MATHEMATICAL BIOSCIENCES
AND ENGINEERING
Volume **10**, Number **5&6**, October & December **2013**

doi:10.3934/mbe.2013.10.1651

pp. **1651–1668**

DIFFERENT TYPES OF BACKWARD BIFURCATIONS DUE TO DENSITY-DEPENDENT TREATMENTS

Baojun Song

Department of Mathematical Sciences
Montclair State University
Montclair, NJ 07043, USA

Wen Du and Jie Lou

Department of Mathematics
Shanghai University
99 Shangda Road, Shanghai 200444, China

Dedicated to Carlos Castillo-Chavez in celebration of his 60th birthday

Abstract. A set of deterministic SIS models with density-dependent treatments are studied to understand the disease dynamics when different treatment strategies are applied. Qualitative analyses are carried out in terms of general treatment functions. It has become customary that a backward bifurcation leads to bistable dynamics. However, this study finds that finds that bistability may not be an option at all; the disease-free equilibrium could be globally stable when there is a backward bifurcation. Furthermore, when a backward bifurcation occurs, the fashion of bistability could be the coexistence of either dual stable equilibria or the disease-free equilibrium and a stable limit cycle. We also extend the formula for mean infection period from density-independent treatments to density-dependent ones. Finally, the modeling results are applied to the transmission of gonorrhea in China, suggesting that these gonorrhea patients may not seek medical treatments in a timely manner.

1. **Introduction.** For a curable transmission disease, one expects that all cases would be treated. However, there are numerous factors that put pressure on exercising treatments: such as hospital capacities, number of skilled health workers (doctors, nurses etc.), public health infrastructure and budgetary constraints. Even when we are able to handle all cases, we could still encounter problems in identifying them all, let alone the asymptomatic ones. An execution of a treatment regime is constrained by the available budget and amount of resources. It is necessary to design different treatment strategies.

When the number of infections is small, we can ignore the aforementioned pressures. Then, it is reasonable to assume that each infected individual has a higher chance of receiving treatment, meaning a fixed portion of infections can be identified and treated. This assumption has led to the conclusion that the per-capita treatment rate is a constant; each infected individual has the same fixed chance to be treated regardless of the number of infections. As we have already seen from the classic modeling approaches in dealing with treatment, the treatment rate is

2010 *Mathematics Subject Classification.* Primary: 92D30, 37G10, 34D20; Secondary: 34C23, 92B05.

Key words and phrases. Treatment, density-dependent, bifurcation, gonorrhea.

a linear function of the number of infections. The classical SIR model is a typical starting point when designing treatment or recovering functions. This linear fashion has also dominated construction of vaccination models, whose rates are also linear. Again, the per-capita vaccination rate is constant. If the pool of infections is large, the limited health infrastructure and budgets prevent us from providing treatments to all infected individuals, hence the reduction in per-capita treatment rate.

Let S and I be the number of susceptible and infected individuals at time t, respectively. Let us suppose that total resources are fixed and all infected individuals are equally treated, then the likelihood of each infected individual to be treated is a function of the number of infected individuals. The per-capita treatment rate is denoted by $p(I)$. If $p(I)$ is a constant, as has been seen in traditional epidemic models, the corresponding treatment is density-independent; otherwise it is density-dependent. As a result, the total treatment rate is $p(I)I$.

There are many forms for the per-capita treatment function $p(I)$. For example, α, $\alpha+\gamma I$, $\alpha e^{-\gamma I}$, $\alpha_2+\alpha_1 e^{-\gamma I}$, and $\frac{A}{1+BI^n}$ are all good candidates. In this paper, we are more interested in the specific forms of $p(I)$, such as $p(I)=\alpha+\gamma I$ and $p(I)=\alpha_2+\alpha_1 e^{-\gamma I}$. The parameter γ in $p(I)=\alpha e^{-\gamma I}$ is a density-dependent factor of the treatment. It catches the impact of the infections to the treatment. Particularly, $\gamma=0$ corresponds to the density-independent per-capita treatment rate; and as γ increases, so does density-dependence.

A similar approach in epidemiology study has appeared in [5, 7, 8, 11, 12] using continuous dynamical models, but from the perspective of saturated treatment rates. Wang [11] introduced a piecewise linear function for the treatment rate

$$T(I)=\begin{cases} \alpha I, & 0\le I\le I_0,\\ rI_0, & I>I_0,\end{cases}$$

where r and I_0 are some positive constants. Zhang and Liu [12] introduced a rational function $T(I)=\frac{\alpha I}{1+\gamma I}$ for the treatment rate, where γ is a nonnegative parameter to measure the extent of the delaying treatment to the infected and α is the cure rate. In dealing with incidence rate, three specific functions have typical been seen in the recent research [5, 7, 8, 11, 12]: mass-action law βSI [5], standard incidence $\frac{\beta SI}{S+I}$ [7] and $\frac{\beta SI}{1+kI}$ [8]. Distinct combinations of saturated treatment rates and incidence rates have resulted in [5, 7, 8, 11, 12] with minor modifications, such as self recovery, etc. Discrete-time epidemiological models have also incorporated density-dependent treatments [2].

2. Mathematical models and basic reproduction number.

We consider the following epidemic models of SIS type:

$$\begin{cases} \dfrac{dS}{dt}=\Lambda-\beta S\dfrac{I}{N}-\mu S+p(I)I,\\ \dfrac{dI}{dt}=\beta S\dfrac{I}{N}-(\mu+d)I-p(I)I,\\ N=S+I. \end{cases} \tag{1}$$

Λ is the recruitment rate into the population; μ is the natural death rate; d is the additional death rate caused by the disease. The infected individuals are treated at rate $p(I)I$.

Since $\Omega=\{(S,I)|I\ge 0, S\ge 0, S+I\le\frac{\Lambda}{\mu}\}$ is positively invariant for model (1), we only study it in the feasible domain Ω. The disease-free equilibrium $E_0=(\frac{\Lambda}{\mu},0)$

always exists and the Jacobian matrix around E_0 is

$$J(E_0) = \begin{pmatrix} -\mu & -\beta + p(0) \\ 0 & \beta - \mu - d - p(0) \end{pmatrix}. \tag{2}$$

Using the next generation operator [10], we compute the basic reproductive number $\mathcal{R}_0 = \frac{\beta}{\mu+d+p(0)}$. The eigenvalues of matrix $J(E_0)$ are $\lambda_1 = -\mu < 0, \lambda_2 = \beta - (\mu + d + p(0)) = (\mu + d + p(0))(\mathcal{R}_0 - 1)$. Therefore, if $\mathcal{R}_0 < 1$, all of the eigenvalues are negative. Then we have the following standard threshold theorem.

Theorem 2.1. *The disease-free equilibrium E_0 of model (1) is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$.*

The per-capital treatment rate $p(I)$ impacts the basic reproductive number through $p(0)$. Since $\mathcal{R}_0$ only picks up information of $p(I)$ locally, it cannot fully characterize the dynamics of the model. We will deal with this in Section 5.

3. **Average infection period.** It is well known that in the study of epidemic models, when $p(I) = \alpha$ is a constant, the average infection period is $\frac{1}{\alpha+\mu+d}$. If the treatment is density-dependent, this is no longer true. Now we formulate the average infection period when $p(I)$ is *not* constant.

Given that a cohort of I_0 individuals who are infected simultaneously at $t = 0$. We will look for the average time of these infected individuals stay in the I-class. The dynamics of these individuals is governed by

$$\begin{cases} \dfrac{dI}{dt} = -(\mu + d)I - p(I)I, \\ I(0) = I_0. \end{cases} \tag{3}$$

Using model (3), we can formulate the average infection period. At time t, $(\mu + d + p(I))I$ of these infected individuals are removed–be it by treatment, natural death or death due to the disease–from I-class per unit of time. These removed individuals at time t all have an infection time (age) of exact t units of time. Therefore, the total infection time for these removed individuals is $(\mu + d + p(I))It$ per unit of time. The grand total infection time for the whole group is $\int_0^\infty (\mu + d + p(I))Itdt$. This produces a formula for the average infection period

$$t_{av} = \frac{\int_0^\infty (\mu + d + p(I(t)))I(t)tdt}{I_0}. \tag{4}$$

Since $(\mu + d + p(I(t)))I(t) = -I'(t)$, we can express (4) in another way,

$$t_{av} = \frac{\int_0^\infty -I'(t)tdt}{I_0} = -\frac{I(t)t}{I_0}\bigg|_0^\infty + \frac{\int_0^\infty I(t)dt}{I_0} = \frac{\int_0^\infty I(t)dt}{I_0}, \tag{5}$$

where $\lim_{t\to\infty} -\frac{I(t)t}{I_0} = 0$ is due to the fact $I(t) \le I_0 e^{-(\mu+d)t}$.

A probabilistic argument for (5), for which a simple case can be found in Section 1.7 of [1], is as follows. Let T be the random variable that denotes the time of an individual to leave the I-class. In other words, T is the infection period of an infected individual. $\frac{I(t)}{I_0}$ is the proportion of the these initially infected individuals who are still in class I at time t. The infection period for them is at least t, Hence, $P(T > t) = \frac{I(t)}{I_0}$ $(t \ge 0)$. The CDF of T is $F_T(t) = P(T \le t) = 1 - P(T > t) =$

$1-\frac{I(t)}{I_0}$ and the PDF of T is $-\frac{I'(t)}{I_0}$. The expected value of T is the average infection period:

$$t_{av} = E[T] = \int_0^\infty \frac{-I'(t)}{I_0} t dt, \tag{6}$$

which is identical to (5).

It is almost impossible to obtain a closed-form solution to IVP (3) for an arbitrary $p(I)$ in order to evaluate t_{av}. However, $p(I)$ does give us some insights into an implicit solution to (3): $I(t) = I_0 e^{-(\mu+d)t-\int_0^t p(I(s))ds}$, which leads to

$$\begin{aligned} t_{av} &= \frac{\int_0^\infty (\mu + d + p(I(t)))I(t)tdt}{I_0} \\ &= \int_0^\infty (\mu + d + p(I(t)))e^{-(\mu+d)t-\int_0^t p(I(s))ds} t dt \\ &= -(\mu + d + p(I(t)))e^{-(\mu+d)t-\int_0^t p(I(s))ds} t\Big|_0^\infty + \int_0^\infty e^{-(\mu+d)t-\int_0^t p(I(s))ds} dt \end{aligned}$$

Since $-(\mu + d + p(I(t)))e^{-(\mu+d)t-\int_0^t p(I(s))ds} t\Big|_0^\infty = 0$, we formulate the expected infection period as

$$t_{av} = \int_0^\infty e^{-(\mu+d)t-\int_0^t p(I(s))ds} dt. \tag{7}$$

An obvious application of expression (7) in terms of the general treatment function is that any treatment will shorten the average infection period because $p(I) \geq 0$ and $t_{av} = \int_0^\infty e^{-(\mu+d)t-\int_0^t p(I(s))ds} dt \leq \int_0^\infty e^{-(\mu+d)t} dt = \frac{1}{\mu+d}$, which is the average infection period in the absence of treatment.

Practically, (7) can be estimated by numerical integration. For instance, if one adapts a right-endpoint approximation in numerical integrals, formula (7) becomes

$$t_{av} \approx \sum_{i=1}^{\infty} e^{-(\mu+d)i-\sum_{j=1}^{i} p(I(j))}. \tag{8}$$

Once one has prevalence data at hands, (8) can be used to estimate the average infection period. Formulas (7) and (8) will be recalled in later sections when we apply our models to the transmission of gonorrhea in China. Following are two examples in computing t_{av} for $p(I) = \alpha$ (constant) and $p(I) = \alpha + \gamma I$.

3.1. $p(I) = \alpha$**.** In this case, the solution to (3) is $I(t) = I_0 e^{-(\mu+d+\alpha)t}$, and the corresponding average infection period is

$$t_{av} = \frac{\int_0^\infty I(t)dt}{I_0} = \frac{\int_0^\infty I_0 e^{-(\mu+d+\alpha)t} dt}{I_0} = \frac{1}{\mu + d + \alpha}.$$

This is the same result as we have seen in the classical epidemic models, where treatment is density-independent.

3.2. $p(I) = \alpha + \gamma I$**.** The corresponding solution to (3) is

$$I(t) = \frac{(\mu + d + \alpha)I_0}{(\mu + d + \alpha + \gamma I_0)e^{(\mu+d+\alpha)t} - \gamma I_0},$$

which leads to

$$\begin{aligned}
t_{av} &= \frac{\int_0^\infty I(t)dt}{I_0} \\
&= \frac{\int_0^\infty \frac{(\mu+d+\alpha)I_0}{(\mu+d+\alpha+\gamma I_0)e^{(\mu+d+\alpha)t}-\gamma I_0}dt}{I_0} \\
&= \int_0^\infty \frac{e^{(\mu+d+\alpha)t}(\mu+d+\alpha)}{e^{(\mu+d+\alpha)t}((\mu+d+\alpha+\gamma I_0)e^{(\mu+d+\alpha)t}-\gamma I_0)}dt \\
&= \int_1^\infty \frac{1}{y((\mu+d+\alpha+\gamma I_0)y-\gamma I_0)}dy \\
&= \frac{1}{\gamma I_0}\int_1^\infty \left(\frac{\mu+d+\alpha+\gamma I_0}{(\mu+d+\alpha+\gamma I_0)y-\gamma I_0}-\frac{1}{y}\right)dy \\
&= \frac{\ln\left(\frac{\mu+d+\alpha+\gamma I_0}{\mu+d+\alpha}\right)}{\gamma I_0} = \frac{1}{\gamma I_0}\ln\left(\frac{\mu+d+\alpha+\gamma I_0}{\mu+d+\alpha}\right)
\end{aligned}$$

$t_{av} = \frac{1}{\gamma I_0}\ln\left(\frac{\mu+d+\alpha+\gamma I_0}{\mu+d+\alpha}\right)$ generalizes the results of case (a), which can be verified by taking the limit as γ approaches zero:

$$\lim_{\gamma\to 0} t_{av} = \lim_{\gamma\to 0}\frac{1}{\gamma I_0}\ln\left(\frac{\mu+d+\alpha+\gamma I_0}{\mu+d+\alpha}\right) = \frac{1}{\mu+d+\alpha}.$$

Once again, this is the exact result when the treatment is density-independent.

4. **General results.** We collect some general results for model (1) in this section. If there are no budgetary and facility hardships, we can keep increasing the chances of treatment as the number of infected cases increases. Thus, it would be useful to consider that $p(I)$ is increasing. For this situation, there exists a uniqueness of endemic equilibrium when $\mathcal{R}_0 > 1$, as stated in the following theorem.

Theorem 4.1. *When $\mathcal{R}_0 > 1$, there exists a unique endemic equilibrium for model (1) if $p'(I) > 0$.*

Proof. At endemic (S^*, I^*), $N^* = \frac{\Lambda - dI^*}{\mu}$ and I^* is a solution to $f(x) = 0$, where

$$f(x) = \beta\frac{(\frac{\Lambda-dx}{\mu}-x)}{\frac{\Lambda-dx}{\mu}} - (\mu+d) - p(x).$$

$f(x)$ is a decreasing function because $f'(x) = -\frac{\beta\Lambda\mu}{(\Lambda-dx)^2} - p'(x) < 0$. If $\mathcal{R}_0 < 1$, $f(x) < 0$ holds for all $x > 0$, since $f(0) = (\mathcal{R}_0 - 1)(\mu + d + p(0))$, and there is no endemic equilibrium. Noticing $\lim_{x\to\frac{\Lambda}{d}-} f(x) = -(\mu+d) - p(\frac{\Lambda}{d}) < 0$, then $\mathcal{R}_0 > 1$ implies $f(x) = 0$ has a unique solution. Therefore, when $\mathcal{R}_0 > 1$, model (1) has a unique endemic equilibrium. □

Our next theorem deals with the stability of the endemic equilibrium.

Theorem 4.2. *For system (1), if $\mathcal{R}_0 > 1$, the endemic equilibrium is asymptotically stable assuming $p''(I) > 0$.*

Proof. The Jacobian matrix $J(E)$ of system (1) around the endemic equilibrium E^* is

$$J(E^*) = \begin{pmatrix} -\frac{\beta I^2}{N^2} - \mu & -\frac{\beta S^2}{N^2} + p(I) + Ip'(I) \\ \frac{\beta I^2}{N^2} & \frac{\beta S^2}{N^2} - (\mu + d) - p(I) - Ip'(I) \end{pmatrix}.$$

We can examine the trace and the determinant of $J(E^*)$, to determine the stability of E^*.

$$\begin{aligned} tr(J) &= \beta\frac{S^2 - I^2}{N^2} - \mu - (\mu + d) - p(I) - Ip'(I) \\ &= \beta\frac{2S - N}{N} - \mu - (\mu + d) - p(I) - Ip'(I) \\ &= -\beta + 2\frac{\beta S}{N} - (\mu + d + \alpha) - \mu - p(I) - Ip'(I) \quad (\text{Using } \beta\frac{S}{N} = \mu + d + p(I)) \\ &= -\beta + (\mu + d + p(I)) - \mu - Ip'(I) \\ &= (\mu + d + p(0))(1 - \mathcal{R}_0) - \mu + p(I) - p(0) - Ip'(I) \\ &\quad (\text{Using mean value theorem for } p(I)) \\ &= (\mu + d + p(0))(1 - \mathcal{R}_0) - \mu - I(p'(I) - p'(c)) \quad (c \le I) \end{aligned}$$

The Mean Value Theorem was applied to $p(I)$ on the interval $[0, I]$ in this process. $p'(I) - p'(c) > 0$ is obtained from $c \le I$ and $p'' > 0$. Hence, if $\mathcal{R}_0 > 1$, the trace of J is negative. Now we check the determinant of J and use $\beta\frac{S}{N} = \mu + d + p(I)$ again.

$$\begin{aligned} det(J) &= \left(-\frac{\beta I^2}{N^2} - \mu\right)\left(\frac{\beta S^2}{N^2} - (\mu + d) - p(I) - Ip'(I)\right) \\ &\quad - \left(-\frac{\beta S^2}{N^2} + p(I) + Ip'(I)\right)\left(\frac{\beta I^2}{N^2}\right) \\ &= \left(\frac{\beta I^2}{N^2}\right)(\mu + d) - \mu\left(\frac{\beta S^2}{N^2} - (\mu + d) - p(I) - Ip'(I)\right) \\ &= \mu\frac{\beta I^2}{N^2} - \mu\left(\frac{\beta S^2}{N^2} - (\mu + d) - p(I) - Ip'(I)\right) + \frac{\beta d I^2}{N^2} \\ &= \mu\left(\frac{\beta I^2}{N^2} - \frac{\beta S^2}{N^2} + (\mu + d) + p(I) + Ip'(I)\right) + \frac{\beta d I^2}{N^2} \\ &= \mu\left(\frac{I^2 - S^2}{N^2}\beta + (\mu + d) + p(I) + Ip'(I)\right) + \frac{\beta d I^2}{N^2} \\ &= \mu\left(\frac{\beta(I - S)}{N} + (\mu + d) + p(I) + Ip'(I)\right) + \frac{\beta d I^2}{N^2} \\ &= \mu\left(\frac{\beta(N - 2S)}{N} + (\mu + d) + p(I) + Ip'(I)\right) + \frac{\beta d I^2}{N^2} \\ &= \mu\left(\beta - \frac{2S}{N}\beta + (\mu + d) + p(I) + Ip'(I)\right) + \frac{\beta d I^2}{N^2} \\ &= \mu\left(\beta - 2(\mu + d + p(I)) + (\mu + d) + p(I) + Ip'(I)\right) + \frac{\beta d I^2}{N^2} \end{aligned}$$

$$
\begin{aligned}
&= \mu\left(\beta - (\mu + d + p(I)) + Ip'(I)\right) + \frac{\beta d I^2}{N^2} \\
&= \mu\left(\beta - (\mu + d + p(0)) - p(I) + p(0) + Ip'(I)\right) + \frac{\beta d I^2}{N^2} \\
&= \mu\left(\beta - (\mu + d + p(0)) - Ip'(c) + Ip'(I)\right) + \frac{\beta d I^2}{N^2} \\
&= \mu\left((\mathcal{R}_0 - 1)(\mu + d + p(0)) + I(p'(I) - p'(c))\right) + \frac{\beta d I^2}{N^2} > 0
\end{aligned}
$$

Therefore, when $\mathcal{R}_0 > 1$, the endemic equilibrium is locally asymptotically stable. □

To study the global dynamics for the planar system (1), we can rule out the existence of closed orbits for some cases.

Theorem 4.3. *For system (1), if $p'(I) > 0$, then there is no limit cycle.*

Proof. To prove this theorem, we rewrite (1) by using variables $N = S + I$ and I. The equivalent system is

$$
\begin{cases}
\dfrac{dN}{dt} = \Lambda - \mu N - dI := F, \\
\dfrac{dI}{dt} = \beta\dfrac{(N - I)I}{N} - (\mu + d)I - p(I)I := G.
\end{cases} \tag{9}
$$

A selection of the Dulac function $D = \frac{1}{I}$ arrives at $\dfrac{\partial(FD)}{\partial N} + \dfrac{\partial(GD)}{\partial I} = -\frac{\mu}{I} - p'(I) - \frac{\beta}{N} < 0$. □

A combination of Theorems 4.2 and 4.3 features the global dynamics of model (1).

Theorem 4.4. *Assume $p'(I) \geq 0$ and $p''(I) \geq 0$. The endemic equilibrium of (1) is globally asymptotically stable if $\mathcal{R}_0 > 1$.*

Examples that meet the hypothesis of Theorem 4.4 include $p(I) = \alpha$(constant), $p(I) = \alpha I$, polynomial functions of positive coefficients like $p(I) = \alpha I^2$, and exponential functions like $p(I) = e^{\gamma I}$. $p(I)$=constant was used for modeling density-independent treatment, which gives clear dynamics. For developed countries, there may not be any limitations on treatment capability. Hence the more cases, the more attention is paid. For this scenario treatment strategy with $p'(I) \geq 0$ and $p''(I) \geq 0$ is applicable.

Complete dynamics analysis could be carried out if the assumptions in Theorem 4.4 are not satisfied. For instance, $p(I) = \frac{B + AI}{C + I}$ was studied in [5]). The scenario of $p(I) < 0$ corresponds to the situation of limited budget or limited resources. Thus as the number of cases increases, the likelihood of an individual to be treated decreases. We shall focus further on the case where $p(I) = \alpha e^{-\gamma I}$ and $p(I) = \alpha_2 + \alpha_1 e^{-\gamma I}$ in the following section.

5. **Exponential decay of density-dependent treatment.** We will first analyze system (1) when $p(I) = \alpha e^{-\gamma I}$, an exponential function. The model becomes

$$\begin{cases} \dfrac{dS}{dt} = \Lambda - \beta S\dfrac{I}{N} - \mu S + \alpha e^{-\gamma I} I, \\ \dfrac{dI}{dt} = \beta S\dfrac{I}{N} - (\mu + d)I - \alpha e^{-\gamma I} I, \\ N = S + I. \end{cases} \tag{10}$$

5.1. **Global stability of endemic equilibria.** Since $p(I) = \alpha e^{-\gamma I}$ is an exponential function, one can not get an analytic expression for endemic equilibria for system (10). But through analysis, we can show the existence and stability of endemic equilibria.

At the nonzero equilibrium $E^*(S^*, I^*)$ of (10), S^* and I^* are governed by

$$\begin{cases} \alpha e^{-\gamma I^*} - \beta\dfrac{\mu\Lambda}{d}\dfrac{1}{dI^* - \Lambda} - \dfrac{(\mu + d)(\beta - d)}{d} = 0, \\ S^* = \dfrac{\Lambda - (\mu + d)I^*}{\mu}. \end{cases}$$

For convenience, we assume $d \le \mu$, so $I < \frac{\Lambda}{\mu} \le \frac{\Lambda}{d}$. This assumption is usually reasonable for SIS models. For the cases adapted to the SIS model such as gonorrhea, influenza, etc, the disease-related death rate is always very small.

Theorem 5.1. *When $\mathcal{R}_0 > 1$, there exists a unique endemic equilibrium $E^*(S^*, I^*)$ for system (10).*

Proof. Define

$$f(I) = \alpha e^{-\gamma I} - A\frac{1}{dI - \Lambda} - B \quad \text{for } 0 \le I < \frac{\Lambda}{d} \tag{11}$$

where $A = \beta\frac{\mu\Lambda}{d}$ and $B = \frac{(\mu+d)(\beta-d)}{d}$. It suffices to show that $f(I) = 0$ has a unique solution when $\mathcal{R}_0 > 1$.

If $\mathcal{R}_0 > 1$, then $f(0) = -\beta + \mu + d + \alpha < 0$ and $\lim\limits_{I \to \frac{\Lambda}{d}^-} f(I) = +\infty$. So when $R_0 > 1$, there is at least one I^* such that $f(I^*) = 0$. For the uniqueness of I^*, we let $x = -(dI - \Lambda)$ and change function $f(I)$ into

$$g(x) = Ce^{Dx} + \frac{A}{x} - B \quad \text{for } 0 < x \le \Lambda, \tag{12}$$

where $C = \alpha e^{-\frac{\gamma\Lambda}{d}}$ and $D = \frac{\gamma}{d}$. Equivalently, we show that $g(x) = 0$ has only one solution on $(0, \Lambda]$. $g'(x) = CDe^{Dx} - \dfrac{A}{x^2}$ gives

$$\lim_{x \to 0^+} g'(x) = -\infty \quad \text{and} \quad g'(\Lambda) = \frac{\alpha\gamma\Lambda - \beta\mu}{d\Lambda},$$

which is followed by $g''(x) = CD^2e^{Dx} + \frac{2A}{x^3} > 0$, for all x on $(0, \Lambda]$. This implies that $g'(x)$ is a monotonic increasing function over the interval. We finish our proof by considering the different cases resulting from the sign of $g'(\Lambda)$.

$g'(\Lambda) < 0$**:** In this case, $g'(x)$ is monotonic increasing, then for all $x \in (0, \Lambda]$, $g'(x) < 0$. So $g(x)$ is a monotonic decreasing function. Also, we can calculate

$$\lim_{x \to 0^+} g(x) = +\infty \quad \text{and} \quad g(\Lambda) = -\beta + \mu + d + \alpha < 0.$$

By the Intermediate Value Theorem and monotonicity, there exists unique x^* ($0 < x^* \leq \Lambda$) such that $g(x^*) = 0$. The uniqueness is guaranteed by the monotonicity of $g(x)$.

$g'(\Lambda) \geq 0$**:** By the Intermediate Value Theorem and monotonicity, there exists a unique $x_1 \in (0, \Lambda]$ such that $g'(x_1) = 0$. When $x \in (x_1, \Lambda]$, because $g'(x)$ is monotonic increasing, $g(x) < g(\Lambda) < 0$. So $g(x) = 0$ has no solution on $(x_1, \Lambda]$. On $(0, x_1]$, we encounter the same situation as $g'(\Lambda) < 0$. For both cases, we have shown that if $\mathcal{R}_0 > 1$, the endemic equilibrium is unique.

□

The local stability of the endemic equilibrium when $\mathcal{R}_0 > 1$ is guaranteed by Theorem 4.3 because $p''(I) = \gamma^2 \alpha e^{-\gamma I} > 0$.

Theorem 5.2. *If $\mathcal{R}_0 > 1$, the unique endemic equilibrium is locally asymptotically stable for system (10).*

Finally, we show that the endemic equilibrium is globally asymptotically stable.

Theorem 5.3. *Assume $e\mu > \alpha$, the endemic equilibrium $E^*(S^*, I^*)$ is globally asymptotically stable if $\mathcal{R}_0 > 1$ for system (10).*

Proof. Let $F = \Lambda - \beta S \dfrac{I}{S+I} - \mu S + \alpha e^{-\gamma I} I$ and $G = \beta S \dfrac{I}{S+I} - (\mu + d) I - \alpha e^{-\gamma I} I$ be the vector field of system (10). We take a Dulac function $D = \dfrac{1}{SI}$.

$$\begin{aligned}
\frac{\partial (DF)}{\partial S} + \frac{\partial (DG)}{\partial I} &= \frac{-\alpha I e^{-\gamma I}}{IS^2} + \frac{\alpha \gamma I e^{-\gamma I} S - \Lambda}{IS^2} \\
&\leq \frac{-\alpha I e^{-\gamma I}}{IS^2} + \frac{\alpha \gamma I e^{-\gamma I} \dfrac{\Lambda}{\mu} - \Lambda}{IS^2} \\
&= \frac{-\alpha I e^{-\gamma I}}{IS^2} + \frac{\Lambda}{IS^2} \left(\frac{\alpha \gamma I e^{-\gamma I}}{\mu} - 1 \right).
\end{aligned}$$

Noticing that $I e^{-\gamma I}$ has the absolute maximum $\dfrac{1}{\gamma e}$. Then it follows from $e\mu > \alpha$ that

$$\begin{aligned}
\frac{\partial (DF)}{\partial S} + \frac{\partial (DG)}{\partial I} &\leq \frac{-\alpha I e^{-\gamma I}}{IS^2} + \frac{\Lambda}{IS^2} \left(\frac{\alpha}{e\mu} - 1 \right) \\
&< \frac{-\alpha I e^{-\gamma I}}{IS^2} < 0;
\end{aligned}$$

and the Dulac's criterion rejects the appearance of a limit cycle for planar system (10). Therefore, we conclude that if $\mathcal{R}_0 > 1$, the endemic equilibrium (S^*, I^*) is globally asymptotically stable by virtue of Poincare-Bendixson Theorem. □

5.2. **Type-I backward bifurcation.** In this and the next subsection, we investigate the bifurcation of the proposed models at $\mathcal{R}_0 = 1$. The following Theorem from [3] will be used to classify the type of the bifurcation at $\mathcal{R}_0 = 1$.

Theorem 5.4. *Consider a system of ordinary differential equations*

$$\frac{dx}{dt} = f(x, \phi), \quad f : \mathbb{R}^n \times \mathbb{R} \to \mathbb{R}^n \text{ and } f \in \mathbb{C}^2(\mathbb{R}^n \times \mathbb{R}), \tag{13}$$

with a parameter ϕ. Assume that:

1. *0 is an equilibrium point of the system, that is, $f(0,\phi)\equiv 0$ for all ϕ; and*
2. *Zero is a simple eigenvalue of $A = D_x f(0,0) = \left(\frac{\partial f_i}{\partial x_j}(0,0)\right)$ and all other eigenvalues of A have negative real parts*

Let $\mathbf{W} = [w_1, w_2, \cdots, w_n]^T$ and $\mathbf{V} = [v_1, v_2, \cdots, v_n]$ be a right and a left eigenvector matrix A, respectively, associated to eigenvalue zero and $f_k(x,\phi)$ be the kth component of $f(x,\phi)$. Then the local dynamics of system (13) around the equilibrium point 0 is totally determined by the signs of a and b below:

$$a = \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0), \tag{14}$$

$$b = \sum_{k,i=1}^{n} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \phi}(0,0). \tag{15}$$

Particularly, if $a > 0$ and $b > 0$, then a backward bifurcation occurs at $\phi = 0$ for system (13).

We use β as the bifurcation parameter and apply Theorem 5.4 to model (10) to determine the bifurcation at $\mathcal{R}_0 = 1$. When $\mathcal{R}_0 = 1$, which is equivalent to $\beta = \mu + d + \alpha$, the Jacobian matrix (2) has a right eigenvector $\mathbf{W} = [1, \frac{\mu}{\alpha-\beta}]^T$ and a left eigenvector $\mathbf{V} = [0, 1]$ associated with the zero eigenvalue. Direct computation from (14) and (15) leads to $b = \frac{\mu}{\mu+d} > 0$ and $a = 2(\frac{\mu}{\mu+d})^2(\alpha\gamma - \frac{\mu\beta}{\Lambda})$. Then, $a > 0$ is equivalent to $R_1 < 1$, where

$$R_1 = \frac{\beta}{\frac{\Lambda}{\mu}\alpha\gamma} < 1. \tag{16}$$

Therefore, we have established the following theorem.

Theorem 5.5. *Consider the system (10). If $R_1 = \frac{\beta}{\frac{\Lambda}{\mu}\alpha\gamma} < 1$, the bifurcation at $\mathcal{R}_0 = 1$ is backward, while if $R_1 > 1$, the bifurcation at $\mathcal{R}_0 = 1$ is forward.*

R_1 is an indicator to the occurrence of a backward bifurcation. This is driven by the density-dependent treatment because $\gamma = 0$ cannot make $R_1 = \frac{\beta}{\frac{\Lambda}{\mu}\alpha\gamma} < 1$. Notice that if $\gamma = 0$, the typical SIS model is characterized by a forward (most of the time, it is globally) bifurcation. That is, regular linear treatment (density-independent) rate αI can not result in a backward bifurcation.

When I is very small, the behaviors of αI and $\alpha e^{-\gamma I} I$ are the same. Hence, around the disease-free equilibrium, there is no difference in using αI or $\alpha e^{-\gamma I} I$ as the treatment rate. The behaviors of αI and $\alpha e^{-\gamma I} I$ differ drastically when I is large. αI tends to treat more infections, shutting down the chances for infections to stay in the I-compartment. $\alpha e^{-\gamma I} I$, on the other hand, tends to treat fewer infections, so the chance of infections staying in the I-compartment increases. The use of $\alpha e^{-\gamma I} I$ creates a locally favorable environment for infections to stay infectious and favor the appearance of a local endemic equilibrium.

The population size $\frac{\Lambda}{\mu}$ usually is a huge number, which appears in the denominator of R_1. Observing the components of R_1, one can find that it is very easy to satisfy $R_1 < 1$ when $\mathcal{R}_0 = 1$. So, one would pretty much ensure the appearance of bi-stability when $\mathcal{R}_0 < 1$, meaning the disease may persist even when $\mathcal{R}_0 < 1$.

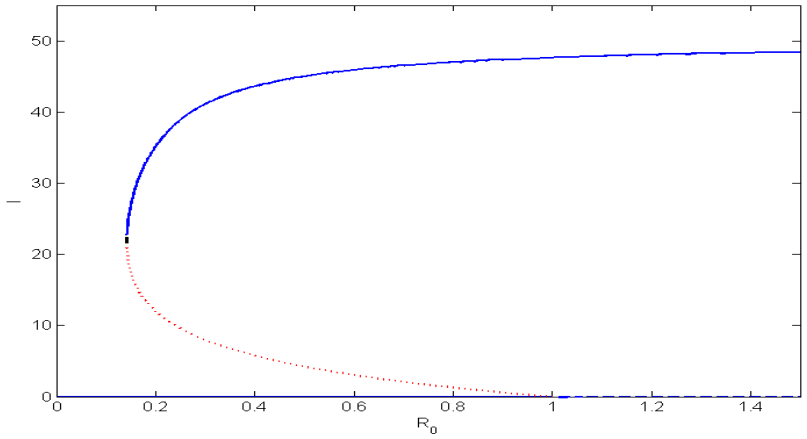

FIGURE 1. Type-I backward bifurcation of model (10). The disease-free equilibrium coexists with an endemic equilibrium. Parameters $\Lambda = 1$, $\mu = 0.01$, $d = 0.01$, $\alpha = 0.2$, $\gamma = 0.2$ and $0.03124 \leq \beta \leq 0.22$ are used in this figure.

Figure 1 shows the existence of backward bifurcation for system (10) and a corresponding phase portrait is illustrated in Figure 2. These figures suggest that, as has been pointed out in virtually all references of backward bifurcation, the classical requirement for the basic reproduction number $\mathcal{R}_0$ to be below unity though necessary, is not sufficient for disease control. The basic reproduction number, $\mathcal{R}_0$, alone cannot determine the dynamics of the disease. We have seen that a secondary measure is required to further advance the study of epidemic models. We hope R_1 will shed some lights in this regard.

We want to emphasize that Theorem 5.4 is about a *local* bifurcation. When there is a backward bifurcation, it can only guarantee there exists an unstable positive equilibria close to the disease-free equilibrium. It cannot determine the stability of the other positive equilibrium, if any. If the other positive equilibrium is stable when the backward bifurcation happens, it is said to be type-I. That is, when there is a type-I backward bifurcation, the disease-free equilibrium coexists with an endemic equilibrium. It has become common to admit that there exists only type-I backward bifurcation. However, this article has identified other types of backward bifurcation.

5.3. **Type-II backward bifurcation.** A disadvantage of $p(I) = \alpha_1 e^{-\gamma I}$ is $\lim_{I\to\infty} p(I)I = 0$. To overcome this, we could consider to use $p(I) = \alpha_2 + \alpha_1 e^{-\gamma I}$. Accordingly, model (1) becomes

$$\begin{cases} \dfrac{dS}{dt} = \Lambda - \beta S\dfrac{I}{N} - \mu S + (\alpha_2 + \alpha_1 e^{-\gamma I})I, \\ \dfrac{dI}{dt} = \beta S\dfrac{I}{N} - (\mu + d)I - (\alpha_2 + \alpha_1 e^{-\gamma I})I, \\ N = S + I. \end{cases} \tag{17}$$

Applying Theorem 5.4 again to model (17), we obtain the same criterion for the occurrence of backward bifurcation as the one for model (10). Specifically, for model

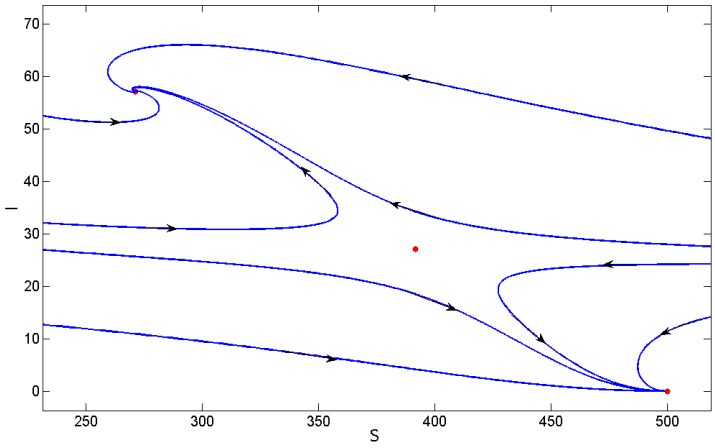

FIGURE 2. A phase portrait of system (10). The disease-free equilibrium coexists with an endemic equilibrium. The saddle separatrixes separate the domain of attraction of each stable equilibrium. Parameter values are $\Lambda = 50, \mu = 0.1, d = 0.3, \beta = 0.5, \alpha = 0.3, \gamma = 0.055$.

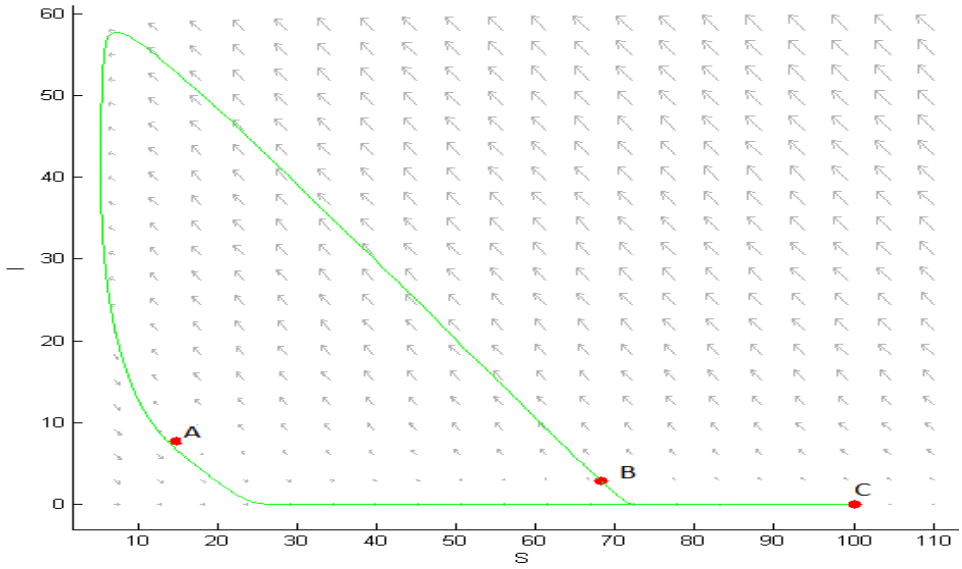

FIGURE 3. A phase-portrait of system (17) corresponding to type-II backward bifurcation. A heteroclinic cycle connects the saddle B and the disease-free equilibrium C. The disease-free equilibrium is globally stable. Parameter values are $\beta = 4.5$, $\Lambda = 1$, $\mu = 0.01$, $d = 0.1$, $\alpha_1 = 5$, $\alpha_2 = 0.3539$, and $\gamma = 0.09$.

(17), if $R_1 = \frac{\beta}{\frac{\Lambda}{\mu}(\alpha\gamma)} < 1$, a backward bifurcation happens at $\mathcal{R}_0 = \frac{\beta}{\mu+d+\alpha_1+\alpha_2} = 1$;

while $R_1 = \frac{\beta}{\frac{\Lambda}{\mu}(\alpha\gamma)} > 1$, the bifurcation at $\mathcal{R}_0 = 1$ is forward. However, when a backward bifurcation occurs, two new types of dynamics are observed.

The first is when a backward bifurcation occurs, the disease-free equilibrium is globally stable. It is observed that one positive equilibrium is an unstable spiral and the other is a saddle; and there is a heteroclinic cycle orbit that connects the saddle with the disease-free equilibrium.

For example, if we take $\beta = 4.5$, $\Lambda = 1$, $\mu = 0.01$, $d = 0.1$, $\alpha_1 = 5$, $\alpha_2 = 0.3539$, and $\gamma = 0.09$, a backward bifurcation appears. The heteroclinic cycle that connects the saddle and the disease-free equilibrium, and the other equilibrium is an unstable spiral that is located inside of the heteroclinic cycle. A phase portrait for this scenario is shown in Figure 3. This is the case where we observe a backward bifurcation, but bistability does dot appear and the disease-free equilibrium is globally stable. We name this as type-II backward bifurcation. Figure 4 is a bifurcation diagram for type-II backward bifurcation, which shows that neither positive equilibrium is stable. Type-II backward bifurcation shows that backward bifurcations cannot always generate bi-stability.

5.4. **Type-III backward bifurcation.** The second new dynamics from model (17) is that when a backward bifurcation occurs, the disease may persist in a periodic fashion. It is observed that neither positive equilibrium is stable and there is a stable limit cycle, as shown in Figure 5; and a corresponding phase portrait can be seen in Figure 6.

The appearance of the stable limit cycle is driven by the Hopf mechanics. We will perform a full analysis of Hopf bifurcation analysis in a separated paper later. In this paper we only present the result and numerical simulation, mainly to address epidemiological implications of those new observations. For instance, we fix parameters $\beta = 4.5$,$\Lambda = 1$, $\mu = 0.01$, $d = 0.1$, $\alpha_1 = 4.8113$, $\alpha_2 = 0.3539$, $\gamma = 0.09$,

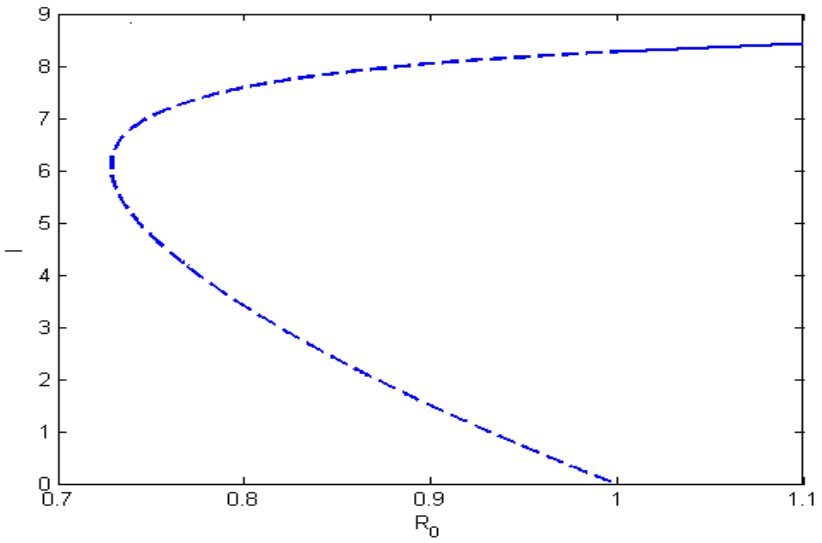

FIGURE 4. Diagram of type-II backward bifurcation. Neither positive equilibrium is stable.

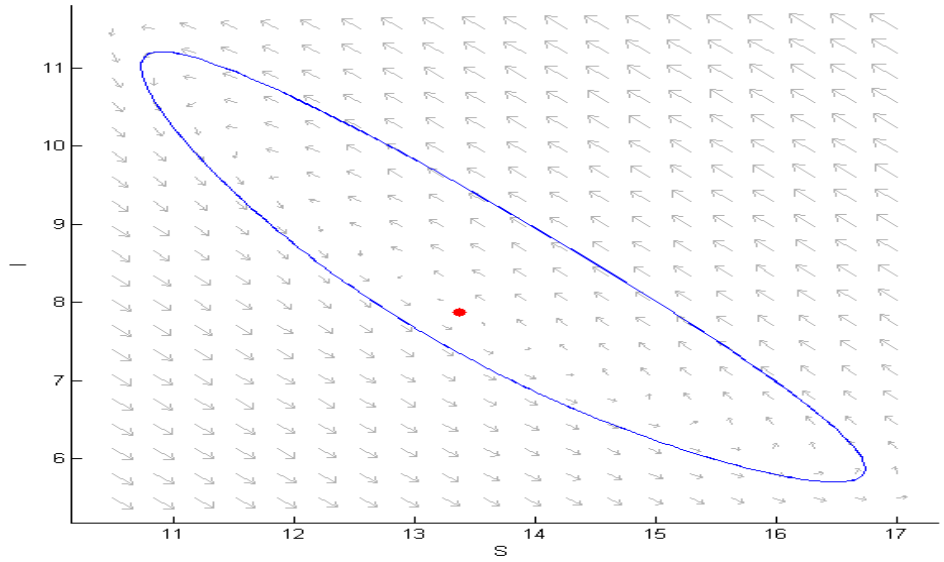

FIGURE 5. A stable limit cycle of system (17) when parameter values are $\beta = 4.5$, $\Lambda = 1$, $\mu = 0.01$, $d = 0.1$, $\alpha_1 = 0.8113$, $\alpha_2 = 0.3539$, and $\gamma = 0.09$.

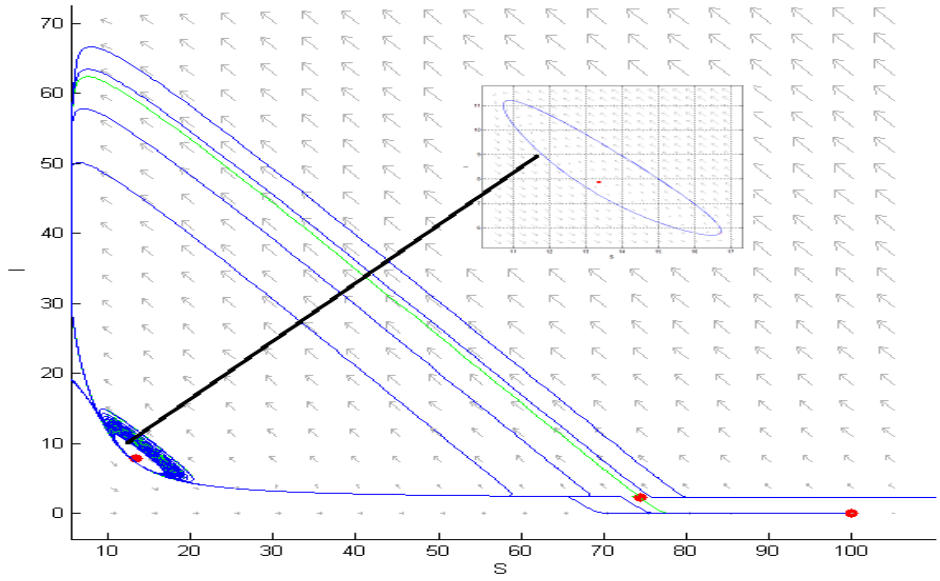

FIGURE 6. A phase-portrait of system (17) corresponding to type-III backward bifurcation. Parameter values are $\beta = 4.5$,$\Lambda = 1$, $\mu = 0.01$, $d = 0.1$, $\alpha_1 = 4.8113$, $\alpha_2 = 0.3539$, and $\gamma = 0.09$. The disease-free equilibrium and a stable limit cycle coexist.

and the let α_2 vary. When $\alpha_1 = 4.8106$, the spiral is stable. but when $\alpha_1 = 4.8113$, the spiral becomes unstable, thus appearing a stable limit cycle.

The backward bifurcation that gives rise to a coexistence of the disease-free equilibrium and a stable limit cycle is named as type-III backward bifurcation. A bifurcation diagram of type-III backward bifurcation is illustrated in Figure 7; and Figure 6 is a snap shot of phase portrait corresponding to type-III backward bifurcation. Type-III backward bifurcation shows that the disease can sustainably oscillate when $\mathcal{R}_0 < 1$.

6. **Application to the transmission of gonorrhea in China.** Gonorrhea is a very old and common infectious sexually transmitted disease (STD) -caused by the gonococcus bacterium, Neisseria gonorrheal. It can grow easily in the warm, moist areas of the reproductive tract, including the cervix, uterus, and fallopian tubes in women and in the urethra in women and men. The bacterium can also grow in the mouth, throat, eyes, and anus. People get gonorrhea by having sex with someone who has the disease. Gonorrhea can also be spread from an untreated mother to her baby during childbirth. Untreated gonorrhea can also increase a person's risk of acquiring or transmitting HIV [13].

Before 1949, the incidence rate of gonorrhea in some urban areas was about 20% in China. After implementation of the national gonorrhea control program, gonorrhea has largely disappeared. But as the new strain of Penicillinase-Producing Neisseria Gonorrhoea (PPNG) came out in 1976 in West Africa and East Asia, gonorrhea cases in China have increased substantially. In recent years, the gonorrhea ranked number one of all sexually transmitted diseases (STD) in China. Especially in Shanghai, it accounts for about 90% of all STD cases [4].

Gonorrhea is treatable. Infected individuals can recover within two weeks after receiving treatment. However, people who have had gonorrhea and have been

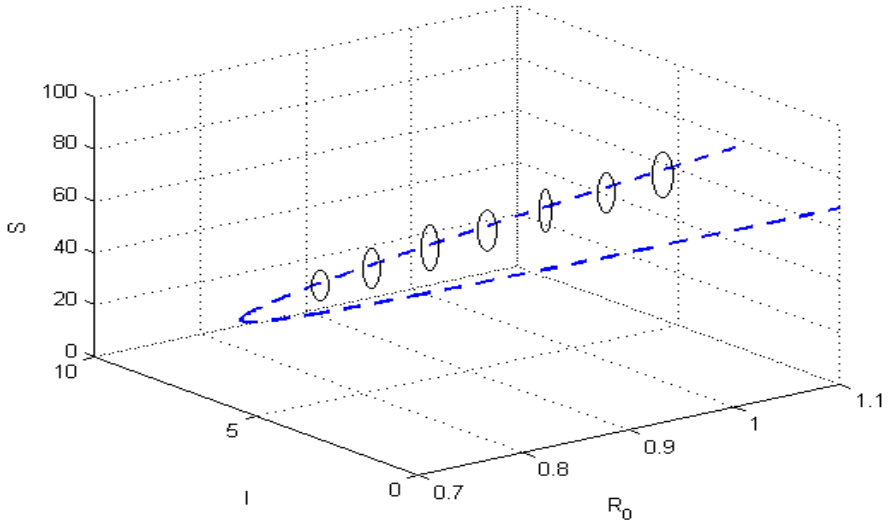

FIGURE 7. Bifurcation diagram of type-III backward bifurcation.

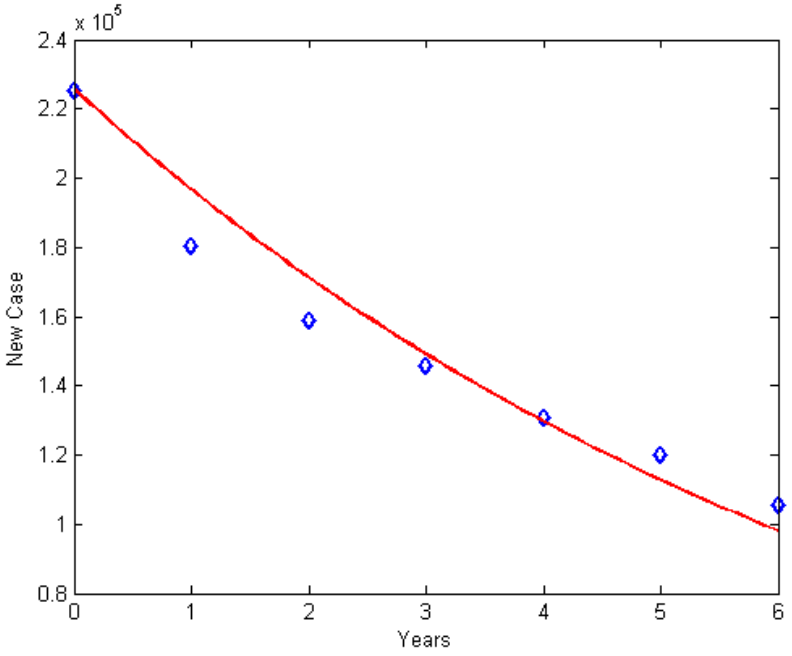

FIGURE 8. New cases of gonorrhea in China from 2004 to 2010 (in diamonds) and model solution.

treated may get reinfected if they have sexual contact with another person infected with gonorrhea [13]. Hence, using SIS models is appropriate for gonorrhea. In this section, we apply models (10) and (17) to the transmission of gonorrhea in China.

The adjusted natural death rate can be computed by $\frac{1}{65-18} \approx 0.02128$ since we consider the population aging from 18 to 65 [14]. With the available data for the new cases of gonorrhea from 2004 to 2010 in China [15], we use Markov chain Monte Carlo (MCMC) methods to estimate the other parameters, which are tabulated in Table 1. Figure 8 shows that the model solution fits the data.

TABLE 1. Estimation of parameters

Para	definition	Estimation
Λ	annual recruitment of population	6.5048×10^7
μ	aging out and natural death rate	0.02128
d	disease-related death rate	1.951×10^{-5}
β	transmission rate	0.79395
α	cure rate	0.91422
γ	density-dependent factor of the treatment	1.605×10^{-8}

Using the estimated parameter values in Table 1 and formula (8) derived in Section 3, we are able to estimate the average infection period of gonorrhea in China. The estimated value is .65 years; that's more than 200 days. The symptoms of gonorrhea emerge very quickly. For instance, infected men get painful or swollen

testicles a few (usually 1 to 14) days after contracting gonorrhea. For that reason, we speculate that these infected individuals did not seek medical attention in a timely manner.

7. **Conclusions and discussions.** We are concerned with the persistence of curable transmission diseases, such as gonorrhea, in this article. This persistence is an effect of a combination of numerous reasons, where a lack of proper treatment strategy at the population level might have played a role. Density dependent and independent treatment regimens draw different pictures of the dynamics of the disease.

Comparing treatment rates $\alpha e^{-\gamma I} I$ with αI, we can see that the significant change is the appearance of bi-stability when $\mathcal{R}_0 < 1$, where a stable equilibrium co-exists with the disease-free equilibrium (type-I backward bifurcation). Density-dependent treatment tends to treat fewer patients than density-independent ones. This reduction in treatment effort leads to complex dynamics, typically with the appearance of backward bifurcation which helps to establish the disease by generating an endemic when $\mathcal{R}_0 < 1$. The nonlinear treatment form of $(\alpha_2 + \alpha_1 e^{-\gamma I})I$ does not reduce treatment efforts as compared to the linear form αI. The dynamical outcomes become more complicated as type-II and type-III backward bifurcations emerge.

In addition to the appearance of type-II and type-III backward bifurcations due to the density-dependent treatments, a forward-backward bifurcation has been found. For instance, [2,11] studied this using continuous-time and discrete-time dynamical models, respectively. It seems to be an endless research to classify the bifurcations at $\mathcal{R}_0 = 1$. Further work is expected to find the criteria upon which distinguish the types of backward bifurcation and the mechanics behind them. For higher dimensional epidemic models, we expect the emergence of even more types of dynamics.

Acknowledgments. Part of the research in this paper was conducted in MTBI (Mathematical and Theoretical Biological Institute) where Wen was a visiting graduate student. We would like to give special thanks to this wonderful institute for offering the opportunity in research. JL's work was supported by the Natural Science item of China under grant No. 11271246 and the International Development Research Center of Canada (Number 104519-010).

REFERENCES

[1] F. Brauer and C. Castillo-Chavez, "Mathematical Models in Population Biology and Epidemiology," Second edition, Texts in Applied Mathematics, **40**, Springer-Verlag, New York, 2012.

[2] H. Cao, Y. Zhou and B. Song, *Complex dynamics of discrete SEIS models with simple demography*, Discrete Dynamics in Nature and Society, **2011**, Art. ID 653937, 21 pp.

[3] C. Castillo-Chavez and B. Song, *Dynamical models of tuberculosis and their applications*, Math. Biosc. Eng., **1** (2004), 361–404.

[4] X. S. Chen, X. D. Gong, G. J. Liang and G. C. Zhang, *Epidemiologic trends of sexually transmitted diseases in China,* Sex Transm. Dis., **27** (2000), 138–142.

[5] J. Cui, X. Mu and H. Wan, *Saturation recovery leads to multiple endemic equilibria and backward bifurcation*, J. Theor. Biol., **254** (2008), 275–283.

[6] H. W. Hethcote and J. A. Yorke, "Gonorrhea Transmission Dynamics and Control," Lecture Notes in Biomathematics, Vol. 56, Springer-Verlag, New York, 1984.

[7] Z. Hu, S. Liu and H. Wang, *Backward bifurcation of an epidemic model with standard incidence rate and treatment rate,* Nonlinear Analysis, **9** (2008), 2302–2312.

[8] X. Li, W. Li and Mini Ghosh, *Stability and bifurcation of an epidemic model with nonlinear incidence and treatment,* Applied Mathematics and Computation, **210** (2009), 141–150.
[9] B. R. Morin, L. Medina-Rios, E. T. Camacho and C. Castillo-Chavez, *Static behavioral effects on gonorrhea transmission dynamics in a MSM population*, J. Theor. Biol., **267** (2012), 35–40.
[10] P. van den Driessche and J. Watmough, *Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission*, Math. Biosci., **180** (2002), 29–48.
[11] W. Wang, *Backward bifurcation of an epidemic model with treatment,* Math. Biosci., **201** (2006), 58–71.
[12] X. Zhang and X. Liu, *Bifurcation of an epidemic model with saturated treatment function*, J. Math. Anal. Appl., **348** (2008), 433–443.
[13] Centers for Disease Control and Prevention, *Gonorrhea-CDC fact sheet*, June 2012. Available from: http://www.cdc.gov/std/gonorrhea/STDFact-gonorrhea-detailed.htm.
[14] China Yearbook. Available from: http://www.yearbook.cn/.
[15] Ministry of Health of the People's Republic of China. Available from: http://www.moh.gov.cn/publicfiles/business/htmlfiles/mohjbyfkzj/s2907/index.htm.

Received October 17, 2012; Accepted May 18, 2013.

E-mail address: songb@mail.montclair.edu
E-mail address: duwen@shu.edu.cn
E-mail address: jie.lou@staff.shu.edu.cn