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ARTICLE *in* INTERNATIONAL JOURNAL OF BIOMATHEMATICS · MAY 2012

Impact Factor: 0.65 · DOI: 10.1142/S1793524512600017

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International Journal of Biomathematics
Vol. 5, No. 3 (May 2012) 1260001 (18 pages)

DOI: 10.1142/S1793524512600017

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A MULTI-GROUP SVEIR EPIDEMIC MODEL WITH DISTRIBUTED DELAY AND VACCINATION

JINLIANG WANG*

School of Mathematical Science
Heilongjiang University
Harbin 150080, P. R. China
jinliangwang@hit.edu.cn

YASUHIRO TAKEUCHI

Graduate School of Science and Technology
Shizuoka University
Hamamatsu 432-8561, Japan
takeuchi@sys.eng.shizuoka.ac.jp

SHENGQIANG LIU

The Academy of Fundamental and Interdisciplinary Science
Harbin Institute of Technology
3041#, 2 Yi-Kuang Street
Harbin 150080, P. R. China
sqliu@hit.edu.cn

Received 28 January 2011
Accepted 17 November 2011
Published 5 March 2012

In this paper, based on a class of multi-group epidemic models of SEIR type with bilinear incidences, we introduce a vaccination compartment, leading to multi-group SVEIR model. We establish that the global dynamics are completely determined by the basic reproduction number R_0^V which is defined by the spectral radius of the next generation matrix. Our proofs of global stability of the equilibria utilize a graph-theoretical approach to the method of Lyapunov functionals. Mathematical results suggest that vaccination is helpful for disease control by decreasing the basic reproduction number. However, there is a necessary condition for successful elimination of disease. If the time for the vaccines to obtain immunity or the possibility for them to be infected before acquiring immunity is neglected in each group, this condition will be satisfied and the disease can always be eradicated by suitable vaccination strategies. This may lead to over evaluation for the effect of vaccination.

Keywords: Multi-group SVEIR model; vaccination strategy; global stability; Lyapunov functionals; graph theory.

Mathematics Subject Classification 2010: 34D30, 92D30

*Corresponding author.

1. Introduction

Over the last years, multi-group epidemic models have been proposed to describe the transmission dynamics of many infectious disease in heterogeneous populations, such as measles, mumps, gonorrhea, or to investigate infectious disease with multiple hosts such as West-Nile virus and vector borne diseases such as Malaria. A heterogeneous host population can be divided into several homogeneous groups according to modes of transmission, contact patterns, or geographic distributions, so that within-group and inter-group interactions could be modeled separately. One of main mathematical challenges in the analysis of multi-group models is the global stability of the endemic equilibrium, see e.g. [1, 9, 10, 12].

In Lajmanovich and Yorke [15], the authors proposed multi-group models to study the transmission of gonorrhea. For a class of n-group SIS models, they have completely established the global dynamics and proved the global stability of a unique endemic equilibrium using a quadratic global Lyapunov function. Hethcote [9] proved global stability of the endemic equilibrium for multigroup SIR model without vital dynamics. Beretta and Capasso [1] derived sufficient conditions for global stability of the endemic equilibrium for multigroup SIR model with constant population in each group. Thieme [24] proved global stability of the endemic equilibrium of multigroup SEIRS models under certain restrictions. In [5] and [6], for a class of multi-group SEIR models described by ordinary differential equations, a graph-theoretic approach to the method of global Lyapunov functions was proposed and used to establish the global stability of a unique endemic equilibrium.

Liu *et al.* [19] studied the vaccination effects via two SVIR models considering continuous vaccination strategy and pulse vaccination strategy (PVS), respectively. The authors showed that both systems exhibit strict threshold dynamics which depend on the basic reproduction number. If this number is below unity, the disease can be eradicated. And if it is above unity, the disease is endemic in the sense of global asymptotic stability of a positive equilibrium for continuous vaccination strategy and disease permanence for PVS. Mathematical results suggest that vaccination is helpful for disease control by decreasing the basic reproduction number.

Recently, Röst and Wu [23] presented an SEIR model for an infectious disease that includes infected individuals with infection-age structure to allow for varying infectivity. The incidence is of mass action type, but because of the varying infectivity, has the form $\beta S(t)\int_0^\infty k(a)i(t,a)da$. The authors identify the basic reproduction number R_0 as a threshold quantity regarding the local asymptotic stability of the disease-free equilibrium and endemic equilibrium. They also proved disease-free equilibrium is globally stable but leaving out the global stability of the endemic equilibrium. Moreover, McCluskey [20] resolved the open problem in [23] by using a Lyapunov functional that includes an integral over all previous states.

Li *et al.* [18] extended the results in Röst and Wu [23] and McCluskey [20] to a class of multi-group epidemic models with distributed delays, and established

the threshold dynamics by utilizing a graph-theoretical approach to the method of Lyapunov functionals.

Motivated by the above works, in the present paper, we will establish that the dynamical behaviors are completely determined by values of R_0^V. More specifically, if $R_0^V \leq 1$, the disease-free equilibrium is globally asymptotically stable and the disease dies out, if $R_0^V > 1$, a unique endemic equilibrium exists and is globally asymptotically stable, and the disease persists at the endemic equilibrium. The key to our analysis is a complete description of the complicated patterns exhibited in the derivative of the Lyapunov functionals by using graph-theoretical approach which has been successfully extended in [5, 6, 17, 18].

The paper is organized as follows. In the next section, we introduce the models and address the well-posedness. Our main results are stated in Sec. 3. In Sec. 4, vaccination effects implied by the mathematical analysis are given. For the convenience of the reader, we include in Appendix A results from graph theory that are needed for our proof.

2. Model Equations and Well-Posedness

Taking into consideration a general age-structure and varying infectivity in heterogeneous populations, Li *et al.* [18] proposed following differential equations

$$\begin{aligned} S_k' &= \Lambda_k - \sum_{j=1}^{n} \beta_{kj} S_k \int_0^\infty h_j(r) i_j(t,r) dr - d_k^S S_k, \\ E_k' &= \sum_{j=1}^{n} \beta_{kj} S_k \int_0^\infty h_j(r) i_j(t,r) dr - (d_k^E + \epsilon_k) E_k, \\ I_k' &= \epsilon_k E_k - (d_k^I + \gamma_k) I_k, \\ R_k' &= \gamma_k I_k - d_k^R R_k, \quad k = 1, 2, \ldots, n, \end{aligned} \tag{2.1}$$

where S_k, E_k, I_k and R_k denote the susceptible, infected but non-infectious, infectious, and recovered populations in the kth group, respectively. Let $i_k(t,r)$ denote the population of infectious individuals in the kth group with respect to the age of infection r at time t, and $I_k(t) = \int_0^\infty i_k(t,r)dr$. $h_k(r) \geq 0$ be a continuous kernel function that represents the infectivity at the age of infection r. β_{kj} represents the transmission coefficient between compartments S_k and I_j. Let Λ_k represents influx of individuals into the kth group, d_k^S, d_k^E, d_k^I and d_k^R represent death rates of S, E, I and R populations in the kth group, respectively, ϵ_k represents the rate of becoming infectious after a latent period in the kth group, and γ_k represents the recovery rate of infectious individuals in the kth group. The disease incidence in the kth group, $\sum_{j=1}^n \beta_{kj} S_k \int_0^\infty h_j(r) i_j(t,r) dr$, takes into account cross-infections from all groups. All parameter values are assumed to be nonnegative and $\Lambda_k, d_k^S, d_k^E > 0$ for all k.

In the present paper, we incorporate model (2.1) with a vaccination compartment V_k and investigate its global dynamics. Our model is described by the following

equations

$$\begin{aligned}
S_k' &= \Lambda_k - \sum_{j=1}^{n} \beta_{kj} S_k \int_0^\infty h_j(r) i_j(t,r) dr - (d_k + \alpha_k) S_k, \\
V_k' &= \alpha_k S_k - \sum_{j=1}^{n} \beta_{kj}^1 V_k \int_0^\infty h_j(r) i_j(t,r) dr - (d_k + \delta_k) V_k, \\
E_k' &= \sum_{j=1}^{n} (\beta_{kj} S_k + \beta_{kj}^1 V_k) \int_0^\infty h_j(r) i_j(t,r) dr - (d_k + \varepsilon_k) E_k, \qquad (2.2) \\
I_k' &= \varepsilon_k E_k - (d_k + \gamma_k) I_k, \\
R_k' &= \delta_k V_k + \gamma_k I_k - d_k R_k, \quad k = 1, 2, \ldots, n.
\end{aligned}$$

Here S_k, V_k, E_k, I_k, R_k denote the population in the kth group that are susceptible to the disease, vaccines (those who are vaccinated to defeat disease), infected but non-infectious, infectious and recovered, respectively. Within the kth group, Λ_k, ε_k, γ_k are the same meaning as (2.1). Let d_k denote the death rates of S_k, V_k, E_k, I_k and R_k compartments in the kth group. β_{kj}^1 is the transmission coefficients between compartments V_k and I_j. We assume that before obtaining immunity the vaccines individuals in V_k compartments still have the possibility of infection with a disease transmission rate β_{kj}^1 while contacting with infected individuals in I_j compartment. β_{kj}^1 may be assumed to be less than β_{kj} because the vaccinating individuals may have some partial immunity during the process or they may recognize the transmission characters of the disease and hence decrease the effective contacts with infected individuals. α_k be the rate at which susceptible individuals are moved into the vaccination process. They will obtain vaccine-induced immunity during or after the process in the kth group. δ_k be the average rate (and hence $1/\delta_k$ is the average time) for them to obtain immunity and move into recovered population in the kth group. All parameter values are assumed to be nonnegative.

If $\alpha_k = 0$, then $\lim_{t\to\infty} V_k(t) = 0$, which means there are no vaccinations and have been studied in Li *et al.* [18]. Moreover, if $\alpha_k = 0$ and $h_j(r) = 1$ for all $r \geq 0$, then

$$\int_0^\infty h_j(r) \varepsilon_j E_j(t-a) e^{(d_j+\gamma_j)r} dr = \int_0^\infty i_j(t,r) dr = I_j(t),$$

and model (2.2) will be reduced to a multi-group SEIR model with a basic reproduction number R_0. By Guo *et al.* [6, Theorem 1.1], when $R_0 > 1$, the system has a unique endemic equilibrium P^*, and P^* is globally asymptotically stable.

Note that

$$\left(\frac{\partial}{\partial t} + \frac{\partial}{\partial r}\right) i_k(t,r) = -(d_k + \gamma_k) i_k(t,r),$$

$$i_k(t,0) = \varepsilon_k E_k(t),$$

we have that

$$i_k(t,r) = i_k(t-r,0)e^{-(d_k+\gamma_k)r} = \varepsilon_k E_k(t-r)e^{-(d_k+\gamma_k)r}. \tag{2.3}$$

Substituting Eq. (2.3) into (2.2) we have

$$\begin{aligned}
S_k' &= \Lambda_k - \sum_{j=1}^{n} \beta_{kj} S_k \int_0^\infty h_j(r)\varepsilon_j E_j(t-r)e^{-(d_j+\gamma_j)r}dr - (d_k+\alpha_k)S_k,\\
V_k' &= \alpha_k S_k - \sum_{j=1}^{n} \beta_{kj}^1 V_k \int_0^\infty h_j(r)\varepsilon_j E_j(t-r)e^{-(d_j+\gamma_j)r}dr - (d_k+\delta_k)V_k,\\
E_k' &= \sum_{j=1}^{n} (\beta_{kj} S_k + \beta_{kj}^1 V_k)\int_0^\infty h_j(r)\varepsilon_j E_j(t-r)e^{-(d_j+\gamma_j)r}dr - (d_k+\varepsilon_k)E_k,\\
I_k' &= \varepsilon_k E_k - (d_k+\gamma_k)I_k,\\
R_k' &= \delta_k V_k + \gamma_k I_k - d_k R_k, \quad k = 1,2,\ldots,n.
\end{aligned} \tag{2.4}$$

Observe that the variable I_k and R_k do not appear in the first three equations of (2.4). This allows us to consider the following reduced system with distributed delays and general kernel functions

$$\begin{aligned}
S_k' &= \Lambda_k - \sum_{j=1}^{n} \beta_{kj} S_k \int_0^\infty f_j(r)E_j(t-r)dr - (d_k+\alpha_k)S_k,\\
V_k' &= \alpha_k S_k - \sum_{j=1}^{n} \beta_{kj}^1 V_k \int_0^\infty f_j(r)E_j(t-r)dr - (d_k+\delta_k)V_k,\\
E_k' &= \sum_{j=1}^{n} (\beta_{kj} S_k + \beta_{kj}^1 V_k)\int_0^\infty f_j(r)E_j(t-r)dr - (d_k+\varepsilon_k)E_k, \quad k = 1,2,\ldots,n.
\end{aligned} \tag{2.5}$$

Here the kernel function $f_k(r) \geq 0$ is continuous and $\int_0^\infty f_k(r)dr = a_k > 0$. We will establish the global dynamics of model (2.5).

Assume the kernel functions $f_k(r)$ satisfy

$$\int_0^\infty f_k(r)e^{\lambda_k r}dr < \infty, \tag{2.6}$$

where λ_k are positive number, $k = 1,2,\ldots,n$. Due to the infinite delay, it is necessary to define the following Banach space of fading memory type (see e.g. [7, 11] and references therein). Let

$$\begin{aligned}
C_k = \Big\{ &\phi \in C((-\infty,0],\mathbb{R}) : \phi(s)e^{\lambda_k s} \text{ is uniformly continuous on } (-\infty,0],\\
&\text{and} \sup_{s\leq 0} |\phi(s)|e^{\lambda_k s} < \infty \Big\},
\end{aligned}$$

with norm $\|\phi\|_k = \sup_{s\le 0}|\phi(s)|e^{\lambda_k s}$. Let $\phi \in C_k$ be such that $\phi_t(s) = \phi(t+s)$, $s \in (-\infty, 0]$. Let $S_{k,0}, V_{k,0} \in \mathbb{R}_+$ and $\phi_k \in C_k$ such that $\phi_k(s) \ge 0$, $s \in (-\infty, 0]$. For any given initial conditions

$$S_k(0) = S_{k,0}, \quad V_k(0) = V_{k,0}, \quad E_{k0} = \phi_k, \quad k = 1, 2, \ldots, n. \tag{2.7}$$

Standard theory of functional differential equations [11] implies $E_{kt} \in C_k$ for $t > 0$. We consider model (2.5) in the phase space

$$X = \prod_{k=1}^{n} (\mathbb{R} \times \mathbb{R} \times C_k).$$

It can be verified that solutions of (2.5) in X with initial conditions (2.7) remain nonnegative.

The matrices $B = (\beta_{kj})$ and $B^1 = (\beta^1_{kj})$ encode the patterns of contact and transmission among groups that are built into the model. Associated to $B(B^1)$, one can construct a directed graph $L = G(B)(G(B^1))$ whose vertex k represents the kth group, $k = 1, 2, \ldots, n$. A directed edge exists from vertex j to vertex k if and only if $\beta_{kj}(\beta^1_{kj}) > 0$. Throughout the paper, we assume that B and B^1 are both irreducible. Biologically, this is the same as assuming that any two groups k and j have a direct or indirect route of transmission. More specifically, individuals in I_j can infect ones in S_k and V_k directly or indirectly.

For each k, adding the three equations in (2.5) gives $(S_k(t) + V_k(t) + E_k(t)) \le \Lambda_k - d_k(S_k(t) + V_k(t) + E_k(t))$. Hence $\lim_{t\to\infty} \sup(S_k(t) + V_k(t) + E_k(t)) \le \Lambda_k/d_k$. It follows from the first equation in (2.5) that $\lim_{t\to\infty} \sup S_k(t) \le \Lambda_k/(d_k + \alpha_k)$. Therefore, omega limit sets of model (2.5) are contained in the following bounded region in the non-negative cone of $\mathbb{R}^{3n}$:

$$\begin{aligned}\Gamma = \{&(S_1, V_1, E_1(\cdot); \ldots; S_n, V_n, E_n(\cdot)) \in \mathbb{R}^{3n}_+ \mid S_k \le \Lambda_k/(d_k + \alpha_k),\\ &S_k + V_k + E_k(0) \le \Lambda_k/d_k, E_k(s) \ge 0, s \in (-\infty, 0], \quad k = 1, 2, \ldots, n\}.\end{aligned}$$

So we have the following result.

Lemma 2.1. *Every forward orbit in* $\mathbb{R}^{3n}_+$ *of* (2.5) *eventually enters into* Γ, *and* Γ *is positively invariant for* (2.5).

Model (2.5) always has the disease-free equilibrium $P_0 = (S^0_1, V^0_1, 0; \ldots; S^0_n, V^0_n, 0)$ on the boundary of Γ, where $S^0_k = \Lambda_k/(d_k + \alpha_k)$, $V^0_k = \alpha_k\Lambda_k/[(d_k + \alpha_k)(d_k + \delta_k)]$. An equilibrium $P^* = (S^*_1, V^*_1, E^*_1; \ldots; S^*_n, V^*_n, E^*_n)$ in the interior of Γ is called an endemic equilibrium, where $S^*_k, V^*_k, E^*_k > 0$ satisfy the equilibrium equations

$$\Lambda_k = \sum_{j=1}^{n} \beta_{kj} a_j S^*_k E^*_j + (d_k + \alpha_k) S^*_k, \tag{2.8}$$

$$\alpha_k S^*_k = \sum_{j=1}^{n} \beta^1_{kj} a_j V^*_k E^*_j + (d_k + \delta_k) V^*_k, \tag{2.9}$$

$$\sum_{j=1}^{n}(\beta_{kj}S_k^* + \beta_{kj}^1 V_k^*)a_j E_j^* = (d_k + \varepsilon_k)E_k^*. \tag{2.10}$$

Following the method of Diekmann *et al.* [4], the parameter R_0^V is defined as the expected number of secondary cases produced in an entirely susceptible or vaccinated population by a typical infected individual during its entire infectious period. Its biological significance is that if $R_0^V < 1$ the disease dies out while if $R_0^V > 1$ the disease becomes endemic (also see Thieme [26], van den Driessche and Watmough [27]). Intuitively, if $R_0^V < 1$, the disease dies out from the host population, and if $R_0^V > 1$, the disease will persist. The next generation matrix for model (2.5) is

$$M_0 = \left(\frac{(\beta_{kj}S_k^0 + \beta_{kj}^1 V_k^0)a_k}{d_k + \varepsilon_k}\right)_{n\times n}. \tag{2.11}$$

Motivated by works of [4, 27], we define the basic reproduction number as the spectral radius of M_0,

$$R_0^V = \rho(M_0).$$

2.1. *Permanence*

The following results show that $R_0^V > 1$ actually implies that model (2.5) admits at least the one positive equilibrium and the disease is uniformly persistent.

Theorem 2.2. *If $R_0^V > 1$, then* (2.5) *admits at least one positive equilibrium, and there is a positive constant ε such that every solution $(S(t), V(t), E(s))$ of* (2.4) *satisfies*

$$\begin{aligned}&\liminf_{t\to\infty} E_i(s) \geq \varepsilon, \quad s \in (-\infty, 0],\\ &\liminf_{t\to\infty} I_i(t) > \varepsilon_i\varepsilon/(d_i + \gamma_i), \quad i = 1, 2, \ldots, n.\end{aligned}$$

Proof. Following the uniform persistence theorem developed by [23, 30], we prove our result as follows. For convenience, we denote the positive solution $(S_1(t), V_1(t), E_1(s), \ldots, S_n(t), V_n(t), E_n(s))$ of (2.5) by $(S(t), V(t), E(s))$. Define

$$\begin{aligned}X &= \{(S(t), V(t), E(s)) : S_i \geq 0, V_i \geq 0, E_i(s) \geq 0, s \in (-\infty, 0], i = 1, 2, \ldots, n\},\\ X_0 &= \{(S(t), V(t), E(s)) \in X : E_i(s) > 0, s \in (-\infty, 0], i = 1, 2, \ldots, n\},\\ \partial X_0 &= X\backslash X_0.\end{aligned}$$

It then suffices to prove that (2.5) is uniformly persistent with respect to $(X_0, \partial X_0)$. By the form of (2.5), it is easy to see that both X and X_0 are positively invariant. Clearly, ∂X_0 is relatively closed in X. Furthermore, model (2.5) is point dissipative from Lemma 2.1. Set

$$M_\partial = \{(S(0), V(0), \phi) : (S(t), V(t), E(s)) \in \partial X_0, \forall t \geq 0\}.$$

We next show that

$$M_\partial = \{(S, V, 0) : S \geq 0, V \geq 0\}. \tag{2.12}$$

Note that $M_\partial \supseteq \{(S,V,0) : S \geq 0, V \geq 0\}$. To show that $M_\partial \backslash \{(S,V,0) : S \geq 0, V \geq 0\} = \emptyset$, it suffices to prove that $E(s) = 0$ for all $s \in (-\infty, 0]$. Suppose not. Then there exists i_0, $1 \leq i_0 \leq n$, and a t_0 such that $E_{i_0}(t_0) > 0$. Thus set $\{1, 2, \ldots, n\}$ can be departed into Q_1 and Q_2, where

$$E_i(t_0) = 0, \quad \forall\, i \in Q_1, \quad E_i(t_0) > 0, \quad \forall\, i \in Q_2.$$

Q_1 and Q_2 are both nonempty. For any $j \in Q_1$, $i_0 \in Q_2$, we have

$$E_j'(t) \geq (\beta_{ji_0} S_j + \beta^1_{ji_0} V_j) \int_{r=0}^{\infty} f_{i_0}(r) E_{i_0}(t_0 - r) dr > 0.$$

It follows that there is an ϵ_0 such that $E_j(s) > 0$, $j \in Q_1$, for any $s \in (-\infty, 0]$, $t_0 < t < t_0 + \epsilon_0$. Also, we can restrict $\epsilon_0 > 0$ to be small enough such that $E_i(s) > 0$, $\forall\, i \in Q_2$, for $t_0 < t < t_0 + \epsilon_0$. This means that $(S(t), V(t), E(s)) \notin \partial X_0$ for $t_0 < t < t_0 + \epsilon_0$, which contradicts the assumption that $(S(0), V(0), \phi) \in M_\partial$. This proves (2.12).

Clearly, there is one equilibrium $(S^0, V^0, 0)$ in M_∂. When $R_0^V > 1$, we see that there exists a small enough $\eta > 0$ such that

$$R_0^V(\eta) = \rho \left(\frac{(\beta_{kj}(S_k^0 - \eta) + \beta^1_{kj}(V_k^0 - \eta))a_k}{d_k + \varepsilon_k} \right)_{n \times n} > 1.$$

Let us consider an arbitrary positive solution $(S(t), V(t), E(s))$ of (2.5). We will show that $0 \leq E(s) \leq \xi_1$ for any $s \in (-\infty, 0]$ and arbitrary small $\xi_1 > 0$ is impossible. Suppose that this is not true and consider following system

$$\begin{aligned} S_k' &= \Lambda_k - \sum_{j=1}^{n} \beta_{kj} S_k a_k \xi_1 - (d_k + \alpha_k) S_k, \\ V_k' &= \alpha_k S_k - \sum_{j=1}^{n} \beta^1_{kj} V_k a_k \xi_1 - (d_k + \delta_k) V_k, \quad k = 1, 2, \ldots, n. \end{aligned} \tag{2.13}$$

Note that for any $\xi_1 > 0$, (2.13) admits a unique positive equilibrium $(S_k^0(\xi_1), V_k^0(\xi_1))$ which is globally asymptotically stable. Thus, we can restrict ξ_1 small enough such that $S_k^0(\xi_1) > S_k^0 - \eta, V_k^0(\xi_1) > V_k^0 - \eta$. By the implicit function theorem, it follows that $S_k^0(\xi_1)$ and $V_k^0(\xi_1)$ are continuous in ξ_1. There exists a large enough $T_1 > 0$ such that $S_k(t) > S_k^0 - \eta, V_k(t) > V_k^0 - \eta$ for $t > T_1$, where $(S_k(t), V_k(t))$ is a solution of (2.13). Then, we obtain for $t > T_1$, $k = 1, 2, \ldots, n$.

$$E_k' \geq \sum_{j=1}^{n} (\beta_{kj}(S_k^0 - \eta) + \beta^1_{kj}(V_k^0 - \eta)) \int_{r=0}^{\infty} f_j(r) E_j(t - r) dr - (d_k + \varepsilon_k) E_k. \tag{2.14}$$

By $R_0^V(\eta) > 1$ and the comparison principle, it is easy to see that $E_k(t) \to \infty$ as $t \to \infty$, $k = 1, 2, \ldots, n$, which leads to a contradiction. Here $E_k(s)$ is component of a solution of (2.5) satisfying $0 \leq E(s) \leq \xi_1$.

Since $(S_k^0, V_k^0, 0)$ is isolated invariant set in X, $W^s((S_k^0, V_k^0, 0)) \cap X_0 = \emptyset$. We can apply [8, Theorem 4.2] to have that $\lim_{t\to\infty} \inf E(t) > \varepsilon$. Clearly, every orbit in M_∂ converges to $(S_k^0, V_k^0, 0)$, and $(S_k^0, V_k^0, 0)$ is acyclic in M_∂. By [25] (for a stronger repelling property of ∂X_0), we conclude that model (2.4) is uniformly persistent with respect to $(X_0, \partial X_0)$. Finally, we can use a standard comparison argument to obtain $\lim_{t\to\infty} \inf I_k(t) > \varepsilon_k \varepsilon/(d_k + \gamma_k)$. □

By a similar argument as [20, Lemma 4.1], we have the following corollary.

Corollary 2.3. *Suppose that $R_0^V > 1$ and $(S(t), V(t), E(s))$ is a solution to (2.5) that lies in Γ, then there exists a positive constant $\bar{\epsilon} > 0$ such that $\bar{\epsilon} < S(t), V(t), E(s) < \bar{\Delta}$ for all $t \in R$.*

Remark 2.4. Uniform persistence of (2.5), together with uniform boundedness of solutions in the interior of Γ, implies the existence of a positive equilibrium of (2.4) (see [3, Theorem 2.8.6]).

3. Main Results

With the uniform persistence of (2.5), we are ready to state and prove the following global stability result.

Theorem 3.1. *Assume that $B = (\beta_{kj})$ and $B^1 = (\beta_{kj}^1)$ are both irreducible.*

(i) *If $R_0^V \leq 1$, then the disease-free equilibrium P_0 of (2.5) is globally asymptotically stable in Γ. If $R_0^V > 1$, then P_0 is unstable.*
(ii) *If $R_0^V > 1$, then the endemic equilibrium P^* of (2.5) is globally asymptotically stable in the interior of Γ.*

Biologically, Theorem 3.1 implies that, if the basic reproduction number $R_0^V \leq 1$, then the disease always dies out in all groups, if $R_0^V > 1$, then the disease always persists in all groups at the unique endemic equilibrium level, irrespective of the initial conditions.

3.1. *Proof of Theorem* 3.1(i)

Since $B = (\beta_{kj})$ and $B^1 = (\beta_{kj}^1)$ are irreducible, we know that matrix

$$M_0 = \left(\frac{(\beta_{kj} S_k^0 + \beta_{kj}^1 V_k^0) a_k}{d_k + \varepsilon_k} \right)_{n \times n}$$

is also irreducible, and has a positive left eigenvector $(\omega_1, \omega_2, \ldots, \omega_n)$ corresponding to the spectral radius $\rho(M_0) > 0$ and thus $\rho(M_0) = R_0^V \leq 1$. Let $c_k = \frac{\omega_k}{d_k + \varepsilon_k}$,

$\alpha_k(r) = \int_{\sigma=r}^{\infty} f_k(\sigma)d\sigma$ and $f(z) = z - 1 - \ln z$. Consider a lyapunov functional

$$L_1 = \sum_{k=1}^{n} c_k \left(S_k^0 f\left(\frac{S_k}{S_k^0}\right) + V_k^0 f\left(\frac{V_k}{V_k^0}\right) + E_k \right.$$
$$\left. + \sum_{j=1}^{n} (\beta_{kj} S_k^0 + \beta_{kj}^1 V_k^0) \int_{r=0}^{\infty} \alpha_j(r) E_j(t-r)dr \right).$$

Since $f(z) = z - 1 - \ln z$, $z \in R^+$, has the global minimum at $z = 1$ and $f(1) = 0$, we have

$$S_k - S_k^0 - S_k^0 \ln \frac{S_k}{S_k^0} = S_k^0 f\left(\frac{S_k}{S_k^0}\right) \geq 0, \quad V_k - V_k^0 - V_k^0 \ln \frac{V_k}{V_k^0} = V_k^0 f\left(\frac{V_k}{V_k^0}\right) \geq 0,$$

for any $S_k, V_k > 0$. The definition of the fading memory space and Corollary 2.3 imply L_1 is well-defined, that is, L_1 is bounded for all $t > 0$. Thus, $L_1 \geq 0$ with equality if and only if $S_k = S_k^0$, $V_k = V_k^0$ and $E_k(t-r) = 0$ for almost all $r \in [0, \infty)$, which is a global minimum.

Differentiating L_1 along the solution of (2.5) and using integration by parts, we obtain

$$\begin{aligned}
L_1' &= \sum_{k=1}^{n} c_k \Bigg[\Lambda_k - d_k S_k - (d_k + \delta_k) V_k - (d_k + \varepsilon_k) E_k \\
&\quad - \frac{\Lambda_k S_k^0}{S_k} + \sum_{j=1}^{n} \beta_{kj} S_k^0 \int_{r=0}^{\infty} f_j(r) E_j(t-r)dr + (d_k + \alpha_k) S_k^0 \\
&\quad - \frac{\alpha_k S_k V_k^0}{V_k} + \sum_{j=1}^{n} \beta_{kj}^1 V_k^0 \int_{r=0}^{\infty} f_j(r) E_j(t-r)dr + (d_k + \delta_k) V_k^0 \\
&\quad + \sum_{j=1}^{n} (\beta_{kj} S_k^0 + \beta_{kj}^1 V_k^0) \int_{r=0}^{\infty} \alpha_j(r) \left(\frac{-\partial E_j(t-r)}{\partial r} \right) dr \Bigg] \\
&= \sum_{k=1}^{n} c_k \Bigg[d_k S_k^0 \left(2 - \frac{S_k}{S_k^0} - \frac{S_k^0}{S_k} \right) + \alpha_k S_k^0 \left(3 - \frac{V_k}{V_k^0} - \frac{S_k^0}{S_k} - \frac{S_k V_k^0}{S_k^0 V_k} \right) \\
&\quad + \sum_{j=1}^{n} (\beta_{kj} S_k^0 + \beta_{kj}^1 V_k^0) \int_{r=0}^{\infty} f_j(r) E_j(t-r)dr - (d_k + \varepsilon_k) E_k \Bigg] \\
&\quad + \sum_{j=1}^{n} (\beta_{kj} S_k^0 + \beta_{kj}^1 V_k^0) \left(a_j E_j - \int_{r=0}^{\infty} f_j(r) E_j(t-r)dr \right) \\
&\leq \sum_{k=1}^{n} \omega_k \left[\frac{\sum_{j=1}^{n} (\beta_{kj} S_k^0 + \beta_{kj}^1 V_k^0) a_j}{d_k + \varepsilon_k} E_j - E_k \right] \\
&= (\omega_1, \omega_2, \ldots, \omega_n)(M_0 E - E) = (\rho(M_0) - 1)(\omega_1, \omega_2, \ldots, \omega_n) E \leq 0.
\end{aligned}$$

Here $E(t) = (E_1(t), E_2(t), \ldots, E_n(t))^T$. And we note that $\Lambda_k = (d_k + \alpha_k)S_k^0$ and $d_k + \delta_k = \frac{\alpha S_k^0}{V_k^0}$. Denote $Y = \{(S_1, V_1, E_1(\cdot); \ldots; S_n, V_n, E_n(\cdot)) \in \Gamma \mid L_1' = 0\}$ and Z be the largest compact invariant set in Y, we will show $Z = \{P_0\}$. $L_1' = 0$ implies that $S_k = S_k^0$ and $V_k = V_k^0$. Hence, from the second equation of (2.5), we have

$$\sum_{j=1}^{n} \beta_{kj}^1 \int_{r=0}^{\infty} f_j(r) E_j(t-r) dr = 0,$$

and thus

$$\beta_{kj}^1 \int_{r=0}^{\infty} f_j(r) E_j(t-r) dr = 0, \quad \text{for } 1 \le k, j \le n.$$

Then, by irreducibility of B^1, for each j, there exists $k \neq j$ such that $\beta_{kj}^1 \neq 0$, which implies $\int_{r=0}^{\infty} f_j(r) E_j(t-r) dr = 0$. Furthermore, from the third equation, we have $E_{jt}(s) = 0$, $s \in (-\infty, 0]$, $j = 1, 2, \ldots, n$. Therefore $Z = \{P_0\}$. By the classical LaSalle–Lyapunov invariance principle (see [7, Theorem 3.4.7] or [16, Theorem 5.3.1]), E_0 is globally stable. This completes the proof of Theorem 3.1(i).

3.2. *Proof of Theorem* 3.1(ii)

Let $P^* = (S_1^*, V_1^*, E_1^*; \ldots; S_n^*, V_n^*, E_n^*)$, $S_k^*, V_k^*, E_k^* > 0$ for $1 \le k \le n$, denote an endemic equilibrium whose existence is established in Theorem 2.2. We prove that P^* is globally stable when $R_0^V > 1$. In particular, this implies that the endemic equilibrium is unique in the interior of Γ when it exists. Set

$$\bar{\beta}_{kj} = \beta_{kj} a_j S_k^* E_j^*, \quad \bar{\beta}_{kj}^1 = \beta_{kj}^1 a_j V_k^* E_j^*, \quad 1 \le k, j \le n, \quad n \ge 2, \tag{3.1}$$

and

$$\bar{B} = \begin{bmatrix} \Sigma_{l \neq 1} \bar{\beta}_{1l} & -\bar{\beta}_{21} & \cdots & -\bar{\beta}_{n1} \\ -\bar{\beta}_{12} & \Sigma_{l \neq 2} \bar{\beta}_{2l} & \cdots & -\bar{\beta}_{n2} \\ \vdots & \vdots & \ddots & \vdots \\ -\bar{\beta}_{1n} & -\bar{\beta}_{2n} & \cdots & \Sigma_{l \neq n} \bar{\beta}_{nl} \end{bmatrix}, \quad \bar{B}^1 = \begin{bmatrix} \Sigma_{l \neq 1} \bar{\beta}_{1l}^1 & -\bar{\beta}_{21}^1 & \cdots & -\bar{\beta}_{n1}^1 \\ -\bar{\beta}_{12}^1 & \Sigma_{l \neq 2} \bar{\beta}_{2l}^1 & \cdots & -\bar{\beta}_{n2}^1 \\ \vdots & \vdots & \ddots & \vdots \\ -\bar{\beta}_{1n}^1 & -\bar{\beta}_{2n}^1 & \cdots & \Sigma_{l \neq n} \bar{\beta}_{nl}^1 \end{bmatrix}.$$

Note that $\overline{B}(\overline{B^1})$ is the Laplacian matrix of the matrix $(\bar{\beta}_{kj})((\bar{\beta}_{kj}^1))$ (see Appendix A). Since $(\beta_{kj})((\beta_{kj}^1))$ is irreducible, matrices $(\bar{\beta}_{kj})((\bar{\beta}_{kj}^1))$ and $\bar{B}(\bar{B}^1)$ are also irreducible. Let C_{kj} denote the cofactor of the (k, j) entry of $\bar{B}$. We know that system $\bar{B}v = 0$ has a positive solution $v = (v_1, v_2, \ldots, v_n)$, where $v_k = C_{kk} > 0$ for $k = 1, 2, \ldots, n$, by Theorem A.1. Consider a Lyapunov functional

$$L_2 = L_{21} + L_{22}, \tag{3.2}$$

where

$$L_{21} = \sum_{k=1}^{n} v_k \left[S_k^* f\left(\frac{S_k}{S_k^*}\right) + V_k^* f\left(\frac{V_k}{V_k^*}\right) + E_k^* f\left(\frac{E_k}{E_k^*}\right) \right], \tag{3.3}$$

$$L_{22} = \sum_{k,j=1}^{n} v_k \left[\beta_{kj} S_k^* + \beta_{kj}^1 V_k^*\right] \int_{r=0}^{\infty} \alpha_j(r) E_j^* f\left(\frac{E_j(t-r)}{E_j^*}\right) dr. \tag{3.4}$$

The definition of the fading memory space, Theorem 2.2 and Corollary 2.3 imply L_2 is well-defined, that is, L_2 is bounded for all $t > 0$. We also note that f has only one extreme value, which is the global minimum: $f(1) = 0$. Thus, $L_2 \geq 0$ with equality if and only if $S_k(t) = S_k^*$, $V_k(t) = V_k^*$, $E_k(t) = E_k^*$ and $E_k(t-\xi) = E_k^*$ for almost all $\xi > 0$.

Differentiating L_{21} along the solution of (2.5) and using equilibrium Eqs. (2.8)–(2.10), we obtain

$$\begin{aligned}
L_{21}' = \sum_{k=1}^{n} v_k \Bigg[& \Lambda_k - d_k S_k(t) - (d_k + \delta_k) V_k(t) - (d_k + \varepsilon_k) E_k(t) \\
& - \frac{\Lambda_k S_k^*}{S_k(t)} + \sum_{j=1}^{n} \beta_{kj} S_k^* \int_0^\infty f_j(r) E_j(t-r) dr + (d_k + \alpha_k) S_k^* \\
& - \frac{\alpha_k S_k V_k^*}{V_k(t)} + \sum_{j=1}^{n} \beta_{kj}^1 V_k^* \int_0^\infty f_j(r) E_j(t-r) dr + (d_k + \delta_k) V_k^* \\
& - \sum_{j=1}^{n} (\beta_{kj} S_k + \beta_{kj}^1 V_k) \frac{E_k^*}{E_k(t)} \int_0^\infty f_j(r) E_j(t-r) dr + (d_k + \varepsilon_k) E_k^* \Bigg] \\
= \sum_{k=1}^{n} v_k \Bigg\{ & d_k S_k^* \left(2 - \frac{S_k(t)}{S_k^*} - \frac{S_k^*}{S_k(t)} \right) \\
& + \alpha_k S_k^* \left(3 - \frac{V_k(t)}{V_k^*} - \frac{S_k^*}{S_k(t)} - \frac{S_k(t) V_k^*}{S_k^* V_k(t)} \right) \\
& + \sum_{j=1}^{n} \beta_{kj} S_k^* E_j^* \left[a_j \left(2 - \frac{S_k^*}{S_k} - \frac{E_k}{E_k^*} \right) \right. \\
& \left. + \int_0^\infty f_j(r) \left(\frac{E_j(t-r)}{E_j^*} - \frac{S_k E_k^* E_j(t-r)}{S_k^* E_k E_j^*} \right) dr \right] \\
& + \sum_{j=1}^{n} \beta_{kj}^1 V_k^* E_j^* \left[a_j \left(\frac{V_k}{V_k^*} - \frac{E_k}{E_k^*} \right) \right. \\
& \left. + \int_0^\infty f_j(r) \left(\frac{E_j(t-r)}{E_j^*} - \frac{V_k E_k^* E_j(t-r)}{V_k^* E_k E_j^*} \right) dr \right] \Bigg\}. \qquad (3.5)
\end{aligned}$$

Differentiating L_{22} along the solution of (2.5) and using integration by parts, we obtain

$$L_{22}' = \sum_{k,j=1}^{n} v_k (\beta_{kj} S_k^* + \beta_{kj}^1 V_k^*) \int_0^\infty \alpha_j(r) \frac{\partial}{\partial t} \left(E_j^* f \left(\frac{E_j(t-r)}{E_j^*} \right) \right) dr$$

$$= \sum_{k,j=1}^{n} v_k(\beta_{kj}S_k^* + \beta_{kj}^1 V_k^*)\int_0^\infty \alpha_j(r)\left[-\frac{\partial}{\partial t}\left(E_j^* f\left(\frac{E_j(t-r)}{E_j^*}\right)\right)\right]dr$$

$$= \sum_{k,j=1}^{n} v_k(\beta_{kj}S_k^* + \beta_{kj}^1 V_k^*)E_j^*$$

$$\times\left[\frac{a_j E_j}{E_j^*} - \int_0^\infty f_j(r)\left(\frac{E_j(t-r)}{E_j^*} + \ln\frac{E_j(t)}{E_j(t-r)}\right)dr\right]. \tag{3.6}$$

Combining Eqs. (3.5) and (3.6), we have

$$\begin{aligned}
L_2' = \sum_{k=1}^{n} v_k &\left[d_k S_k^*\left(2 - \frac{S_k(t)}{S_k^*} - \frac{S_k^*}{S_k(t)}\right)\right.\\
&\left.+ (d_k + \delta_k)V_k^*\left(3 - \frac{V_k(t)}{V_k^*} - \frac{S_k^*}{S_k} - \frac{S_k(t)V_k^*}{S_k^* V_k(t)}\right)\right]\\
&+ \sum_{k,j=1}^{n} v_k\beta_{kj}S_k^*E_j^*\left[a_j\left(2 - \frac{S_k^*}{S_k} - \frac{E_k}{E_k^*} + \frac{E_j}{E_j^*}\right)\right.\\
&\left.- \int_0^\infty f_j(r)\left(\frac{S_k E_k^* E_j(t-r)}{S_k^* E_k E_j^*} + \ln\frac{E_j}{E_j(t-r)}\right)dr\right]\\
&+ \sum_{k,j=1}^{n} v_k\beta_{kj}^1 V_k^* E_j^*\left[a_j\left(3 - \frac{S_k^*}{S_k} - \frac{S_k V_k^*}{S_k^* V_k} - \frac{E_k}{E_k^*} + \frac{E_j}{E_j^*}\right)\right.\\
&\left.- \int_0^\infty f_j(r)\left(\frac{V_k E_k^* E_j(t-r)}{V_k^* E_k E_j^*} + \ln\frac{E_j}{E_j(t-r)}\right)dr\right].
\end{aligned}$$

In the above derivation, when we apply the following facts: $\frac{S_k}{S_k^*} + \frac{S_k^*}{S_k} \geq 2$, $\frac{S_k^*}{S_k} + \frac{V_k}{V_k^*} + \frac{S_k V_k^*}{S_k^* V_k} \geq 3$ with equality holding if and only if $S_k = S_k^*$, $V_k = V_k^*$, we have

$$\begin{aligned}
L_2' \leq \sum_{k,j=1}^{n} v_k\beta_{kj}S_k^*E_j^*\int_0^\infty f_j(r)&\left[-f\left(\frac{S_k^*}{S_k}\right) - f\left(\frac{S_k E_k^* E_j(t-r)}{S_k^* E_k E_j^*}\right)\right.\\
&\left.+\left(\frac{E_j}{E_j^*} - \frac{E_k}{E_k^*} - \ln\frac{S_k^*}{S_k}\cdot\frac{S_k E_k^* E_j(t-r)}{S_k^* E_k E_j^*}\cdot\frac{E_j(t)}{E_j(t-r)}\right)\right]dr\\
+ \sum_{k,j=1}^{n} v_k\beta_{kj}^1 V_k^* E_j^*\int_0^\infty f_j(r)&\left[-f\left(\frac{S_k^*}{S_k}\right) - f\left(\frac{S_k V_k^*}{S_k^* V_k}\right) - f\left(\frac{V_k E_k^* E_j(t-r)}{V_k^* E_j^* E_k}\right)\right.\\
&\left.+\left(\frac{E_j}{E_j^*} - \frac{E_k}{E_k^*} - \ln\frac{S_k^*}{S_k}\cdot\frac{S_k V_k^*}{S_k^* V_k}\cdot\frac{V_k E_k^* E_j(t-r)}{V_k^* E_k E_j^*}\cdot\frac{E_j(t)}{E_j(t-r)}\right)\right]dr
\end{aligned}$$

$$\leq \sum_{k,j=1}^{n} v_k(\bar{\beta}_{kj} + \bar{\beta}^1_{kj}) \left(\frac{E_j}{E^*_j} - \frac{E_k}{E^*_k} \right) - \sum_{k,j=1}^{n} v_k(\bar{\beta}_{kj} + \bar{\beta}^1_{kj}) \ln \frac{E^*_k E_j}{E_k E^*_j}$$

$$=: H_n - H^1_n.$$

Here we used fact that $f(z) = z - 1 - \ln z$, $z \in R^+$, has the global minimum at $z = 1$ and $f(1) = 0$. It follows from $\bar{B}v = 0$ and $\bar{B}^1 v = 0$ that

$$\sum_{j=1}^{n} \bar{\beta}_{jk} v_j = \sum_{i=1}^{n} \bar{\beta}_{ki} v_k, \quad \sum_{j=1}^{n} \bar{\beta}^1_{jk} v_j = \sum_{i=1}^{n} \bar{\beta}^1_{ki} v_k$$

or, using Eq. (3.1), we have

$$\sum_{j=1}^{n} \beta_{jk} a_k S^*_j E^*_k v_j = \sum_{i=1}^{n} \beta_{ki} a_i S^*_k E^*_i v_k, \quad \sum_{j=1}^{n} \beta^1_{jk} a_k V^*_j E^*_k v_j = \sum_{i=1}^{n} \beta^1_{ki} a_i V^*_k E^*_i v_k. \tag{3.7}$$

This implies that

$$\begin{aligned}
\sum_{k,j=1}^{n} v_k \beta_{kj} a_j S^*_k E_j &= \sum_{k=1}^{n} E_k \sum_{j=1}^{n} \beta_{jk} a_k S^*_j v_j \\
&= \sum_{k=1}^{n} \frac{E_k}{E^*_k} \sum_{i=1}^{n} \beta_{ki} a_i S^*_k E^*_i v_k \\
&= \sum_{k,j=1}^{n} v_k \beta_{kj} a_j S^*_k E^*_j \frac{E_k}{E^*_k}, \\
\sum_{k,j=1}^{n} v_k \beta^1_{kj} a_j S^*_k E_j &= \sum_{k=1}^{n} E_k \sum_{j=1}^{n} \beta^1_{jk} a_k S^*_j v_j \\
&= \sum_{k=1}^{n} \frac{E_k}{E^*_k} \sum_{i=1}^{n} \beta^1_{ki} a_i S^*_k E^*_i v_k \\
&= \sum_{k,j=1}^{n} v_k \beta^1_{kj} a_j S^*_k E^*_j \frac{E_k}{E^*_k}.
\end{aligned}$$

So we have $H_n \equiv 0$ for all $E_1, E_2, \ldots, E_n > 0$.

Next, it is reasonable to show that $H^1_n \equiv 0$ for all $E_1, E_2, \ldots, E_n > 0$ in the interior of Γ. Since the arguments are essentially the same in the Proof of [5, Theorem 1.1]; [6] and [18, Sec. 5], we omit the details here. Thus $H_n \leq 0$, $H^1_n \leq 0$ implies that $L'_2 \leq 0$. $L'_2 = 0$ if and only if $S_k(t) = S^*_k$, $V_k(t) = V^*_k$ and $E_k(t-s) = E^*_k$ for almost all $s \in [0, \infty)$. Again by the Lyapunov–LaSalle invariance principle, all solutions of (2.5) are attracted to M, which is the largest invariant subset of $L'_2 \leq 0$. Since M is invariant with respect to (2.5), it is ease to verify that $M = (S^*, V^*, E^*) = P^*$.

This shows that $\lim_{t\to\infty}(S(t), V(t), E(t)) = P^*$. This completes the proof of Theorem 3.1(ii).

Remark 3.2. Compared to results in [5, 6], the group structure in model (2.4) greatly increases the complexity exhibited in the derivatives of the Lyapunov functionals. These Lyapunov functionals are motivated by the works by Huang *et al.* [13], Korobeinikov [14], McCluskey [21] and Wang *et al.* [28, 29]. The key to our analysis is a complete description of the patterns exhibited in the derivative of the Lyapunov functionals using graph theory.

4. Vaccination Effects

Theorem 3.1 implies that the disease global dynamics of (2.5) is completely determined by the basic reproduction number R_0^V. Hence the vaccination effects depend on whether the basic reproduction number can be reduced to be below the unity or not. Recall that when $\alpha_k = 0$, (2.5) will become the model of [18] with a basic reproduction number $R_0^1 = \rho(\frac{\beta_{kj}a_k\Lambda_k}{(d_k+\varepsilon_k)(d_k+\alpha_k)})_{1\le k,j\le n}$. By Theorem 3.1 of Michael *et al.* [18], when $R_0^1 > 1$, then system has a unique endemic equilibrium P^*, and P^* is globally asymptotically stable. We now consider the vaccination effects by the continuous vaccination strategy. Let

$$R_1^V \triangleq R_0^V|_{\beta_{kj}^1=0 \text{ or } \delta_k\to\infty} = \rho\left(\frac{\beta_{kj}a_k\Lambda_k}{(d_k+\varepsilon_k)(d_k+\alpha_k)}\right)_{1\le k,j\le n}$$

which are the basic reproduction number of (2.4) if we neglect the possibility for vaccines to be infected ($\beta_{kj}^1 = 0$), $1 \le k, j \le n$ or neglect the time for them to obtain immunity ($\delta_k \to \infty$). It is obvious that $R_1^V \le R_0^V$. Since $\beta_{kj} > \beta_{kj}^1$, $1 \le k, j \le n$. Calculating the derivative of R_0^V with respect to α_k, we can obtain

$$\frac{\partial R_0^V}{\partial \alpha_k} = \rho\left(\frac{[(\beta_{kj}^1 - \beta_{kj})\Lambda_k d_k - \beta_{kj}\Lambda_k\delta_k]a_k}{(d_k+\varepsilon_k)(d_k+\alpha_k)^2(d_k+\delta_k)}\right)_{1\le k,j\le n} < 0. \tag{4.1}$$

It follows that $R_0^V \le R_0^V|_{\alpha_k=0} = R_0^*$. Moreover, we have

$$\lim_{\alpha_k\to\infty} R_1^V = 0 \quad \text{and} \quad \lim_{\alpha_k\to\infty} R_0^V = \rho\left(\frac{\beta_{kj}^1\Lambda_k a_k}{(d_k+\varepsilon_k)(d_k+\delta_k)}\right)_{1\le k,j\le n} \triangleq R_2.$$

To understand the effects of vaccinations, we should suppose that without vaccinations the disease is in endemic state, i.e. $R_0^* > 1$. Since $\frac{\partial R_0^V}{\partial \alpha_k} < 0$, vaccination always has a good effect for disease control by decreasing the basic reproduction number. Next, we will discuss this issue in the following two cases:

Case I. If we neglect the possibility for vaccines to be infected $\beta_{kj}^1 = 0$ or neglect the time for them to obtain complete immunity $\delta_k \to \infty$, then by $\frac{\partial R_1^V}{\partial \alpha_k} < 0$, $\lim_{\alpha_k\to\infty} R_1^V = 0$, we can conclude that the disease always can be eradicated by some suitable vaccination strategy.

Case II. If we consider the possibility for vaccines to be infected $\beta_{kj}^1 > 0$ and the time for them to obtain immunity (δ_k is finite), by $\frac{\partial R_0^V}{\partial \alpha_k} < 0$ and $\lim_{\alpha_k \to \infty} R_0^V = R_2$. If $R_2 < 1$, then there is a unique $\aleph$ for continuous strategy such that $R_0^V = 1$ for $\alpha_k = \aleph$. Hence $R_0^V < 1$ for $\alpha_k > \aleph$. By Theorem 3.1, the disease can be eliminated by some suitable vaccination strategies (satisfying $\alpha_k > \aleph$). If $R_2 \geq 1$, then $R_0^V > R_2 \geq 1$. By Theorem 3.1, the situation is so serious that disease cannot be eradicated by any vaccination strategies (for any values of α_k). Note that R_2 means the average new infections produced by one infected individual during his lifespan when the whole population is vaccinated. And clearly, $R_2 < 1$ is the necessary condition for disease elimination. The validity of the necessary condition requires that the possibility for the vaccines to be infected is small (β_{kj}^1 is small) or the time for them to gain immunity is short (δ_k is large). These two improvements of the efficacy of vaccines may lead to disease eradication. If the time for the vaccines to obtain immunity or the possibility for them to be infected before gaining immunity neglected, this necessary condition is automatically satisfied and the disease can always be eradicated by some suitable vaccination strategies. This warns over evaluation for the effect of vaccination.

Acknowledgments

The authors are very grateful to the anonymous referees for carefully reading and valuable comments which leads to a significant improvement of the original manuscript. This work is supported by a scholarship from the China Scholarship Council while the first author visiting Shizuoka University. Y. Takeuchi is supported in part by the Grand-in-Aid for Scientific Research(C) No. 22540122, Japan Society for the Promotion of Science. S. Liu is supported by SRF of Harbin Institute of Technology (HITC200714) and program of excellent Team in Harbin Institute of Technology.

Appendix A. Kirchhoff's Matrix-Tree Theorem

Given a nonnegative matrix $A = (a_{ij})$, the *directed graph* $G(A)$ associated with $A = (a_{ij})$ has vertices $1, 2, \ldots, n$ with a directed arc (i, j) from i to j if and only if $a_{ij} = 0$. It is *strongly connected* if any two distinct vertices are joined by an oriented path. Matrix A is irreducible if and only if $G(A)$ is strongly connected [2]. A *tree* is a connected graph with no cycles. A subtree T of a graph G is said to be *spanning* if T contains all the vertices of G. A *directed tree* is a tree in which each edge has been replaced by an arc directed one way or the other. A directed tree is said to be *rooted* at a vertex, called the root, if every arc is oriented in the direction towards to the root. An *oriented cycle* in a directed graph is a simple closed oriented path. A *unicyclic graph* is a directed graph consisting of a collection of disjoint rooted directed trees whose root are on an oriented cycle. We refer the reader to [22, Theorem 5.5] for more details of these concepts.

For a given nonnegative matrix $A = (a_{ij})$, let

$$L = \begin{bmatrix} \Sigma_{l\neq 1}\bar{a}_{1l} & -\bar{a}_{21} & \cdots & -\bar{a}_{n1} \\ -\bar{a}_{12} & \Sigma_{l\neq 2}\bar{a}_{2l} & \cdots & -\bar{a}_{n2} \\ \vdots & \vdots & \ddots & \vdots \\ -\bar{a}_{1n} & -\bar{a}_{2n} & \cdots & \Sigma_{l\neq n}\bar{a}_{nl} \end{bmatrix}$$

be the Laplacian matrix of the directed graph $G(A)$ and C_{ij} denote the cofactor of the (i, j) entry of L. For the linear system

$$Lv = 0, \tag{A.1}$$

the following results hold (see details in [6]).

Theorem A.1. *Assume that $n \geq 2$ and that A is irreducible. Then following results hold*

(i) *The solution space of* (A.1) *has dimension* 1, *with a basis*

$$(v_1, v_2, \ldots, v_n) = (C_{11}, C_{22}, \ldots, C_{nn}).$$

(ii) *For $1 \leq k \leq n$,*

$$C_{kk} = \sum_{T\in \mathrm{T}_k} w(T) = \sum_{T\in \mathrm{T}_k} \prod_{(r,m)\in E(T)} a_{rm} > 0,$$

where T_k is the set of all directed spanning subtrees of $G(A)$ that are rooted at vertex k, $w(T)$ is the weight of a directed tree T, and $E(T)$ denotes the set of directed arcs in T.

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