MODELING THE EFFECTS OF CARRIERS ON TRANSMISSION DYNAMICS OF INFECTIOUS DISEASES

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ABSTRACT. An $S-I_c-I-R$ epidemic model is investigated for infectious diseases
that can be transmitted through carriers, infected individuals who are conta-
gious but do not show any disease symptoms. Mathematical analysis is carried
out that completely determines the global dynamics of the model. The im-
pacts of disease carriers on the transmission dynamics are discussed through
the basic reproduction number and through numerical simulations.

1. Introduction. For certain infectious diseases, there are individuals who are able
to transmit their illness but do not exhibit any symptoms. These individuals are
called “carriers” and they play an important role in the transmission of the disease.
There are two types of carriers. Genetic carriers carry the illness on their recessive
genes. They can only pass on their disease to their children and are not contagious.
The focus of our study is on infectious disease carriers. These individuals are
asymptomatic and are likely unaware of their conditions, and therefore are more
likely to infect others. An infectious disease that produces long-term asymptotic
carriers is the Typhoid fever caused by the bacteria Salmonella Typhi. Typhoid fever
reached public notoriety at the beginning of the 20th century with the cases of “Mr.
N the milker” in England and Typhoid Mary in the US. These individuals infected
hundreds of people over the decades while they worked in the food production
industry and private homes. Even today, Typhoid fever infects 21 million people and
kills 200,000 worldwide every year. Asymptomatic carriers are believed to play an
essential role in the evolution and global transmission of Typhi, and their presence
greatly hinders the eradication of Typhoid fever using treatment and vaccination
[13].

Another major infectious disease that causes long-term asymptomatic carriage
is hepatitis B, a liver disease caused by the HBV virus of the Hepadnavirus family.
Most people infected with HBV recover completely and develop a lifelong immunity
to the virus. However, about 5-10% of adults will develop chronic HBV infection,
and 15-25% of these will develop liver disease. Hepatitis B’s symptoms include jaundice, abdominal pain, nausea, fatigue and joint pain. About 30% of people with the disease do not show any of these symptoms. A major public-health challenge in the control of hepatitis B infection in many countries is the existence of a large pool of chronic carriers who are responsible for transmitting most of the new infections. Infections of other pathogens are also known to produce asymptomatic carriers. The Epstein-Barr Virus (EBV) of the herpes family is one of the most common viruses in humans. EBV infection commonly causes infectious mononucleosis, also known as glandular fever. Most people infected with EBV are asymptomatic, as it remains dormant in those who have had it for the rest of their lives in the cells of the throat and the immune system. Clostridium difficile is a bacterium that causes Clostridium difficile-associated diseases (CDAD). CDAD remains the most common cause of acute hospital-acquired diarrhea, responsible for more than 300,000 cases of diarrhea annually in acute-care facilities in the United States. Asymptomatic carriage rates of up to 30% have been reported in long-term care facilities. It is believed that carriers are responsible for transmission and large outbreaks of CDAD in Europe and North America [12].

Despite their public health significance, the effects of carriers on the transmission dynamics of the disease have not received adequate research attention in the mathematical modeling literature. One of the earlier attempts was Kemper [7], in which a general mathematical model that incorporates disease carriers was developed and analyzed. Medley et al. [10] used a mathematical model for hepatitis B with carriers to discuss the effects of HBV vaccination. Several other studies using large-scale computational models with carriers are specifically aimed at hepatitis B and other diseases [15, 1, 2, 14, 11]. In the present paper, we propose a general mathematical model for infectious diseases with asymptomatic carriers to investigate the effects of carriers on the transmission dynamics. We have derived the basic reproduction number \( R_0 \) and show that the global dynamics of the model are completely determined by the values of \( R_0 \). Since \( R_0 \) explicitly involves parameters related to disease carriage, we are able to discuss the impact of disease carriage on \( R_0 \). We have also carried out numerical simulations of the model using parameter values that are pertinent to hepatitis B infection, and investigated the effects of carriers on the HBV transmission dynamics. Mathematically, our proof of the global stability of the unique endemic equilibrium when \( R_0 > 1 \) nontrivially utilizes the method of global Lyapunov functions.

The model derivation is given in the next section. The basic reproduction number is derived and discussed in Section 3. Global stability of the disease-free and endemic equilibrium is proved in Section 4 and 5, respectively. In Section 6, effects of carriers on the transmission of chronic hepatitis B infection are discussed.

2. A general epidemic model with asymptomatic carriers.

2.1. Model formulation. We formulate an \( S-I_c-I-I-R \) compartmental model where \( S, I_c, I, \) and \( R \) represent the susceptible, carrier, symptomatically infectious or infectious for short, and removed classes, respectively. A susceptible individual can be infected through direct contact with an infectious individual or a carrier. A newly infected individual can become a carrier with probability \( p \), or shows disease symptoms with probability \( 1 - p \). We assume that the rate of transmission \( \beta \) for carriers is higher than the rate \( \gamma \) of symptomatically infected individuals due to the fact that they are more likely to be unaware of their condition, and therefore continue
CARRIERS’ EFFECTS ON INFECTIOUS DISEASES

with their regular behaviours. Carriers may become symptomatic at a rate \( \alpha \). For infections such as HBV for which carriage can remain life-long, \( \alpha \) can be regarded as rate of diagnosis. We assume a constant influx \( b \) of susceptibles, and let \( d_1, d_2, d_3, d_4 \) denote the death rates of those in the susceptible, carrier, infectious, and removed classes, respectively. Here \( d_1, d_4 \) can be considered as natural death rates, while \( d_2 \) and \( d_3 \) may include both natural and disease-related death. We incorporate a simple vaccination strategy in which a fraction \( \theta \) of the susceptible population is vaccinated and is fully protected by the vaccine. Symptomatically infected individual recover with rate \( \pi \), and we assume that recovered individuals are permanently immune.

Parameters in the model are summarized and explained in Table 1, and the model is depicted in the transfer diagram in Figure 1. We assume that all parameters in the model are nonnegative and that \( b > 0, d_i > 0, i = 1, 2, 3, 4 \).

### Table 1. Parameters in the Model

- **\( b \)**: Rate of influx of susceptibles
- **\( d_1, d_4 \)**: Natural death rates
- **\( d_2, d_3 \)**: Death rates for \( I_c \) and \( I \) compartments, respectively, including both natural and disease-caused death
- **\( \beta \)**: Transmission coefficient for the carrier compartment \( I_c \)
- **\( \gamma \)**: Transmission coefficient for the symptomatically infected compartment \( I \)
- **\( \alpha \)**: Rate at which carriers develop symptoms
- **\( \pi \)**: Rate of recovery
- **\( p \)**: Probability of a newly infected individual is asymptomatic
- **\( \theta \)**: Vaccination rate

### Figure 1. Transfer diagram of model (1).
Based on our assumptions and the transfer diagram, we can derive the following system of differential equations that govern our model.

\[
\begin{align*}
S' &= b - d_1S - S(\beta I_c + \gamma I) - \theta S \\
I'_c &= pS(\beta I_c + \gamma I) - (d_2 + \alpha)I_c \\
I' &= (1 - p)S(\beta I_c + \gamma I) - (d_3 + \pi)I + \alpha I_c \\
R' &= \pi I + \theta S - d_4R.
\end{align*}
\]  

(1)

We note that disease carriage is different from disease latency in that individuals in the carrier state are infectious while those in the latent period are not. Our model (1) is thus different from the traditional SEIR models that incorporate disease latency. In the special case when $\beta = 0$, the $I_c$ class is not infectious and can be considered as latent, and our model becomes a modified SEIR model in which new infections can be either latent or infectious. While both $I_c$ and $I$ are infectious, model (1) is different from the differential infectivity models considered in [5], since new infections from $I_c$ or $I$ may enter either compartment with certain probability. Our model is more general than the carrier model in [7] in that we incorporate demography and disease-caused death. We also allow carriers to become symptomatic over their lifetime. Our model is different from the carrier model in [10] in that we allow new infections to be either symptomatic or asymptomatic with certain probabilities.

2.2. Feasible region and equilibria. From (1) we have that $S' \leq b - (d_1 + \theta)S$, and thus $\limsup_{t \to \infty} S(t) \leq \frac{b}{d_1 + \theta}$ along each solution. Also from (1) we see that

\[
N' = b - d_1S - d_2I_c - d_3I - d_4R = b - \bar{d}N,
\]

where $\bar{d} = \min\{d_1, d_2, d_3, d_4\}$. Therefore $\limsup_{t \to \infty} N(t) \leq b/\bar{d}$. The equation for $R$ can be omitted in our analysis as $R$ does not appear in the other equations. This shows that the model can be studied in the feasible region

\[
\Gamma = \{ (S, I_c, I) \in \mathbb{R}_+^3 : S \leq \frac{b}{d_1 + \theta}, S + I_c + I \leq \frac{b}{\bar{d}} \}.
\]

It can be verified that $\Gamma$ is positively invariant with respect to (1). Once the dynamics of $(S, I_c, I)$ are understood, those of $R$ can then be determined from the equation $R' = \pi I + \theta S - d_4R$.

The first step in our analysis is to find equilibria $(S^*, I^*_c, I^*)$ from equations

\[
\begin{align*}
0 &= b - d_1S^* - S^*(\beta I^*_c + \gamma I^*) - \theta S^*, \\
0 &= pS^*(\beta I^*_c + \gamma I^*) - (d_2 + \alpha)I^*_c, \\
0 &= (1 - p)S^*(\beta I^*_c + \gamma I^*) - (d_3 + \pi)I^* + \alpha I^*_c.
\end{align*}
\]

(2)

Model (1) always has a disease-free equilibrium $R_0 = \left(\frac{b}{d_1 + \theta}, 0, 0\right)$. An endemic equilibrium $P^* = (S^*, I^*_c, I^*)$ satisfies $S^*, I^*_c, I^* > 0$. From the equilibrium equations we can show that a unique $P^*$ exists with

\[
S^* = \frac{(d_3 + \pi)(d_2 + \alpha)}{pd_3\beta + (d_2 + \alpha)\gamma + p(\pi\beta - d_2\gamma)}.
\]

For $P^*$ to exist in the feasible region $\Gamma$, it is necessary and sufficient that $0 < S^* \leq \frac{b}{d_1 + \theta}$, or equivalently, $\frac{b}{(d_1 + \theta)S^*} \geq 1$. Define

\[
R_0 = \frac{1}{S^*} \frac{b}{d_1 + \theta} = \frac{b}{d_1 + \theta} \frac{pd_3\beta + (d_2 + \alpha)\gamma + p(\pi\beta - d_2\gamma)}{(d_3 + \pi)(d_2 + \alpha)}.
\]

(3)
Then $R_0$ is a threshold parameter that determines the number of equilibria. We will show in Section 3 that $R_0$ is the basic reproduction number.

**Proposition 1.** If $R_0 \leq 1$ then $P_0$ is the only equilibrium in $\Gamma$; if $R_0 > 1$, then there are two equilibria, $P_0$ and a unique endemic equilibrium $P^*$.

### 3. The basic reproduction number

Rewrite $R_0$ in (3) as

$$R_0 = \left[ (1 - p)\gamma \frac{1}{d_3 + \pi} + p \left( \frac{\beta}{d_2 + \alpha} + \frac{\alpha}{d_2 + \alpha} \gamma \frac{1}{d_3 + \pi} \right) \right] \frac{b}{d_1 + \theta}. \quad (4)$$

In the following, we show that $R_0$ is the basic reproduction number, namely, it represents the average number of secondary infections caused by a single infective in an entirely susceptible population during its entire infectious period.

When a single infective is introduced into the population, with probability $1 - p$ it is a non-carrier, hence makes $\gamma$ effective contacts per unit time. This is multiplied by the average infectious period $\frac{1}{d_3} + \frac{\pi}{d_3}$ for non-carriers; with probability $p$ the infective is a carrier, and hence makes $\beta$ effective contacts per unit time during the average period $\frac{1}{d_2}$ it remains a carrier. This number should be augmented by the number of infections $\frac{\gamma}{d_3 + \pi}$ caused by this infective after it becomes a non-carrier, with probability $\frac{\alpha}{d_2 + \alpha}$ to survive the carrier stage. Therefore, the expression in the big square brackets in (4) is the per capita average number of secondary infections. This number multiplied by the number of susceptibles at the disease-free equilibrium, $\frac{b}{d_1 + \theta}$, gives $R_0$.

The carriers in our system can have a great effect on $R_0$. The parameters $\beta$, $\alpha$, and $p$ are all related to the carrier class and all appear in the basic reproductive number. It is straightforward from (3) that $R_0$ increases as $\beta$ increases. This agrees with the intuition that higher transmissibility increases the basic reproduction number.

To see the effect of $p$ on $R_0$ we note

$$\frac{\partial R_0}{\partial p} = \left[ -\frac{\gamma}{d_3 + \pi} + \frac{\beta}{d_2 + \alpha} + \frac{\alpha}{d_2 + \alpha} \frac{\gamma}{d_3 + \pi} \right] \frac{b}{d_1 + \theta} = \frac{b(d_2 + \alpha)}{d_1 + \theta} \left[ \beta - \frac{d_2}{d_2 + \alpha} \right],$$

and thus $\frac{\partial R_0}{\partial p} > 0$ if

$$\beta > \frac{d_2}{d_3 + \pi}. \quad (5)$$

We see that a greater probability to develop carriage will increase the basic reproduction number under the condition (5).

We can also analyze the effect of diagnosis rate $\alpha$ on $R_0$. Straightforward computation gives

$$\frac{\partial R_0}{\partial \alpha} = p \left[ -\frac{\beta}{(d_2 + \alpha)^2} + \frac{\gamma}{d_3 + \pi} \frac{d_2}{(d_2 + \alpha)^2} \right] \frac{b}{d_1 + \theta} = -\frac{bp}{(d_2 + \alpha)^2(d_1 + \theta)} \left[ \beta - \frac{d_2}{d_3 + \pi} \right],$$

and thus $\frac{\partial R_0}{\partial \alpha} > 0$ if the same condition (5) holds.

From these analysis we see that parameter $p$ and $\alpha$ have opposite effects on $R_0$: while a higher probability $p$ of carriage increases $R_0$, a higher diagnosis rate $\alpha$ of
We want to show, when $R_0 > 0$, that the transmissibility $\beta$ of carriers is not too small compared to that of the symptomatically infected. This is likely to hold for many diseases with carriers since carriers can unknowingly infect many people.

4. **Stability of the disease-free equilibrium.** To examine the local stability of the disease-free equilibrium $P_0$ we evaluate the Jacobian matrix at $P_0 = \left( \frac{b}{d_1 + \theta}, 0, 0 \right)$

$$J(P_0) = \begin{bmatrix}
-d_1 - \theta & -\beta \left( \frac{b}{d_1 + \theta} \right) & -\gamma \left( \frac{b}{d_1 + \theta} \right) \\
0 & p\beta \left( \frac{b}{d_1 + \theta} \right) - (d_2 + \alpha) & p\gamma \left( \frac{b}{d_1 + \theta} \right) \\
0 & (1 - p)\beta \left( \frac{b}{d_1 + \theta} \right) + \alpha & (1 - p)\gamma \left( \frac{b}{d_1 + \theta} \right) - (d_3 + \pi)
\end{bmatrix}.$$

We have the following stability result that shows $R_0$ is a sharp threshold.

**Proposition 2.** $P_0$ is locally asymptotically stable if $R_0 < 1$ and is unstable if $R_0 > 1$.

**Proof.** One eigenvalue of $J(P_0)$ is $\lambda_1 = -(d_1 + \theta) < 0$. The other two eigenvalues $\lambda_2, \lambda_3$ are eigenvalues of the $2 \times 2$ matrix

$$A = \begin{bmatrix}
p\beta \left( \frac{b}{d_1 + \theta} \right) - (d_2 + \alpha) & p\gamma \left( \frac{b}{d_1 + \theta} \right) \\
(1 - p)\beta \left( \frac{b}{d_1 + \theta} \right) + \alpha & (1 - p)\gamma \left( \frac{b}{d_1 + \theta} \right) - (d_3 + \pi)
\end{bmatrix}.$$

We want to show, when $R_0 < 1$, that the Routh-Hurwitz conditions hold, namely, $\text{tr}(A) < 0$ and $\text{det}(A) > 0$. Simple calculations show that

$$\text{tr}(A) = (d_2 + \alpha)\left[ p\beta \left( \frac{b}{d_1 + \theta} \right) -(d_2 + \alpha) \right] + (d_3 + \pi)\left[ (1 - p)\gamma \left( \frac{b}{d_1 + \theta} \right) - (d_3 + \pi) \right].$$

Using our assumption that $R_0 = \frac{p\beta \left( \frac{b}{d_1 + \theta} \right) - (d_2 + \alpha)}{d_2 + \alpha} + \frac{p\alpha \gamma \left( \frac{b}{d_1 + \theta} \right)}{(d_2 + \alpha)(d_3 + \pi)} + \frac{(1 - p)\gamma \left( \frac{b}{d_1 + \theta} \right)}{(d_3 + \pi)} < 1$ we have

$$\frac{p\beta \left( \frac{b}{d_1 + \theta} \right)}{d_2 + \alpha} < 1 \quad \text{and} \quad \frac{(1 - p)\gamma \left( \frac{b}{d_1 + \theta} \right)}{d_3 + \pi} < 1.$$

Therefore

$$\frac{p\beta \left( \frac{b}{d_1 + \theta} \right)}{d_2 + \alpha} - 1 < 0 \quad \text{and} \quad \frac{(1 - p)\gamma \left( \frac{b}{d_1 + \theta} \right)}{d_3 + \pi} - 1 < 0.$$

This shows that $\text{tr}(A) < 0$. Now we calculate

$$\text{det}(A) = \left[ p\beta \left( \frac{b}{d_1 + \theta} \right) - (d_2 + \alpha) \right] \left[ (1 - p)\gamma \left( \frac{b}{d_1 + \theta} \right) - (d_3 + \pi) \right]$$

$$- \left[ (1 - p)\beta \left( \frac{b}{d_1 + \theta} \right) + \alpha \right] p\gamma \left( \frac{b}{d_1 + \theta} \right)$$

$$= (d_2 + \alpha)(d_3 + \pi) - (d_3 + \pi)p\beta \frac{b}{d_1 + \theta} - d_2(1 - p)\gamma \frac{b}{d_1 + \theta}$$

$$= (d_2 + \alpha)(d_3 + \pi)(1 - R_0).$$

Therefore, $\text{det}(A) > 0$ if and only if $R_0 < 1$. This proves the proposition. \(\square\)

**Theorem 4.1.** $P_0$ is globally asymptotically stable in the feasible region $\Gamma$ if $R_0 \leq 1$.

**Proof.** To prove the global asymptotic stability of $P_0$ we use the method of Lyapunov functions. Define

$$L = \left[ \frac{\beta}{d_2 + \alpha} + \frac{\gamma \alpha}{(d_3 + \pi)(d_2 + \alpha)} \right] I_c + \frac{\gamma}{d_3 + \pi} I.$$
Therefore the largest invariant set in the closure \( \bar{\Gamma} \) of \( \Gamma \) where

Then

\[
\frac{dL}{dt} = \left[ \frac{\beta}{d_2 + \alpha} + \frac{\gamma \alpha}{(d_3 + \pi)(d_2 + \alpha)} \right] I_c' + \frac{\gamma}{d_3 + \pi} I' \\
= \left[ \frac{p\beta}{d_2 + \alpha} + \frac{p\gamma \alpha}{(d_3 + \pi)(d_2 + \alpha)} + \frac{(1-p)\gamma}{d_3 + \pi} \right] S(\beta I_c + \gamma I) - (\beta I_c + \gamma I) \\
= \left[ \frac{d_1 + \theta}{b} - R_0 S - 1 \right] (\beta I_c + \gamma I).
\]

Using \( S \leq \frac{b}{d_1 + \theta} \) we know

\[
\frac{dL}{dt} \leq (R_0 - 1)(\beta I_c + \gamma I) \leq 0.
\]

So \( \frac{dL}{dt} \leq 0 \) if \( R_0 \leq 1 \). Furthermore, \( \frac{dL}{dt} = 0 \iff I_c = I = 0 \) or \( R_0 = 1 \) and \( S = \frac{b}{d_1 + \theta} \).

Therefore the largest invariant set in the closure \( \bar{\Gamma} \) of \( \Gamma \) where \( \frac{dL}{dt} = 0 \) is the singleton \( \{P_0\} \). By LaSalle’s Invariance Principle [9], \( P_0 \) is globally asymptotically stable in \( \Gamma \), completing the proof.

5. Stability of the endemic equilibrium \( P^* \).

**Theorem 5.1.** If \( R_0 > 1 \), then \( P^* \) is globally asymptotically stable with respect to the interior of \( \Gamma \).

**Proof.** To study the global stability of the endemic equilibrium, we make use of a Lyapunov function \( V \) of form

\[
V(S, I_c, I) = x_1(S - S^* \ln S) + x_2(I_c - I_c^* \ln I_c) + x_3(I - I^* \ln I),
\]

where \( x_1, x_2, x_3 > 0 \) are constants to be specified. Note that \( V \) has a global minimum at \( P^* = (S^*, I_c^*, I^*) \) and \( V(S, I_c, I) - V(P^*) \) is positive definite. We show that suitable constants \( x_1, x_2, x_3 \) can be chosen such that the Lyapunov derivative of \( V \) is negative definite with respect to \( P^* \). Direct calculation and applying the identity \( b = d_1 S^* + \theta S^* + \beta I_c^* S^* + \gamma I^* S^* \) lead to

\[
\frac{dV}{dt} = x_1(S' - S^* \frac{S'}{S}) + x_2(I_c' - I_c^* \frac{I_c'}{I_c}) + x_3(I' - I^* \frac{I'}{I}) \\
= x_1 \left[ b - (d_1 + \theta)S - (\beta I_c + \gamma I)S - b \frac{S^*}{S} + (d_1 + \theta)S^* + (\beta I_c + \gamma I)S^* \right] \\
+ x_2 \left[ (1-p)(\beta I_c + \gamma I)S - (d_2 + \alpha)I_c - (1-p)I_c \frac{\beta I_c S^* I_c}{I_c} - (1-p) \frac{\gamma I S I_c^* I_c}{I_c} \right] \\
+ x_3 \left[ p(\beta I_c + \gamma I)S - \alpha I_c - (d_3 + \pi)I - p \frac{\beta I_c S^* I_c}{I} \right] \\
- p^2 \frac{\gamma I S I_c^*}{I} + \frac{\alpha I_c I^*}{I} + (d_3 + \pi)I^* \\
= \left[ x_1 (d_1 + \theta)S^* (2 - \frac{S^*}{S} - \frac{S}{S^*}) \right] \\
+ \left[ x_1 (\beta I_c^* + \gamma I^*)S^* + x_2 (d_2 + \alpha)I_c^* + x_3 (d_3 + \pi)I^* \right] \\
- \left[ x_1 (\beta I_c^* + \gamma I^*)S^2 \frac{S}{S} + x_2 (1-p)\beta SI_c^* I_c + x_2 (1-p) \frac{\gamma I S I_c^* I_c}{I_c} \right] \\
+ x_3 p \frac{\beta I_c S^* I_c}{I} + x_3 p \frac{\gamma SI^* I_c^*}{I} - x_3 \frac{\alpha I_c I^*}{I} \right].
\]
Positive constants \( x_1, x_2, \) and \( x_3 \) are chosen as
\[
x_1 = 1, \quad x_2 = \frac{(d_3 + \pi)\beta S^* + \gamma\alpha S^*}{(d_2 + \alpha)(d_3 + \pi)}, \quad x_3 = \frac{\gamma S^*}{(d_3 + \pi)}.
\] (7)

It can be verified that they satisfy relations
\[
-x_1 + x_2(1 - p) + x_3p = 0,
\]
\[
x_1\gamma S^* - x_3(d_3 + \pi) = 0,
\]
\[
x_1\beta S^* - x_2(d_2 + \alpha) + x_3\alpha = 0.
\] (8)

We re-group terms in \( \frac{dV}{dt} \) such that \( \frac{dV}{dt} = V_1 + V_2 + V_3 \), where
\[
V_1 = (d_1 + \theta)S^*(2 - \frac{S}{S^*} - \frac{S^*}{S}),
\]
\[
V_2 = x_1(\beta S^*I_c^* + \gamma I^*S^*) + x_2(d_2 + \alpha)I_c^* + x_3(d_3 + \pi)I^*,
\]
\[
V_3 = -\frac{x_1(\beta I_c^*S^* + \gamma I^*S^*)S^*}{S} - x_2(1 - p)\beta SI_c^* - x_3p\gamma SI^* - \frac{x_2(1 - p)\gamma ISI_c^*}{I} - \frac{x_3\alpha I_c I^*}{I}.
\]

We see that \( V_1 \leq 0 \) from the inequality \( x + \frac{1}{x} \geq 2 \) for all \( x > 0 \), and that \( V_1 = 0 \) if and only if \( S = S^* \). We are left to show that \( V_2 + V_3 \leq 0 \). We begin by examining \( V_2 \). Using the values for \( x_1, x_2, \) and \( x_3 \) in (7), relations in (8), and the equilibrium relation
\[
(pd_2 + \alpha)I_c^* = (1 - p)(d_2 + \pi)I^*,
\] (9)

we can rewrite \( V_2 \) as
\[
V_2 = 2px_3\gamma I^*S^* + 2(1 - p)x_2\beta I_c^*S^* + 4px_3\beta I_c^*S^* + \frac{3(1 - p)\alpha}{(pd_2 + \alpha)}\gamma I^*S^*.
\] (10)

Similarly, we can rewrite \( V_3 \) as
\[
V_3 = \left[ -x_2(1 - p)\beta I_c^*S - \frac{(1 - p)x_2\beta S^2I_c^*}{S} \right] + \left[ -x_3p\gamma SI^* - \frac{px_3\gamma I^*S^2}{S} \right] + \left[ -\frac{x_2(1 - p)\gamma ISI_c^*}{I_c} - \frac{x_3\alpha I_c I^*}{I} - (1 - y)\frac{x_2\gamma I^*S^2}{S} \right] + \left[ -\frac{x_2(1 - p)\gamma ISI_c^*}{I_c} - \frac{x_3p\beta I_c SI^*}{I} - (1 - y)\frac{(1 - p)x_2\gamma I^*S^2}{S} \right] - \frac{px_3\beta S^2I_c^*}{S},
\]

where
\[
y = \frac{(1 - p)\alpha}{(pd_2 + \alpha)(1 - p)x_2}, \quad 1 - y = \frac{(1 - p)\beta S^*}{(pd_2 + \alpha)(1 - p)x_2}.
\]

Write \( V_3 = V_a + V_b + V_c + V_d \), with each term representing the expression enclosed in a pair of big square brackets. We will estimate each term in \( V_3 \) by applying the inequality
\[
\frac{a_1 + a_2 + \cdots + a_n}{n} \geq (a_1 \cdot a_2 \cdots a_n)^{1/n}, \quad \text{for } a_i > 0.
\]
We obtain
\[ V_a = -x_2(1-p)\beta I_c^* S - \frac{(1-p)x_2\beta S^*^2 I_c^*}{S} \]
\[ \leq -2\sqrt{(x_2(1-p))^2(\beta I_c^* S^*)^2} = -2(1-p)x_2\beta I_c^* S^*, \] (11)
and
\[ V_b = -x_3 p \gamma SI^* - \frac{px_3 \gamma I^* S^*^2}{S} \leq -2\sqrt{(x_3 p)^2(\gamma I^* S^*)^2} = -2px_3 \gamma I^* S^*. \] (12)

Similarly,
\[ V_c = -y \frac{x_2(1-p)\gamma ISI_c^*}{I_c} - \frac{x_3 \alpha I_c^* I}{I} - y \frac{(1-p)x_2\gamma I^* S^*^2}{S} \]
\[ \leq -3[(x_2(1-p))^2x_3\alpha I_c^*y^2(\gamma I^* S^*)^2] = \frac{3(1-p)\alpha}{(pd_2 + \alpha)} \gamma I^* S^*, \] (13)
and
\[ V_d = -(1-y) \frac{x_2(1-p)\gamma ISI_c^*}{I_c} = -x_3 p \beta I_c^* S I - (1-y) \frac{px_2\gamma I^* S^*^2}{S} \]
\[ \leq -4[(x_2(1-p))^2(px_3)^2(1-y)^2\gamma I^* S^*^2 \beta I_c^* S^*^2 \beta I^* I_c^*] = -4px_3 \beta I_c^* S^*. \] (14)

Therefore, (11) - (14) imply
\[ V_3 \leq -2(1-p)x_2\beta I_c^* S^* - 2px_3 \gamma I^* S^* - 4px_3 \beta I_c^* S^* - \frac{3(1-p)\alpha}{(pd_2 + \alpha)} \gamma I^* S^*. \] (15)

It follows from (10) and (15) that \( V_2 + V_3 \leq 0 \) and thus \( \frac{dV}{dt} \leq 0 \). Furthermore, \( \frac{dV}{dt} = 0 \) if and only if \( V_1 = 0 \) and \( V_2 + V_3 = 0 \). Using (10) - (15), we can show that \( \frac{dV}{dt} = 0 \Leftrightarrow (S, I_c, I) = (S^*, I_c^*, I^*) \), and thus \( \frac{dV}{dt} \) is negative definite with respect to \( P^* \). The global stability of \( P^* \) follows from the classical stability theorem of Lyapunov. 

We remark that the form of Lyapunov function in (6) was motivated by those used in Korobeinikov and Maini [8], Guo [3], and Guo and Li [4].

6. Impact of carriers on the transmission dynamics: chronic hepatitis B infection. To further illustrate the impact of disease carriers on the transmission dynamics, we use chronic hepatitis B infection as an example. Hepatitis B is a liver disease caused by the HBV virus. It is transmitted through sexual contact, the sharing of infected needles, or from mother to infant. Chronic HBV infection is more common: children infected with HBV rarely develop acute illness and up to 90% of infected children become chronically infected; adults infected with HBV usually recover from acute illness, but 5-10% will become chronically infected. About 30% of people infected with HBV do not show any symptoms. These people are the asymptomatic carriers. According to WHO statistics, about 2 billion people worldwide have been infected with HBV and about 350 million live with chronic infection. An estimated 600,000 persons die each year due to the acute or chronic consequences of hepatitis B. Safe and effective hepatitis B vaccines became available in 1982. Integration of the HBV vaccines into childhood immunization programs since 1991 has produced a great decline in the amount of children infected. In many countries where 8% to 15% of children used to become chronically infected
with HBV, vaccination has reduced the rate of chronic infection to less than 1% among immunized children [18, 16, 17].

Our model (1) can be used as a crude approximation for the transmission dynamics of chronic hepatitis B infection among an adult population. The compartment $S$ contains individuals who are susceptible to HBV infection, compartment $I$ contains individuals who are chronically infected with HBV and are symptomatic or have been tested and are aware of their condition, and compartment $I_c$ contains individuals who are asymptomatic carriers of HBV and have no knowledge that they are infected. Recall that in this model, $\alpha$ represents the rate of diagnosis - the rate at which people carrying the disease are made aware of their infection, either through testing or through appearance of symptoms. Based on epidemiological data from WHO, CDC (US), and PHAC (Canada) [18, 16, 17], we have estimated the values of our model parameters as follows:

\[
b = 90,000, \quad d_1 = 1/80, \quad d_2 = d_1 + 0.004, \quad d_3 = d_2, \quad \beta = 1.5\gamma, \quad \pi = 0.75.
\]

(16)

We carry out numerical simulations of our model (1) in a hypothetical population of size 200,000. We will vary key parameters to investigate the impact of asymptomatic carriers and HBV vaccinations.

![Figure 2](image)

**Figure 2.** Simulation results showing the impact of testing and diagnosis of carriers. In (a), diagnosis rate $\alpha = 0.1$. In (b), $\alpha = 0.5$. Other parameter values are the same as in (16).

In the first set of simulations, we fix a vaccination coverage rate at 70% where the vaccine has a success rate of 85%. This means that $\theta = 0.85 \times 0.7 = 0.585$. We vary the parameter $\alpha$ to see the effects of diagnosis rate at which carriers move into the infected class.

We see in Figure 2 that, if only 1% of chronic carriers become aware of their disease, the number of symptomatically infected individuals decreases significantly, but the number of carriers is still high. This is not a desirable result as it is the carriers that are responsible for most of the new infections. If we increase $\alpha$ from 1% to 5%, a more dramatic change occurs in the disease dynamics: the number of carriers shows a much greater decline while the number of symptomatically infected remains low. This demonstrates that testing and diagnosis of carriers can be an effective control measure in high HBV prevalence countries.

In the second set of simulations, we will fix $\alpha = 0.01$ and vary $\theta$ to see the effect of increasing the vaccination rate. If we set $\theta = 0.1$, we see in Figure 3 that though the number of symptomatically infected reduces rapidly, the number of carriers remains...
high. Increasing $\theta$ to 0.6 only slightly alters the disease dynamics; the number of carriers only shows a moderate decline.

![Graph](image)

**Figure 3.** Simulation results showing the impact of vaccination. In (a), vaccination rate $\theta = 0.1$. In (b), $\theta = 0.6$. Other parameter values are the same as in (16)

Our model simulations demonstrate the challenges of chronic HBV infection: the existence of a large number of carriers who are infectious but show no symptoms. Because carriers do not show symptoms, they will not be part of any treatment program. Comparing our simulation results in Figures 2 and 3, we conclude that, in high HBV prevalence countries, testing and increasing awareness of carriers will have a much greater impact on the disease burden than increasing vaccination rates. While this conclusion may have practical implications for the control of chronic HBV infections, more realistic models that are specific for HBV infection and more detailed data need to be employed to further explore its significance in future studies.

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