Global analysis of an SEIR model with varying population size and vaccination

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ABSTRACT

An SEIR model with varying population size and vaccination strategy is investigated. Three threshold parameters $\mathscr{R}_0, \widehat{\mathscr{R}}_0, \overline{\mathscr{R}}_0$ and $\widetilde{\mathscr{R}}_0$ are obtained to govern the disease eradication, which involve the total number of infectives and their proportion in the population. Parameter conditions on the uniform persistence, the global stability of the disease – "free" equilibrium and the "endemic" equilibrium are derived. The global dynamics of model in population size are studied. The correlations of the two systems in terms of disease eradication, endemicity and disease explosion are summarized and compared. We conjecture that substantially low product of vaccination rate and low vaccine efficacy may lead to complicated dynamics for the system in question.

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1. Introduction

Mathematical modeling for disease transmission in host population is of great practical value in predicting and controlling disease spread (West Nile virus in North America 1990s, Avian influenza worldwide 2000s, SARS in Asia 2003, etc.). The battle between infectious diseases and humans was heavily lopsided for much of the history. Since the pioneering work of Edward Jenner (a doctor, who worked in Gloucestershire, UK, noticed that individuals who had contracted cowpox rarely caught smallpox) on smallpox [1], the process of protecting individuals from infection by vaccination has become routine, with substantial historical success in reducing both morbidity and mortality (see [2,3] and references cited therein). In this paper, we will incorporate a vaccination strategy for disease control into a single host population.

Typically, after the initial infection, the host remains in a latent stage for a period of time before becoming infectious. For some diseases, the latent period is neither short nor negligible comparing with the infectious period (scarlet fever: 1–2 days versus 14–21 days [4]; measles: 4–12 days versus 17–31 days [5]). Distinguished by the evolution history of disease, the heterogeneous population is partitioned into four homogeneous classes: the susceptible $S(t)$, the exposed (in the latent period) $E(t)$, the infective $I(t)$, and the recovered $R(t)$. The total number of population $N(t)$ is denoted by $N(t) = S(t) + E(t) + I(t) + R(t)$, where $N(t)$ is assumed to vary with time since individuals enter and leave the population either through migration, demographics or the disease-induced death, which imbalances the inflows and outflows of a given population. The disease transmission flow is depicted in Fig. 1.

Here the disease is assumed to transmit horizontally, which can occur either by direct contact (licking, touching, biting), or indirect contact (vectors or fomites) with no physical contact. All the offsprings at birth are assumed susceptible to the disease (Cholera, Polio and Hepatitis A are of this case).

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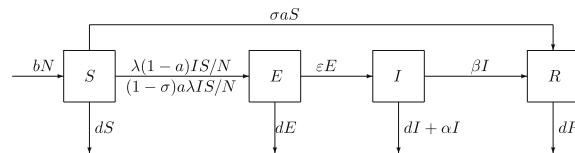 E-mail address: sunc@cc.umanitoba.ca (C. Sun).

Fig. 1. A schematic representation of the flow of individuals between epidemiological class.

Parameters b and d are the inflow rate (including birth and immigration) and outflow rate (including natural death and emigration), respectively. And α is the constant rate of disease-related death. The proportionate mixing incidence rate is $\lambda IS/N$, i.e., standard incidence, where λ is the effective per capita contact rate of infectious individuals, and I/N is the proportion of contacts between susceptibles and infectives, that is, random mixing is assumed. We assume that susceptible individuals are vaccinated at a constant per capita rate $a(0 \leqslant a < 1)$ (i.e., vaccine coverage rate). Due to the partial efficiency of the vaccine, only $\sigma(0 \leqslant \sigma \leqslant 1)$ fraction of the vaccinated susceptibles goes to the recovered class (i.e., σ is the vaccine efficacy). The remained $1 - \sigma$ fraction of the vaccinated susceptibles has no immunity at all and goes to the exposed class after infected by contact with the infectives. When $\sigma = 0$, it means the vaccine has no effect at all, and when $\sigma = 1$, the vaccine is perfectly effective. The parameter ε is the constant rate, at which the exposed individuals become infectious. and $1/\varepsilon$ is then the mean latent period. In the limit when $\varepsilon \to \infty$, the latent period is negligible, and the SEIR model can reduce to an SIR model (see [2,6,7]). Parameter β is the constant rate, at which the infectious individuals recover with acquire permanent immunity. Hence, there is no transfer from class S. R back to class $1/\beta$ is the mean infectious period. When $\beta = 0$, the mean infectious period goes to infinity, which implies that there is no recovery from the disease. The SEIR model then reduces to an SEI model (for example, HIV [8,9]). All the parameters (except the non-negative a, σ) here are assumed positive.

Using these definitions, assumptions and Fig. 1, we derive the following general SEIR model with vaccination and varying population size in a homogeneously mixing population.

$$
\begin{aligned}
S' &= bN - \lambda(1-a)IS/N - (1-\sigma)a\lambda IS/N - (\sigma a + d)S, \\
E' &= \lambda(1-a)IS/N + (1-\sigma)a\lambda IS/N - (d + \varepsilon)E, \\
I' &= \varepsilon E - (\alpha + \beta + d)I, \\
R' &= \sigma aS + \beta I - dR,
\end{aligned}
\tag{1}
$$

where the derivative d/dt is denoted by $'$.

Moreover, the differential equation of total population size $N(t)$ takes the form:

$$
N' = (b - d)N - \alpha I,
\tag{2}
$$

which is derived by adding the four equations in (1).

The global stability of an SEIR model with nonlinear incidence rates is studied by Sun et al. [10]. Feng [11] give out the final and peak epidemic sizes for SEIR models with quarantine and isolation. Li and Wang [12] systematically analyze the global dynamics of the SEIR model with constant recruitment, and with disease vertical transmission and incorporating perfect vaccination strategy, respectively. Arino et al. [13] consider the vaccine efficacy and waning in an SIRS model and present the occurrence of backward bifurcation leading to bi-stability. The latent time delay is incorporated into the SEIR model by Yan and Liu [14]. All the models above are with constant population size. Busenberg–van den Driessche [15], and Li et al. [16] investigate an SIRS model and an SEIR model with varying population size, respectively. As far as we know, this paper is very novel in analyzing the SEIR model with varying population size and vaccination strategy. The paper is organized in the following manner: We give some well-posed preliminary results and the stability properties of disease-"free" equilibrium of the model in Section 2. Section 3 devotes to the uniform persistence, the existence, local and global stability of the "endemic" equilibrium for the reduced proportional system. In Section 4, we determine the dynamic behaviors of original population model, and obtain the correlation between the original and the reduced models from the perspective of epidemiology. The paper ends up with a discussion.

Remark 1. We have to point out here that there have two distinct concepts of disease eradication and persistence which involve the total number of infectives and their proportion in the population. The quotation marks in disease-"free" and "endemic" only refer to the latter, and however, it can not guarantee the same outcomes happening to the total number of infectives.

2. Disease "eradication"

2.1. Preliminary results

In the situation that the total population size $N(t)$ is not constant, it is often necessary to consider the proportions of individuals in four epidemiological classes, namely,

$$s = S/N, \quad e = E/N, \quad i = I/N, \quad r = R/N.$$

It is easy to verify that s, e, i and r satisfy the following system of differential equations

$$
\begin{aligned}
s' &= b - (\sigma a + b)s - (1 - a\sigma)\lambda is + \alpha is, \\
e' &= (1 - a\sigma)\lambda is - (b + \varepsilon)e + \alpha ei, \\
i' &= \varepsilon e - (\alpha + \beta + b)i + \alpha i^2, \\
r' &= \sigma as + \beta i - br + \alpha ir
\end{aligned}
\tag{3}
$$

with subject to the restriction $s + e + i + r = 1$. It notices that the variable r does not appear in the first three equations of (3). We can first study the reduced system

$$
\begin{aligned}
s' &= b - (\sigma a + b)s - (1 - a\sigma)\lambda is + \alpha is, \\
e' &= (1 - a\alpha)\lambda is - (b + \varepsilon)e + \alpha ei, \\
i' &= \varepsilon e - (\alpha + \beta + b)i + \alpha i^2,
\end{aligned}
\tag{4}
$$

and determine r from $r = 1 - s - e - i$ or from $r' = as + \beta i - br + \alpha ir$.

The feasible region of (4) is

$$\Delta := \{(s, e, i) \in \mathbb{R}_+^3 \,|\, 0 \leqslant s + e + i \leqslant 1\}, \tag{5}$$

which can be verified positively invariant (i.e., given non-negative initial values in Δ, all solutions to (4) have non-negative components and stay in Δ for $t \geqslant 0$) and globally attracting in $\mathbb{R}_+^3$ with respect to (4). Therefore, we restrict our attention to the dynamics of (4) in Δ. The boundary and the interior of Δ are denoted by $\partial\Delta$ and $\mathit{\Delta}$, respectively.

2.2. Disease-"free" equilibrium (DFE)

There are two distinct ways of considering a disease as being eradicated in a population with varying size. The stricter way requires that the total number of the infected $E(t) + I(t) \to 0$, while a weaker requirement is that the proportion sum $e(t) + i(t) \to 0$ (see details in [17]). We are thus inspired to seek the conditions for the existence and stability of the disease-"free" equilibrium (DFE) $P_0(s_0, 0, 0)$ and the "endemic" proportion equilibrium $P^*(s^*, e^*, i^*)$.

Clearly, $P_0(b/(\sigma a + b), 0, 0) \in \Delta$ is the DFE of (4), which exists for all positive parameters. The Jacobian matrix of (4) at an arbitrary point $P(s, e, i)$ takes the form:

$$
J(P) = \begin{pmatrix}
-(\sigma a + b) - (1 - a\sigma)\lambda i + \alpha i & 0 & -(1 - a\sigma)\lambda s + \alpha s \\
(1 - a\sigma)\lambda i & -(b + \varepsilon) + \alpha i & (1 - a\sigma)\lambda s + \alpha e \\
0 & \varepsilon & -(\alpha + \beta + b) + 2\alpha i
\end{pmatrix}.
\tag{6}
$$

To analyze the stability of DFE, we calculate the characteristic equation of $J(P)$ at $P = P_0$ as follows:

$$
(\bar{\lambda} + \sigma a + b)\left(\bar{\lambda}^2 + (\alpha + \beta + \varepsilon + 2b)\bar{\lambda} + (b + \varepsilon)(\alpha + \beta + b) - \frac{b\varepsilon\lambda(1 - a\sigma)}{\sigma a + b}\right) = 0.
\tag{7}
$$

The stability of P_0 is equivalent to all eigenvalues of (7) being with negative real parts, which can be guaranteed by

$$\mathscr{R}_0 := \frac{b\varepsilon\lambda(1 - a\sigma)}{(b + \varepsilon)(\sigma a + b)(\alpha + \beta + b)} < 1. \tag{8}$$

Here $\mathscr{R}_0$ is the epidemiological threshold parameter. Consequently, the DFE is locally asymptotically stable if $\mathscr{R}_0 < 1$.

2.3. Global stability of the DFE

In this sub-section, we show that the parameter restrictions of local stability of the DFE guarantee its global stability. Here we define another threshold parameter

$$\widehat{\mathscr{R}}_0 = \frac{\epsilon\lambda(1 - a\sigma)}{(\varepsilon + b)(\alpha + \beta + b)}.$$

It notices that $\widehat{\mathscr{R}}_0 < 1$ guarantees $\mathscr{R}_0 < 1$, but the vice versa is not true.

Theorem 2.1. *The DFE $P_0(b/(\sigma a + b), 0, 0)$ of (4) is globally asymptotically stable in Δ if $\widehat{\mathscr{R}}_0 \leqslant 1$; it is unstable if $\mathscr{R}_0 > 1$. In the latter case, the solutions of (4) starting sufficiently close to P_0 in Δ move away from P_0, except those starting on the invariant s-axis which approach P_0 along this axis.*

Proof. We prove the global stability of P_0 by constructing a suitable Lyapunov function $L_1 = \varepsilon e + (\varepsilon + b)i$. Differentiating L_1 along (4) obtains that

$$L_1'|_{(4)} = \varepsilon[(1-a\sigma)\lambda is - (\varepsilon+b)e + \alpha ei] + (\varepsilon+b)[\varepsilon e - (\alpha+\beta+b)i + \alpha i^2]$$
$$= \varepsilon\lambda(1-a\sigma)is + \varepsilon\alpha ei - (\varepsilon+b)(\alpha+\beta+b)i + \alpha(\varepsilon+b)i^2$$
$$= i[\varepsilon\lambda(1-a\sigma)s - (\varepsilon+b)(\alpha+\beta+b) + \varepsilon\alpha e + \alpha(\varepsilon+b)i] \tag{9}$$

The maximum value of (9) in Δ is achieved at the extremal points: $A_1(0,0,0)$, $A_2(1,0,0)$, $A_3(0,1,0)$ and $A_4(0,0,1)$. It is easy to verify that at these four points, $L_1'|_{(4)} \leqslant 0$ when $\mathcal{R}_0 \leqslant 1$. (9) becomes an equality, i.e., $L_1'|_{(4)} = 0$ if $i = 0$ or $\widehat{\mathcal{R}}_0 = 1$. The maximum invariant set in $\{(s,e,i) \in \Delta | L_1'|_{(4)} = 0\}$ is the singleton $\{P_0\}$. By LaSalle's Invariance Principle ([18], Chapter 2, Theorem 6.4), the DFE P_0 is globally asymptotically stable when $\widehat{\mathcal{R}}_0 \leqslant 1$.

If $\mathcal{R}_0 > 1$, we define $L_2 = \varepsilon e + (\varepsilon+b)i$. Then

$$L_2'|_{(4)} = \varepsilon[(1-a\sigma)\lambda is - (\varepsilon+b)e + \alpha ei] + (\varepsilon+b)[\varepsilon e - (\alpha+\beta+b)i + \alpha i^2]$$
$$= \varepsilon(1-a\sigma)\lambda is + \varepsilon\alpha ei - (\varepsilon+b)(\alpha+\beta+b)i + \alpha(\varepsilon+b)i^2$$
$$= i[\varepsilon(1-a\sigma)\lambda s - (\varepsilon+b)(\alpha+\beta+b) + \varepsilon\alpha e + \alpha(\varepsilon+b)i]. \tag{10}$$

Observe that $L_2'|_{(4)} > 0$ for s sufficiently close to $b/(\sigma a + b)$ except when $e = i = 0$. Solutions starting sufficiently close to P_0 leave a neighborhood of P_0 except those on the invariant s-axis, where (4) reduces to $s' = b - (\sigma a + b)s$ and thus $s(t) \to b/(\sigma a + b)$ as $t \to \infty$, completing the proof. $\square$

It points out here that the unstable property of DFE P_0 when $\mathcal{R}_0 > 1$ can also be proved by the eigenvalue analysis of (7). The threshold parameters $\mathcal{R}_0$ and $\widehat{\mathcal{R}}_0$ govern whether the infected fractions (i.e., $e(t)$, $i(t)$) vanish in time locally and globally, respectively. Reducing R_0 to values less than unity can "eradicate" disease with a small magnitude. However, when $\widehat{\mathcal{R}}_0$ is adjusted less than or equal to unity, the disease can be "eradicated" even with a large magnitude. $\mathcal{R}_0$ and $\widehat{\mathcal{R}}_0$ can be interpreted epidemiologically as the disease transmission by contacts being strengthened through both the increase of susceptible inflow and the increase of the infectious individuals coming from the exposed ones, while weakened through the outflow of the infected and the susceptible fractions. It is found that both $\mathcal{R}_0$ and $\widehat{\mathcal{R}}_0$ are decreasing functions of σ. $\mathcal{R}_0$ increases with a if $\sigma < b/(1+b)$ and decreases with a if $\sigma > b/(1+b)$, which imply that the high vaccination rate with low vaccine efficacy is likely to make the disease "persistent". $\widehat{\mathcal{R}}_0$ decreases as the vaccination rate a increases.

3. Disease "persistence"

3.1. Uniform persistence

In this sub-section, we attempt to explore the uniform persistence of (4) when the threshold parameter $\mathcal{R}_0 > 1$, by applying the acyclicity Theorem (see [19, p. 18]).

Definition 3.1 [20]. System (4) is said to be uniformly persistent if there exists a constant $0 < c < 1$ such that any solution $(s(t), e(t), i(t))$ with $(s(0), e(0), i(0)) \in \Delta$ satisfies

$$\min\{\liminf_{t\to\infty} s(t), \liminf_{t\to\infty} e(t), \liminf_{t\to\infty} i(t)\} \geqslant c. \tag{11}$$

Let X be a locally compact metric space with metric $\mathtt{d}$ and let Γ be a closed nonempty subset of X with boundary $\partial\Gamma$ and interior $\overset{\circ}{\Gamma}$. Clearly, $\partial\Gamma$ is a closed subset of Γ. Let Φ_t be a dynamical system defined on Γ. A set B in X is said to be invariant if $\Phi(B, t) = B$. Define $M_\partial := \{x \in \partial\Gamma : \Phi_t x \in \partial\Gamma, \forall t \geqslant 0\}$.

Lemma 3.1 [19]. *Assume*
(A_1) Φ_t *has a global attractor;*
(A_2) *There exists an $M = \{M_1, \ldots, M_k\}$ of pair-wise disjoint, compact, and isolated invariant set on $\partial\Gamma$ such that*
(a) $\bigcup_{x\in M_\partial} \omega(x) \subset \bigcup_{j=1}^k M_j$;
(b) *No subsets of M form a cycle on $\partial\Gamma$;*
(c) *Each M_j is also isolated in Γ;*
(d) $W^s(M_j) \bigcap \overset{\circ}{\Gamma} \doteq \phi$ *for each $1 \leqslant j \leqslant k$, where $W^s(M_j)$ is the stable manifold of M_j. Then Φ_t is uniformly persistent with respect to $\overset{\circ}{\Gamma}$.*

In this application, let

$$\Gamma = \Delta := \{(s,e,i) \in \mathbb{R}_+^3 | 0 \leqslant s + e + i \leqslant 1\},$$
$$\overset{\circ}{\Gamma} := \{(s,e,i) \in E : e, i > 0\}, \quad \text{and} \quad \partial\Gamma = \Gamma/\overset{\circ}{\Gamma}$$

Obviously, $M_\partial = \partial\Gamma$.

We next show $M = \{P_0\}$, $\omega(x) = \{P_0\}$ for all $x \in M_\partial$. On $\partial\Gamma$, system (4) reduces to $s' = b - (\sigma a + b)s$, in which $s(t) \to \frac{b}{\sigma a + b}$ as $t \to \infty$. It is concluded that $M = \{P_0\}$, $\omega(x) = \{P_0\}$ for all $x \in M_\partial$, which indicates that hypothesis (a) and (b) hold. When $\mathcal{R}_0 > 1$, the disease-"free" equilibrium (DFE) P_0 is unstable from Theorem 2.1, and also $W^s(M) = \partial\Gamma$. Hypothesis (c) and (d)

are then satisfied. Due to the ultimate boundedness of all solutions to system (4), there always admits a global attractor, making (A1) true.

Theorem 3.2. *When $\mathscr{R}_0 > 1$, system (4) is uniformly persistent.*

3.2. Existence of the "endemic" equilibrium (EE)

Sub-section 2.3 shows that the disease-"free" equilibrium (DFE) is globally asymptotically stable when $\mathscr{R}_0 \leqslant 1$. This implies that there is no endemic equilibrium. The disease can be "wiped out" in the end. From the epidemiological perspective, it is more important to investigate the existence of EE and its properties when $\mathscr{R}_0 > 1$.

Suppose that $P_*(s_*, e_*, i_*) \in \varDelta$ is an "endemic" equilibrium (EE). From (4), its coordinates should satisfy

$$
\begin{aligned}
&b - (\sigma a + b)s_* - (1 - a\sigma)\lambda i_* s_* + \alpha i_* s_* = 0, \\
&(1 - a\sigma)\lambda i_* s_* - (\varepsilon + b)e_* + \alpha e_* i_* = 0, \\
&\varepsilon e_* - (\alpha + \beta + b)i_* + \alpha i_*^2 = 0.
\end{aligned}
\tag{12}
$$

with $s^* > 0$, $e^* > 0$ and $i^* > 0$. Adding the above equations leads to

$$
(\sigma a + b - \alpha i_*)(1 - s_* - e_* - i_*) = \beta i_* + \sigma a(1 - e_* - i_*),
$$

which gives the following range of i^*

$$
0 < i_* < \min\{1, (\sigma a + b)/\alpha\}.
\tag{13}
$$

It is noted from (13) that when the excess death rate α is less than the product of vaccine coverage rate a and vaccine efficacy σ, or the natural birth rate b, or the sum of σa and b, i^* will lie in the interval $(0,1)$. Eliminating s^* and e^* from (12), i^* satisfies.

$$
\begin{aligned}
&(1 - a\sigma)\varepsilon b\lambda i_* + (\alpha i_* - (\varepsilon + b))((\alpha + \beta + b)i_* - \alpha i_*^2) \\
&\quad \times [\sigma a + b + (1 - a\sigma)\lambda - \alpha)i_*] = 0 \\
&\Rightarrow ((\varepsilon + b) - \alpha i_*)((\alpha + \beta + b) - \alpha i_*)[(\sigma a + b) + (1 - a\sigma)\lambda - \alpha)i_*] \\
&\quad = (1 - a\sigma)\varepsilon b\lambda \\
&\Rightarrow \left(1 - \frac{\alpha}{\varepsilon + b}i_*\right)\left(1 - \frac{\alpha}{\alpha + \beta + b}i_*\right)\left(1 + \frac{(1 - a\sigma)\lambda - \alpha}{\sigma a + b}i_*\right) = R_0,
\end{aligned}
\tag{14}
$$

where $\mathscr{R}_0$ is defined as in (8). Furthermore, s^* and e^* can be uniquely determined from i^* by

$$
\begin{aligned}
s_* &= \frac{b}{\sigma a + b + (1 - a\sigma)\lambda - \alpha i_*}, \\
e_* &= \frac{(\alpha + \beta + b)i^* - \alpha i_*^2}{\varepsilon},
\end{aligned}
\tag{15}
$$

In (15), e^*, $s^* > 0$ are, respectively, guaranteed by the fact that $0 < i^* < 1$ and $\mathscr{R}_0 > 1$ implying $(1 + a(1 - \sigma))\lambda > \alpha$

Case i: Suppose $\alpha < \min\{\sigma a + b, \varepsilon + b\}$. From (13) we know that $0 < i^* < 1$. Define

$$
f(i) = \left(1 - \frac{\alpha i}{\varepsilon + b}\right)\left(1 - \frac{\alpha i}{\alpha + \beta + b}\right)\left(1 + \frac{((1 - a\sigma)\lambda - \alpha)i}{\sigma a + b}\right),
\tag{16}
$$

and then the roots of $f(i)$ are $i_1 = (\varepsilon + b)/\alpha$, $i_2 = (\alpha + \beta + b)/\alpha$, and $i_3 = -(\sigma a + b)/((1 - a\sigma)\lambda - \alpha)$, all of which lie outside $(0,1)$. Moreover, $f(0) = 1$ and under the parameter restriction $b \geqslant \alpha, f(1) = (\varepsilon + b - \alpha)(\beta + b)(\sigma a + b + (1 - a\sigma)\lambda - \alpha)/((\varepsilon + b)(\alpha + \beta + b)(\sigma a + b)) > \mathscr{R}_0$. These observations lead to the conclusion that the line $y = \mathscr{R}_0$ has exactly one intersection $(i^*, f(i^*))$ with the function $f(i)$ where i^* satisfies (13).

Case ii: $\sigma a + b < \alpha < b + \epsilon$.

From (13) we know that $0 < i^* < (\sigma a + b)/\alpha$. If $f\left(\frac{\sigma a + b}{\alpha}\right) \geqslant \mathscr{R}_0$, there is an unique positive root to (14). One can verify that $f\left(\frac{\sigma a + b}{\alpha}\right) \geqslant \mathscr{R}_0$ is equivalent to

$$
(\sigma a - \varepsilon)(\sigma a - \alpha - \beta)(\sigma a + b) \geqslant b\alpha\varepsilon,
\tag{17a}
$$

$$
\Rightarrow (\sigma a)^3 - (\alpha - \beta - \varepsilon - b)(\sigma a)^2 + (\varepsilon(\alpha + \beta) - b(\alpha + \beta + \varepsilon))(\sigma a) + b\varepsilon\beta \geqslant 0.
\tag{17b}
$$

Next, we seek sufficient conditions that guarantee $f\left(\frac{\sigma a + b}{\alpha}\right) \geqslant \mathscr{R}_0$. Define the left-hand side of (17b) as $f_1(\sigma a)$. Obviously, $f_1(0) \geqslant 0$. And $f_1(1) > 0$ if and only if

$$
b \geqslant \frac{(1 - \varepsilon)(\alpha + \beta - 1)}{(1 - \varepsilon)(1 - \beta) - \alpha} =: b_0.
$$

Differentiating $f_1(x)$ with respect to x, we obtain that f_1 reaches its local minimum value at

$$x_{\min} = \frac{\alpha + \beta + \varepsilon - b + \sqrt{(\alpha - \beta + \varepsilon - b)^2 - 3(\varepsilon(\alpha + \beta) - b(\alpha + \beta + \epsilon))}}{3}.$$

Since $0 \leqslant \sigma a < 1$ (from assumptions in Section 1), then $x_{\min} \geqslant 1$ makes inequality (17) true, namely, $f\left(\frac{\sigma a + b}{\alpha}\right) \geqslant \mathcal{R}_0$. A straightforward calculation can verify that $x_{\min}$ is no less than the unity if

$$\alpha + \beta + \varepsilon - 3 \geqslant b. \tag{18}$$

In summary, regarding the existence and the number of the "endemic" equilibria (EE), we have

Theorem 3.3. *Suppose that $\mathcal{R}_0 > 1$. System (4) has a unique "endemic" equilibrium $P^*(s^*, e^*, i^*)$ with coordinates satisfying (14) and (15) if*

$$b \geqslant \alpha, \text{ or} \tag{19a}$$

$$\sigma a < \alpha - b,$$
$$\max\{\alpha - \varepsilon, b_0\} < b \leqslant \alpha + \beta + \varepsilon - 3. \tag{19b}$$

3.3. Local stability of the EE

From (6) and (12), the Jacobian matrix compound matrix $J(P)$ at the EE P^* can take the form:

$$J(P_*) = \begin{pmatrix} -\frac{b}{s_*} & 0 & \frac{-b + (\sigma a + b)s_*}{i_*} \\ (1 - a\sigma)\lambda i_* & \frac{(1 - a\sigma)\lambda i_* s_*}{e_*} & (1 - a\sigma)\lambda s + \alpha e \\ 0 & \varepsilon & \frac{-\varepsilon e_* + \alpha i_*^2}{i_*} \end{pmatrix}.$$

To show the locally asymptotical stability of the EE is equivalent to show that $J(P^*)$ is stable. Denote the diagonal matrix $Q = \text{diag } (i^*, s^*, s^*)$. Obviously, $J(P^*)$ is similar to $QJ(P^*)Q^{-1}$, where

$$QJ(P_*)Q^{-1} = \begin{pmatrix} -\frac{b}{s_*} & 0 & -\frac{b}{s_*} + \sigma a + b \\ (1 - a\sigma)\lambda s_* & \frac{(1 - a\sigma)\lambda i_* s_*}{e_*} & (1 - a\sigma)\lambda s + \alpha e \\ 0 & \varepsilon & \frac{-\varepsilon e_* + \alpha i_*^2}{i_*} \end{pmatrix}.$$

The matrix $J(P^*)$ is stable if and only if $QJ(P^*)Q^{-1}$ is stable, since similarity preserves the eigenvalues. It is observed that the diagonal elements of the matrix $QJ(P^*)Q^{-1}$ are negative. An easy argument applying Geršgorin discs (see [21]) shows that it is stable if it is diagonally dominant in rows. Set $\mu_1 = \max\{g_1, g_2, g_3\}$, where

$$g_1 = -\sigma a - b,$$
$$g_2 = 2(1 - a\sigma)\lambda s_* - \frac{(1 - a\sigma)\lambda i_* s_*}{e_*} + \alpha e_*, \tag{20}$$
$$g_3 = \varepsilon - \frac{\varepsilon e_*}{i_*} + \alpha i_*,$$

since $-b/s^* + \sigma a + b < 0$ from (15).

The last two equations of (12) can be rewritten as

$$\frac{i_* s_*}{e_*} = \frac{\varepsilon + b - \alpha i_*}{(1 - a\sigma)\lambda},$$
$$\frac{e_*}{i_*} = \frac{\alpha + \beta + b - \alpha i_*}{\varepsilon}, \tag{21}$$

Substituting (21) into (20) yields

$$\mu_1 = \max\{-\sigma a - b, -(\alpha + \beta + b) + \varepsilon + 2\alpha i_*, 2(1 - a\sigma)\lambda s_* + \alpha(e_* + i_*) - (b + \varepsilon)\}.$$

Assume $\frac{2b(1 - a\sigma)\lambda}{\sigma a + b} \leqslant \varepsilon \leqslant \beta$. Since $\alpha \leqslant b$, the last two elements inside the braces of last equation are negative. We then have $\mu_1 < 0$, which implies the diagonal dominance of $QJ(P^*)Q^{-1}$.

The following theorem summarizes the parameter restrictions on the local stability of the EE.

Theorem 3.4. *Assume $\mathcal{R}_0 > 1$. When*

$$\alpha \leqslant b \text{ and } \frac{2b(1 - a\sigma)\lambda}{\sigma a + b} \leqslant \varepsilon \leqslant \beta \tag{22}$$

the unique "endemic" equilibrium P^* is locally asymptotically stable in Δ.

Locally asymptotical stability by means of eigenvalue analysis, may be of no practical significance for a real epidemiological system since it merely guarantees stability relative to small perturbation of the initial state from an equilibrium. Ideally we would like to establish global stability result relating to all possible displacements of the initial state in the feasible region.

3.4. Global stability of the EE

In this sub-section, we apply a geometric approach developed by Smith [22] and Li-Muldowney [23] to investigate the globally asymptotic stability of the unique endemic equilibrium P^* when $\mathcal{R}_0 > 1$. Here we omit the detailed introduction of this approach and refer readers to [23,22].

Let $x - \mathbf{f}(x) \in \mathbb{R}^n$ be a smooth vector field defined for x in an open set $D \subset \mathbb{R}^n$. We define a differential equation as

$$x' = \mathbf{f}(x), \quad x \in D, \tag{23a}$$

and its corresponding periodic linear system

$$z' = \frac{\partial \mathbf{f}^{[2]}}{\partial x}(p(t))z(t), \tag{23b}$$

where $\frac{\partial \mathbf{f}^{[2]}}{\partial x}$ is the second additive compound matrix ([16,23,12]) of $\frac{\partial \mathbf{f}}{\partial x}$ and $\Theta = \{p(t):0 \leqslant t \leqslant \omega\}$ is the periodic orbit of (23a). The key steps in the proof are summarized as follows (see [16,23,12], [22]):

(i) (23a) has a compact absorbing set $K \subset D$;
(ii) (23a) has a unique equilibrium $\bar{x}$ in D;
(iii) (23a) satisfies the Poincaré–Bendixson property;
(iv) (23b) is asymptotically stable for each periodic solution $x = p(t)$ to (23a) with $p(0) \in D$;
(v) $(-1)^n det\left(\frac{\partial f}{\partial x}(\bar{x})\right) > 0$.

The main idea of the geometric approach by Smith and Li-Muldowney [23,22] is to rule out the existence of periodic solutions inside the variant region Δ and then all trajectories of go to the unique EE P^* from the Poincare–Bendixson property [24]. Now, we apply the methods outlined above to (4) and try to ind out the parameter restrictions. The Jacobian matrix $\frac{\partial \mathbf{f}}{\partial x}$ of (4) at an arbitrary point $P(s, e, i)$ in Δ is given by (6). The second of [2] additive compound matrix $\frac{\partial \mathbf{f}^{[2]}}{\partial x}$ is calculated as

$$\frac{\partial \mathbf{f}^{[2]}}{\partial x} = \begin{pmatrix} a_{11} & (1 - a\sigma)\lambda s + \alpha e & (1 - a\sigma)\lambda s - \alpha s \\ \varepsilon & a_{22} & 0 \\ 0 & (1 - a\sigma)\lambda i & a_{33} \end{pmatrix}, \tag{24a}$$

where

$$\begin{aligned} a_{11} &= -2b - \sigma a - (1 - a\sigma)\lambda i - \varepsilon + 2\alpha i, \\ a_{22} &= -2b - \sigma a - (1 - a\sigma)\lambda i - \alpha - \beta + 3\alpha i, \\ a_{33} &= -2b - \varepsilon - \alpha - \beta + 3\alpha i. \end{aligned} \tag{24b}$$

We then can write (23b) for (4) with respect to a periodic solution $p(t) = (s(t),e(t),i(t))$ as

$$\begin{aligned} z_1' &= (-2b - \sigma a - (1 - a\sigma)\lambda i - \varepsilon + 2\alpha i)z_1 + [(1 - a\sigma)\lambda s + \alpha e]z_2 + [(1 - a\sigma)\lambda s - \alpha a]z_3, \\ z_2' &= \varepsilon z_1 + (-2b - \sigma a - 1(1 - a\sigma)\lambda i - \alpha - \beta + 3\alpha i)z_2 \\ z_3' &= (1 - a\sigma)\lambda i z_2 + (-2b - \varepsilon - \alpha - \beta + 3\alpha i)z_3 \end{aligned} \tag{25}$$

The uniform persistence from sub-Section 3.2 and the boundedness of Δ tell that (4) has a compact absorbing set $K \subset \Delta$ (see [20]). When $\mathcal{R}_0 > 1$, from Theorem 3.1, we know that (4) has a unique EE in Δ under the conditions (19a) or (19b). System (4) satisfies the Poincaré–Bendixson property since it is competitive in the convex set $K \subset \Delta$ (see [24, Chapter 3], Theorem 4.1). As to the definition of competitive system and the proof of competitiveness of (4) in Δ, we here omit the details and refer readers to Section 2 of Li et al. [16], where a similar technique is performed. The locally asymptotical stability of the EE P^* in Theorem 3.4 implies det $\left(\frac{\partial f}{\partial x}(P_*)\right) < 0$.

We now construct the following Lyapunov function to demonstrate the asymptotical stability of the periodic linear system (25).

$$V(z_1, z_2, z_3; s, e, i) = \sup\left\{|z_1|, \frac{e}{i}\left(|z_2| + \frac{(1 - a\sigma)\lambda - \alpha}{(1 - a\sigma)\lambda}|z_3|\right)\right\}. \tag{26}$$

From Theorem 3.2, we know that the orbit γ of $p(t)$ remains at a positive distance from $\partial\Delta$. Hence there exists a constant $c > 0$ such that

$$V(z_1, z_2, z_3; s, e, i) \geqslant c|(z_1, z_2, z_3)|, \tag{27}$$

for all $(z_1, z_2, z_3) \in \mathbb{R}^3$ and $(s,e,i) \in \gamma$. We next calculate the right-hand derivative of $V(t)$, which is described in Ref. [25] and obtain the following differential inequalities:

$$
\begin{aligned}
D_+|z_1(t)| \leqslant & -(\sigma a + 2b + \varepsilon + (1-a\sigma)\lambda i - 2\alpha i)|z_1(t)| \\
& + ((1-a\sigma)\lambda s + \alpha e)|z_2(t)| + ((1-a\sigma)\lambda s - \alpha s)|z_3(t)| \\
= & -(\sigma a + 2b + \varepsilon + (1-a\sigma)\lambda i - 2\alpha i)|z_1(t)| \\
& + \left(\frac{(1-a\sigma)\lambda si}{e} + \alpha i\right)\frac{e}{i}|z_2(t)| \\
& + \frac{(1-a\sigma)\lambda - \alpha}{(1-a\sigma)\lambda} \cdot \frac{(1-a\sigma)\lambda si}{e}\frac{e}{i}|z_3(t)| \\
\leqslant & -(\sigma a + 2b + \varepsilon + (1-a\sigma)\lambda i - 2\alpha i)|z_1(t)| \\
& + \left(\frac{(1-a\sigma)\lambda si}{e} + \alpha i\right)\frac{e}{i}\left(|z_2(t)| + \frac{(1-a\sigma)\lambda - \alpha}{(1-a\sigma)\lambda}|z_3(t)|\right)
\end{aligned}
\tag{28a}
$$

$$
D_+|z_2(t)| \leqslant \varepsilon|z_1(t)| - (2b + \sigma a + \alpha + \beta + \lambda i - 3\alpha i)|z_2(t)|,
\tag{28b}
$$

$$
D_+|z_3(t)| \leqslant (1-a\sigma)\lambda i|z_2(t)| - (2b + \varepsilon + \alpha + \beta - 3\alpha i)|z_3(t)|.
\tag{28c}
$$

Using (28b) and (28c), we have

$$
\begin{aligned}
& D_+ \frac{e}{i}\left(|z_2(t)| + \frac{(1-a\sigma)\lambda - \alpha}{(1-a\sigma)\lambda}|z_3(t)|\right) \\
= & \left(\frac{e'}{e} - \frac{i'}{i}\right)\frac{e}{i}\left(|z_2(t)| + \frac{(1-a\sigma)\lambda - \alpha}{(1-a\sigma)\lambda}|z_3(t)|\right) \\
& + D_+ \frac{e}{i}\left(|z_2(t)| + \frac{(1-a\sigma)\lambda - \alpha}{(1-a\sigma)\lambda}|z_3(t)|\right) \\
\leqslant & \left(\frac{e'}{e} - \frac{i'}{i}\right)\frac{e}{i}\left(|z_2(t)| + \frac{(1-a\sigma)\lambda - \alpha}{(1-a\sigma)\lambda}|z_3(t)|\right) \\
& + \frac{e}{i}(\varepsilon|z_1(t)| - (2b + \sigma a + \alpha + \beta - 2\alpha i)|z_2(t)|) \\
& - \frac{(1-a\sigma)\lambda - \alpha}{(1-a\sigma)\lambda}(2b + \varepsilon + \alpha + \beta - 3\alpha i)|z_3(t)|) \\
\leqslant & \left(\frac{e'}{e} - \frac{i'}{i}\right)\frac{e}{i}\left(|z_2(t)| + \frac{(1-a\sigma)\lambda - \alpha}{(1-a\sigma)\lambda}|z_3(t)|\right) \\
& + \frac{e}{i}(\varepsilon|z_1(t)| - (2b + \alpha + \beta - 2\alpha i)|z_2(t)|) \\
& - \frac{(1-a\sigma)\lambda - \alpha}{(1-a\sigma)\lambda}(2b + \alpha + \beta - 3\alpha i)|z_3(t)| \\
\leqslant & \frac{\varepsilon e}{i}|z_1(t)| + \left(\frac{e'}{e} - \frac{i'}{i} - 2b - \alpha - \beta + 3\alpha i\right)\frac{e}{i}\left(|z_2(t)| + \frac{(1-a\sigma)\lambda - \alpha}{(1-a\sigma)\lambda}|z_3(t)|\right).
\end{aligned}
\tag{29}
$$

Inequalities (28a) and (29) lead to

$$
D_+V(t) \leqslant \max\{g_1(t)\}V(t),
\tag{30}
$$

where

$$
\begin{aligned}
g_1 &= -\sigma a - 2b - (1-a\sigma)\lambda i - \varepsilon + 3\alpha i + \frac{(1-a\sigma)\lambda si}{e}, \\
g_2 &= \frac{e'}{e} - \frac{i'}{i} - 2b - \alpha - \beta + 3\alpha i + \frac{\varepsilon e}{i}.
\end{aligned}
\tag{31}
$$

We rewrite the last two equations of (4) as

$$
\begin{aligned}
\frac{(1-a\sigma)\lambda si}{e} + \alpha i &= \frac{e'}{e} + (\varepsilon + b), \\
\frac{\varepsilon e}{i} + \alpha i &= \frac{i'}{i} + b + \alpha + \beta.
\end{aligned}
\tag{32}
$$

Substituting (32) into (31) leads to

$$g_1 = -\sigma a - b + 2\alpha i - \lambda(1 - \sigma a)i + \frac{e'}{e}$$
$$\leqslant -\sigma a - b + 2\alpha i + \frac{e'}{e}, \tag{33}$$
$$g_2 = -b + 2\alpha i + \frac{e'}{e}.$$

From (33) we obtain that

$$\max\{g_1, g_2\} \leqslant -b + 2\alpha i + \frac{e'}{e},$$

and thus if $2\alpha \leqslant b$,

$$\int_0^\omega \max\{g_1, g_2\}dt \leqslant \log e(t)|_0^\omega + \int_0^\omega (2\alpha i - b)dt = -\int_0^w (-2\alpha i + b)dt = -M < 0,$$

which implies that $V(t) \to 0$ as $t \to \infty$, and in turn that $(z_1(t), z_2(t), z_3(t)) \to 0$ as $t \to \infty$ by (27). As a result, the second compound system (23b) is asymptotically stable and the periodic solution $(s(t), e(t), i(t))$ is asymptotically orbitally stable. This verifies the condition (iv). Hence P^* is globally stable in Δ, which gives the following result.

Theorem 3.5. *Assume* $\mathscr{R}_0 > 1$. *When*

$$2\alpha \leqslant b \text{ and } \frac{2b(1 - a\sigma)\lambda}{\sigma a + b} \leqslant \varepsilon \leqslant \beta, \tag{34}$$

the unique "endemic" equilibrium P^* *attracts all trajectories of* Δ *except those on the invariant s-axis which converge to the disease-"free" equilibrium* P_0 *along this axis.*

Conditions (34) tell that the locally asymptotical stability of P^* can not guarantee its global stability, which requires stricter parameter restrictions, biologically, larger recruitment or inflow rate of susceptibles.

4. Epidemiology correlations of systems in proportion and in population

In the previous sections, we investigate the global dynamics of the reduced proportional system (4) and obtain the parameter restrictions for disease "persistence" and "eradication". Are these conclusions compatible with the original epidemic model (1)? And does disease "persistence" or "eradication" in system (3) or (4) imply disease persistence or eradication in model (1), respectively? In this section, we focus on finding out the correlations between them.

Let's turn to the original model (1). Clearly, (1) is not well defined at $(0,0,0,0)$, so following the technique by Smith [24] we study the redefined system

$$S' = bN - \lambda(1 - a)IS/N - (1 - \sigma)a\lambda IS/N - (\sigma a + d)S \triangleq F_1(S, E, I, N),$$
$$E' = \lambda(1 - a)IS/N + (1 - \sigma)a\lambda IS/N - (d + \varepsilon) \triangleq F_2(S, E, I, N),$$
$$I' = \varepsilon E - (\alpha + \beta + d)I \triangleq F_3(S, E, I, N), \tag{35}$$
$$N' = (b - d)N - \alpha I \triangleq F_4(S, E, I, N),$$
$$F_1' = F_2' = F_3 = F_4' = 0, when (S, E, I, N) = (0, 0, 0, 0),$$

in its feasible region

$$\overline{\Delta} = \left\{(S, E, I, N) \in \mathbb{R}_+^4 \,\middle|\, 0 \leqslant S + E + I \leqslant N\right\}.$$

Due to the boundedness of term $\frac{IS}{N}$ around the origin in (35), we see that

$$\lim_{(S,E,I,N) \to 0,0,0,0} F_j(S, E, I, N) = 0, \quad j = 1, 2, 3, 4.$$

We conclude that $F_j(j = 1,2,3,4)$ are continuous functions on $\mathbb{R}_+^4 = \{(S, E, I, N) : S, E, I, N \geqslant 0\}$. Straightforward computation shows that system (35) are Lipschizian on $\overline{\Delta}$. Hence a solution of (35) with non-negative initial condition exists and is unique. It is also easy to see that these solutions exist for all $t \geqslant 0$ and stay non-negative. When $b - d \leqslant 0$ and $\alpha > 0$, or $b - d < 0$ and $\alpha > 0$, the total population $N(t)$ in system (35) will die out with the initial condition $E(0) + I(0) > 0$ due to the larger natural death rate and disease-caused excess death. When $b - d = 0$ and $\alpha = 0$, the total population size $N(t)$ will remain constant so that system (35) reduces to a SEIR model with constant population, whose dynamic behaviors are very similar to (3) or (4). In the rest of this section, we assume that $b - d > 0$, $\alpha \geqslant 0$ or $b - d > 0$, $\alpha = 0$. The latter does not incorporate disease-related death in population and the whole population will increase exponentially. Sections 2 and 3 show that the dynamics of system (4) with $\alpha = 0$ are similar to that with $\alpha > 0$ except the parameter conditions for the existence of EE (see Theorem 3.3).

We now consider the case $b - d > 0$ and $\alpha > 0$. For the convenience of readers, we summarize the existence and stability of equilibria for system (4) in Table 1.

Table 1
Existence and stability of equilibrium for system (4).

$\mathscr{R}_0$	$\widehat{\mathscr{R}}_0$	Condition	# of Equilibria	Type of equilibria	Respective stability
<1	>1	NA	1	DFE	LAS
<1	⩽1	NA	1	DFE	GAS
>1	NA	(22)	2	DFE/EE	Unstable/LAS
>1	NA	(34)	2	DFE/EE	Unstable GAS

Table 2
Existence and stability of equilibrium for system (35).

Relationship between $\mathscr{R}_o$ and $\widetilde{\mathscr{R}}_o$	# of Equilibria	Type of equilibria	Stability
$\mathscr{R}_0 < \widetilde{\mathscr{R}}_0$	1	Trivial	Unstable
$\mathscr{R}_0 > \widetilde{\mathscr{R}}_0$	1	Trivial	Stable
$\mathscr{R}_0 = \widetilde{\mathscr{R}}_0$	∞	Trivial/EE line	Unstable/stable

"GAS" denotes globally asymptotically stable
"LAS" denotes locally asymptotically stable.
"NA" is the abbreviation of "not applicable".

Model (35) always has the trivial equilibrium $\widetilde{P}_o$ (0,0,0,0). We are interested in determining whether (35) has an endemic equilibrium (EE). Suppose $\widetilde{P}_*(\widetilde{S}_*, \widetilde{E}_*, \widetilde{I}_*, \widetilde{N}_*)$ is the EE of model (35). The right-hand side of (35) equal to zero (i.e., $Fj = 0, j = 1,2,3,4$) leads to

$$0 = b - (\sigma a + d)\frac{\widetilde{S}_*}{\widetilde{N}_*} - (1 - a\sigma)\lambda \frac{\widetilde{I}_*}{\widetilde{N}_*} \cdot \frac{\widetilde{S}_*}{\widetilde{N}_*},$$

$$\frac{\widetilde{S}_*}{\widetilde{N}_*} = \frac{d + \varepsilon}{\lambda(1 - a\sigma)} \cdot \frac{\alpha + \beta + d}{\varepsilon},$$

$$\frac{\widetilde{E}_*}{\widetilde{N}_*} = \frac{\alpha + \beta + d}{\varepsilon} \cdot \frac{\widetilde{I}_*}{\widetilde{N}_*},$$

$$\frac{\widetilde{I}_*}{\widetilde{N}_*} = \frac{b - d}{\alpha}.$$

Eliminating $\widetilde{S}_*, \widetilde{E}_*, \widetilde{I}_*$ and $\widetilde{N}_*$ from these equations leads to the following condition

$$b = \frac{(d + \varepsilon)(\alpha + \beta + d)}{\lambda\varepsilon(1 - a\sigma)} \left[(\sigma a + d) + \frac{(1 - \sigma a)\lambda}{\alpha} \cdot (b - d)\right].$$

which is equivalent to

$$\widetilde{\mathscr{R}}_o := f\left(\frac{b - d}{\alpha}\right) = \left(1 - \frac{b - d}{\varepsilon + b}\right)\left(1 - \frac{b - d}{\alpha + \beta + b}\right)\left(1 + \frac{b - d}{\alpha} \cdot \frac{(1 - a\sigma)\lambda - \alpha}{\sigma a + b}\right) = \mathscr{R}_0$$

where $f(x)$ is the cubic polynomial defined in (16) in sub-Section 3.2.

Theorem 4.1. If $\widetilde{\mathscr{R}}_o \neq \mathscr{R}_o$, system (35) only has a trivial equilibrium $\widetilde{P}_0(0,0,0,0)$; if $\widetilde{\mathscr{R}}_0 = \mathscr{R}_0$, system (35) has an equilibrium line $\widetilde{L}$:

$$\left(\frac{(d + \varepsilon)(\alpha + \beta + d)\widetilde{N}_*}{\lambda\varepsilon}, \frac{(b - d)(\alpha + \beta + d)\widetilde{N}_*}{\alpha\varepsilon}, \frac{(b - d)\widetilde{N}_*}{\alpha}, \widetilde{N}_*\right)$$

Denote the endemic equilibrium (EE) on $\widetilde{L}$ as $\widetilde{P}_*(\widetilde{S}_*, \widetilde{E}_*, \widetilde{I}_*, \widetilde{N}_*)$.

We summarize the existence and stability of equilibria for system (35) in Table 2.
The stability conclusion in Table 2 can be obtained from the context below.
Theorem 2.1 shows that when $\widehat{\mathscr{R}}_0 \leqslant 0, (s(t), e(t), i(t), r(t)) \to (b/(\sigma a + b), 0, 0, \sigma a/(\sigma a + b))$ exponentially as $t \to \infty$. From (2), we know that $N'(t) = ((b - d) - \alpha i)N$. We therefore claim that $N(t)$ increases exponentially due to the fact that $i(t) \to 0$ as $t \to \infty$ (see [26]). The trajectories of $S(t)$ and $R(t)$ go to infinity following from the facts that $s(t) = S(t)/N(t) \to b/(\sigma a + b)$ and $r(t) = R(t)/N(t) \to \sigma a/(\sigma a + b)$ as $t \to \infty$, respectively. Consider the equation for E and I

Table 3
Limit values of variables in proportions and in population sizes for systems (4) and (35).

$\mathscr{R}_0$	$\widehat{\mathscr{R}}_0$	$\overline{\mathscr{R}}_0$	$\widetilde{\mathscr{R}}_0$	(s,e,i)	(S, E, I, R, N)
NA	$\leqslant 1$	$\leqslant 1^{a}$	NA	$(b/(\sigma a + b),0,0)$	$(\infty,0,0,\infty,\infty)$
NA	$\leqslant 1$	$>1^{a}$	NA	$(b/(\sigma a + b),0,0)$	$(\infty,\infty,\infty,\infty,\infty)$
>1	NA	NA	$> \mathscr{R}_0^{\star}$	(s^{*},e^{*},i^{*})	$(\infty,\infty,\infty,\infty,\infty)$
>1	NA	NA	$< \mathscr{R}_0^{\star}$	(s^{*},e^{*},i^{*})	$(0, 0, 0, 0, 0)$
>1	NA	NA	$= \mathscr{R}_0^{\star}$	(s^{*},e^{*},i^{*})	$\widetilde{S}_{*},\widetilde{E}_{*},\widetilde{I}_{*},\widetilde{R}_{*},\widetilde{N}_{*}$

"NA" is the abbreviation of "not applicable".

Note: When $\mathscr{R}_0 > 1$, all the conclusions are obtained under the conditions (34).

[a] Necessary condition for system (35), but not for system (4).

$$E' = -(d+\varepsilon)E + \frac{(1-a\sigma)b\lambda}{\sigma a + b}I + (1-a\sigma)\lambda\left(s - \frac{b}{\sigma a + b}\right)I,$$
$$I' = \varepsilon E - (\alpha + \beta + d)I,$$

(36)

which is a perturbation of a linear system. Since the perturbation decays exponentially as $t \to \infty$, the perturbed system (36) behaves almost the same as the principal part as $t \to \infty$ (see [26]). Through the characteristic equation analysis of (36) at $(0,0)$, we have the following two eigenvalues

$$\mu_1 = \frac{-(\alpha + \beta + \varepsilon + 2d) + \sqrt{(\alpha + \beta + \varepsilon + 2d)^2 - 4c_o}}{2},$$
$$\mu_2 = \frac{-(\alpha + \beta + \varepsilon + 2d) - \sqrt{(\alpha + \beta + \varepsilon + 2d)^2 - 4c_o}}{2},$$

(37)

where $c_0 = [(\varepsilon + d)(\alpha + \beta + d) - b\varepsilon(1 - a\sigma)\lambda/(\sigma a + b)]$.

Let $\overline{\mathscr{R}}_0 := b\varepsilon(1 - a\sigma)\lambda/((\sigma a + b)(\varepsilon + d)(\alpha + \beta + d))$ be another parameter threshold for the population size model (35). From (37), $\mu_1 > 0$ if $\overline{\mathscr{R}}_0 > 1$. And it follows that $(E(t), I(t))$ goes to infinity as $t \to \infty$. When $\overline{\mathscr{R}}_0 < 1$, we have $\mu_{1,2} < 0$ and $(E(t), I(t))$ goes to $(0, 0)$ as $t \to \infty$.

From the discussion above, we summarize the results as follows.

Theorem 4.2. *If assume $\mathscr{R}_0 \leqslant 1$. Then $S(t), R(t), N(t)$ go to infinity exponentially with exponential rate $b - d$ as $t \to \infty$. Moreover, $(E(t), I(t))$ goes to $(0,0)$ or infinity as $t \to \infty$ when $\overline{\mathscr{R}}_0 < 1$ or $\overline{\mathscr{R}}_0 > 1$, respectively.*

Next, we consider the dynamical behavior of $S(t), E(t), I(t), R(t), N(t)$ when $\mathscr{R}_0 > 1$. Since $\widetilde{\mathscr{R}}_0 = f\left(\frac{b-d}{\alpha}\right)$ and $\mathscr{R}_0 = (fi_*)$, from the analysis of function f in sub-Section 3.2, we know that $\widetilde{\mathscr{R}}_0 > R_0$ or $\widetilde{\mathscr{R}}_0 < \mathscr{R}_0$ are equivalent to the relations $b - d - \alpha i^* > 0$ or $b - d - \alpha i^* < 0$, respectively. Eq. (2) can be rewritten as

$$N' = [(b - d - \alpha i_*) - \alpha(i(t) - i_*)]N.$$

(38)

Under the parameter restrictions (34), using the global stability of (s^*,e^*,i^*) in Theorem 3.5, we conclude that if $b - d - \alpha i^* > 0$, $N(t) \to \infty(t \to \infty)$ in (38), which implies $(S(t), E(t), I(t), R(t)) \to (\infty,\infty, \infty, \infty)$ as $t \to \infty$; if $b - d - \alpha i^* < 0$, $N(t) \to 0(t \to \infty)$ in (38), which implies $(S(t), E(t), I(t), R(t)) \to (0,0,0,0)$ as $t \to \infty$; if $b - d - \alpha i_* = 0$, $N(t) \to \widetilde{N}_*(t \to \infty)$ in (38), which implies $(S(t),E(t),I(t),R(t)) \to (\widetilde{S}_*, \widetilde{E}_*, \widetilde{I}_*, \widetilde{N}_*)$.

We then have the following results.

Theorem 4.3. *Suppose $\mathscr{R}_0 > 1$ and conditions (34) being satisfied. As $t \to \infty$ when $\widetilde{\mathscr{R}}_0 > \mathscr{R}_0$ $(S(t), E(t), I(t), R(t), N(t)) \to (\infty,\infty,\infty,\infty,\infty)$; when $\widetilde{\mathscr{R}}_0 < \mathscr{R}_0$ $(S(t), E(t), I(t), R(t)) \to (0,0,0,0)$; when $\widetilde{\mathscr{R}}_0 = \mathscr{R}_0$ $(S(t),E(t),I(t),R(t)) \to (\widetilde{S}_*, \widetilde{E}_*, \widetilde{I}_*, \widetilde{N}_*)$.*

When $b - d > 0$ and $\alpha = 0$, system (35) has only the trivial equilibrium $\widetilde{P}_*$ $(0,0,0,0)$. In this case, $(S(t), E(t), I(t), R(t), N(t)) \to (\infty,\infty,\infty,\infty,\infty)$ as $t \to \infty$. Hence the trivial equilibrium $\widetilde{P}_*$ is unstable.

Finally, we summarize the limiting values of variables in proportions and in population sizes for system (4) and system (35) in Table 3.

5. Discussion

In this paper, we propose an SEIR model with varying population size and vaccination strategy towards susceptible individuals. The vaccine effectiveness is also taken into account. We investigate the global dynamics of the reduced proportional system and the original population model, respectively, and give out the dynamic correlations between the two.

We first note that the parameter threshold for proportions $\mathscr{R}_0 := \varepsilon\lambda b(1 - a\sigma)/(\varepsilon + b)(\sigma a + b)(\alpha + \beta + b)$ has a clear epidemiological interpretation for system (3), where $b/(\sigma a + b)$ is the susceptible fraction at DFE, P_0, which, multiplied by $\lambda(1 - a\sigma)$ gives the fraction of infections caused by an infective per time unit; $\varepsilon/(\varepsilon + b)$ is the probability for the infected fraction

becoming infective; and $1/(\alpha + \beta + b)$ is the mean infectious period of an infective fraction. Subsequently, the product of the three terms above yields the expected infective fraction generated by a given infective fraction $i(t)$. We also note that the threshold considerations obtained for fractions are in general different from that of the population itself. See [8,9] for detailed discussions under similar scenarios. Similarly, the parameter threshold for population sizes $\overline{\mathscr{R}}_0 := b\varepsilon\lambda(1 - a\sigma)/((\sigma a + b)(\varepsilon + d)(\alpha + \beta + d))$ also can be interpreted biologically. Consider the system for population sizes in (1), $b/(\sigma a + b)$ is again the susceptible fraction at DFE P_0 which is multiplied by $\lambda(1 - a\sigma)$ to give the fraction of infections caused by an infective per time unit; $\varepsilon/(\varepsilon + d)$ is the probability for the infected individual becoming infective; and $1/(\alpha + \beta + d)$ is the mean infectious period of an infective individual. The product of the above three terms yields the number of individuals infected by the infective population at time t, $I(t)$.

We have shown in Theorem 2.1 that when $\widehat{\mathscr{R}}_0 \leqslant 1$, the DFE P_0 is globally asymptotically stable. However, $\mathscr{R}_0 < 1$ implies that P_0 is locally asymptotically stable. For the case $\mathscr{R}_0 > 1$, P_0 is unstable and system (4) is uniformly persistent. We obtain sufficient conditions for the existence and uniqueness of the "endemic" equilibrium P^*. Under these conditions we further investigate the global dynamics of the system in questions.

When the product of the vaccination rate and the vaccine efficacy $\sigma a < \frac{b(2\lambda - \varepsilon)}{2b\lambda + \varepsilon}$, which violates the assumption of Theorem 3.4, the EE P^* may be unstable. Consequently there may exist stable periodic solutions around P^* in system (4), which also makes considerable difference in the dynamics of the corresponding system (35) with varying population size. Hence the substantially low product of vaccination rate or low vaccine efficacy (e.g., $\sigma a < \frac{b(2\lambda - \varepsilon)}{2b\lambda + \varepsilon}$) may lead to complicated dynamics for the system in question. We leave these problems for future investigation.

Also, we note from (2) or (35) that, when $b < d$, the inflow rate exceeds the outflow rate (the excess disease-related death is not included) and, subsequently, the total population $N(t)$ must decrease monotonically to zero, regardless of whether it is asymptotically in endemic fractions or not. Therefore, the analysis for this case is of little practical significance. When the parameter threshold $\widehat{\mathscr{R}}_0 \leqslant 1$, the disease "die out" the proportional system (4). However, this phenomenon only occurs in the population size system (35) when $\overline{\mathscr{R}}_0 \leqslant 1$ and the disease explodes when $\overline{\mathscr{R}}_0 > 1$ (see Table 3). When $\mathscr{R}_0 > 1$, the disease in proportional system (4) goes to the "endemic" or "persistent" state. However, this phenomenon only happens to the case when $\mathscr{R}_0 = \widetilde{\mathscr{R}}_0$. For $\mathscr{R}_0 > \widetilde{\mathscr{R}}_0$ and $\mathscr{R}_0 < \widetilde{\mathscr{R}}_0$ the disease in the population size system (35) goes extinct and explodes, respectively.

We have to point out in the end that in this paper we do not compare the continuous vaccination strategy to pulse vaccination since the pulse vaccination strategy consisting of periodical repetitions of impulsive vaccinations in a population and all vaccine doses are applied in a very short time comparing with the dynamics of targeted diseases. Anderson and May [2] guided the design of two pulse vaccination programs (two dose strategy for measles in Great Britain), and this strategy was started in Canada in 1996/97. The pulse vaccination sometimes is cost-effective and indeed yields great success in controlling some well-known viral childhood diseases, such as measles, smallpox, chickenpox, etc. However, for some newly emerging diseases, such as influenza A H1N1 (Swine Flu) outbreak early 2009 in Mexico, the viral stain is unknown or partially known, and in addition, the vaccine is not very reliable and its effectiveness is low to some extent, one or two dose pulse vaccinations seem not to be enough in disease eradication. Mathematically, the disease-free equilibrium states of epidemic models with continuous vaccination may be periodic solutions of impulsive models due to the introduction of pulse vaccination.

Acknowledgements

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