Journal of Theoretical Biology 291 (2011) 56–64

Contents lists available at SciVerse ScienceDirect

Journal of Theoretical Biology

journal homepage: www.elsevier.com/locate/yjtbi

Dynamics of a multigroup epidemiological model with group-targeted vaccination strategies

Lamwah Chow [a,b,1], Meng Fan [a,*,1], Zhilan Feng [c,2]

[a] School of Mathematics and Statistics, Northeast Normal University, 5268 Renmin Street, Changchun, Jilin 130024, PR China
[b] Department of Applied Mathematics, School of Science, Changchun University of Science and Technology, 7089 Weixing Road, Changchun, Jilin 130022, PR China
[c] Department of Mathematics, Purdue University, West Lafayette, IN 47907, USA

ARTICLE INFO

Article history:
Received 26 June 2011
Received in revised form
27 August 2011
Accepted 7 September 2011
Available online 21 September 2011

Keywords:
Multigroup epidemiological model
Vaccination strategy
Control reproduction number
Type reproduction number

ABSTRACT

A multigroup *SIR* epidemiological model is used to study the effects of group-targeted vaccination strategies on disease control and prevention. The model takes into consideration both proportionate and preferential mixing patterns between groups. We show that the dynamical behaviors of the model are determined by the control reproduction number $\mathcal{R}_v$ and, under certain conditions, by the type-reproduction number T_{1v}. These reproduction numbers provide criteria for evaluating control strategies including targeted vaccination programs and reduction of interactions between groups. We also illustrate how these reproduction numbers can be used to examine the influence of population heterogeneities such as group preferences, activity levels, and mixing patterns. Criteria are also established for disease eradication from the entire network of populations by applying vaccination strategies in one or some sub-populations.

1. Introduction

Control and prevention of infectious diseases can become increasingly difficult as the connectivity between multiple groups of populations (e.g., different schools or countries) increases. The SARS outbreak in 2003 and the A-H1N1 influenza outbreak in 2009 are two examples which demonstrated the challenges for disease control when multiple populations are connected. Common characteristics of these epidemics/pandemics include a rapid spread across multiple countries and transmission between different subgroups in a population. Population heterogeneities that may have significant influence on disease spread and control include sizes of sub-populations, activity levels, susceptibility (immunity) and infectivity, and contact (mixing) patterns within and between populations. This makes it crucial to study mathematical models that take into consideration these heterogeneities.

Multigroup models have been used to study transmission dynamics of infectious diseases in heterogeneous populations (see, for example, Lloyd and May, 1996; Thieme, 2003 and references therein). Examples of using multigroup models to study specific infectious diseases include the following: Huang et al. (1992) on HIV/AIDS; Feng and Velasco-Hernandez (1997) on dengue; Bowman et al. (2005) on West Nile virus; Feng et al. (2005) on age-structured multigroup models; Edwards et al. (2010) on sexually transmitted diseases; and so on. Global stability results on multigroup disease models have also been studied, including those presented by Guo et al. (2006), some of which can be applied to the model considered in this paper. The results in Guo et al. (2006) focus more on stability properties of their model, whereas the current paper has its emphasis on applications of the model to the evaluation of disease control programs. More importantly, we investigate how preferential mixing (an important type of population heterogeneity) may influence the effectiveness of disease control strategies.

One of the most effective control measures against infectious diseases is to increase population immunity via vaccination. The uses of vaccine have played a critical role in reducing the prevalence of measles worldwide. Before a measles vaccine was discovered in 1962, an infection with measles would occur in almost all children. However, the measles incidence has decreased dramatically with an increase in measles vaccination. One of such examples is the successful vaccination program used in Australia according to the information provided by the Better Health Channel (2011), a website supported by the Department of Health of the Victorian State Government. In Australia, several measles vaccine programs have been available, including the National Immunization Program in 1983, the introduction of a second measles vaccine dose in 1994, and the primary school Measles Control Campaign in 1998 (Better Health Channel, 2011; Gidding, 2005). The average number of measles cases in Australia

* Corresponding author.
E-mail address: mfan@nenu.edu.cn (M. Fan).
[1] The authors are supported by NSFC, NCET-08-0755, and FRFCU.
[2] The author's research is partially supported by the NSF grants DMS-0719697 and DMS-1022758.

0022-5193/$ - see front matter © 2011 Published by Elsevier Ltd.
doi:10.1016/j.jtbi.2011.09.020

as a result of these programs has decreased from 75 cases per year between 1997 and 1999 to five cases per year from 2005 to 2007.

Various mathematical models have been used to study the effects of vaccinations for infectious diseases, including Castillo-Chavez and Feng (1998) on TB; Shulgin et al. (1998) on pulse vaccination strategy; Kribs-Zaleta and Martcheva (2002) using a model structured by age-since-infection; Keeling et al. (2003) on foot-and-mouth disease; Shim et al. (2006) on rotavirus; and Towers and Feng (2009), Glasser et al. (2010) and Qiu and Feng (2010) on influenza. Most of these models assume a homogeneous mixing in the population being considered. In the case when vaccine resources or vaccine uptake can vary significantly across different countries or different social groups, models with heterogeneous mixing are needed in order to better evaluate vaccination strategies. Particulary, interesting questions to explore include: (1) What are the effects of vaccination programs when applied to one or more of the sub-populations? (2) How will different mixing patterns between the sub-populations affect the outcomes of the vaccination programs? (3) Is it possible to eradicate the infection from the entire population by vaccinating only one or several of the sub-populations? The main objective of this paper is to study some of these questions.

When multiple groups or multiple populations are considered in a single model, one of the factors that can significantly influence the disease transmission dynamics is the mixing pattern between the sub-populations. A more commonly used mixing assumption is proportionate mixing, which makes the mathematical analysis much easier. Under this assumption, the probability that an individual in group i will have a contact with people in group j is proportional to the total number of contacts from group j. An extension of this mixing function is the preferential mixing, which assumes that each subgroup will reserve a fraction of its contacts to individuals within the same group and distribute the rest of its contacts proportionally among all other groups. The model we study in this paper will include both proportionate mixing and preferential mixing. Incorporation of preferential mixing in the model can provide more valuable information about control programs, although it will make the mathematical analysis more challenging. We will use the model to examine how the effects of vaccination programs might be affected by various factors including the degree of preference within subgroups, group activity levels, and population sizes of subgroups. The evaluations will be based on the control reproduction numbers and the epidemic sizes.

We will also consider the use of a *type reproduction number* as defined by Roberts and Heesterbeek (2003) and Heesterbeek and Roberts (2007) for the evaluation of vaccination strategies. As pointed out in these studies, for multigroup models the standard basic reproduction number ($\mathcal{R}_0$) may be less useful in some cases because it will underestimate the control effort required. They developed a new threshold quantity, which they termed the type reproduction number, as a measure for control efforts when a particular subgroup is targeted. Our results show that it is possible to eradicate the disease if sufficient vaccination efforts are applied to only the reservoir population of the infection. In addition, we demonstrate that the usual control reproduction number for the entire network ($\mathcal{R}_v$) and the type reproduction number (T_{1v}) can provide different information regarding the role of vaccination in reducing these threshold quantities.

The paper is organized as follows. In Section 2, we present an n-groups model which includes a general mixing function and vaccination. This model is used to compute the control reproduction numbers including $\mathcal{R}_v$ and T_{1v}. Some qualitative and stability results of the model system are also included in this section. In Section 3, we use the model results to investigate the effects of various vaccination strategies and their dependence on model parameters. Some conclusions and discussions are included in Section 4.

2. Model formulation and analysis

The uses of proportionate and preferential functions in metapopulation models have been previously considered. For example, Busenberg and Castillo-Chavez (1991) provided detailed descriptions on proportionate mixing. Various formulations of preferential mixing functions are considered by Nold (1980), Jacquez et al. (1988), Hethcote (1996), Feng et al. (in review), and Glasser et al. (in revision). In this section, we introduce the metapopulation model for n subgroups that may have different properties including activity levels, population sizes, and preferences for within and between sub-populations. The model is used to derive the control reproduction number and the type reproduction number. We present threshold conditions determined by these reproduction numbers and examine how vaccination strategies can be influenced by various factors representing population heterogeneities.

2.1. Model formulation

Consider a network of n populations whose sizes are denoted by N_i for $i=1,2,\ldots,n$. These population sizes remain constant for all time by assuming equal per-capita birth and death rates (μ). Each of the sub-populations (or subgroups) is divided into three epidemiological classes: susceptible (S_i), infectious (I_i), and removed either by recovery from infection or by vaccination (R_i). The recovery rate (γ) is assumed to be the same for all sub-populations. All individuals are born susceptible. For each sub-population i, a fraction p_i is vaccinated and immune. Our multigroup model is a system consisting of the following ordinary differential equations:

$$\begin{cases} \dfrac{dS_i}{dt} = \mu N_i(1-p_i) - (\lambda_i(t)+\mu)S_i, \\ \dfrac{dI_i}{dt} = \lambda_i(t)S_i - (\gamma+\mu)I_i, \\ \dfrac{dR_i}{dt} = \mu N_i p_i + \gamma I_i - \mu R_i, \\ N_i = S_i + I_i + R_i, \quad i=1,2,\ldots,n. \end{cases} \tag{2.1}$$

Here, λ_i represents the force of infection for susceptibles in group i given by

$$\lambda_i = a_i\beta \sum_{j=1}^{n} c_{ij}\frac{I_j}{N_j}, \tag{2.2}$$

where a_i denotes the average number of contacts an individual in sub-population i has per unit of time (which represents the activity level of group i), and β is the probability of infection per contact when the contact is with an infectious individual. The fraction I_j/N_j gives the probability that a contact is with an infectious individual in sub-population j. The contact matrix (c_{ij}) has the same form as the preferential mixing considered by Jacquez et al. (1988) with

$$c_{ij} = \varepsilon_i\delta_{ij} + (1-\varepsilon_i)f_j, \quad i,j=1,2,\ldots,n. \tag{2.3}$$

The parameter ε_i is the fraction of contacts with individuals in the same sub-population, δ_{ij} is the Kronecker delta (i.e., 1 when $i=j$ and 0 otherwise), and

$$f_j = (1-\varepsilon_j)a_jN_j \Big/ \sum_k (1-\varepsilon_k)a_kN_k, \quad j=1,2,\ldots,n.$$

Clearly, unless all the subgroups are isolated (i.e., no interactions between any groups), there must be some i with $\varepsilon_i<1$. All parameters and their meanings are listed in Table 1. It is easy to verify that solutions of (2.1) remain nonnegative for all nonnegative initial conditions. Thus, the model is well posed.

Table 1
Parameter definitions and values used in the simulations illustrated in the figures.

Symbol	Definition	Value/ range
N_i	Total population of sub-population i	
S_i	Susceptible population of sub-population i	
I_i	Infected population of sub-population i	
R_i	Removed population of sub-population i	
x_i	Fraction of susceptible population of sub-population i	[0,1]
y_i	Fraction of infected population of sub-population i	[0,1]
β	Probability of infection per contact when the contact is with an infectious individual	0.03
γ	Recovery rate	0.15
μ	Per-capita birth and death rates	0.00016
ε_i	Fraction of contacts with individuals in the same sub-population	[0,1]
a_i	Average number of contacts an individual in sub-population i has per unit of time	[1,50]
p_i	Vaccination proportion of newborns of sub-population i	[0,1]
c_{ij}	Proportion of contacts a member of sub-population i has with those in sub-population j	[0,1]

Note: $i,j=1,2,\ldots,n$.

2.2. Control reproduction number and stability of equilibria

To study the dynamics of system (2.1), we only need to consider the S_i and I_i equations as they are independent of R_i. Furthermore, as the population sizes N_i are constant, it is easier to consider the fractions:

$$x_i=\frac{S_i}{N_i},\quad y_i=\frac{I_i}{N_i},\quad i=1,2,\ldots,n.$$

Thus, our analysis will focus on the following reduced system for the fractions:

$$\begin{cases}\dfrac{dx_i}{dt}=\mu(1-p_i)-(\lambda_i+\mu)x_i,\\ \dfrac{dy_i}{dt}=\lambda_i x_i-(\gamma+\mu)y_i,\\ \lambda_i=a_i\beta\displaystyle\sum_{j=1}^{n}c_{ij}y_j,\quad i=1,2,\ldots,n.\end{cases}\tag{2.4}$$

It can be shown that the biologically feasible region:

$$\mathcal{D}=\{(x_1,y_1,\ldots,x_n,y_n)\in\mathbb{R}_+^{2n}\,|\,0\le x_i+y_i\le 1,\ i=1,2,\ldots,n\}$$

is positively invariant with respect to (2.4).

For each sub-population i, if all contacts are with people within the same group (i.e., $c_{ii}=1$ and $c_{ij}=0$ for $i\neq j$), then the basic and control reproduction numbers for group i are, respectively,

$$\mathcal{R}_{0i}=\frac{\beta a_i}{\mu+\gamma},\quad \mathcal{R}_{vi}=\mathcal{R}_{0i}(1-p_i),\quad i=1,2,\ldots,n.\tag{2.5}$$

When there are contacts between sub-populations, i.e., $c_{ii}<1$ or $\varepsilon_i<1$ for some i, we can derive the basic and control reproduction numbers for the metapopulation. These reproduction numbers will be functions of $\mathcal{R}_{0i}$ or $\mathcal{R}_{vi}$. Following the approach of Diekmann et al. (1990) we can obtain from model (2.4) the next generation matrix K_v (v for vaccination):

$$K_v=\begin{pmatrix}\mathcal{R}_{01}c_{11}(1-p_1) & \mathcal{R}_{01}c_{12}(1-p_1) & \ldots & \mathcal{R}_{01}c_{1n}(1-p_1)\\ \mathcal{R}_{02}c_{21}(1-p_2) & \mathcal{R}_{02}c_{22}(1-p_2) & \ldots & \mathcal{R}_{02}c_{2n}(1-p_2)\\ \vdots & \vdots & \ddots & \vdots\\ \mathcal{R}_{0n}c_{n1}(1-p_n) & \mathcal{R}_{0n}c_{n2}(1-p_n) & \ldots & \mathcal{R}_{0n}c_{nn}(1-p_n)\end{pmatrix}$$

$$=\begin{pmatrix}\mathcal{R}_{v1}c_{11} & \mathcal{R}_{v1}c_{12} & \ldots & \mathcal{R}_{v1}c_{1n}\\ \mathcal{R}_{v2}c_{21} & \mathcal{R}_{v2}c_{22} & \ldots & \mathcal{R}_{v2}c_{2n}\\ \vdots & \vdots & \ddots & \vdots\\ \mathcal{R}_{vn}c_{n1} & \mathcal{R}_{vn}c_{n2} & \ldots & \mathcal{R}_{vn}c_{nn}\end{pmatrix}.\tag{2.6}$$

The control reproduction number $\mathcal{R}_v$ for the metapopulation is given by

$$\mathcal{R}_v=\rho(K_v),\tag{2.7}$$

where $\rho(K_v)$ denotes the dominant eigenvalue of K_v (Diekmann and Heesterbeek, 2000). Note that $\mathcal{R}_v=\mathcal{R}_v(p_1,p_2,\ldots,p_n)$ is a function of vaccination fractions p_i. The basic reproduction number $\mathcal{R}_0$ for the metapopulation is given by $\mathcal{R}_v$ when $p_i=0$ for all i, i.e., $\mathcal{R}_0=\mathcal{R}_v(0,0,\ldots,0)$.

2.2.1. Equilibria of system (2.4) and their stability

System (2.4) always has the disease-free equilibrium:

$$E_0=(x_1^0,0,x_2^0,0,\ldots,x_n^0,0),$$

where $x_i^0=(1-p_i)(i=1,2,\ldots,n)$. Let $\overset{\circ}{\mathcal{D}}$ denote the interior of $\mathcal{D}$. Then system (2.4) may have an endemic equilibrium $E^*=(x_1^*,y_1^*,x_2^*,y_2^*,\ldots,x_n^*,y_n^*)$ in $\overset{\circ}{\mathcal{D}}$, that is, $x_i^*<1$ and $y_i^*>0$ for $i=1,2,\ldots,n$. The existence and stability of these equilibria are summarized in the following result, which demonstrates that the control reproduction number $\mathcal{R}_v$ will determine whether or not the disease can be controlled.

Theorem 2.1. *Consider system* (2.4) *and let* $\mathcal{R}_v$ *be the reproduction number defined in* (2.7).

(1) *If* $\mathcal{R}_v\le 1$, *then the disease-free equilibrium* E_0 *is the only equilibrium and is globally asymptotically stable* (*g.a.s.*) *in* $\mathcal{D}$. *Thus, the disease can be eradicated when* $\mathcal{R}_v\le 1$.
(2) *If* $\mathcal{R}_v>1$, *then* E_0 *is unstable. In this case, a unique endemic equilibrium* E^* *exists and is g.a.s. in* $\overset{\circ}{\mathcal{D}}$. *Moreover, the system is uniformly persistent in* $\overset{\circ}{\mathcal{D}}$, *which implies persistence of the disease in the population.*

A proof of Theorem 2.1 can be carried out using arguments similar to those used by Guo et al. (2006). If we let $B=(b_{ij})$ be the matrix with $b_{ij}=a_i\beta c_{ij}$, then the system (2.4) has a similar mathematical structure as the system (1.3) in Guo et al. (2006). We omit the details here, as the main focus of this study is on the application of the model to the evaluation of disease control strategies.

It is clear that the control reproduction number $\mathcal{R}_v$ is a very useful quantity in disease control. An effective vaccination strategy should aim to achieve $\mathcal{R}_v<1$ so that the disease will eventually be eradicated in the whole population. If $\mathcal{R}_v>1$, the disease will become endemic in some sub-populations or the entire population.

2.3. Type reproduction number for targeted sub-populations

Although the control reproduction number $\mathcal{R}_v$ is the most commonly used quantity for a multigroup model or a metapopulation model to provide threshold conditions for eradicating an infection from the entire population, it may not be as useful for a particular sub-population which the control program targets. In some cases, the use of $\mathcal{R}_v$ may lead to an underestimate of the control efforts required to achieve a certain goal. Roberts and Heesterbeek (2003) developed a new threshold quantity, which they termed the *type reproduction number*, and explained how it

can be used to evaluate effects of control measures when a specific sub-population is targeted. Without loss of generality, we consider the case when sub-population 1 (or type 1 hosts) is being targeted by control efforts. The type reproduction number for sub-population 1, denoted by T_1, is the cumulative number of infected individuals in sub-population 1 produced by one primary infection from sub-population 1 as a result of chains of infection that link sub-populations 2 to n without other infected individuals in sub-population 1 being allowed to reproduce.

Let $\mathcal{R}_0$ be the basic reproduction number in the absence of control measures, i.e., $\mathcal{R}_0=\rho(K)$ where

$$K=\begin{pmatrix}\mathcal{R}_{01}c_{11} & \mathcal{R}_{01}c_{12} & \dots & \mathcal{R}_{01}c_{1n}\\ \mathcal{R}_{02}c_{21} & \mathcal{R}_{02}c_{22} & \dots & \mathcal{R}_{02}c_{2n}\\ \vdots & \vdots & \ddots & \vdots\\ \mathcal{R}_{0n}c_{n1} & \mathcal{R}_{0n}c_{n2} & \dots & \mathcal{R}_{0n}c_{nn}\end{pmatrix}.$$

Note that the (i,j) element, $\mathcal{R}_{0i}c_{ij}$, represents the expected number of secondary infections in sub-population i that can be generated by a typical primary infection in sub-population j within the susceptible population. To derive the type reproduction number T_1, let $\mathbf{e}$ denote the unit vector with the first element being 1 and others being 0, I denote the $n\times n$ identity matrix, and $P=(p_{ij})$ denote the projection matrix on sub-population 1 (i.e., $p_{11}=1$ and $p_{ij}=0$ for all other entries). The second generation of infected individuals is described by the vector $K\mathbf{e}$, whose i-th element $(K\mathbf{e})_i$ gives the new infections in sub-population i generated by the primary infected individual in sub-population 1.

Note that the second generation of infected individuals in sub-populations $2,3,\dots,n$ can also be expressed by $(I-P)K\mathbf{e}$, and these infected individuals will produce new infections in the third generation of infection given by the vector $K(I-P)K\mathbf{e}$. It includes $PK(I-P)K\mathbf{e}$ new infections in sub-population 1 and $(I-P)K(I-P)K\mathbf{e}$ in sub-populations $2,3,\dots,n$. Notice that the new infections described by $K(I-P)K\mathbf{e}$ do not include the contribution from infected individuals in sub-population 1 in the second infection generation. If this counting process is continued, then at the $(j+1)$-th infection generation, the expected number of infections in sub-population 1 is $\mathbf{e}^{\mathbf{T}}K((I-P)K)^{j-1}\mathbf{e}$. Thus, the total number of the secondary infections in sub-population 1 arising from the primary infected individual is $\mathbf{e}^{\mathbf{T}}K\sum_{j=1}^{\infty}((I-P)K)^{j-1}\mathbf{e}$. This series is convergent under the condition $\rho((I-P)K)<1$ (i.e., the disease will die out if there is no infection in sub-population 1), and it converges to $\mathbf{e}^{\mathbf{T}}K(I-(I-P)K)^{-1}\mathbf{e}$. Thus,

$$T_1=\mathbf{e}^{\mathbf{T}}K(I-(I-P)K)^{-1}\mathbf{e}. \tag{2.8}$$

Let K_v be the matrix given in (2.6), and let

$$T_{1v}=\mathbf{e}^{\mathbf{T}}K_v(I-(I-P)K_v)^{-1}\mathbf{e}. \tag{2.9}$$

Then, the following result can be proved using arguments similar to those in Roberts and Heesterbeek (2003, Appendix A (c) and (d)).

Theorem 2.2. *Let T_1 and T_1v be defined in* (2.8) *and* (2.9), *respectively. Assume that the conditions $\rho((I-P)K)<1$ and $\rho((I-P)K_v)<1$ hold.*

(i) *$T_1>1$ ($T_{1v}>1$) if and only if $\mathcal{R}_0>1$ ($\mathcal{R}_v>1$);*
(ii) *If only sub-population 1 is targeted for vaccination, then an infection will be eliminated over time from the entire population if the vaccination fraction p_1 satisfies $p_1>1-1/T_1$;*
(iii) *The disease will be eradicated from the entire population if $T_{1v}<1$.*

Remark 2.1. As pointed out by Roberts and Heesterbeek (2003), the above results can be generalized to consider targeted control efforts in several of the n sub-populations. Without loss of generality, assume that sub-populations i $(i=1,2,\dots s)$ are targeted. Let E_s and P_s be $n\times s$ and $n\times n$ projection matrices defined by $(E_s)_{ii}=(P_s)_{ii}=1$ for $i=1\dots s$, $(E_s)_{ij}=(P_s)_{ij}=0$ otherwise. Then,

$$T_s=\rho(\mathbf{E_s^T}K(I-(I-P_s)K)^{-1}\mathbf{E_s}),\quad T_s^v=\rho(\mathbf{E_s^T}K_v(I-(I-P_s)K_v)^{-1}\mathbf{E_s})$$

are the type reproduction numbers of (2.1) without and with vaccination, respectively.

3. Vaccination strategies

Results in the previous section suggest that threshold conditions such as $\mathcal{R}_v<1$, $p_1>1-1/T_1$, or $T_{1v}<1$ can be used to evaluate vaccination programs. How likely these conditions can be satisfied may depend highly on the degree of population heterogeneity. Particularly, the effect of vaccination on the reduction of $\mathcal{R}_v$ can be influenced by the preferential mixing (ε_i), activity levels (a_i), and population sizes (N_i). In this section, we present some analytical results for the case of $n=2$ sub-populations. Some numerical simulations are carried out for $n>2$ sub-populations.

3.1. Vaccination strategies based on the control reproduction number $\mathcal{R}_v$

In the case of $n=2$, an explicit formula for $\mathcal{R}_v$ can be obtained

$$\mathcal{R}_v=\frac{1}{2}\left[A+D+\sqrt{(A-D)^2+4BC}\right], \tag{3.1}$$

where $A=\mathcal{R}_{01}c_{11}(1-p_1)$, $B=\mathcal{R}_{01}c_{12}(1-p_1)$, $C=\mathcal{R}_{02}c_{21}(1-p_2)$, $D=\mathcal{R}_{02}c_{22}(1-p_2)$, and $\mathcal{R}_{0i}$ $(i=1,2)$ are given in (2.5). If $p_1=p_2=0$, then $\mathcal{R}_v$ reduces to

$$\mathcal{R}_0=\tfrac{1}{2}\left[\mathcal{R}_{01}c_{11}+\mathcal{R}_{02}c_{22}+\sqrt{(\mathcal{R}_{01}c_{11}-\mathcal{R}_{02}c_{22})^2+4\mathcal{R}_{01}c_{12}\mathcal{R}_{02}c_{21}}\right].$$

To study effects of vaccination strategies, assume that $\mathcal{R}_0>1$ in the absence of vaccination and

$$\mathcal{R}_{01}>1,\quad \mathcal{R}_{02}>1. \tag{3.2}$$

Let

$$\Omega=\{(p_1,p_2)|\ 0\le p_1\le 1, 0\le p_2\le 1\}. \tag{3.3}$$

Then each point $(p_1,p_2)\in\Omega$ represents a vaccination strategy.

To demonstrate the influence of preferential mixing on the effectiveness of vaccination, we consider $\mathcal{R}_v=\mathcal{R}_v(\varepsilon_1,\varepsilon_2)$ as a function of ε_1 and ε_2. Let Δ_2 denote the set consisting of all values of ε_1 and ε_2 in [0,1] except $\varepsilon_1=\varepsilon_2=1$, which represents the case when the two sub-populations do not interact. That is,

$$\Delta_2=\{(\varepsilon_1,\varepsilon_2,)|\ 0\le\varepsilon_i\le 1, i=1,2\}\backslash\{(\varepsilon_1,\varepsilon_2)|\varepsilon_1=\varepsilon_2=1\}. \tag{3.4}$$

It can be shown that

$$\frac{\partial\mathcal{R}_v}{\partial\varepsilon_1}>0,\quad \frac{\partial\mathcal{R}_v}{\partial\varepsilon_2}>0\quad \text{for all } (\varepsilon_1,\varepsilon_2)\in\Delta_2. \tag{3.5}$$

The result in (3.5) is based on the inequality

$$\begin{aligned}\frac{\partial\mathcal{R}_v}{\partial\varepsilon_1}=\frac{1}{2}\Bigg[&\mathcal{R}_{01}(1-p_1)\frac{[(1-\varepsilon_2)a_2N_2]^2}{[(1-\varepsilon_1)a_1N_1+(1-\varepsilon_2)a_2N_2]^2}\\ &+\mathcal{R}_{02}(1-p_2)\frac{(1-\varepsilon_2)^2a_1N_1a_2N_2}{[(1-\varepsilon_1)a_1N_1+(1-\varepsilon_2)a_2N_2]^2}\\ &+\frac{[\mathcal{R}_{01}(1-p_1)a_1N_1-\mathcal{R}_{02}(1-p_2)a_2N_2]^2(1-\varepsilon_2)^2a_2N_2}{[(1-\varepsilon_1)a_1N_1+(1-\varepsilon_2)a_2N_2]^3\sqrt{(A-D)^2+4BC}}\Bigg]\ge 0\end{aligned} \tag{3.6}$$

and a similar one for $\partial\mathcal{R}_v/\partial\varepsilon_2$. For ease of presentation, we first consider the simpler case in which

$$\varepsilon_1=\varepsilon_2=\varepsilon$$

and consider $\mathcal{R}_v=\mathcal{R}_v(\varepsilon)$ as a function of ε. Then, for each fixed $\varepsilon\in[0,1)$, the curve $\mathcal{R}_v(\varepsilon)=1$ divides the region Ω into two parts: one

is the region

$$\Omega_\varepsilon = \{(p_1,p_2)|\ 0 \le \mathcal{R}_v(\varepsilon) < 1, (p_1,p_2) \in \Omega, 0 \le \varepsilon < 1\},$$

which includes all points above the curve, and another is the region

$$D_\varepsilon = \{(p_1,p_2)|\ \mathcal{R}_v(\varepsilon) > 1, (p_1,p_2) \in \Omega, 0 \le \varepsilon < 1\},$$

which includes all points below the curve. It can be shown that

$$\Omega_{\tilde\varepsilon} \supseteq \Omega_{\hat\varepsilon}, \quad D_{\tilde\varepsilon} \subseteq D_{\hat\varepsilon}, \quad \text{if } 0 < \tilde\varepsilon < \hat\varepsilon < 1.$$

This implies that if $\tilde\varepsilon < \hat\varepsilon$, then the curve corresponding to $\mathcal{R}_v(\tilde\varepsilon) = 1$ is below the curve corresponding to $\mathcal{R}_v(\hat\varepsilon) = 1$ (see Fig. 1). All these curves intersect at a single point (p_{1c},p_{2c}) with

$$p_{1c} = 1 - \frac{1}{\mathcal{R}_{01}}, \quad p_{2c} = 1 - \frac{1}{\mathcal{R}_{02}}. \tag{3.7}$$

Let

$$\Omega^* \subseteqq \bigcap_{0 \le \varepsilon < 1} \Omega_\varepsilon, \quad D^* \subseteqq \bigcap_{0 \le \varepsilon < 1} D_\varepsilon. \tag{3.8}$$

Fig. 1 depicts these two regions Ω^* and D^* as subsets of Ω. We observe from Fig. 1 that the region Ω^* (lighter-shaded) is determined by the two inequalities

$$p_{1c} < p_1 < 1, \quad p_{2c} < p_2 < 1, \tag{3.9}$$

where p_{1c} and p_{2c} are defined in (3.7). For region D^* (darker shaded), the upper bound is determined by the line

$$p_2 = -\mathcal{A}p_1 + \mathcal{B}, \tag{3.10}$$

where

$$\mathcal{A} = \frac{\mathcal{R}_{01}a_1N_1}{\mathcal{R}_{02}a_2N_2}, \quad \mathcal{B} = \frac{(\mathcal{R}_{01}-1)a_1N_1 + (R_{02}-1)a_2N_2}{\mathcal{R}_{02}a_2N_2}. \tag{3.11}$$

The two regions intersect at the point (p_{1c},p_{2c}).

The above analysis for the case of $\varepsilon_1 = \varepsilon_2$ can be extended to the case when $\varepsilon_1 \ne \varepsilon_2$. Let

$$\Omega^* = \{(p_1,p_2)|p_{1c} < p_1 < 1,\ p_{2c} < p_2 < 1\},$$

$$D^* = \{(p_1,p_2)|0 < p_1 < 1,\ p_2 > -\mathcal{A}p_1 + \mathcal{B}\}, \tag{3.12}$$

where p_{1c} and p_{2c} are defined in (3.7), and $\mathcal{A}$ and $\mathcal{B}$ are given in (3.11). Note that the regions Ω^* and D^* defined in (3.12) are the same regions as shown in Fig. 1. The following result is helpful for understanding how the effect of vaccination strategies may be influenced by mixing patterns (represented by ε_1 and ε_2).

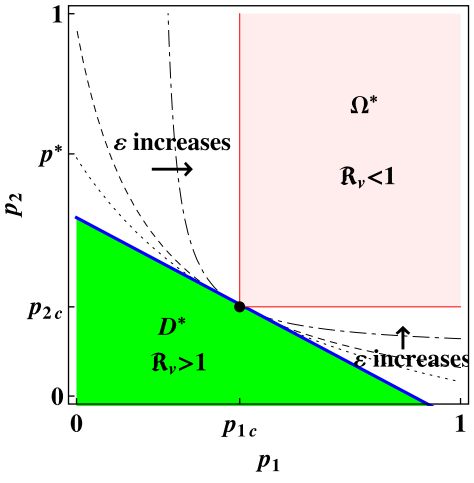

Fig. 1. Plot showing the regions Ω^* and D^* defined in (3.8). Several curves of $\mathcal{R}_v(\varepsilon) = 1$ for different ε values are also shown, with the dashed curves corresponding to $0 < \varepsilon < 1$, the thin solid lines (boundary of Ω^*) corresponding to $\varepsilon = 1$, and the thick line corresponding to $\varepsilon = 0$ (the upper bound of the region D^*). The arrows indicate the direction of change of the curve $\mathcal{R}_v(\varepsilon) = 1$ as ε increases from 0 to 1. All of the $\mathcal{R}_v(\varepsilon) = 1$ curves intersect at the single point (p_{1c},p_{2c}).

Theorem 3.1. *Let Ω^* and D^* be the regions defined in* (3.12) *and let Δ_2 be the set defined in* (3.4).

(i) *If $(p_1,p_2) \in \Omega^*$, then $\mathcal{R}_v < 1$ for all $(\varepsilon_1,\varepsilon_2) \in \Delta_2$.*
(ii) *If $(p_1,p_2) \in D^*$, then $\mathcal{R}_v > 1$ for all $(\varepsilon_1,\varepsilon_2) \in \Delta_2$.*
(iii) *For every point $(\varepsilon_1,\varepsilon_2) \in \Delta_2$, the curve determined by $\mathcal{R}_v = 1$ lies in the region $\Omega \backslash (\Omega^* \cup D^*)$, and all of these curves intersect at a single point (p_{1c},p_{2c}). Moreover, these curves have the property that the curve corresponding to $(\tilde\varepsilon_1,\tilde\varepsilon_2)$ is higher than that corresponding to $(\hat\varepsilon_1,\hat\varepsilon_2)$ if $\tilde\varepsilon_1 < \hat\varepsilon_1$ and $\tilde\varepsilon_2 < \hat\varepsilon_2$.*

The proof of Theorem 3.1 is provided in Appendix.

Remark 1. The result in part (i) of Theorem 3.1 suggests that there is a "lower bound" for vaccination efforts (p_1,p_2), above which the infection can be eradicated regardless of mixing patterns. Similarly, part (ii) of Theorem 3.1 provides an "upper bound" for vaccination efforts (p_1,p_2), below which the infection cannot be eradicated regardless of mixing patterns. For an "intermediate level" vaccination strategy (p_1,p_2), part (iii) of Theorem 3.1 shows that mixing parameters ε_1 and ε_2 can play an important role in influencing the effect of vaccination strategies on reducing $\mathcal{R}_v$. Thus, when designing vaccination strategies, one should take into consideration mixing patterns within and between sub-populations.

Notice that for given ε_1 and ε_2,

$$\frac{\partial \mathcal{R}_v}{\partial p_1} = -\frac{1}{2}\left[\mathcal{R}_{01}c_{11} + \mathcal{R}_{02}c_{22} + \frac{\mathcal{R}_{01}c_{11}(1-p_1) + \mathcal{R}_{01}\mathcal{R}_{02}(1-p_2)(1+c_{12}c_{21})}{\sqrt{(A-D)^2+4BC}}\right] < 0, \tag{3.13}$$

and similarly, $\partial \mathcal{R}_v/\partial p_2 < 0$. When the curve $\mathcal{R}_v = 1$ lies between regions D^* and Ω^*, the curve intersects the p_1-axis and p_2-axis at $(p_1^*,0)$ and $(0,p_2^*)$, respectively, where

$$p_1^* = 1 - \frac{1-\mathcal{R}_{02}c_{22}}{\mathcal{R}_{01}c_{11}(1-\mathcal{R}_{02}c_{22}) + \mathcal{R}_{01}\mathcal{R}_{02}c_{12}c_{21}},$$
$$p_2^* = 1 - \frac{1-\mathcal{R}_{01}c_{11}}{\mathcal{R}_{02}c_{22}(1-\mathcal{R}_{01}c_{11}) + \mathcal{R}_{22}\mathcal{R}_{01}c_{12}c_{21}}. \tag{3.14}$$

Since $\mathcal{R}_{0i} > 1$ for $i = 1,2$, it is possible that $\mathcal{R}_{01}c_{11} > 1$ and/or $\mathcal{R}_{02}c_{22} > 1$. Thus, it is possible that $p_1^* > 1$ and/or $p_2^* > 1$. When $p_1^* > 1$, we know from (3.13) that $\mathcal{R}_v > 1$ for any vaccination strategy $(p_1,0)$. Thus, it is impossible to eradicate the infection if only sub-population 1 is vaccinated.

Fig. 2 illustrates all four possible cases, which are $p_i^* > 1$ $(i = 1,2)$ (see (a)); $p_1^* < 1$ and $p_2^* > 1$ (see (b)); $p_1^* < 1$ and $p_2^* > 1$ (see (c)); $p_i^* < 1$ $(i = 1,2)$ (see (d)).

The results described above are based on the control reproduction number. Fig. 3 shows some simulation results illustrating the effect of vaccination on the prevalence of infection. System (2.4) is used in these simulations with $\varepsilon_1 = 0.2$, $\varepsilon_2 = 0.4$. This represents a scenario in which the second group has a higher preference (0.4) of contacting people in its own group. Other parameter values used are $\beta = 0.03$, $\gamma = 0.15$ (an infectious period of about 6 days), and $a_1 = 12$, $a_2 = 8$, $\mu = 0.00016$ (a duration of 17 years in school). These values correspond to $\mathcal{R}_{01} = 2.4$ and $\mathcal{R}_{02} = 1.6$. Since some people have natural immunity to certain infectious diseases, such as most people have natural immunity to the seasonal flu (U.S. Department of Health and Human Services, 2011), the initial conditions used are $x_1(0) = S_1(0)/N_1(0) = 0.4$, $y_1(0) = I_1(0)/N_1(0) = 0.00002$, $x_2(0) = S_2(0)/N_2(0) = 0.6$, $y_2(0) = I_2(0)/N_2(0) = 0.00002$. For this set of parameters, $p_1^* = 0.77$ and $p_2^* \gg 1$. Fig. 3(a) is for a vaccination strategy $(p_1,0)$ with $p_1 = 0.2 < p_1^*$, for which the infection persists $(\mathcal{R}_v = 1.8)$, and Fig. 3(b) is for a vaccination strategy $(p_1,0)$ with $p_1 = 0.8 > p_1^*$, in which case the infection dies out $(\mathcal{R}_v = 0.97)$.

3.2. Vaccination strategies based on the type reproduction number T_{1v}

Notice that for $n=2$, $\rho((I-P)K)=\mathcal{R}_{02}c_{22}$ and $\rho((I-P)K_v)=\mathcal{R}_{02}c_{22}(1-p_2)$. Here, we consider two cases. Case 1: The sub-population 1 is the only reservoir of the infection so that it is possible to eradicate the infection by vaccinating sub-population 1 only. In this case, from Theorem 2.2, the condition $\mathcal{R}_{02}c_{22}<1$ holds, and the disease will die out with the vaccination effort $p_1>1-1/T_1$, where T_1 is given in (2.8).

Case 2: The sub-population 2 is also a reservoir, i.e., $\mathcal{R}_{02}c_{22}>1$. In this case, both sub-populations need to be vaccinated to eradicate the infection. Assume that for a given vaccination level p_2 the sub-population 2 is no longer a reservoir. This can be achieved if $\mathcal{R}_{02}c_{22}(1-p_2)<1$, which is equivalent to

$$p_2>1-\frac{1}{\mathcal{R}_{02}c_{22}}.$$

From Theorem 2.2, the infection can be eradicated if $T_{1v}<1$, where T_{1v} is defined in (2.9), and $T_{1v}<1$ if and only if $\mathcal{R}_v<1$. Notice that T_{1v} depends on both the vaccination effort p_i and the mixing parameter ε_i. For any given $(\varepsilon_1,\varepsilon_2)\in\Delta_2$, T_{1v} and $\mathcal{R}_v$ are both functions of p_1 and p_2 and the intersection of the two surfaces is determined by $T_{1v}=\mathcal{R}_v=1$, which is a curve in the p_1–p_2 plane (see Fig. 4). Although these two quantities T_{1v} and $\mathcal{R}_v$ provide the same threshold value 1 for disease eradication, their evaluations for other vaccination strategies (p_1,p_2) can be very different. As pointed out by Roberts and Heesterbeek (2003), T_{1v} focuses on the disease risk in sub-population 1, while $\mathcal{R}_v$ reflects the average risk in the whole population. From Fig. 4, we observe that when T_{1v} and $\mathcal{R}_v$ are both greater than 1, $T_{1v}>\mathcal{R}_v$ with the difference $T_{1v}-\mathcal{R}_v$ varying with (p_1,p_2). In addition, when $p_1=1$, $T_{1v}=0$ for all $p_2\le 1$ while $\mathcal{R}_v>0$ for $p_2<1$. Hence, the disease transmission risk in sub-population 1 is higher than that predicted by the control reproduction number $\mathcal{R}_v$. These differences can have important implications for disease control.

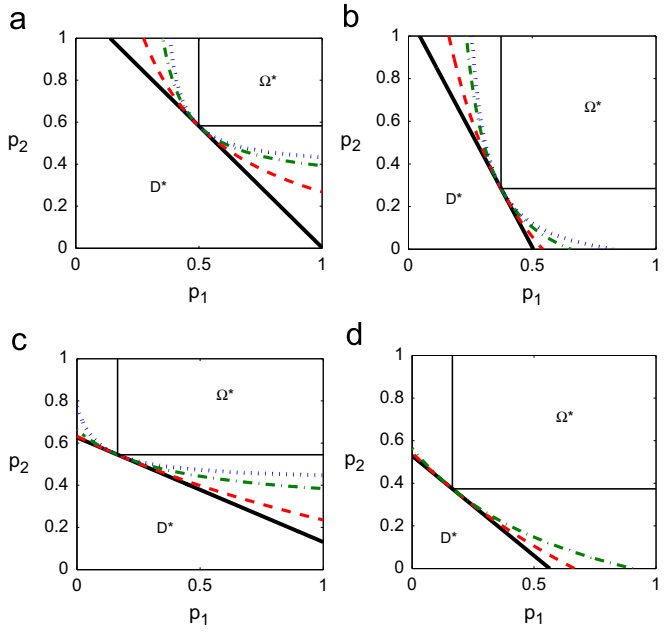

Fig. 2. Effective sets of vaccination in p_1-p_2 plane. The curves are created by $\mathcal{R}_v=1$ with different preference parameters $(\varepsilon_1,\varepsilon_2)\in\Delta_2$ and the region above $\mathcal{R}_v=1$ is the effective set of vaccination with respect to $(\varepsilon_1,\varepsilon_2)$. Ω^* is the absolutely effective set of vaccination and D^* is the absolutely ineffective set of vaccination, which are independent of the preference parameters $(\varepsilon_1,\varepsilon_2)\in\Delta_2$. (a) $p_1^*>1,p_2^*>1$; $a_1=10$, $a_2=12$. One has to vaccinate both sub-populations simultaneously with $(p_1,p_2)\in\Omega_{(\varepsilon_1,\varepsilon_2)}$. (b) $p_1^*<1,p_2^*>1$; $a_1=8$, $a_2=7$. One can vaccinate both sub-populations simultaneously with $(p_1,p_2)\in\Omega_{(\varepsilon_1,\varepsilon_2)}$ or vaccinate sub-population 1 alone provided that $p_1^*<p_1\le 1$ for given $(\varepsilon_1,\varepsilon_2)\in\Delta_2$. (c) $p_1^*>1,p_2^*<1$; $a_1=6$, $a_2=11$. One can vaccinate both sub-populations simultaneously with $(p_1,p_2)\in\Omega_{(\varepsilon_1,\varepsilon_2)}$ or vaccinate sub-population 2 alone provided that $p_2^*<p_2\le 1$ for $(\varepsilon_1,\varepsilon_2)\in\Delta_2$. (d) $p_1^*<1,p_2^*<1$; $a_1=6$, $a_2=8$. One can vaccinate both sub-populations simultaneously with $(p_1,p_2)\in\Omega_{(\varepsilon_1,\varepsilon_2)}$, vaccinate the sub-population 1 alone with $p_1^*<p_1\le 1$, or just vaccinate the sub-population 2 such that $p_2^*<p_2\le 1$ for $(\varepsilon_1,\varepsilon_2)\in\Delta_2$. Here, $N_1=50\,000$, $N_2=30\,000$, $(\varepsilon_1,\varepsilon_2)=(0.2,0.3)$ for the dash curve, $(\varepsilon_1,\varepsilon_2)=(0.4,0.5)$ for the dot dash curve, $(\varepsilon_1,\varepsilon_2)=(0.6,0.5)$ for the dot curve, other parameters are given in Table 1.

4. Discussion

In this paper, we considered a multigroup model with the focus on investigating the effects of mixing patterns (proportional and preferential mixing) and group-targeted vaccination programs on the control and prevention of infectious diseases. We derived the threshold conditions for the disease elimination with group-targeted vaccination strategies based on the use of the type reproduction number T_{1v} (see Theorem 2.2). Our results described in Theorem 3.1 demonstrate that the degree of mixing preference (ε_i) can play a critical role in the effects of vaccination strategies (p_i). It suggests that to identify the best disease control strategies in a heterogeneous population, policymakers must take into account the structure of mixing both within and between the sub-populations. This may have significant implications for public health.

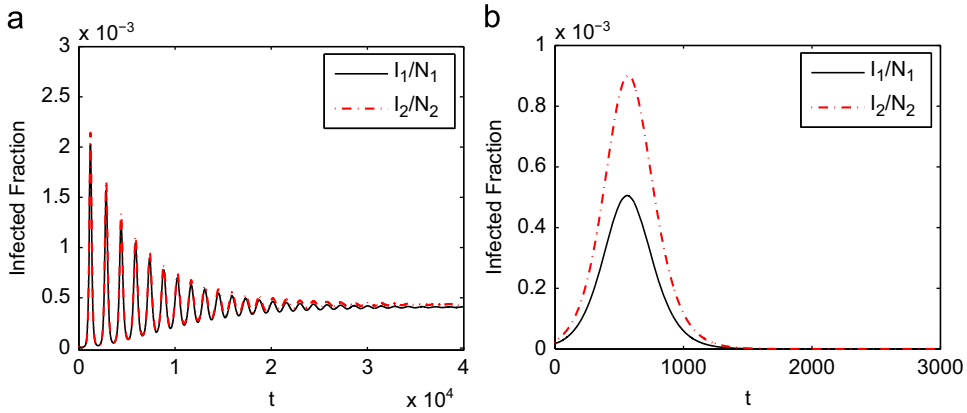

Fig. 3. When $p_1^*<1$ and $p_2^*>1$, the disease is eventually eradicated if the vaccination is applied to sub-population 1 alone at a level above p_1^*. (a) $(p_1,p_2)=(0.2,0)$ and $p_1<p_1^*=0.77$, the disease persists $(\mathcal{R}_v=1.8)$; (b) $(p_1,p_2)=(0.8,0)$ and $p_1>p_1^*=0.77$, the disease eventually disappears $(\mathcal{R}_v=0.97)$. Here, $x_1(0)=S_1(0)/N_1(0)=0.4$, $y_1(0)=I_1(0)/N_1(0)=0.00002$, $x_2(0)=S_2(0)/N_2(0)=0.6$, $y_2(0)=I_2(0)/N_2(0)=0.00002$, $a_1=12$, $a_2=8$, $\varepsilon_1=0.2$, $\varepsilon_2=0.4$, other parameters are given in Table 1, and then $p_1^*=0.77$, $p_2^*\gg 1$.

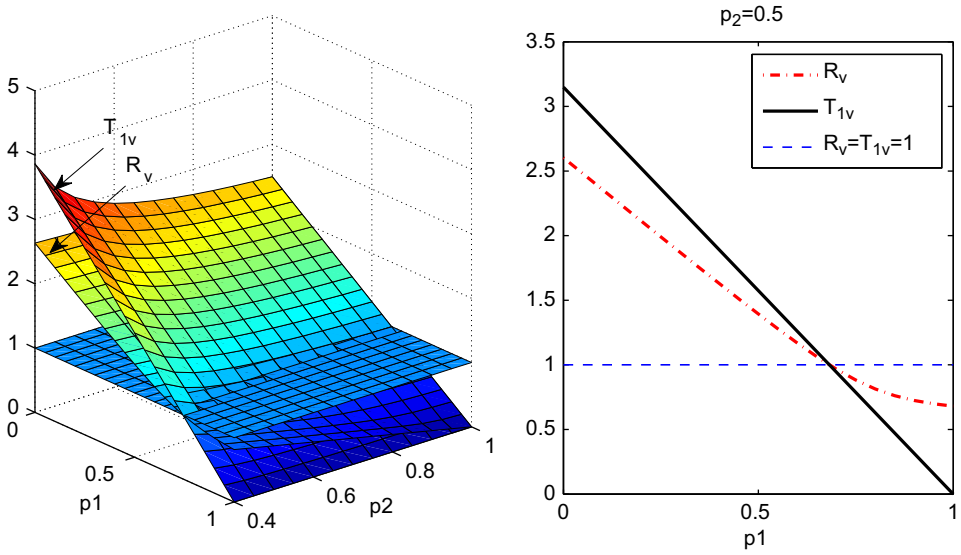

Fig. 4. Effect of (p_1,p_2) on the type reproduction number T_{1v} and the control reproduction number $\mathcal{R}_v$. It is obvious that T_{1v} has the same threshold property as $\mathcal{R}_v$. T_{1v} focuses on the disease risk in sub-population 1 while $\mathcal{R}_v$ reflects the averaging risk in the whole population. In addition, $T_{1v}>\mathcal{R}_v>1$. When $p_1=1$, $T_{1v}=0$ for any $0\le p_2\le 1$ while $\mathcal{R}_v>0$ for $0\le p_2<1$. The risk of the infection in sub-population 1 (i.e., T_{1v}) is larger than that provided by the control reproduction number $\mathcal{R}_v$. Here, $N_1=50\,000$, $N_2=30\,000$, $a_1=15$, $a_2=11$, $\varepsilon_1=0.3$, $\varepsilon_2=0.5$ and $\mathcal{R}_{02}c_{22}=1.36$, other parameters are given in Table 1.

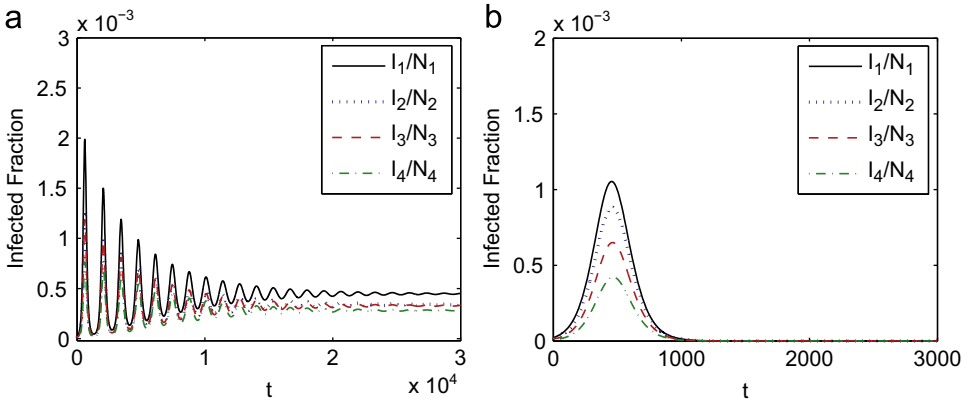

Fig. 5. For a 4-group model ($n=4$), if the vaccination strategy satisfies $p_i>1-1/\mathcal{R}_{0i}$ for $i=1,2,3,4$, then the disease is eventually eradicated without considering the regulation of cross-contacts between different sub-populations (i.e., the values of ε_i, $i=1,2,3,4$). (a) $(p_1,p_2,p_3,p_4)=(0.3,0.3,0.2,0.1)$ and $p_i<1-1/\mathcal{R}_{0i}(i=1,2,3,4)$, then the disease persists ($\mathcal{R}_v=1.88$); (b) $(p_1,p_2,p_3,p_4)=(0.7,0.5,0.4,0.2)$ and $p_i>1-1/\mathcal{R}_{0i}(i=1,2,3,4)$, then the disease eventually disappears ($\mathcal{R}_v=0.94$). Here, $a_1=15$, $a_2=10$, $a_3=8$, $a_4=6$, $\varepsilon_1=0.2$, $\varepsilon_2=0.3$, $\varepsilon_3=0.4$, $\varepsilon_4=0.5$, other parameters are given in Table 1, and then $1-1/\mathcal{R}_{01}=0.67$, $1-1/\mathcal{R}_{02}=0.5$, $1-1/\mathcal{R}_{03}=0.37$, $1-1/\mathcal{R}_{04}=0.17$. Initial conditions are $x_1(0)=0.4$, $x_2(0)=0.4$, $x_3(0)=0.5$, $x_4(0)=0.5$, $y_1(0)=y_2(0)=y_3(0)=y_4(0)=0.00002$.

The analytical results we obtained are for the case of $n=2$ sub-populations. These derivations require the uses of explicit formulas for the control reproduction number $\mathcal{R}_v$ and the type reproduction number T_{1v}. For $n>3$ and preferential mixing (i.e., $0<\varepsilon_i<1$ for some $i=1,2,\ldots,n$), the explicit formulas for these reproduction numbers are very difficult to obtain. Nevertheless, we have conducted numerical simulations to verify some of the threshold conditions and results regarding the effect of vaccination and the influence of mixing patterns (see, e.g., Figs. 5 and 6).

Fig. 5 shows some time plots for a system for four sub-populations and two different vaccination strategies. The numerical simulations suggest that similar threshold conditions still hold. For example, the infection will die out if vaccination efforts p_i satisfy $p_i>1-1/\mathcal{R}_{0i}$ for $i=1,2,3,4$. For the given set of parameters, $1-1/\mathcal{R}_{01}=0.67$, $1-1/\mathcal{R}_{02}=0.5$, $1-1/\mathcal{R}_{03}=0.37$, and $1-1/\mathcal{R}_{04}=0.17$. In Fig. 5(a), $p_i<1-1/\mathcal{R}_{0i}$ for $i=1,2,3,4$. It shows that the fraction of infection size $I_i(t)/N_i$ stabilize at positive levels for all i ($\mathcal{R}_v=1.88$). In Fig. 5(b), $p_i>1-1/\mathcal{R}_{0i}$ for $i=1,2,3,4$. It shows that the fraction of infection $I_i(t)/N_i$ tends to 0 as $t\to\infty$ for $i=1,2,3,4$ ($\mathcal{R}_v=0.94$).

Fig. 6 is similar to Fig. 5 except that only the sub-population 1 is targeted for vaccination, i.e., $p_1>0$ and $p_2=p_3=p_4=0$. For the given set of parameter values, we can numerically compute the value p_1^*, which is defined in a similar way as in (3.14) and $p_1^*=0.78$. In Fig. 6(a), $p_1=0.2<0.78=p_1^*$ and the disease persists ($\mathcal{R}_v=1.95$). In Fig. 6(b), $p_1=0.8>0.78=p_1^*$ and the disease eventually disappears ($\mathcal{R}_v=0.98$).

Figs. 5 and 6 provide two examples showing that the results for $n=2$ also hold for $n=4$. Our additional simulations (not shown here) suggest that, in general, the following results can be extended to the case of n sub-populations.

(i) For any $(\varepsilon_1,\varepsilon_2,\ldots,\varepsilon_n)\in\Delta_n$, the disease will die out if $(p_1,p_2,\ldots,p_n)\in\Omega_{(\varepsilon_1,\varepsilon_2,\ldots,\varepsilon_n)}$.
(ii) If $p_i>1-1/R_{0i}$ for all $i=1,2,\ldots,n$, then the infection will be eradicated regardless of the values of the mixing parameters ε_i $(i=1,2,\ldots,n)$.
(iii) Let p_i^* denote the intersection point of axis-i and the surface determined by $\mathcal{R}_v=1$. If $0<p_i^*<1$ for some $i=1,\ldots,n$, eradication of the infection is possible by vaccinating only

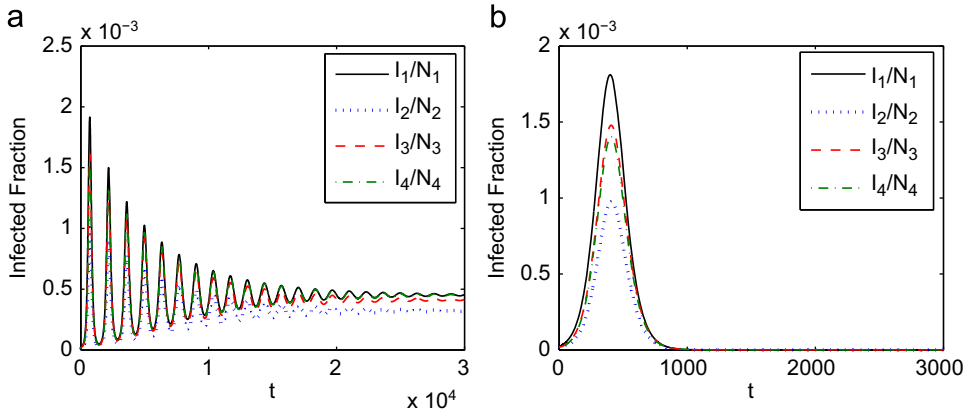

Fig. 6. For a 4-group model ($n=4$), when $0<p_1^*<1$, one could control the epidemic by just vaccinating sub-population 1 alone with $p_1>p_1^*$. (a) $(p_1,p_2,p_3,p_4)=(0.2,0,0,0)$ and $p_1=0.2<0.78=p_1^*$, then the disease persists ($\mathcal{R}_v=1.95$); (b) $(p_1,p_2,p_3,p_4)=(0.8,0,0,0)$ and $p_1=0.8>0.78=p_1^*$, then the disease eventually disappears ($\mathcal{R}_v=0.98$). Here, $a_1=14$, $a_2=6$, $a_3=8$, $a_4=9$, $\varepsilon_1=0.2$, $\varepsilon_2=0.4$, $\varepsilon_3=0.3$, $\varepsilon_4=0.2$, other parameters are given in Table 1, and then $p_1^*=0.78$, $p_i^*>1 (i=2,3,4)$. Initial conditions are $x_1(0)=0.4$, $x_2(0)=0.6$, $x_3(0)=0.6$, $x_4(0)=0.5$, $y_1(0)=y_2(0)=y_3(0)=y_4(0)=0.00002$.

sub-population i with $p_i>p_i^*$. If $p_i^*>1$ for all $i=1,\ldots,n$, all sub-populations need to be vaccinated in order to eliminate the infection.

In this paper, we focused on vaccination alone as a control measure. Similar analyses can be conducted for models that consider other control measures. Our main objective is to explore the influence of population heterogeneities on disease spread and control, particularly, the roles of heterogeneous mixing between multiple sub-populations are examined. We identified scenarios in which the preferential mixing patterns (represented by ε_i) can have a significant impact on the effectiveness of vaccination strategies. Effect of other heterogeneities, such as activity levels (a_i) and populations sizes (N_i), can also be studied using a similar approach. We will leave these studies for future work.

Appendix A

We provide a proof for Theorem 3.1 in this appendix.

For part (i), we prove the result by considering four cases:

$$\mathcal{R}_{01}c_{11}>1,\quad \mathcal{R}_{02}c_{22}>1;\quad \mathcal{R}_{01}c_{11}>1,\quad \mathcal{R}_{02}c_{22}<1;$$

$$\mathcal{R}_{01}c_{11}<1,\quad \mathcal{R}_{02}c_{22}>1;\quad \mathcal{R}_{01}c_{11}<1,\quad \mathcal{R}_{02}c_{22}<1.$$

As the proof for these cases are similar, we provide details for only the case $\mathcal{R}_{01}c_{11}>1, \mathcal{R}_{02}c_{22}>1$. In this case, the fact that $(p_1,p_2)\in\Omega^*$ implies that

$$\mathcal{R}_{01}(1-p_1)<1,\quad \mathcal{R}_{02}(1-p_2)<1. \tag{A.1}$$

Let $\varepsilon_1=1$ and $0\le\varepsilon_2<1$, then $A=\mathcal{R}_{01}(1-p_1)$, $B=C=0$, and $D=\mathcal{R}_{02}(1-p_2)$. From (A.1),

$$\mathcal{R}_v=\tfrac{1}{2}\left[A+D+\sqrt{(A-D)^2+4BC}\right]=\max\{A,D\}$$
$$=\max\{\mathcal{R}_{01}(1-p_1),\mathcal{R}_{02}(1-p_2)\}<1.$$

From $\partial\mathcal{R}_v/\partial\varepsilon_1\ge 0$ (see (3.6)) we have $\mathcal{R}_v<1$ for $0\le\varepsilon_1\le 1$ and $0\le\varepsilon_2<1$. Similarly, it can be shown that $\mathcal{R}_v<1$ for $0\le\varepsilon_1<1$ and $0\le\varepsilon_2\le 1$. This completes the proof of Part (i).

For Part (ii), assume that $(p_1,p_2)\in D^*$. Note that when $\varepsilon_1=\varepsilon_2=0$, the expressions of c_{ij} reduce to

$$c_{11}=c_{21}=\frac{a_1N_1}{a_1N_1+a_2N_2},\quad c_{12}=c_{22}=\frac{a_2N_2}{a_1N_1+a_2N_2}.$$

Using the above expressions and the condition $p_2<-\mathcal{A}p_1+\mathcal{B}$ we can show that $\mathcal{R}_v|_{\varepsilon_1=\varepsilon_2=0}>1$. Then, from $\partial\mathcal{R}_v/\partial\varepsilon_1\ge 0$ and $\partial\mathcal{R}_v/\partial\varepsilon_2\ge 0$, it follows that $\mathcal{R}_v>1$ for all $(\varepsilon_1,\varepsilon_2)\in\Delta_2$. The proof of Part (ii) is finished.

Part (iii) can be proved using the following information. Define

$$\Omega_{(\varepsilon_1,\varepsilon_2)}=\{(p_1,p_2)|\mathcal{R}_v<1,(p_1,p_2)\in\Omega,\ (\varepsilon_1,\varepsilon_2)\in\Delta_2\},$$

$$D_{(\varepsilon_1,\varepsilon_2)}=\{(p_1,p_2)|\mathcal{R}_v>1,(p_1,p_2)\in\Omega,\ (\varepsilon_1,\varepsilon_2)\in\Delta_2\}.$$

Then $\Omega_{(\tilde\varepsilon_1,\tilde\varepsilon_2)}\supseteq\Omega_{(\hat\varepsilon_1,\hat\varepsilon_2)}$ and $D_{(\tilde\varepsilon_1,\tilde\varepsilon_2)}\subseteq D_{(\hat\varepsilon_1,\hat\varepsilon_2)}$ for $\tilde\varepsilon_1<\hat\varepsilon_1$ and $\tilde\varepsilon_2<\hat\varepsilon_2$, and

$$\Omega^*\subseteqq\bigcap_{(\varepsilon_1,\varepsilon_2)\in\Delta_2}\Omega_{(\varepsilon_1,\varepsilon_2)},\quad D^*\subseteqq\bigcap_{(\varepsilon_1,\varepsilon_2)\in\Delta_2}D_{(\varepsilon_1,\varepsilon_2)}.$$

This completes the proof of the Theorem 3.1.

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