_i(t)dt = \int_0^\infty e^{-\gamma_i t}P_i(t)dt\cdot\Gamma_{i-1}\Gamma_{i-2}\cdots\Gamma_1[N-S_\infty], \quad (i\geq 2). \tag{14}$$

Next, we write

$$T_i(t) = \int_0^t C_i(s)Q_i(t-s)ds. \tag{15}$$

The epidemic model consists of the equations (1), (10), (12), and (15).

Differentiation gives

$$T_i'(t) = C_i(t) + \int_0^t C_i(s)Q_i'(t-s)ds.$$

The output from T_i to T_{i+1} at time t is $-\int_0^t C_i(s)Q_i'(t-s)ds$ and thus

$$\begin{aligned} C_1(t) &= \gamma_1 I_1(t) \\ C_{i+1}(t) &= \gamma_{i+1}I_{i+1}(t) - \int_0^t C_i(s)Q_i'(t-s)ds, \quad i>1. \end{aligned}$$

Thus

$$\begin{aligned} \int_0^\infty C_1(t) &= \gamma_1\int_0^\infty I_1(t)dt = \gamma_1\Gamma_1[N-S_\infty] \\ \int_0^\infty C_{i+1}(t)dt &= \gamma_{i+1}\int_0^\infty I_{i+1}(t)dt - \int_0^\infty\int_0^t C_i(s)Q_i'(t-s)dsdt \\ &= \gamma_{i+1}\int_0^\infty I_{i+1}(t)dt + \int_0^\infty C_i(s)ds, \\ &= \gamma_{i+1}\Gamma_{i+1}\Gamma_i\cdots\Gamma_1[N-S_\infty] + \int_0^\infty C_i(s)ds, \quad (i>0). \end{aligned}$$

We now obtain

$$\begin{aligned}\int_0^\infty T_i(t)dt &= \int_0^\infty C_i(s)Q_i(t-s)dsdt \\ &= \int_0^\infty C_i(s)ds\int_0^\infty Q_i(u)du \\ &= [N-S_\infty]\int_0^\infty Q_i(u)du[\gamma_i\Gamma_i\Gamma_{i-1}+\cdots+\gamma_1\Gamma_1].\end{aligned}$$

It is convenient to write

$$\Lambda_i = \gamma_i\Gamma_i\Gamma_{i-1}\cdots\Gamma_1+\gamma_{i-1}\Gamma_{i-1}\cdots\Gamma_1+\cdots+\gamma_1\Gamma_1],$$

so that

$$\int_0^\infty T_i(t)dt = \Lambda_i\int_0^\infty Q_i(u)du[N-S_\infty]. \tag{16}$$

Combination of (14) and (16) gives the control reproduction number

$$\mathcal{R}_c = \beta N\sum_{i=1}^{k}\left[\varepsilon_i\Gamma_{i-1}\Gamma_{i-2}\cdots\Gamma_1\int_0^\infty e^{-\gamma_i t}P_i(t)dt+\delta_i\Lambda_i\int_0^\infty Q_i(t)dt\right], \tag{17}$$

and the same final size relation (9).

The results take a much simpler form if treatment is confined to a single stage. Suppose that $\gamma_i = 0$ if $i \neq j$. Then $\Gamma_i = 1$ if $i \neq j$ and

$$\begin{aligned}\int_0^\infty I_i(t)dt &= [N-S_\infty], \quad (i<j), \quad \int_0^\infty I_i(t)dt = \Gamma_j[N-S_\infty], \quad (i\geq j) \qquad (18)\\ \int_0^\infty T_i(t)dt &= 0, \quad (i<j), \quad \int_0^\infty T_j(t)dt = \gamma_j\Gamma_j\int_0^\infty Q_i(t)dt[N-S_\infty], \quad (i\geq j).\end{aligned}$$

This leads to

$$\mathcal{R}_c = \beta N\sum_{i=1}^{j-1}\left[\varepsilon_i\int_0^\infty P_i(t)dt+\sum_{i=j}\left[\varepsilon_i\Gamma_j\int_0^\infty e^{-\gamma_i t}P_i(t)dt+\delta_i\gamma_j\Gamma_j\int_0^\infty Q_i(t)dt\right].$$

4. **Discrete epidemic models.** We begin with the simplest discrete epidemic model, the discrete analogue of the simple continuous epidemic model

$$\begin{aligned}S' &= -\beta SI\\ I' &= \beta SI-\alpha I.\end{aligned}$$

We define the function

$$G(S,I) = e^{-\beta I},$$

and let

$$G_k = G(S_k, I_k).$$

The discrete model is

$$\begin{aligned}S_{k+1} &= S_kG_k \qquad (19)\\ I_{k+1} &= S_k[1-G_k]+\sigma I_k.\end{aligned}$$

In this model G_k is the fraction of susceptibles at stage k who remain susceptible to stage $(k+1)$, and σ is the fraction of infectives at each stage who remain infective to the next stage. It is clear that

$$0 \leq G_k \leq 1, \quad 0 \leq \sigma \leq 1.$$

Since $G_k \leq 1$, S_k is a decreasing sequence and has a limit $S_\infty \geq 0$ as $t \to \infty$. Since $\sigma \leq 1, S_{k+1} + I_{k+1}$ is a decreasing sequence and has a limit $S_\infty + I_\infty$ as $t \to \infty$. Also, the difference of successive terms in this sequence $-(1-\sigma)I_k$ tends to zero, and this shows that $I_\infty = 0$.

In order to show, as for the continuous epidemic model, that $S_\infty > 0$, we proceed as follows. It is easy to show by induction that

$$\begin{aligned} S_{k+1} &= S_0 G_0 G_1 \cdots G_k \\ \ln \frac{S_{k+1}}{S_0} &= \sum_{j=0}^{k} G_j. \end{aligned} \tag{20}$$

Because $\ln G_j = -\beta I_j$, this gives

$$\ln \frac{S_0}{S_{k+1}} = \beta \sum_{j=0}^{k} I_j.$$

We let $k \to \infty$, and

$$\ln \frac{S_0}{S_\infty} = \beta \sum_{j=0}^{\infty} I_j. \tag{21}$$

From (19) we have

$$S_k - S_{k+1} = I_{k+1} - \sigma I_k,$$

and summing over k we have

$$S_0 - S_\infty = (1-\sigma) \sum_{j=0}^{\infty} I_j - I_0. \tag{22}$$

Using $N = S_0 + I_0$ and combining (21) and (22), we have

$$\ln \frac{S_0}{S_\infty} = \frac{\beta N}{1-\sigma} \left[1 - \frac{S_\infty}{N} \right].$$

Because the mean infective period is

$$1 + \sigma + \sigma^2 + \cdots = \frac{1}{1-\sigma},$$

the basic reproduction number is

$$\mathcal{R}_0 = \frac{\beta N}{1-\sigma},$$

the final size relation becomes

$$\ln \frac{S_0}{S_\infty} = \mathcal{R}_0 \left[1 - \frac{S_\infty}{N} \right]. \tag{23}$$

4.1. **The discrete staged progression epidemic.** Let $I_j^{(i)}$ denote the fraction of infected in stage i $(i = 1, 2, \cdots, k)$ at time j. We assume initial conditions

$$I_0^{(1)} = I_0, \quad I_0^{(2)} = I_0^{(3)} = \cdots = I_0^{(k)} = 0, \quad S_0 + I_0 = N.$$

Consider the system

$$\begin{aligned} S_{j+1} &= S_j G_j \\ I_{j+1}^{(1)} &= S_j (1 - G_j) + \sigma_1 I_j^{(1)} \\ I_{j+1}^{(i)} &= (1 - \sigma_{i-1}) I_j^{(i-1)} + \sigma_i I_j^{(i)}, \quad i = 2, \cdots, k, \ j \geq 0, \end{aligned} \tag{24}$$

where

$$G_j = e^{-\beta \sum_{i=1}^{k} \epsilon_i I_j^{(i)}}. \tag{25}$$

From the S equation in (24) we have

$$S_{n+1} = S_n G_n = S_{n-1} G_{n-1} G_n = \cdots = S_0 \prod_{j=1}^{n} G_j.$$

Thus,

$$\ln S_{n+1} = \ln S_0 + \sum_{j=1}^{n} \ln G_j. \tag{26}$$

From (25) we have

$$\begin{aligned} \sum_{j=1}^{n} \ln G_j &= -\beta \sum_{j=1}^{n} \sum_{i=1}^{k} \epsilon_i I_j^{(i)} \\ &= -\beta \sum_{i=1}^{k} \epsilon_i \sum_{j=1}^{n} I_j^{(i)}. \end{aligned} \tag{27}$$

Thus, (26) can be written as

$$\ln S_{n+1} = \ln S_0 - \beta \sum_{i=1}^{k} \epsilon_i \sum_{j=1}^{n} I_j^{(i)}.$$

We let $n \to \infty$ and obtain

$$\ln \frac{S_0}{S_\infty} = \beta \sum_{i=1}^{k} \epsilon_i \sum_{j=1}^{\infty} I_j^{(i)}. \tag{28}$$

From the $I^{(1)}$ equation in (24) and using $S_j G_j = S_{j+1}$, we have

$$I_{j+1}^{(1)} - \sigma_1 I_j^{(1)} = S_j - S_{j+1},$$

and taking summation on both sides:

$$\sum_{j=0}^{n} I_{j+1}^{(1)} - \sigma_1 \sum_{j=0}^{n} I_j^{(1)} = \sum_{j=0}^{n} S_j - \sum_{j=0}^{n} S_{j+1},$$

$\Rightarrow$

$$I_{n+1}^{(1)} + \sum_{j=0}^{n} I_j^{(1)} - I_0 - \sigma_1 \sum_{j=0}^{n} I_j^{(1)} = \sum_{j=0}^{n} S_j - \sum_{j=0}^{n} S_j - S_{n+1} + S_0.$$

Assume that $I_{n+1}^{(1)} \to 0$ as $n \to \infty$. Taking the limit $n \to \infty$ in the above equation and using $S_0 + I_0 = N$we have

$$(1 - \sigma_1) \sum_{j=0}^{\infty} I_j^{(1)} = N - S_\infty,$$

or

$$\sum_{j=0}^{\infty} I_j^{(1)} = \frac{1}{1 - \sigma_1} \big(N - S_\infty\big). \tag{29}$$

Using the $I^{(i)}$ equation in (24) for $i \geq 2$, and noticing that $I_0^{(i)} = 0$, we can get

$$\big(1-\sigma_i\big)\sum_{j=0}^{\infty} I_j^{(i)} = \big(1-\sigma_{i-1}\big)\sum_{j=0}^{\infty} I_j^{(i-1)}, \quad i \geq 2. \tag{30}$$

From (29) and (30) we have

$$\sum_{j=0}^{\infty} I_j^{(i)} = \frac{1}{1-\sigma_i}\big(N - S_\infty\big), \quad i \geq 1. \tag{31}$$

Substituting (31) into (28) we get

$$\ln \frac{S_0}{S_\infty} = \beta \sum_{i=1}^{k} \frac{\epsilon_i (N - S_\infty)}{1-\sigma_i}.$$

Since the reproduction number is

$$\mathcal{R}_0 = \beta \sum_{i=1}^{k} \frac{\epsilon_i N}{1-\sigma_i}, \tag{32}$$

we obtain

$$\ln \frac{S_0}{S_\infty} = \mathcal{R}_0 \left[1 - \frac{S_\infty}{N}\right]. \tag{33}$$

5. **Discrete treatment models.** For discrete epidemic models we think of events occurring only at discrete times, and the selection of members for treatment occurs only at the beginning of a stage.

Let $I_j^{(i)}$ and $T_j^{(i)}$ denote the numbers of infected and treated, individuals respectively, in stage i $(i = 1, 2, \cdots, k)$ at time j. Let σ_i^I denote the probability that an infected individual in the $I^{(i)}$ stage continues on to the next stage, either treated or untreated, and let σ_i^T denote the probability that an individual in the $T^{(i)}$ stage continues on to the next treated stage.

In addition, as in the continuous case, of the members leaving an infected stage $I_j^{(i)}$, a fraction p_i enters treatment in $T_{j+1}^{(i+1)}$ while the remaining fraction q_i continues to I_{i+1}. We let m_i denote the fraction of infected members who go through the stage I_i and n_i the fraction of infected members who go through the stage T_i. Then, as in the continuous case,

$$\begin{aligned} m_1 &= q_1, m_2 = q_1 q_2, \cdots, m_k = q_1 q_2 \cdots q_k \\ n_1 &= p_1, p_2 = p_1 + q_1 p_2, \cdots, n_k = p_1 + q_1 p_2 + \cdots + q_1 q_2 \cdots q_{k-1} p_k. \end{aligned} \tag{34}$$

We use initial conditions

$$I_0^{(1)}(0) = q_1 I_0, \quad T_0^{(1)}(0) = p_1 I_0, \; I_0^{(i)}(0) = T_0^{(i)}(0) = 0, \; i \geq 2, \quad S_0 + I_0 = N.$$

The treatment system is

$$\begin{aligned}
S_{j+1} &= S_j G_j,\\
I_{j+1}^{(1)} &= q_1 S_j(1-G_j) + \sigma_1^I I_j^{(1)},\\
T_{j+1}^{(1)} &= p_1 S_j(1-G_j) + \sigma_1^T T_j^{(1)},\\
I_{j+1}^{(i)} &= q_i(1-\sigma_{i-1}^I) I_j^{(i-1)} + \sigma_i^I \eta_i I_j^{(i)},\\
T_{j+1}^{(i)} &= p_i(1-\sigma_{i-1}^I) I_j^{(i-1)} + (1-\sigma_{i-1}^T) T_j^{(i-1)} + \sigma_i^T T_j^{(i)},\\
&\qquad\qquad i = 2,\cdots,k, \quad j \geq 0,
\end{aligned} \tag{35}$$

with

$$G_j = e^{-\beta \sum_{i=1}^{k} \left(\epsilon_i I_j^{(i)} + \delta_i T_j^{(i)}\right)}.$$

From the S equation in (35) and similarly to the case of no treatment we can obtain

$$\ln \frac{S_0}{S_\infty} = \beta \sum_{i=1}^{k} \Big(\epsilon_i \sum_{j=1}^{\infty} I_j^{(i)} + \delta_i \sum_{j=1}^{\infty} T_j^{(i)} \Big). \tag{36}$$

Using the $I^{(1)}$ equation in (35) we have (assuming again that $I_n^{(i)} \to 0$ as $n \to \infty$)

$$(1-\sigma_1^I) \sum_{j=0}^{\infty} I_j^{(1)} = q_1 \big(N - S_\infty\big). \tag{37}$$

Using the $I^{(i)}$ equation in (35) we have

$$(1-\sigma_i^I) \sum_{j=0}^{\infty} I_j^{(i)} = q_i \big(1-\sigma_{i-1}^I\big) \sum_{j=0}^{\infty} I_j^{(i-1)}, \quad i \geq 2,$$

which leads to

$$(1-\sigma_i^I) \sum_{j=0}^{\infty} I_j^{(i)} = q_i q_{i-1} \cdots q_2 (1-\sigma_1^I) \sum_{j=0}^{\infty} I_j^{(1)}, \quad i \geq 2. \tag{38}$$

Using (37) and $m_i = q_i q_{i-1} \cdots q_1$ (with $m_0 = 1$) we rewrite (38) as

$$(1-\sigma_i^I) \sum_{j=0}^{\infty} I_j^{(i)} = m_i (N - S_\infty), \quad i \geq 2. \tag{39}$$

Using the $T^{(1)}$ equation in (35) we have

$$(1-\sigma_1^T) \sum_{j=0}^{\infty} T_j^{(1)} = p_1 (N - S_\infty). \tag{40}$$

Using the $T^{(i)}$ equation in (35) we have

$$(1-\sigma_i^T) \sum_{j=0}^{\infty} T_j^{(i)} = (1-\sigma_{i-1}^T) \sum_{j=0}^{\infty} T_j^{(i-1)} + p_i (1-\sigma_{i-1}^I) \sum_{j=0}^{\infty} I_j^{(i-1)}, \quad i \geq 2,$$

which leads to

$$\begin{aligned}
(1-\sigma_i^T)\sum_{j=0}^{\infty} T_j^{(i)} &= (1-\sigma_{i-2}^T)\sum_{j=0}^{\infty} T_j^{(i-2)} + p_{i-1}(1-\sigma_{i-2}^I)\sum_{j=0}^{\infty} I_j^{(i-2)} \\
&\quad + p_i(1-\sigma_{i-1}^I)\sum_{j=0}^{\infty} I_j^{(i-1)} \\
&= \cdots\cdots \\
&= (1-\sigma_1^T)\sum_{j=0}^{\infty} T_j^{(1)} + \sum_{l=2}^{i}\Big[p_l(1-\sigma_{l-1}^I)\sum_{j=0}^{\infty} I_j^{(l-1)}\Big] \\
\text{(from (39), (40))} \quad &= p_1(N-S_\infty) + \sum_{l=2}^{i}\Big[p_l m_{l-1}(N-S_\infty)\Big] \\
&= \big(N-S_\infty\big)\sum_{l=1}^{i} p_l m_{l-1}, \quad i \geq 2.
\end{aligned}$$

Thus, using $n_i = \sum_{l=1}^{i} p_l m_{l-1}$ we have

$$\sum_{j=0}^{\infty} T_j^{(i)} = \frac{n_i(N-S_\infty)}{1-\sigma_i^T}, \quad i \geq 2. \tag{41}$$

Substituting (39) and (41) into (36) we get

$$\ln\frac{S_0}{S_\infty} = \beta\sum_{i=1}^{k}\Big[\frac{\epsilon_i m_i}{1-\sigma_i^I} + \frac{\delta_i n_i}{1-\sigma_i^T}\Big]\big(N-S_\infty\big). \tag{42}$$

Let

$$\mathcal{R}_c = \beta N\sum_{i=1}^{k}\Big[\frac{\epsilon_i m_i}{1-\sigma_i^I} + \frac{\delta_i n_i}{1-\sigma_i^T}\Big], \tag{43}$$

then the equation (42) becomes

$$\ln\frac{S_0}{S_\infty} = \mathcal{R}_c\left[1-\frac{S_\infty}{N}\right]. \tag{44}$$

The calculation of the control reproduction number takes a simpler form if treatment takes place in only one stage, say at the beginning of stage j. Then $p_1 = 0$ if $i \neq j$, and

$$\begin{aligned}
m_i &= 1, \quad (i<j), \quad m_i = 1-p_j, \quad (i \geq j) \\
n_i &= 0, \quad (i<j), \quad n_i = q_{j-1}p_j, \quad (i \geq j).
\end{aligned}$$

6. **Conclusions.** The SARS epidemic of 2003 brought to our attention the importance of developing theory that would allow us to test the impact of intervention policies in the context of single-epidemic outbreaks. Theoreticians had been 'distracted' from this important task putting emphasis on the study of the long-term (asymptotic) dynamics of epidemic models (models that include vital dynamics) for which there is a rich mathematical theory. Hence, the theoretical emphasis had been on the study of endemic behavior or on the identification of mechanisms that would generate 'non-typical' long-term dynamics, like oscillations. Furthermore,

the exploration of the impact of control measures had as its driving goal the elimination or eradication of a disease via long-term policies that focus primarily on the evaluation of vaccination or education long-term policies [20]. The SARS epidemic [14, 19, 28], fears of the avian flu [6, 16, 17, 18, 25, 26] and the most recent H1N1 pandemic have brought to the forefront the importance of having a theory that allow us for the exploration of measures that can contain, in real time, single epidemic outbreaks [6, 8, 16, 17, 18, 25, 26]

In this note, we present elements of this theory in the context of discrete and continuous-time single outbreak models with some degree of epidemiological heterogeneity. Specifically, we have extended the simple continuous epidemic model to include staged progression models and have developed the analogous results for discrete epidemic models. The basic results on reproduction numbers have analogues for discrete models, and the final size relations discrete models for discrete models are identical to those for continuous models. However, important and obvious challenges remain. The most critical has to do with finding a theory that manages to deal with single epidemic outbreaks in the context of meta-populations. In other words, dealing with realistic levels of heterogeneity, particularly those driven by the movement of people between different environments or communities or incorporating the role of behavior in single-outbreak models has yet to be carried out.

REFERENCES

[1] L. J. S. Allen, *Some discrete-time SI, SIR, and SIS epidemic models*, Math. Biosci., **124** (1994), 83–105.

[2] L. J. S Allen, "An Introduction to Mathematical Biology," Prentice-Hall, 2007.

[3] L. J. S. Allen and A. M. Burgin, *Comparison of deterministic and stochastic SIS and SIR models in discrete time*, Math. Biosci., **163** (2000), 1–33.

[4] L. J. S. Allen, M. A. Jones and C. F. Martin, *A discrete-time model with vaccination for a measles epidemic*, Math. Biosci., **105** (1991), 111–131.

[5] R. M. Anderson and R. M. May, "Infectious Diseases of Humans," Oxford Science Publications, Oxford, 1991.

[6] J. Arino, F. Brauer, P. van den Driessche, J. Watmough and J. Wu, *Simple models for containment of a pandemic*, J. Roy. Soc. Interface, **3** (2006), 453–457.

[7] N. T. J. Bailey, "The Mathematical Theory of Infectious Diseases," Hafner, New York, second ed., 1975.

[8] L. M. A. Bettencourt, R. M. Ribeiro, G.Chowell, T. Lant and C. Castillo- Chavez, *Towards real time epidemiology: Data assimilation, modeling and anomaly detection of health surveillance data streams*, in "Intelligence and security informatics: Biosurveillance" (G.D. Zeng, K. Komatsu, C. Lynch,Eds.), Proceedings of the 2nd NSF Workshop, Biosurveillance, Lecture Notes in Computer Science, New Brunswick, NJ Springer- Verlag (2007), 79–90.

[9] F. Brauer, *Age-of-infection and the final size relation*, Math. Biosc. and Eng., **5** (2008), 681–690.

[10] F. Brauer and C. Castillo-Chavez, "Mathematical Models in Population Biology and Epidemiology," Springer-Verlag, 2001.

[11] C. Castillo-Chavez and A-A. Yakubu, *Dispersal, disease and life-history evolution*, Math. Biosci., **173** (2001), 35–53.

[12] C. Castillo-Chavez and A-A. Yakubu, *Discrete-time S-I-S models with complex dynamics*, Nonlinear Analysis, **47** (2001), 4753–4762.

[13] C. Castillo-Chavez and A-A. Yakubu, *Discrete-time S-I-S models with simple and complex population dynamics*, in "Mathematical Approaches for Emerging and Reemerging Infectious Diseases" (eds., C. Castillo-Chavez, et al.), Springer-Verlag, IMA, **125** (2001), 153–163.

[14] G. Chowell, P. W. Fenimore, M. A. Castillo - Garsow and C. Castillo - Chavez, *SARS outbreaks in Ontario, Hong Kong, and Singapore: the role of diagnosis and isolation as a control mechanism*, J. Theor. Biol., **224** (2003), 1–8.

[15] Z. Feng, *Final and peak epidemic sizes for SEIR models with quarantine and isolation*, Math. Biosc. and Eng., **4** (2007), 675–686.
[16] N. M. Ferguson, D. A. T. Cummings, S. Cauchemez, C. Fraser, S. Riley, A. Meeyai, S. Iamsirithaworn and D. S. Burke, *Strategies for containing an emerging influenza pandemic in Southeast Asia*, Nature, **437** (2005), 209–214.
[17] N. M. Ferguson, D. A. T. Cummings, C. Fraser, J. C. Cajka, P. C. Cooley and D. S. Burke, *Strategies for mitigating an influenza pandemic*, Nature, **442** (2006), 448–452.
[18] T. C. Germann, K. Kadau, I. M. Longini and C. A. Macken, *Mitigation strategies for pandemic influenza in the United States*, Proc. Nat. Acad. Sci., **103** (2006), 5935–5940.
[19] A. Gumel, S. Ruan, T. Day, J. Watmough, P. van den Driessche, F. Brauer, D. Gabrielson, C. Bowman, M. E. Alexander, S. Ardal, J. Wu and B. M. Sahai, *Modeling strategies for controlling SARS outbreaks based on Toronto, Hong Kong, Singapore and Beijing experience*, Proc. Roy. Soc. London, **271** (2004), 2223–2232.
[20] H. W. Hethcote, *The mathematics of infectious diseases*, SIAM Review, **42** (2000), 599–653,
[21] J. M. Hyman, J. Li and E. A. Stanley, *The differential infectivity and staged progression models for the transmission of HIV*, Math. Biosci., **155** (1999), 77–109.
[22] J. M. Hyman and J. Li, *Infection-age structured epidemic models with behavior change or treatment*, J. Biol. Dyn., **1** (2007), 109–131.
[23] W. O. Kermack and A. G. McKendrick, *A contribution to the mathematical theory of epidemics*, Proc. R. Soc. London, **115** (1927), 700–721.
[24] J. Li, Z. Ma and F. Brauer, *Global analysis of discrete-time SI and SIS epidemic models*, Math. Biosc. and Eng., **4** (2007), 699–710.
[25] I. M. Longini, M. E. Halloran, A. Nizam and Y. Yang, *Containing pandemic influenza with antiviral agents*, Am. J. Epidem., **159** (2004), 623–633.
[26] I. M. Longini, A. Nizam, S. Xu, K. Ungchusak, W. Hanshaoworakul, D. T. Cummings and M. E. Halloran, *Containing pandemic influenza at the source*, Science, **309** (2004), 623–633.
[27] J. Ma and D. J. D. Earn, *Generality of the final size formula for an epidemic of a newly invading infectious disease*, Bull. Math. Biol., **68** (2006), 679–702.
[28] S. Riley, C. Fraser, C. A. Donnelly, A. C. Ghani, L. J. Abu-Raddad, A. J. Hedley, G. M. Leung, L-M Ho, T-H Lam, T.Q. Thach, P. Chau, K-P Chan, S-V Lo, P-Y Leung, T. Tsang, W. Ho, K-H Lee, E. M. C. Lau, N. M. Ferguson and R. M. Anderson, *Transmission dynamics of the etiological agent of SARS in Hong Kong: Impact of public health interventions*, Science, **300** (2003), 1961–1966.
[29] C. K. Yang and F. Brauer, *Calculation of $\mathcal{R}_0$ for age-of-infection models*, Math. Biosc. and Eng., **5** (2008), 585–599.
[30] Y. Zhou, Z. Ma and F. Brauer, *A discrete epidemic model for SARS transmission and control in China*, Math. and Computer Modelling, **40** (2004), 1491–1506.

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