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IMPACTS OF MIGRATION AND IMMIGRATION ON DISEASE TRANSMISSION DYNAMICS IN HETEROGENEOUS POPULATIONS

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Abstract. Population migration and immigration have greatly increased the spread and transmission of many infectious diseases at a regional, national and global scale. To investigate quantitatively and qualitatively the impact of migration and immigration on the transmission dynamics of infectious diseases, especially in heterogeneous host populations, we incorporate immigration/migration terms into all sub-population compartments, susceptible and infected, of two types of well-known heterogeneous epidemic models: multi-stage models and multi-group models for HIV/AIDS and other STDs. We show that, when migration or immigration into infected sub-population is present, the disease always becomes endemic in the population and tends to a unique asymptotically stable endemic equilibrium P^*. The global stability of P^* is established under general and biological meaningful conditions, and the proof utilizes a global Lyapunov function and the graph-theoretic techniques developed in Guo et al. (2008).

1. **Introduction.** Population migrations are occurring at a global scale: mass of migrant workers are moving from rural regions into large cities in developing countries, and immigrants and refugees are moving from developing countries to industrialized countries. Migration and immigration greatly increase the spread of many infectious diseases at a regional, national and global scale. The impact of migration and immigration on the transmission dynamics of infectious diseases, especially within a heterogeneous population, needs to be investigated using mathematical models. Standard compartment models customarily incorporate an immigration/migration term into the susceptible sub-population or compartment. When natural birth is not considered, such an immigration term provides influx of susceptibles into the population that makes it possible for the disease to remain endemic in the population. Fewer models, however, considered a more realistic situation where immigrants or migrants move into infected sub-populations. There is usually

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no public health screening of migrants among different regions of the same country, and hence infected people are free to migrate. Industrialized countries has standardized health screening procedures for new immigrants, while such a screening standard is generally lacking for refugees. Furthermore, for certain diseases such as tuberculosis (TB), current screening procedures can not detect infected individuals who are in early latent stage, and as a result, many latently infected immigrants would develop active TB within 2-5 years of their landing. An earlier work of Brauer and van den Driessche [3] has incorporated immigration into the infectious compartment in a simple HIV model for a prison population. McCluskey and van den Driessche [20] considered a TB model with immigration into a latent compartment. It is shown in these simple models that, if infected immigrants or migrants are allowed into the host population, the disease will always become and remain endemic: a unique endemic equilibrium always exists and is globally asymptotically stable. Whether these results continue to hold in more complex models for heterogeneous disease transmissions has remained open.

Two classes of heterogeneous epidemic models have been well studied in the literature. For infectious diseases with a long infectious or latent period such as HIV/AIDS, staged progression models have been constructed to describe disease progression through a discrete set of stages, and with varying degrees of transmissibility at different stages [11, 23]. Global dynamics of staged progression models and various modifications have been well studied [2, 5, 8, 11, 19, 23]. Another class of heterogeneous transmission models consists of multi-group models that were developed to describe the heterogeneous mixing and transmission of HIV/AIDs and other STDs [1, 9, 10, 13, 15, 18, 22]. In this case, the host population is partitioned into homogeneous groups, and the model accounts for both within-group and intergroup mixing and transmission. Multi-group models can also be used to describe diseases with multiple hosts such as West-Nile virus and other vector borne diseases [23]. The global dynamics of an n-group models of SEIR type with bilinear incidence have been completely established by Guo et al. [6, 7]. We note that, in all works on heterogeneous epidemic models in the literature, none has considered the effects of immigration into the infective subpopulation.

In the present paper, we incorporate a migration/immigration term into all compartments, susceptible and infected, in these two classes of heterogeneous epidemic models, to investigate the impact of immigration on complex disease transmission dynamics. We prove that, when immigration is present in at least one infected compartment (latent or infectious), the disease will persists in all sub-populations, and a unique endemic equilibrium is globally asymptotically stable in the feasible region. The global stability is established using a global Lyapunov function and an adaptation of the graph-theoretic approach developed in [6, 7, 16]. Our results are the first to show that the graph-theoretic approach developed in [6, 7, 16] is applicable to heterogeneous epidemic models with immigration and migration into infected compartments. Our results also generalize the earlier result in [3] on simple HIV models. Biologically, our results have significant implications for disease control and prevention in countries and regions that receive significant number of immigrants or migrants. It is not sufficient for these countries and regions to focus their public health efforts to only within their boarders; eradication of an infectious disease needs to be achieved at its source outside their boarders.

The paper is organized as follows: in Section 2, a class of multi-stage models with infected immigration is formulated and the global dynamics are established. In Section 3, a class of multi-group models with infected immigration is formulated. The uniqueness and global-stability of the endemic equilibrium is proved. Conclusions and discussions are given in Section 4.

2. **A multi-stage $\mathbf{SEI_nR}$ model with immigration.** In this section, we consider a multi-stage (MS) progression model with constant immigration distributed to every compartment. In this section and hereafter, the term "immigration" is used to include both immigrants between countries and migrants between regions. Typical MS models such as staged-progression models and their variations have been studied extensively, see [19, 5, 2, 12, 8] and reference therein. This class of models contain classical SEIR models with a single latent and infectious stage as a special case [1, 23].

The population is divided into a susceptible compartment S, a latent compartment E, a removed compartment R and n successive infectious compartments I_i, $i = 1, \cdots, n$. A fraction p of the total immigration π moves into the latent compartment, a fraction q_i into the i-th infectious compartment, a fraction q_{n+1} into the recovered compartment, and the remaining fraction $1 - p - \sum_{i=1}^{n+1} q_i$ into the susceptible compartment. We assume that $0 \le p, q_i < 1$, $i = 1, \cdots, n+1$, and $0 < p + \sum_{i=1}^{n+1} q_i < 1$. The total force of infection is described by a linear term $\sum_{i=1}^{n} \beta_i I_i$, where β_i is the transmission coefficient between a susceptible individual and an infective in the i-th infectious compartment. Parameter $1/\delta$ denotes the mean latent period, and $1/\gamma_i$ the mean period an individual stays in the compartment I_i, $i = 1, \cdots, n$. Parameter $d_\# > 0$ denotes the removal rate of the respective compartment, where '#' represents $S, E, 1, \cdots, n$ or R. All parameters are assumed to be nonnegative, and we require that all death rates d_S, d_E, d_{I_i}, $i = 1, \cdots, n$, are positive so that the total host population remains bounded. The transfer diagram for the model is shown in Figure 1. Based on these assumptions, we derive the

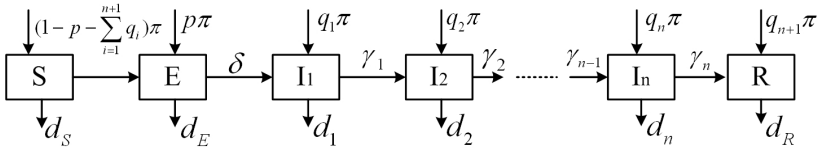

FIGURE 1. Flow diagram of a multi-stage progression model with immigration.

following system of ordinary differential equations:

$$\begin{aligned}
S' &= (1 - p - \sum_{i=1}^{n+1} q_i)\pi - \sum_{i=1}^{n} \beta_i S I_i - d_S S, \\
E' &= p\pi + \sum_{i=1}^{n} \beta_i S I_i - (d_E + \delta) E, \\
I_1' &= q_1\pi + \delta E - (d_1 + \gamma_1) I_1, \\
I_i' &= q_i\pi + \gamma_{i-1} I_{i-1} - (d_i + \gamma_i) I_i, \quad i = 2, \cdots, n-1, \\
I_n' &= q_n\pi + \gamma_{n-1} I_{n-1} - (d_n + \gamma_n) I_n, \\
R' &= q_{n+1}\pi + \gamma_n I_n - d_R R.
\end{aligned} \tag{1}$$

When $p = 0$ and all $q_i = 0$, model (1) reduces to SP models considered in [5, 12, 8], where the global dynamics are established by a global Lyapunov function. Also our model generalizes the low dimensional models in [3, 17, 20, 19].

2.1. **Uniqueness of the endemic equilibrium.** Let $\Pi \doteq (1-p-\sum_{i=1}^{n+1} q_i)\pi > 0$. Since the variable R does not appear in other equations of (1), we may consider the following reduced system:

$$\begin{aligned} S' &= \Pi - \sum_{i=1}^{n} \beta_i S I_i - d_S S, \\ E' &= p\pi + \sum_{i=1}^{n} \beta_i S I_i - (d_E + \delta) E, \\ I_1' &= q_1\pi + \delta E - (d_1 + \gamma_1) I_1, \\ I_i' &= q_i\pi + \gamma_{i-1} I_{i-1} - (d_i + \gamma_i) I_i, \quad i = 2, \cdots, n-1, \\ I_n' &= q_n\pi + \gamma_{n-1} I_{n-1} - (d_n + \gamma_n) I_n. \end{aligned} \tag{2}$$

Let $N = S + E + \sum_{i=1}^{n} I_i$ denote the total population at risk and let

$$d = \min\{d_S, d_E, d_1, \cdots, d_n\} > 0.$$

Then N satisfies

$$N' = (1 - q_{n+1})\pi - d_S S - d_E E - \sum_{i=1}^{n} d_i I_i - \gamma_n I_n \le (1 - q_{n+1})\pi - dN.$$

It follows that $\lim_{t\to\infty} \sup N(t) \le (1 - q_{n+1})\pi/d$. Similarly, from the first equation in (2) we obtain $S' \le \Pi - d_S S$, and thus $\lim_{t\to\infty} \sup S(t) \le \Pi/d_S$. The feasible region for (2) can be defined as the closed set

$$\begin{aligned} \Gamma = \{(S, E, I_1, \cdots, I_n) \in \mathbb{R}_+^{n+2} : 0 \le S \le \Pi/d_S, \\ 0 \le S + E + \sum_{i=1}^{n} I_i \le (1 - q_{n+1})\pi/d\}. \end{aligned} \tag{3}$$

It can be verified that Γ is positively invariant with respect to (2).

Next we show that model (2) only admits endemic equilibria in Γ and has no disease-free equilibrium, due to immigration into E and I_i compartments. Let $P^* = (S^*, E^*, I_1^*, \cdots, I_n^*) \in \Gamma$ denote an equilibrium of (2). Then $S^*, E^*, I_1^*, \cdots, I_n^*$ satisfy the following equilibrium equations

$$\begin{aligned} \Pi &= \sum_{i=1}^{n} \beta_i S I_i + d_S S, \\ p\pi + \sum_{i=1}^{n} \beta_i S I_i &= (d_E + \delta) E, \\ q_1\pi + \delta E &= (d_1 + \gamma_1) I_1, \\ q_i\pi + \gamma_{i-1} I_{i-1} &= (d_i + \gamma_i) I_i, \quad i = 2, \cdots, n. \end{aligned} \tag{4}$$

It is straightforward to see that $E = I_1 = \cdots = I_n = 0$ do not satisfy (4) if $p + \sum_{i=1}^{n+1} q_i > 0$. Thus the model has no disease-free equilibrium. To find an endemic equilibrium, we rewrite the first equation of (4) as

$$S = \frac{\Pi}{d_S + \sum_{i=1}^{n} \beta_i I_i}. \tag{5}$$

Eliminating E from the second and third equations of (4), we have

$$p\pi + \frac{d_E+\delta}{\delta} q_1\pi + \sum_{i=1}^{n} \beta_i S I_i = \frac{d_E+\delta}{\delta}(d_1+\gamma_1) I_1. \tag{6}$$

Let $a_1 = (d_E+\delta)/\delta$. Substituting (5) into (6) gives

$$(p\pi + a_1 q_1 \pi)(d_S + \sum_{i=1}^{n} \beta_i I_i) + \Pi \sum_{i=1}^{n} \beta_i I_i = a_1(d_1+\gamma_1) I_1 (d_S + \sum_{i=1}^{n} \beta_i I_i). \tag{7}$$

From the remaining n equations in (4), a recursion formula can be obtained

$$I_i = \frac{q_i \pi}{d_i+\gamma_i} + \frac{\gamma_{i-1}}{d_i+\gamma_i} I_{i-1}, \quad i = 2, \cdots, n.$$

It follows that

$$\begin{aligned}
\sum_{i=2}^{n} \beta_i I_i &= \sum_{i=2}^{n} \frac{\beta_i q_i \pi}{d_i+\gamma_i} + \sum_{i=2}^{n} \beta_i \frac{\gamma_{i-1}}{d_i+\gamma_i} I_{i-1} \\
&= \sum_{i=2}^{n} \frac{\beta_i q_i \pi}{d_i+\gamma_i} + \sum_{i=3}^{n} \beta_i \frac{\gamma_{i-1}}{d_i+\gamma_i} \left(\frac{q_{i-1}\pi}{d_{i-1}+\gamma_{i-1}} + \frac{\gamma_{i-2} I_{i-2}}{d_{i-1}+\gamma_{i-1}} \right) \\
&\quad + \frac{\beta_2 \gamma_1}{d_2+\gamma_2} I_1 \\
&= \sum_{i=2}^{n} \frac{\beta_i q_i \pi}{d_i+\gamma_i} + \sum_{i=3}^{n} \beta_i \frac{\gamma_{i-1}}{d_i+\gamma_i} \frac{q_{i-1}\pi}{d_{i-1}+\gamma_{i-1}} \\
&\quad + \sum_{i=3}^{n} \beta_i \frac{\gamma_{i-1}}{d_i+\gamma_i} \frac{\gamma_{i-2}}{d_{i-1}+\gamma_{i-1}} I_{i-2} + \frac{\beta_2\gamma_1}{d_2+\gamma_2} I_1 \\
&\quad \cdots \\
&\doteq K_1 + \tilde{K} I_1,
\end{aligned} \tag{8}$$

where K_1 is the sum of all constant terms and $\tilde{K}$ is the coefficient of I_1. Substituting (8) into (7) and defining $K_2 \doteq \tilde{K} + \beta_1$, we get

$$\begin{aligned}
&(p\pi + a_1 q_1 \pi)(d_S + K_1 + K_2 I_1) + \Pi(K_1 + K_2 I_1) \\
&= a_1(d_1+\gamma_1) I_1 (d_S + K_1 + K_2 I_1).
\end{aligned} \tag{9}$$

Then we obtain a quadratic equation about variable I_1 as following

$$a I_1^2 + b I_1 + c = 0,$$

where

$$\begin{aligned}
a &= a_1(d_1+\gamma_1) K_2 > 0, \\
b &= a_1(d_1+\gamma_1)(d_S+K_1) - K_2\Pi - (p\pi + a_1 q_1 \pi) K_2, \\
c &= -(p\pi + a_1 q_1 \pi)(d_S + K_1) - K_1 \Pi < 0.
\end{aligned} \tag{10}$$

The signs of a, c imply that the quadratic equation has exactly one positive solution. Therefore, system (2) always has a unique endemic equilibrium $P^* = (S^*, E^*, I_1^*, \cdots, I_n^*)$, with $S^* > 0, E^* > 0, I_i^* > 0$, $i = 1, \cdots, n$. The direction of the vector fields of (2) on the boundary of Γ is transversal to the boundary. As a result, the boundary of Γ is a repellor and system (2) is uniformly persistent. We thus have obtained the following result.

Proposition 1. *Assume that* $0 < p^2 + \sum_{i=1}^n q_i^2 < 1$. *Then system* (2) *has no disease-free equilibrium, and a unique endemic equilibrium* P^* *always exists in the interior of the feasible region* Γ.

2.2. **Global stability of the endemic equilibrium P^*.** We prove the following global-stability result.

Theorem 2.1. *Suppose that* $0 < p^2 + \sum_{i=1}^n q_i^2 < 1$. *Then the unique endemic equilibrium* P^* *is globally asymptotically stable in* Γ.

Proof. Let $P^* = (S^*, E^*, I_1^*, \cdots, I_n^*)$ denote the endemic equilibrium and set $\bar{\beta}_i = \beta_i I_i^* S^*$, $i = 1, \cdots, n$. Consider a Lyapunov function

$$V(x) = \left(S - S^* - S^* \ln \frac{S}{S^*}\right) + \left(E - E^* - E^* \ln \frac{E}{E^*}\right) + \sum_{i=1}^n a_i \left(I_i - I_i^* - I_i^* \ln \frac{I_i}{I_i^*}\right),$$

where

$$a_1 = \frac{d_E + \delta}{\delta} \quad \text{and} \quad a_i = \frac{\sum_{k=i}^n \bar{\beta}_k}{\gamma_{i-1} I_{i-1}^*}, \quad i = 2, \cdots, n.$$

Function $V(x)$ is positive definite with respect to $x^* = P^*$ since $x - x^* \log \frac{x}{x^*}$ has the global minimum value 0 at $x = x^*$. The derivative of V along a solution $(S(t), E(t), I_1(t), \cdots, I_n(t))$ of system (2) is

$$V' = \left(1 - \frac{S^*}{S}\right) S' + \left(1 - \frac{E^*}{E}\right) E' + \sum_{i=1}^n a_i \left(1 - \frac{I_i^*}{I_i}\right) I_i'. \tag{11}$$

By the first equations in (2) and (4), it follows that

$$\begin{aligned}
&\left(1 - \frac{S^*}{S}\right) S' \\
&= \Pi - \sum_{i=1}^n \beta_i S I_i - d_S S - \Pi \frac{S^*}{S} + \sum_{i=1}^n \beta_i S^* I_i + d_S S^* \\
&= \sum_{i=1}^n \bar{\beta}_i + 2 d_S S^* - \sum_{i=1}^n \beta_i S I_i - d_S S - (\sum_{i=1}^n \bar{\beta}_i + d_S S^*) \frac{S^*}{S} + \sum_{i=1}^n \beta_i S^* I_i \\
&= d_S S^* \left(2 - \frac{S^*}{S} - \frac{S}{S^*}\right) - \sum_{i=1}^n \bar{\beta}_i \frac{S}{S^*} \frac{I_i}{I_i^*} + \sum_{i=1}^n \bar{\beta}_i \frac{I_i}{I_i^*} + \sum_{i=1}^n \bar{\beta}_i \left(1 - \frac{S^*}{S}\right).
\end{aligned} \tag{12}$$

Similarly, by (2) and endemic equilibrium equations in (4), we have

$$\begin{aligned}
\left(1 - \frac{E^*}{E}\right) E' &= p\pi + \sum_{i=1}^n \beta_i S I_i - (d_E + \delta) E - p\pi \frac{E^*}{E} \\
&\quad - \sum_{i=1}^n \beta_i S I_i \frac{E^*}{E} + (d_E + \delta) E^* \\
&= \sum_{i=1}^n \bar{\beta}_i \frac{S}{S^*} \frac{I_i}{I_i^*} - (d_E + \delta) E^* \frac{E}{E^*} + p\pi \left(2 - \frac{E^*}{E}\right) \\
&\quad + \sum_{i=1}^n \bar{\beta}_i \left(1 - \frac{S I_i E^*}{S^* I_i^* E}\right),
\end{aligned} \tag{13}$$

$$\begin{aligned}
&\left(1-\frac{I_1^*}{I_1}\right)I_1' \\
&= q_1\pi + \delta E - (d_1+\gamma_1)I_1 - q_1\pi\frac{I_1^*}{I_1} - \delta E\frac{I_1^*}{I_1} + (d_1+\gamma_1)I_1^* \\
&= \delta E^*\frac{E}{E^*} - (d_1+\gamma_1)I_1^*\frac{I_1}{I_1^*} + q_1\pi\left(2-\frac{I_1^*}{I_1}\right) + \delta E^*\left(1-\frac{E}{E^*}\frac{I_1^*}{I_1}\right),
\end{aligned} \tag{14}$$

and, for $i = 2, \cdots, n$,

$$\begin{aligned}
&\left(1-\frac{I_i^*}{I_i}\right)I_i' \\
&= q_i\pi + \gamma_{i-1}I_{i-1} - (d_i+\gamma_i)I_i - q_i\pi\frac{I_i^*}{I_i} - \gamma_{i-1}I_{i-1}\frac{I_i^*}{I_i} + (d_i+\gamma_i)I_i^* \\
&= \gamma_{i-1}I_{i-1}^*\frac{I_{i-1}}{I_{i-1}^*} - (d_i+\gamma_i)I_i^*\frac{I_i}{I_i^*} + q_i\pi\left(2-\frac{I_i^*}{I_i}\right) \\
&+ \gamma_{i-1}I_{i-1}^*\left(1-\frac{I_{i-1}}{I_{i-1}^*}\frac{I_i^*}{I_i}\right).
\end{aligned} \tag{15}$$

Substituting (12) – (15) into (11) and rearranging terms, we obtain

$$\begin{aligned}
V' =& d_S S^*\left(2-\frac{S^*}{S}-\frac{S}{S^*}\right) \\
&+ \sum_{i=1}^n \bar{\beta}_i\left(3-\frac{S^*}{S}-\frac{SI_iE^*}{S^*I_i^*E}-\frac{E}{E^*}\frac{I_1^*}{I_1}\right) + p\pi\left(3-\frac{E^*}{E}-\frac{E}{E^*}\frac{I_1^*}{I_1}\right) \\
&+ \sum_{i=1}^n a_i q_i\pi\left(2-\frac{I_i^*}{I_i}\right) + \sum_{i=2}^n a_i\gamma_{i-1}I_{i-1}^*\left(1-\frac{I_{i-1}}{I_{i-1}^*}\frac{I_i^*}{I_i}\right) \\
&+ \left(\sum_{i=1}^n \beta_i S^* I_i - a_1(d_1+\gamma_1)I_1 + \sum_{i=2}^n a_i\left[\gamma_{i-1}I_{i-1} - (d_i+\gamma_i)I_i\right]\right).
\end{aligned} \tag{16}$$

Here we have used relation $a_1\delta E^* = p\pi + \sum_{i=1}^n \bar{\beta}_i$.

Using the definition of a_i and exchanging the order of summation, we can show

$$\begin{aligned}
\sum_{i=2}^n a_i\gamma_{i-1}I_{i-1}^* &= \sum_{i=2}^n\sum_{k=i}^n \bar{\beta}_i = \sum_{i=2}^n (i-1)\bar{\beta}_i, \\
\sum_{i=2}^n a_i\gamma_{i-1}I_{i-1}^*\frac{I_{i-1}}{I_{i-1}^*}\frac{I_i^*}{I_i} &= \sum_{i=2}^n\sum_{k=i}^n \bar{\beta}_k\frac{I_{i-1}}{I_{i-1}^*}\frac{I_i^*}{I_i} = \sum_{i=2}^n \bar{\beta}_i\sum_{k=2}^i \frac{I_{k-1}}{I_{k-1}^*}\frac{I_k^*}{I_k}.
\end{aligned} \tag{17}$$

Substituting (17) into (16) gives

$$\begin{aligned} V' =& \Big[d_S S^* \left(2 - \frac{S^*}{S} - \frac{S}{S^*}\right) + p\pi \left(3 - \frac{E^*}{E} - \frac{E}{E^*}\frac{I_1^*}{I_1}\right) + \sum_{i=1}^{n} a_i q_i \pi \left(2 - \frac{I_i^*}{I_i}\right) \\ &+ \bar{\beta}_1 \left(3 - \frac{S^*}{S} - \frac{S I_1 E^*}{S^* I_1^* E} - \frac{E}{E^*}\frac{I_1^*}{I_1}\right) \\ &+ \sum_{i=2}^{n} \bar{\beta}_i \left((i+2) - \frac{S^*}{S} - \frac{S I_i E^*}{S^* I_i^* E} - \frac{E}{E^*}\frac{I_1^*}{I_1} - \sum_{k=2}^{i} \frac{I_{k-1}}{I_{k-1}^*}\frac{I_k^*}{I_k}\right) \Big] \\ &+ \left(\sum_{i=1}^{n} \beta_i S^* I_i - a_1(d_1+\gamma_1) I_1 + \sum_{i=2}^{n} a_i \gamma_{i-1} I_{i-1} - \sum_{i=2}^{n} a_i (d_i + \gamma_i) I_i\right) \\ \doteq& V_1 + V_2. \end{aligned} \tag{18}$$

Using endemic equations in (4) and rearranging V_2 leads to

$$\begin{aligned} V_2 =& \sum_{i=1}^{n} \beta_i S^* I_i - a_1(d_1+\gamma_1) I_1 + \sum_{i=2}^{n} a_i \gamma_{i-1} I_{i-1} - \sum_{i=2}^{n} a_i (d_i + \gamma_i) I_i \\ =& \sum_{i=1}^{n} \bar{\beta}_i \frac{I_i}{I_i^*} - a_1(d_1+\gamma_1) I_1 + \sum_{i=2}^{n} a_i \gamma_{i-1} I_{i-1} - \sum_{i=2}^{n} a_i (d_i + \gamma_i) I_i \\ =& \frac{I_1}{I_1^*}\left(\bar{\beta}_1 - a_1(d_1+\gamma_1) I_1^* + a_2 \gamma_1 I_1^*\right) + \frac{I_2}{I_2^*}\left(\bar{\beta}_2 - a_2(d_2+\gamma_2) I_2^* + a_3 \gamma_2 I_2^*\right) \\ &+ \cdots + \frac{I_n}{I_n^*}\left(\bar{\beta}_n - a_n(d_n+\gamma_n) I_n^*\right) \\ =& \frac{I_1}{I_1^*}\left(\bar{\beta}_1 - a_1 q_1 \pi - (p\pi + \sum_{i=1}^{n} \bar{\beta}_i) + a_2 \gamma_1 I_1^*\right) \\ &+ \frac{I_2}{I_2^*}\left(\bar{\beta}_2 - a_2 q_2 \pi - a_2 \gamma_1 I_1^* + a_3 \gamma_2 I_2^*\right) \\ &+ \cdots + \frac{I_n}{I_n^*}\left(\bar{\beta}_n - a_n q_n \pi - a_n \gamma_{n-1} I_{n-1}^*\right). \end{aligned}$$

From relation $a_i \gamma_{i-1} I_{i-1}^* = \sum_{k=i}^{n} \bar{\beta}_k$, $i = 2, \cdots, n$, it follows that

$$-a_i \gamma_{i-1} I_{i-1}^* + a_{i+1} \gamma_i I_i^* = -\sum_{k=i}^{n} \bar{\beta}_k + \sum_{k=i+1}^{n} \bar{\beta}_k = -\bar{\beta}_i, \quad i = 2, \cdots, n-1.$$

Therefore

$$\begin{aligned} V_2 &= \frac{I_1}{I_1^*}\left(-a_1 q_1 \pi - p\pi\right) + \frac{I_2}{I_2^*}\left(-a_2 q_2 \pi\right) + \cdots + \frac{I_n}{I_n^*}\left(-a_n q_n \pi\right) \\ &= -p\pi \frac{I_1}{I_1^*} - \sum_{i=1}^{n} a_i q_i \pi \frac{I_i}{I_i^*}. \end{aligned} \tag{19}$$

Now substituting V_2 back into (18) we obtain

$$\begin{aligned} V' =& d_S S^* \left(2 - \frac{S^*}{S} - \frac{S}{S^*}\right) + p\pi \left(3 - \frac{E^*}{E} - \frac{E}{E^*}\frac{I_1^*}{I_1} - \frac{I_1}{I_1^*}\right) \\ &+ \sum_{i=1}^{n} a_i q_i \pi \left(2 - \frac{I_i^*}{I_i} - \frac{I_i}{I_i^*}\right) + \bar{\beta}_1 \left(3 - \frac{S^*}{S} - \frac{SE^*I_1}{S^*EI_1^*} - \frac{E}{E^*}\frac{I_1^*}{I_1}\right) \\ &+ \sum_{i=2}^{n} \bar{\beta}_i \left((i+2) - \frac{S^*}{S} - \frac{SE^*I_i}{S^*EI_i^*} - \frac{E}{E^*}\frac{I_1^*}{I_1} - \sum_{k=2}^{i} \frac{I_{k-1}}{I_{k-1}^*}\frac{I_k^*}{I_k}\right). \end{aligned} \tag{20}$$

By the inequality of arithmetic and geometric means:

$$z_1 + z_2 + \cdots + z_n \geq n\sqrt[n]{z_1 z_2 \cdots z_n}, \text{ for } z_i \geq 0,\ i = 1, \cdots, n,$$

we obtain that $V' \leq 0$ for all $(S_1, E_1, I_1, \cdots, I_n) \in \Gamma$. Furthermore, $V' = 0$ if and only if

$$S = S^*, \quad E = E^*, \quad I_i = I_i^*,\ i = 1, \cdots, n. \tag{21}$$

Therefore, V' is negative definite with respect to P^*, and this implies that P^* is globally asymptotically stable in Γ, by the classical Lyapunov stability theorem, completing proof of Theorem 2.1. □

We remark that the same method can be applied to establish Proposition 1 and Theorem 2.1 for the following MS model with amelioration (δ_i) and immigration:

$$\begin{aligned} S' &= (1 - p - \sum_{i=1}^{n+1} q_i)\pi_i - \sum_{i=1}^{n} \beta_i S I_i - d_S S, \\ E' &= p\pi + \sum_{i=1}^{n} \beta_i S I_i - (d_E + \delta)E, \\ I_1' &= q_1\pi + \delta E - (d_1 + \gamma_1)I_1 + \delta_1 I_2, \\ &\cdots \\ I_i' &= q_i\pi + \gamma_{i-1} I_{i-1} - (d_i + \gamma_i + \delta_{i-1})I_i + \delta_i I_{i+1}, \quad i = 2, \cdots, n-1, \\ &\cdots \\ I_n' &= q_n\pi + \gamma_{n-1} I_{n-1} - (d_n + \gamma_n)I_n + \delta_{n-1} I_n, \\ R' &= q_{n+1}\pi + \gamma_n I_n - d_R R. \end{aligned} \tag{22}$$

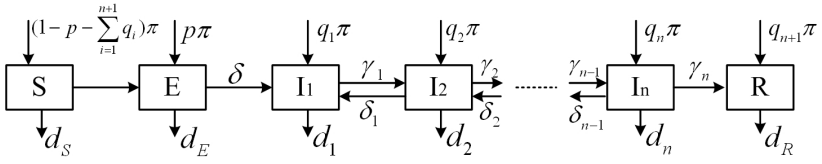

FIGURE 2. Flow diagram of MS model with amelioration (δ_i) and immigration.

3. **A multi-group SEIR model with immigration.** Multi-group models have been studied in the literature since 1970s, motivated by modeling heterogeneous mixing among different social, sexual and risk groups in the transmission of HIV/AIDS and other STDs [1, 9, 10, 13, 15, 18, 22]. These models can be used to describe transmission dynamics of many infectious diseases in heterogeneous host populations. For a recent survey on multi-group models, we refer the reader to [23]. In a seminal work by Lajmanovich and Yorke on a multi-group SIS model of Gonorrhea [15], global dynamics were completely established using a global Lyapunov function. The method of global Lyapunov functions has since been the main tool for establishing global stability of equilibria in these heterogeneous epidemic models. Recently, Guo et al. [6, 7] established the global dynamics of a n-group SIR and SEIR model with bilinear incidence and varying total population size. Their proof of global stability of the endemic equilibrium contains a new graph-theoretical approach to the construction of global Lyapunov functions [6, 7, 16]. We note that these earlier works on multi-group models all restrict immigration into the susceptible population only. The global dynamics of multi-group models with immigration into infected sub-populations have remained open.

In this section, we incorporate immigration into a general multi-group SEIR model, with immigrants moving into all compartments, susceptible and infected, and completely establish its global dynamics. The host population is divided into n groups. For each group i, $1 \le i \le n$, the subpopulation is further divided into four compartments, susceptible S_i, latent E_i, infectious I_i and recovered R_i. Parameter β_{ij}, $i, j = 1, \cdots, n$, represents the transmission coefficient between a susceptible individual in S_i and an infective in I_j, and $1/\delta_i, 1/\alpha_i$ are the mean latent and infectious periods in group i, respectively. Removal rates $d_i^S, d_i^E, d_i^I, d_i^R$ in respective compartments may include both natural and disease-caused death. All parameters are assumed to be nonnegative. We further require that all removal rates $d_i^S, d_i^E, d_i^I, d_i^R$, $i = 1, \cdots, n$, are positive.

Let π be the total immigrants for all groups and $\chi_i (\chi_i > 0)$ be the fraction to the group i. Thus $\sum_{i=1}^n \chi_i = 1$ and $\pi_i \doteq \chi_i \pi$ be the total immigration into the i-th group. One further assumes that a fraction p_i goes into the latent compartment E_i, a fraction q_i into the infectious compartment I_i, a fraction γ_i into the recovered compartment R_i, and the remaining fraction $1 - p_i - q_i - \gamma_i$ into the susceptible compartment S_i. Then our multi-group SEIR model with immigration is described by the following system of ordinary differential equations:

$$\begin{aligned} S_i' &= (1 - p_i - q_i - \gamma_i)\pi_i - \sum_{j=1}^n \beta_{ij} S_i I_j - d_i^S S_i, \\ E_i' &= p_i \pi_i + \sum_{j=1}^n \beta_{ij} S_i I_j - (d_i^E + \delta_i) E_i, \qquad i = 1, 2, \cdots, n. \\ I_i' &= q_i \pi_i + \delta_i E_i - (d_i^I + \alpha_i) I_i, \\ R_i' &= \gamma_i \pi_i + \alpha_i I_i - d_i^R R_i, \end{aligned} \tag{23}$$

Here we assume that $0 \le p_i, q_i, \gamma_i$, $p_i + q_i + \gamma_i < 1$, and $\sum_{i=1}^n (p_i + q_i + \gamma_i) > 0$. If $p_i = q_i = \gamma_i = 0$ for all i, model (23) reduces to the standard multi-group model studied in [7].

Denote $\Pi_i = (1-p_i-q_i-\gamma_i)\pi_i > 0$, $i = 1, \cdots, n$. Since the variable R_i does not appear in other equations of (23), we may consider the following reduced system:

$$\begin{aligned} S_i' &= \Pi_i - \sum_{j=1}^{n} \beta_{ij} S_i I_j - d_i^S S_i, \\ E_i' &= p_i\pi_i + \sum_{j=1}^{n} \beta_{ij} S_i I_j - (d_i^E + \delta_i) E_i, \qquad i = 1, 2, \cdots, n. \\ I_i' &= q_i\pi_i + \delta_i E_i - (d_i^I + \alpha_i) I_i, \end{aligned} \tag{24}$$

3.1. **Feasible region and equilibria.** For each i, adding the three equations in (24) gives $(S_i+E_i+I_i)' \le (1-\gamma_i)\pi_i - d_i^*(S_i+E_i+I_i)$, where $d_i^* = \min\{d_i^S, d_i^E, d_i^I + \alpha_i\} > 0$. Hence $\limsup_{t\to\infty}(S_i+E_i+I_i) \le (1-\gamma_i)\pi_i/d_i^*$. Similarly, from the S_i equation in (24) we obtain $\limsup_{t\to\infty} S_i \le \Pi_i/d_i^S$. Therefore, omega limit sets of system (24) are contained in the following bounded region in the non-negative cone of $\mathbb{R}^{3n}$:

$$\begin{aligned} \Gamma = \{(S_1, E_1, I_1, \cdots, S_n, E_n, I_n) \in \mathbb{R}_+^{3n} \mid\ & S_i \le \Pi_i/d_i^S, \\ & 0 \le S_i + E_i + I_i \le (1-\gamma_i)\pi_i/d_i^*, 1 \le i \le n\}. \end{aligned}$$

It can be verified that Γ is positively invariant with respect to (24).

As expected, the immigration model no longer has the disease-free equilibrium if a positive level of immigration moves into a latent or infective compartment. Let $P^* = (S_1^*, E_1^*, I_1^*, \cdots, S_n^*, E_n^*, I_n^*)$ denote an equilibrium of (24), and set $\bar\beta_{ij} = \beta_{ij} S_i^* I_j^*$, $1 \le i, j \le n$. Then coordinates of P^* satisfy the following system of equations:

$$\begin{aligned} 0 &= \Pi_i - \sum_{j=1}^{n} \bar\beta_{ij} - d_i^S S_i^*, \\ 0 &= p_i\pi_i + \sum_{j=1}^{n} \bar\beta_{ij} - (d_i^E + \delta_i) E_i^*, \qquad i = 1, 2, \cdots, n. \\ 0 &= q_i\pi_i + \delta_i E_i^* - (d_i^I + \alpha_i) I_i^*, \end{aligned} \tag{25}$$

It is clear that $E_i^* = I_i^* = 0$, $i = 1, \cdots, n$, do not satisfy system (25) if there exists $1 \le i \le n$ such that $p_i\pi_i > 0$ or $q_i\pi_i > 0$, and thus model (24) admits no disease-free equilibrium. We assume that transmission matrix $B = (\beta_{ij})$ is irreducible, thus $\overline{B} = (\bar\beta_{ij})$ is irreducible too. It can be further verified that, model (24) admits no equilibria on the boundary of Γ. Since the convex compact set $\Gamma \subset \mathbb{R}^{3n}$ is positively invariant for the flow of system (24), Browder's Fixed Point Theorem implies that system (24) has an equilibrium in Γ. Since no equilibria exist on the boundary, system (24) must have an endemic equilibrium P^*, in the interior of Γ. It can be verified that the vector field of system (24) at the boundary of Γ is transversal to the boundary, and the boundary of Γ is a repellor. This implies the uniform persistence of system (24). In the next subsection, we will establish that any endemic equilibrium of system (24) must be globally asymptotically stable, and as a consequence, system (24) has a unique endemic equilibrium.

Adding the last two equations of (25) and canceling E term give

$$\delta_i p_i \pi_i + \delta_i \sum_{j=1}^{n} \bar\beta_{ij} + (d_i^E + \delta_i) q_i \pi_i = (d_i^E + \delta_i)(d_i^I + \alpha_i) I_i^*, \ i = 1, 2, \cdots, n.$$

Setting $b_i = (d_i^E + \delta_i)/\delta_i$ and dividing by δ_i in the above equation, we obtain the following relation, which will be used in later proof,

$$p_i\pi_i + b_i q_i \pi_i + \sum_{j=1}^{n} \bar{\beta}_{ij} - b_i(d_i^I + \alpha_i)I_i^* = 0, \quad i = 1, 2, \cdots, n. \tag{26}$$

3.2. **Uniqueness and global stability of endemic equilibrium.** In this section, we prove that if infected immigrants are allowed into at least one population group, and the contact network among groups is strongly connected, then the disease will persists in all population groups: a unique endemic equilibrium P^* exists for all feasible parameter values and is globally asymptotically stable. We state our main result in the following theorem.

Theorem 3.1. *Assume that the transmission matrix $B = (\beta_{ij})$ is irreducible. Suppose $\sum_{i=1}^{n}(p_i + q_i) \neq 0$. Then system (24) has a unique endemic equilibrium P^* and it is globally asymptotically stable in Γ.*

Proof. Let $P^* = (S_1^*, E_1^*, I_1^*, \cdots, S_n^*, E_n^*, I_n^*)$ denote an equilibrium of (24). We consider a Lyapunov function

$$V(x) = \sum_{i=1}^{n} c_i V_i,$$

where c_i are positive constants to be specified later, and

$$\begin{aligned} V_i = &\left(S_i - S_i^* - S_i^* \ln \frac{S_i}{S_i^*}\right) + \left(E_i - E_i^* - E_i^* \ln \frac{E_i}{E_i^*}\right) \\ &+ b_i \left(I_i - I_i^* - I_i^* \ln \frac{I_i}{I_i^*}\right) \end{aligned} \tag{27}$$

with $b_i = (d_i^E + \delta_i)/\delta_i$, $i = 1, 2, \cdots, n$, as given earlier. Lyapunov functions in the form of V_i were successfully applied to prove global stability for single-group epidemic models in Korobeinikov and Maini [14], and was further explored in works of Korobeinikov (see e.g. [21]) and others. We refer the reader to a review paper [4] for recent development. We are seeking a suitable linear combination of the Lyapunov functions V_i for single group models, so that $V = \sum_{i=1}^{n} c_i V_i$ is a global Lyapunov function for the multi-group models. Our proof is an adaptation of the graph-theoretical approach to the selection of suitable coefficients c_i developed in [6, 7, 16].

We note that, if $c_i > 0$ for all $1 \leq i \leq n$, function $V(x)$ is positive definite with respect to $x^* = P^*$. The derivative of V along the solution of system (24) is

$$V' = \sum_{i=1}^{n} c_i V_i' = \sum_{i=1}^{n} c_i \left\{ \left(1 - \frac{S_i^*}{S_i}\right) S_i' + \left(1 - \frac{E_i^*}{E_i}\right) E_i' + b_i \left(1 - \frac{I_i^*}{I_i}\right) I_i' \right\}. \tag{28}$$

Using the first equation in (25) and S equation in (24), we obtain

$$\begin{aligned}
&\left(1-\frac{S_i^*}{S_i}\right)S_i' \\
&=\Pi_i-\sum_{j=1}^{n}\beta_{ij}S_iI_j-d_i^SS_i-\Pi_i\frac{S_i^*}{S_i}+\sum_{j=1}^{n}\beta_{ij}S_i^*I_j+d_i^SS_i^* \\
&=\sum_{j=1}^{n}\bar{\beta}_{ij}+2d_i^SS_i^*-\sum_{j=1}^{n}\beta_{ij}S_iI_j-d_i^SS_i-(\sum_{j=1}^{n}\bar{\beta}_{ij}+d_i^SS_i^*)\frac{S_i^*}{S_i}+\sum_{j=1}^{n}\beta_{ij}S_i^*I_j \\
&=d_i^SS_i^*\left(2-\frac{S_i^*}{S_i}-\frac{S_i}{S_i^*}\right)-\sum_{j=1}^{n}\beta_{ij}S_iI_j+\sum_{j=1}^{n}\beta_{ij}S_i^*I_j+\sum_{j=1}^{n}\bar{\beta}_{ij}\left(1-\frac{S_i^*}{S_i}\right).
\end{aligned} \tag{29}$$

Similarly, from (24) and (25) it follows

$$\begin{aligned}
\left(1-\frac{E_i^*}{E_i}\right)E_i' =&p_i\pi_i+\sum_{j=1}^{n}\beta_{ij}S_iI_j-(d_i^E+\delta_i)E_i-p_i\pi_i\frac{E_i^*}{E_i} \\
&-\sum_{j=1}^{n}\beta_{ij}S_iI_j\frac{E_i^*}{E_i}+p_i\pi_i+\sum_{j=1}^{n}\bar{\beta}_{ij}, \\
=&\sum_{j=1}^{n}\beta_{ij}S_iI_j-(d_i^E+\delta_i)E_i+p_i\pi_i\left(2-\frac{E_i^*}{E_i}\right) \\
&+\sum_{j=1}^{n}\bar{\beta}_{ij}\left(1-\frac{S_iI_j}{S_i^*I_j^*}\frac{E_i^*}{E_i}\right),
\end{aligned} \tag{30}$$

$$\begin{aligned}
\left(1-\frac{I_i^*}{I_i}\right)I_i' &= q_i\pi_i+\delta_iE_i-(d_i^I+\alpha_i)I_i-q_i\pi_i\frac{I_i^*}{I_i}-\delta_iE_i\frac{I_i^*}{I_i}+(d_i^I+\alpha_i)I_i^* \\
&=\delta_iE_i-(d_i^I+\alpha_i)I_i+q_i\pi_i\left(2-\frac{I_i^*}{I_i}\right)+\delta_iE_i^*\left(1-\frac{E_i}{E_i^*}\frac{I_i^*}{I_i}\right).
\end{aligned} \tag{31}$$

Then, substituting (29) – (31) into V_i' and rearranging terms, we get

$$\begin{aligned}
V_i' =&d_i^SS_i^*\left(2-\frac{S_i^*}{S_i}-\frac{S_i}{S_i^*}\right)+\sum_{j=1}^{n}\beta_{ij}S_i^*I_j+\sum_{j=1}^{n}\bar{\beta}_{ij}\left(2-\frac{S_i^*}{S_i}-\frac{S_iI_j}{S_i^*I_j^*}\frac{E_i^*}{E_i}\right) \\
&+p_i\pi_i\left(2-\frac{E_i^*}{E_i}\right)+b_iq_i\pi_i\left(2-\frac{I_i^*}{I_i}\right) \\
&-b_i(d_i^I+\alpha_i)I_i+b_i\delta_iE_i^*\left(1-\frac{E_i}{E_i^*}\frac{I_i^*}{I_i}\right)
\end{aligned} \tag{32}$$

$$
\begin{aligned}
&= \left(\sum_{j=1}^{n} \beta_{ij} S_i^* I_j - b_i(d_i^I + \alpha_i) I_i\right) \\
&\quad + p_i \pi_i \left(3 - \frac{E_i^*}{E_i} - \frac{E_i}{E_i^*}\frac{I_i^*}{I_i}\right) + b_i q_i \pi_i \left(2 - \frac{I_i^*}{I_i}\right) \\
&\quad + \sum_{j=1}^{n} \bar{\beta}_{ij} \left(3 - \frac{S_i^*}{S_i} - \frac{S_i}{S_i^*}\frac{I_j}{I_j^*}\frac{E_i^*}{E_i} - \frac{E_i}{E_i^*}\frac{I_i^*}{I_i}\right) + d_i^S S_i^* \left(2 - \frac{S_i^*}{S_i} - \frac{S_i}{S_i^*}\right) \\
&= \left(\sum_{j=1}^{n} \beta_{ij} S_i^* I_j - b_i(d_i^I + \alpha_i) I_i + (p_i \pi_i + b_i q_i \pi_i)\frac{I_i}{I_i^*}\right) \\
&\quad + p_i \pi_i \left(3 - \frac{E_i^*}{E_i} - \frac{E_i}{E_i^*}\frac{I_i^*}{I_i} - \frac{I_i}{I_i^*}\right) + b_i q_i \pi_i \left(2 - \frac{I_i^*}{I_i} - \frac{I_i}{I_i^*}\right) \\
&\quad + \sum_{j=1}^{n} \bar{\beta}_{ij} \left(3 - \frac{S_i^*}{S_i} - \frac{S_i}{S_i^*}\frac{I_j}{I_j^*}\frac{E_i^*}{E_i} - \frac{E_i}{E_i^*}\frac{I_i^*}{I_i}\right) + d_i^S S_i^* \left(2 - \frac{S_i^*}{S_i} - \frac{S_i}{S_i^*}\right).
\end{aligned}
$$

Here we have used the relation $b_i \delta_i E_i^* = p_i \pi_i + \sum_{j=1}^{n} \bar{\beta}_{ij}$ from (25). Now we substitute (32) into (28) and obtain

$$
\begin{aligned}
V' = &\sum_{i=1}^{n} c_i \left(\sum_{j=1}^{n} \beta_{ij} S_i^* I_j - b_i(d_i^I + \alpha_i) I_i + (p_i \pi_i + b_i q_i \pi_i)\frac{I_i}{I_i^*}\right) \\
&+ \sum_{i=1}^{n} c_i p_i \pi_i \left(3 - \frac{E_i^*}{E_i} - \frac{E_i}{E_i^*}\frac{I_i^*}{I_i} - \frac{I_i}{I_i^*}\right) + \sum_{i=1}^{n} c_i b_i q_i \pi_i \left(2 - \frac{I_i^*}{I_i} - \frac{I_i}{I_i^*}\right) \\
&+ \sum_{i=1}^{n} c_i \sum_{j=1}^{n} \bar{\beta}_{ij} \left(3 - \frac{S_i^*}{S_i} - \frac{S_i}{S_i^*}\frac{I_j}{I_j^*}\frac{E_i^*}{E_i} - \frac{E_i}{E_i^*}\frac{I_i^*}{I_i}\right) \\
&+ \sum_{i=1}^{n} c_i d_i^S S_i^* \left(2 - \frac{S_i^*}{S_i} - \frac{S_i}{S_i^*}\right).
\end{aligned} \tag{33}
$$

Constants $c_i > 0$ will be chosen in such a way that the first sum in (33) totally vanishes. Recall that $\bar{\beta}_{ij} = \beta_{ij} S_i^* I_j^*$ and that the transmission matrix $B = (\beta_{ij})$ is irreducible. A lemma in Appendix justifies the choice of c_i and the following holds.

$$
\sum_{i=1}^{n} c_i \Big(\sum_{j=1}^{n} \beta_{ij} S_i^* I_j - b_i(d_i^I + \alpha_i) I_i\Big) + \sum_{i=1}^{n} c_i \left(p_i \pi_i + b_i q_i \pi_i\right) \frac{I_i}{I_i^*} \equiv 0, \tag{34}
$$

for all $I_1, \cdots, I_n \geq 0$.

Substituting (34) into (33) and using the inequality of arithmetic and geometric means, we have

$$\begin{aligned} V' &= \sum_{i=1}^{n} c_i d_i^S S_i^* \left(2 - \frac{S_i^*}{S_i} - \frac{S_i}{S_i^*}\right) \\ &+ \sum_{i=1}^{n} c_i p_i \pi_i \left(3 - \frac{E_i^*}{E_i} - \frac{E_i}{E_i^*}\frac{I_i^*}{I_i} - \frac{I_i}{I_i^*}\right) + \sum_{i=1}^{n} c_i b_i q_i \pi_i \left(2 - \frac{I_i^*}{I_i} - \frac{I_i}{I_i^*}\right) \\ &+ \sum_{i=1}^{n}\sum_{j=1}^{n} c_i \bar{\beta}_{ij} \left(3 - \frac{S_i^*}{S_i} - \frac{S_i}{S_i^*}\frac{I_j}{I_j^*}\frac{E_i^*}{E_i} - \frac{E_i}{E_i^*}\frac{I_i^*}{I_i}\right) \\ &\le \sum_{i=1}^{n}\sum_{j=1}^{n} c_i \bar{\beta}_{ij} \left(3 - \frac{S_i^*}{S_i} - \frac{S_i}{S_i^*}\frac{I_j}{I_j^*}\frac{E_i^*}{E_i} - \frac{E_i}{E_i^*}\frac{I_i^*}{I_i}\right) \doteq H_n. \end{aligned} \tag{35}$$

For the remaining term H_n, following the graph-theoretic arguments in the proof of Theorem 1.1 of [7], we can show that $H_n \le 0$ for all $(S_1, E_1, I_1, \cdots, S_n, E_n, I_n) \in \Gamma$. Furthermore, a similar argument as in [7] shows that $V' = 0$ implies

$$S_i = S_i^*, \quad \frac{E_i}{E_i^*} = \frac{I_i}{I_i^*} = a, \quad i = 1, \cdots, n, \tag{36}$$

for some positive number a. The assumption $\sum_{i=1}^{n}(p_i + q_i) > 0$ of Theorem 3.1 implies that there exists k $(1 \le k \le n)$ such that either $p_k > 0$ or $q_k > 0$. For this index k, from the second or the third term of V' we know that $V' = 0$ implies $I_k = I_k^*$, and thus $a = 1$ in (36). As a result, $V' = 0$ holds only at P^*, and V' is negative definite with respect to P^*. Standard Lyapunov stability theorem implies that P^* is locally asymptotically stable and globally attracting in Γ. The global stability of P^* also implies that P^* is unique in Γ. This establishes Theorem 3.1. □

4. **Conclusions.** In this paper, we have studied two classes of epidemic models for the transmission of infectious diseases in heterogeneous populations. A new feature of our models is that we allow constant immigration or migration into both susceptible and infected compartments or subpopulations. Our results have completely determined the global dynamics of these two classes of models for the first time in the literature.

The first class of model consists of SEI_nR type multi-stage models with possible immigration into all compartments, and the second class includes multi-group models of $SEIR$ type with possible immigration to all compartments in each group. We have established that, as long as infected (exposed or infectious) immigrants or migrants are allowed into at least one compartment or subpopulation, the disease will persist in all subpopulations: there will be no disease-free equilibrium, and a unique endemic equilibrium P^* always exists and is globally asymptotically stable in the entire feasible region. Our results generalize earlier results in the literature on simpler models with infective immigration in [3] and [20], though the later using standard incidence. In comparison to results in [3, 20], our proof is technically much more difficult due to the heterogeneity and the associated high dimensionality as well as complexity in these models. In our proof, we have adapted the new graph-theoretical approach to the construction of global Lyapunov functions for complex models developed in [6, 7, 16]. Our work is the first to expand the applicability of

the graph-theoretic approach in [6, 7, 16] to heterogeneous epidemic models with infective immigration.

While our results have completely determined the global dynamics in two general classes of heterogeneous epidemic models with immigration, interesting questions remain regarding how the dynamics of model with immigration are related to those models without immigration to infected subpopulations. In particular, as it was pointed out in Brauer and van den Driessche [3], when immigration into infected subpopulations exists, the model no longer has the disease-free equilibrium, and the basic reproduction number R_0 has lost its threshold property. Note that R_0 is still well-defined in this case, whether it still plays a mathematical role in determining different asymptotic behaviours of solutions, or a biological role of determining different disease properties remain to be further investigated.

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Appendix. Consider a linear algebraic system

$$\overline{B}v = 0, \tag{37}$$

where

$$\overline{B} = \begin{bmatrix} \sum_{l\neq 1}\bar{\beta}_{1l} & -\bar{\beta}_{21} & \cdots & -\bar{\beta}_{n1} \\ -\bar{\beta}_{12} & \sum_{l\neq 2}\bar{\beta}_{2l} & \cdots & -\bar{\beta}_{n2} \\ \vdots & \vdots & \ddots & \vdots \\ -\bar{\beta}_{1n} & -\bar{\beta}_{2n} & \cdots & \sum_{l\neq n}\bar{\beta}_{nl} \end{bmatrix} \tag{38}$$

with $\bar{\beta}_{ij} \geq 0$, and $v = (v_1, \cdots, v_n)^T$ is a column vector. Note that each column's sum of matrix $\overline{B}$ equals to zero. The following result in graph theory and its proof can be found in [7, Section 3].

Kirchhoff's Matrix-Tree Theorem. Assume that the matrix $(\bar{\beta}_{ij})_{n\times n}$ is irreducible and $n \geq 2$. Then the following statements hold.

(1) The solution space of system (37) has dimension 1, with a basis

$$(v_1, v_2, \ldots, v_n) = (C_{11}, C_{22}, \ldots, C_{nn}), \tag{39}$$

where C_{kk} denotes the cofactor of the k-th diagonal entry of $\bar{B}$, $1 \leq k \leq n$.

(2) For each $1 \leq k \leq n$,

$$C_{kk} = \sum_{T\in\mathbb{T}_k} \prod_{(r,m)\in E(T)} \bar{\beta}_{rm} > 0, \tag{40}$$

where $\mathbb{T}_k$ is the set of all directed n-trees rooted at the k-th vertex, and $E(T)$ denotes the set of arcs in a directed tree T.

Lemma 4.1. *Let c_i be the co-factor of the i-th diagonal element of $\overline{B}$ as (38). Then*

(1) $c_i > 0$, $i = 1, \cdots, n$.

(2) $c = (c_1, \cdots, c_n)^T$ *satisfies* $\overline{B}c = 0$.

(3) *The following identity holds.*

$$\sum_{i=1}^{n} c_i \Big(\sum_{j=1}^{n} \beta_{ij} S_i^* I_j - b_i (d_i^I + \alpha_i) I_i \Big) + \sum_{i=1}^{n} c_i \left(p_i \pi_i + b_i q_i \pi_i \right) \frac{I_i}{I_i^*} = 0,$$

for all $I_1, \cdots, I_n \geq 0$.

Proof. The first two statements follows from the the fact that $\overline{B}$ is the algebraic Laplacian matrix of an irreducible positive matrix $B = (\beta_{ij})$, and from the Kirchhoff Matrix Tree Theorem in the Appendix.

To verify statement (3), we regroup terms in the left hand side of (4.1) according to $\frac{I_i}{I_i^*}$ and obtain

$$\begin{aligned} L_n &\doteq \sum_{i=1}^{n} c_i \Big(\sum_{j=1}^{n} \bar{\beta}_{ij} \frac{I_j}{I_j^*} - b_i (d_i^I + \alpha_i) I_i^* \frac{I_i}{I_i^*} \Big) + \sum_{i=1}^{n} c_i (p_i \pi_i + b_i q_i \pi_i) \frac{I_i}{I_i^*} \\ &= \sum_{i=1}^{n} \Big(\sum_{j=1}^{n} c_j \bar{\beta}_{ji} + c_i (p_i \pi_i + b_i q_i \pi_i) - c_i b_i (d_i^I + \alpha_i) I_i^* \Big) \frac{I_i}{I_i^*}. \end{aligned}$$

We see that $L_n \equiv 0$ for all $I_1, \cdots, I_n \geq 0$ if and only if coefficients of $\frac{I_i}{I_i^*}$ are 0, namely,

$$\sum_{j=1}^{n} c_j \bar{\beta}_{ji} + c_i (p_i \pi_i + b_i q_i \pi_i) - c_i b_i (d_i^I + \alpha_i) I_i^* = 0, \quad i = 1, \cdots, n. \tag{41}$$

Using relation (26), system (41) can be rewritten as

$$\sum_{j=1}^{n} c_j \bar{\beta}_{ji} - \sum_{j=1}^{n} \bar{\beta}_{ij} c_i = 0, \quad i = 1, \cdots, n,$$

which, in a matrix form, is equivalent to $\overline{B} c = 0$. This completes the proof. □

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