Research Article

The Cost-Effectiveness Analysis and Optimal Strategy of the Tobacco Control

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1. Introduction

Tobacco use is the single greatest preventable cause of death in the world today. Currently, about 6 million people die from tobacco-related illnesses each year [1]. By 2030, this figure is expected to reach 10 million deaths [2]. If current patterns of smoking continue, about 500 million of the world’s population alive today will eventually be killed by smoking, half of them in productive middle age, losing 20 to 25 years of life [3]. Statistical data indicate that it will be very difficult to reduce tobacco-related deaths over the next 30–50 years, unless adult smokers are encouraged to quit [4]. Hence, smoking control and reducing smoking-related death are priority concerns that government organizations must face in the respective countries. Since tobacco contains nicotine which is addictive, it is very difficult to quit smoking [5]. Many different measures have been used to control smoking, including regulation of the packaging and labelling of tobacco products, higher taxes and prices of cigarettes, setting special smoking areas, mass media campaigns, and psychosocial and pharmacological treatment, all of which aim to enhance public consciousness and help tobacco users to give up smoking and avoid subsequent relapse [6].

Many studies have been conducted to analyze the smoking phenomenon and investigate the effects of different control measures (Ham [7], Yen et al. [8], Ertürk et al. [9], Castillo et al. [10], Sharomi and Gumel [11], and Guerrero et al. [12]). Rowe et al., in 1992 [13], applied a dynamical model to investigate smoking behavior. Zeb et al., in 2013 [14], proposed a model with square-root incidence rate to describe smoking phenomenon. Lahrouz, et al., in 2011 [15], used deterministic and stochastic models to study the dynamic properties of smokers. Guerrero et al., in 2011 [16], used a mathematical model to successfully describe the characteristics of smoking habit in Spain. In 2002, the
Canadian Cancer Society released a study which indicated that setting health warning on cigarette packages is very effective in discouraging smoking [17]. In 2015 [18], we proposed a mathematical model with saturated incidence rate to explore the effects of controlling smoking by setting special smoking areas and raising the price of cigarettes. Results indicate that setting special smoking areas and putting up the price of cigarettes are very effective in reducing the number of smokers.

As a continuation of our previous work, we will further investigate the effects of media coverage and smoking cessation treatment in controlling smoking. We will use a concrete example to provide an analytical method for strategic decision-makers, so that we can find out which strategy is the most cost-effective for all possible combinations of the two tobacco control measures. The organization of this paper is as follows. In Section 2, we will present a new mathematical model to describe the dynamic behavior of smokers. In Section 3, we will derive the concrete form of the basic reproduction number $R_0$ and perform stability analysis of the model. In Section 4, we will introduce media coverage and smoking cessation treatment into the model to investigate the effects of two control measures as well as the combination of them. In Section 5, the cost-effectiveness analysis is carried out to gain insight to which strategy is most cost-effective in controlling smoking. Finally, the conclusions are summarized in Section 6.

## 2. Construction of the Mathematical Model

In order to facilitate discussion, we introduce new occasional smoker class $L(t)$ and patient class $C(t)$ caused by smoking into our previous model [18]. Hence, we divide the total population into six subpopulations: potential smokers, occasional smokers, smokers, temporary quitters, permanent quitters, and patients caused by smoking, with sizes denoted by $P(t)$, $L(t)$, $S(t)$, $Q_r(t)$, $Q_p(t)$, and $C(t)$, respectively.

The transitions among these subpopulations are shown graphically in Figure 1, which shows that the number of potential smokers is increased at a constant recruitment rate $\Lambda$. In addition, potential smokers can become occasional smokers via effective "contact" with smokers. The incidence rate is bilinear ($\beta$ is effective contact rate). The probability that an occasional smoker converts a smoker is assumed as $\omega$. The rate of quitting smoking for smokers is $\gamma$. Smokers with the proportion $\delta \in (0, 1)$ are shifted into temporary quitters; nevertheless, smokers with the proportion $\gamma(1 - \delta)$ become permanent quitters. The relapse rate of temporary quitters is $\alpha$. The conversion ratios from occasional smokers, smokers, temporary quitters, and permanent quitters to patients caused by smoking are $\tau$, $\tau_\xi$, $\eta \theta (\xi, \theta > 1)$, and $\eta$, respectively. The natural death rates of all the subpopulations are $\mu$, and the mortality rate due to the disease caused by smoking is $d$. Hence, we can establish the following model:

\[
\begin{align*}
\dot{P} &= \Lambda - \mu P - \beta SP, \\
\dot{L} &= \beta SP - (\mu + \omega + \tau)L, \\
\dot{S} &= \omega L + aQ_r - (\mu + \gamma + \tau_\xi)S, \\
\dot{Q}_r &= \gamma \delta S - (\mu + \alpha + \eta \theta)Q_r, \\
\dot{Q}_p &= \gamma (1 - \delta)S - (\mu + \eta)Q_p, \\
\dot{C} &= \tau L + \tau_\xi S + \eta \theta Q_r + \eta Q_p - (\mu + d)C.
\end{align*}
\]

Thus, the total population size is given by $N(t) = P(t) + L(t) + S(t) + Q_r(t) + Q_p(t) + C(t)$ at time $t$. Adding all equations of system (1), we can get

\[
\dot{N} = \Lambda - \mu N - dC \leq \Lambda - \mu N,
\]

which yields that

\[
\lim_{t \to \infty} N(t) = \frac{\Lambda}{\mu}
\]

Therefore, the biologically feasible region

\[
\Omega = \left\{ (P, L, S, Q_r, Q_p, C) \in \mathbb{R}^6_+ : P(t) + L(t) + S(t) + Q_r(t) + Q_p(t) + C(t) \leq \frac{\Lambda}{\mu} \right\}
\]

is positively invariant.

Since the first four equations in system (1) are independent of the variables $Q_p$ and $C$, it is sufficient to consider the following reduced system:

\[
\begin{align*}
\dot{P} &= \Lambda - \mu P - \beta SP, \\
\dot{L} &= \beta SP - (\mu + \omega + \tau)L, \\
\dot{S} &= \omega L + aQ_r - (\mu + \gamma + \tau_\xi)S, \\
\dot{Q}_r &= \gamma \delta S - (\mu + \alpha + \eta \theta)Q_r.
\end{align*}
\]

## 3. Basic Properties of the Model and Parameter Values

In this section, the basic reproductive number $R_0$ of model (5) will be calculated, and the stabilities of equilibria will be investigated. For convenience, we note $a = \mu + \omega + \tau$, $b = \mu + \gamma + \tau_\xi$, $c = \mu + \alpha + \eta \theta$.

### 3.1. The Basic Reproductive Number $R_0$

Apparently, model (5) always has a smoking-free equilibrium $E_0(\Lambda/\mu, 0, 0, 0)$. Let $\mathcal{X} = (L, S, Q_r)$, from equation (5), we have

\[
\dot{X} = F(X) - F(X^0),
\]
where
\[
\mathcal{F}(X) = \begin{pmatrix} \beta SP \\ 0 \\ 0 \end{pmatrix},
\]
\[
\mathcal{V}(X) = \begin{pmatrix} aL \\ -\omega L - \alpha Q_1 + bS \\ eQ_1 - \gamma \delta S \end{pmatrix}.
\] (7)

By calculating, we obtain the Jacobian matrices of \(\mathcal{F}(X)\) and \(\mathcal{V}(X)\) at the smoking-free equilibrium \(E_0\) as follows:
\[
F = \begin{bmatrix} 0 & \frac{\beta \Lambda}{\mu} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix},
\]
\[
V = \begin{bmatrix} a & 0 & 0 \\ -\omega & b & -\alpha \\ 0 & -\gamma \delta & c \end{bmatrix}.
\] (8)

The inverse matrix of \(V\) is given by
\[
V^{-1} = \frac{1}{|V|} \begin{bmatrix} bc - \alpha \gamma \delta & 0 & 0 \\ \omega \gamma \delta & ca & aa \\ \omega \gamma \delta & a \gamma \delta & ab \end{bmatrix},
\] (9)

where
\[
|V| = a(bc - \alpha \gamma \delta),
\]
\[
bc - \alpha \gamma \delta = (\mu + \tau \xi)(\mu + \alpha + \eta \theta) + \gamma(\mu + \alpha + \eta \theta) - \alpha \gamma \delta
\]
\[
= (\mu + \tau \xi)(\mu + \alpha + \eta \theta) + \gamma(\mu + \eta \theta) + \alpha \gamma (1 - \delta).
\] (10)

Clearly, \(bc - \alpha \gamma \delta > 0\) when \(0 < \delta < 1\). Then \(|V| = a(bc - \alpha \gamma \delta) > 0\).

Hence, the basic reproductive number \(R_0\) (i.e., the spectral radius of \(FV^{-1}\) [19]) is equal to
\[
R_0 = \frac{\beta \omega c \Lambda}{\mu a(bc - \alpha \gamma \delta)}.
\] (11)

**Proposition 1.** If \(R_0 > 1\), an unique positive equilibrium \(E_*(P_*, L_*, S_*, Q_*)\) exists in model (5), where \(P_* = \Lambda/\mu R_0\), \(L_* = (\Lambda/a)(R_0 - 1/R_0)\), \(S_* = \mu(R_0 - 1)/\beta\), and \(Q_* = \mu \gamma \delta (R_0 - 1)/\beta c\).

**3.2. The Stability Analysis of the Model**

**Theorem 1.** The smoking-free equilibrium \(E_0\) is globally asymptotically stable if \(R_0 < 1\) and unstable if \(R_0 > 1\).

**Proof.** The Jacobian matrix of model (5) at \(E_0\) is
\[
J(E_0) = \begin{bmatrix} -\mu & 0 & \frac{-\beta \Lambda}{\mu} & 0 \\ 0 & -a & \frac{\beta \Lambda}{\mu} & 0 \\ 0 & \omega & -b & \alpha \\ 0 & 0 & \gamma \delta & -c \end{bmatrix},
\] (12)

whose characteristic equation is given by
\[
(\lambda + \mu)(\lambda^3 + a_1 \lambda^2 + a_2 \lambda + a_3) = 0.
\] (13)

Obviously, \(J(E_0)\) has an eigenvalue \(\lambda_1 = -\mu\), and the remaining eigenvalues satisfy
\[
\lambda^3 + a_1 \lambda^2 + a_2 \lambda + a_3 = 0,
\] (14)

where
Given that $\mathcal{R}_0 < 1$, we can obtain $a_2 > 0$, $a_3 > 0$, and $a_1 a_2 - a_3 > 0$. Hence, by Routh–Hurwitz criterion, the smoking-free equilibrium $E_0$ is locally asymptotically stable if $\mathcal{R}_0 < 1$. If $\mathcal{R}_0 > 1$, then $a_3 < 0$, which implies that the smoking-free equilibrium $E_0$ is unstable.

To discuss the global stability of $E_0$, we use a Lyapunov function

$$V_1 = \omega c P - P^* \ln P + \omega c L + acS + aaQ_t, \quad (16)$$

where $P^* = \Lambda/\mu$.

The derivative of $V_1$ along solutions of model (5) is calculated as follows:

$$\frac{dV_1}{dt} = \omega c \left( P - P^* \frac{dP}{dt} + \omega c \frac{dL}{dt} + ac \frac{dS}{dt} + a \omega c \frac{dQ_t}{dt} \right)$$

$$= \omega c \left( P - P^* \left( \Lambda - \mu P - \beta SP \right) + \omega c \left( \beta SP - aL \right) \right. + a c \left( \omega L + aQ_t - bS \right) + a a \left( \gamma S - cQ_t \right) + \omega c \left( \mu P^* - aP - \beta SP \right) + \omega c \left( \beta SP - aL \right)$$

$$= \omega c \left( \mu P^* - \mu P - \beta SP \right) + \omega c \left( \beta SP - aL \right) + a c \left( \omega L + aQ_t - bS \right) + a a \left( \gamma S - cQ_t \right)$$

$$= \frac{\mu \omega c}{P} \left( P - P^* \right)^2 + a (bc - \alpha \gamma \delta) (\mathcal{R}_0 - 1) S.$$}

Then $(dV_1/dt) \leq 0$ if $\mathcal{R}_0 < 1$, and $(dV_1/dt) = 0$ only if $P = P^*, S = 0$. Hence, $\{(P, L, S, Q_t) | (dV_1/dt) = 0\} = \{E_0\}$. Therefore, by the Lasalle Invariance Principle, every solution of model (5) approaches $E_0$ as $t \rightarrow \infty$. \hfill \Box

**Theorem 2.** The unique smoking-present equilibrium $E_*$ is globally asymptotically stable in $\Omega$ if $\mathcal{R}_0 > 1$.

**Proof.** The Jacobian matrix of system (5) at $E_*$ is

$$J(E_*) = \begin{bmatrix}
-\mu - \beta S_* & 0 & -\beta P_* & 0 \\
\beta S_* & -a & \beta P_* & 0 \\
0 & \omega & -b & a \\
0 & 0 & \gamma \delta & -c
\end{bmatrix}, \quad (18)$$

and the characteristic equation is

$$\lambda^4 + b_1 \lambda^3 + b_2 \lambda^2 + b_3 \lambda + b_4 = 0, \quad (19)$$

where

$$b_1 = \mu + \beta S_* + a + b + c,$$

$$b_2 = \left( \mu + \beta S_* \right) (a + b + c) + (bc - \alpha \gamma \delta) + \mu + \beta S_* + \left( ab - \omega \beta P_* \right) + ac + (bc - \alpha \gamma \delta) + \beta S_* \omega \beta P_* + \left( \mu + \beta S_* \right)\left( a + b + c \right)^2$$

$$- \beta S_* \beta \omega P_* > (\mu + \beta S_*) (a + b + c)^2 - \beta S_* \beta \omega P_* > \beta S_* \beta \omega P_* = (a - \beta \omega P_*)$$

(20)

It is clear that $b_1 > 0$. Note that $ab - \omega \beta P_* = \alpha \gamma \delta c / \omega \beta P_* + abc - \beta \omega P_* c - \alpha \gamma \delta a = c (ab - \omega \beta P_*) - \alpha \gamma \delta a = 0$, then $b_2 > 0$, $b_3 = (\mu + \beta S_*) ((ab - \omega \beta P_*) + ac + (bc - \alpha \gamma \delta)) + \beta S_* \omega \beta P_* > 0$, $b_4 = \beta S_* \beta \omega P_* > 0$, $b_5 = \beta S_* \beta \omega P_* > 0$. We can also prove $b_1 b_2 - b_3 = (\mu + \beta S_*) \left( a + b + c \right) \left( a + b + c \right) + (ab - \omega \beta P_*)^2 + ac + (bc - \alpha \gamma \delta) + (\mu + \beta S_*) (a + b + c)^2 - \beta S_* \beta \omega P_* > (\mu + \beta S_*) (a + b + c)^2 - \beta S_* \beta \omega P_* > \beta S_* \beta \omega P_* = (a - \beta \omega P_*)$.

(21)

Therefore, by the Lasalle Invariance Principle, every solution of model (5) approaches $E_0$ as $t \rightarrow \infty$. \hfill \Box

The uniform persistence, because of boundedness of $\Omega$, is equivalent to the existence of a compact set in the interior of $\Omega$, which is absorbing for system (5).

**Theorem 3.** Denote $x(t) = (P(t), L(t), S(t), Q(t))$ and $m(t) = (X(t), Y(t), Z(t), W(t))$, we assign the vector field generated by system (5) to $f(x)$. Then system (5) can be rewritten as

$$x(t) = f(x),$$

$$m(t) = \omega f^{[3]}(x) m,$$
where $\partial f^{[3]}/\partial x$ stands for the third additive compound matrix for system (5) (see Appendix B for details). It is given by

$$\frac{\partial f^{[3]}}{\partial x} = -(3\mu + \beta S)E + \Phi,$$

(23)

$$\Phi = \begin{bmatrix} -(\omega + \tau + \gamma + \tau \xi) & \alpha & 0 & 0 \\ \gamma \delta & -(\omega + \alpha + \theta \eta) & \beta P & \beta P \\ 0 & \omega & -(\gamma + \tau \xi + \alpha + \eta \theta) & 0 \\ 0 & 0 & \beta S & -(\omega + \tau + \gamma + \theta \eta + \tau \xi + \alpha - \beta S) \end{bmatrix}. $$

(24)

Furthermore, the associated linear compound system is given by

$$\begin{align*}
\dot{X} &= -(3\mu + \beta S + \omega + \tau + \gamma + \tau \xi)X + \alpha Y, \\
\dot{Y} &= \gamma \delta X - (3\mu + \beta S + \omega + \tau + \alpha + \theta \eta)Y + \beta P (Z + W), \\
\dot{Z} &= \omega Y - (3\mu + \beta S + \gamma + \tau \xi + \alpha + \eta \theta)Z, \\
\dot{W} &= \beta S Z - (3\mu + \omega + \gamma + \tau + \tau \xi + \alpha + \theta \eta)W.
\end{align*}$$

(25)

We construct a Lyapunov function given by

$$V_2(x, m) = \max \left\{ |X| + |Y|, \frac{L}{S} (|Z| + |W|) \right\}.$$  

(26)

Let $\|m\| = |X(t)| + |Y(t)| + |Z(t)| + |W(t)|$. Calculating the derivative of $V_2$ along the positive solution of system (25) reduces to the following differential inequalities:

$$D_+[\frac{L}{S} (|Z| + |W|)] \leq -(3\mu + \beta S + \omega + \tau + \gamma + \tau \xi - \gamma \delta)|X|$$

$$= -(3\mu + \beta S + \omega + \tau + \tau \xi + \gamma (1 - \delta))|X|$$

$$= -(3\mu + \beta S + \omega + \tau + \theta \eta)|Y| + \beta P (|Z| + |W|)$$

$$\leq -(3\mu + \beta S + \omega + \tau + \gamma + \tau \xi + \alpha + \theta \eta) (|X| + |Y|)$$

$$+ \frac{S}{L} \beta P \left( \frac{L}{S} (|Z| + |W|) \right).$$

(27)

Similarly, we get

where $E$ is an identity matrix and

$$D_+\left[\frac{L}{S} (|Z| + |W|)\right] = \frac{L}{S} \left( \frac{\dot{L}}{L} - \frac{\dot{S}}{S} \right) (|Z| + |W|)$$

$$+ \frac{L}{S} D_+ (|Z| + |W|)$$

$$\leq \left( \frac{L}{S} - \frac{\dot{S}}{S} \right) (3\mu + \gamma + \tau \xi + \alpha + \theta \eta)$$

$$\cdot \left( \frac{L}{S} (|Z| + |W|) + \frac{\omega L}{S} |Y| \right)$$

$$\leq \frac{\omega L}{S} (|X| + |Y|)$$

$$+ \left( \frac{\dot{L}}{L} - \frac{\dot{S}}{S} \right) (3\mu + \gamma + \tau \xi + \alpha + \theta \eta)$$

$$\cdot \left( \frac{L}{S} (|Z| + |W|) \right).$$

(28)

Combining (27) and (28) yields

$$D_+ |V_2(t)| \leq \sup \{ h_1(t), h_2(t) \} V_2(t),$$

(29)

where

$$\begin{align*}
h_1(t) &= -(3\mu + \beta S + \omega + \tau) + \frac{S}{L} \beta P, \\
h_2(t) &= \frac{\omega L}{S} + \left( \frac{L}{S} - \frac{\dot{S}}{S} \right) (3\mu + \gamma + \tau \xi + \alpha + \theta \eta).
\end{align*}$$

(30)

Form system (5), we have

$$\begin{align*}
\frac{\dot{L}}{L} &= -\frac{\beta S P}{L} - (\mu + \omega + \tau), \\
\frac{\dot{S}}{S} &= \frac{\omega L}{S} + \frac{\alpha Q_1}{S} - (\mu + \gamma + \tau \xi).
\end{align*}$$

(31)

Hence,
persons per year.

\[ h_1(t) = \frac{L}{L} - 2\mu \leq \frac{L}{L} - 2\mu, \]

\[ h_1(t) = \frac{L}{L} - 2\mu - \frac{\alpha Q}{\beta} - \alpha - \theta \eta \leq \frac{L}{L} - 2\mu, \]

which leads to

\[ D_\alpha V_2(t) \leq \left( \frac{L}{L} - 2\mu \right) V_2(t). \]

Accordingly, from (33), we can obtain

\[ V_2(t) \leq \frac{L(f)}{L(0)} V_2(0) e^{-\mu t} \leq \frac{L(f)}{\mu L(0)} e^{-\mu t} \rightarrow 0, \text{ as } t \rightarrow \infty, \]

which indicates that the associated linear compound system (25) is asymptotically stable. Hence, by results found in [25], the smoking-present equilibrium \( E_* \) is globally asymptotically stable.

3.3. Parameter Values. In order to estimate the parameter values of the model (1), we make some reasonable hypothesis. Assume that the average age of people is 70 years old; then, we estimate the natural death rate \( \mu = 1/(365 \times 70) = 4 \times 10^{-5} \) persons per day. We suppose to select a community with size about \( 1.5 \times 10^6 \) person as the object of our investigation. Thus, the recruitment rate of potential smokers is \( \Lambda = 1.5 \times 10^6 \times \mu = 6000 \) persons per day.

The convert rate of occasional smokers into smokers is estimated as \( \omega = 0.03 \) persons per day [14]. The average duration of smoking for a smoker is assumed as 10 years. Thus, the quit rate of a smoker is estimated as \( \gamma = 1/(365 \times 10) = 2.74 \times 10^{-4} \) persons per day. The ratio of quitters who temporarily quit smoking is assumed as \( \delta = 0.2 \).

The average time-span for temporary quitters from the time quitting smoking to the time starting smoking again is assumed as 2 years, then \( \alpha = 1/(2 \times 365) = 0.0014 \) persons per day.

The average duration after which an occasional smoker will develop smoking-related illnesses is about 8 years. Thus, \( \tau \) is estimated as \( 1/(8 \times 365) = 3.42 \times 10^{-4} \) persons per day.

Based on that, a smoker have a higher probability of developing smoking-related illnesses than an occasional smoker; we assume that a smoker develops smoking-related illnesses at a rate \( \tau \xi \) (where \( \xi = 3 \)). Similarly, the average duration after which a permanent quitter will develop smoking-related illnesses is assumed as 10 years. Hence, \( \eta \) is estimated as \( 1/(10 \times 365) = 2.74 \times 10^{-4} \) persons per day.

Because that a temporary quitter have a higher probability of developing smoking-related illnesses than a permanent quitter, we assume that a temporary quitter develops smoking-related illnesses at a rate \( \eta \theta \) (where \( \theta = 6 \)). It is assumed that an individual with smoking-related illnesses can averagely live for 20 years. Thus, the death rate due to illnesses is estimated as \( d = 1/(365 \times 20) = 1.37 \times 10^{-4} \).

Goyal, in 2014, applied the data derived from Canada to deduce the effective contact rate between the potential smoker and the smoker as \( 8.2192 \times 10^{-7} \) persons per year [26]. We take it as the effective contact rate \( \beta \) of this paper, i.e., \( \beta = 8.2192 \times 10^{-7}/365 = 1.3177 \times 10^{-11} \) persons per day.

We list each parameter value of system (1) in Table 1 to provide a quick reference.

From the reasonably estimated parameter values in Table 1, we can calculate the basic reproductive number \( R_0 = 1.4840 > 1 \), which indicates that the smoking-present equilibrium \( E_* \) is globally asymptotically stable, i.e., smoking is one of the enduring problems of society. Corresponding time series plots with different initial values of \( S(t) \) are shown in Figure 2.

4. Application of Optimal Control to the Tobacco Control Model

Based on the analysis results above mentioned, we know that smoking will become a huge social problem in the absence of any control measure. In order to combat this trouble, we will investigate the effects of media coverage and smoking cessation treatment in controlling smoking. (a) Effects of media coverage. The mass media campaigns which propagate that smoking is very harmful to health not only can cut down the relapse probability of an ex-smoker who returns to cigarettes and reduce the convert probability of an occasional smoker into a smoker, but also can decrease the probability of becoming an occasional smoker to a potential smoker due to the contact with a smoker. Based on that, the probability of a potential smoker becoming an occasional smoker is not only influenced by the media coverage, and we denote the relapse rate of an ex-smoker, the conversion rate of an occasional smoker into a smoker, and the probability of a potential smoker becoming an occasional smoker reduced by media coverage as \( \mu_1(t) \), \( \mu_2(t) \), and \( b \mu_1(t) \), (where \( b \in (0, 1) \)), respectively. (b) Effects of smoking cessation treatment. Many treatment measures can be used for smoking cessation, including behavioral counseling and medications (such as nicotine replacement therapy and varenicline). These treatment measures do not only reduce withdrawal symptoms but also increase the success rate of quitting smoking. \( u_1(t) \) represents the success rate of quitting smoking enhanced by smoking cessation treatment. Taking into account the extensions made above, system (1) is modified as the following system:

\[
\begin{align*}
\dot{P} &= \Lambda - \mu P - \beta (1 - b_1 u_1) SP, \\
\dot{L} &= \beta (1 - b_1 u_1) SP - [\mu + \omega (1 - u_1) + \tau] L, \\
\dot{S} &= \omega (1 - u_1) L + \alpha (1 - u_1) Q_v - [\mu + \gamma (1 + u_1) + \tau \xi] S, \\
\dot{Q}_v &= \gamma (1 + u_2) \delta S - [\mu + \alpha (1 - u_1) + \eta \theta] Q_v, \\
\dot{Q}_p &= \gamma (1 + u_2) (1 - \delta) S - (\mu + \eta) Q_p, \\
\dot{C} &= \tau L + \tau \xi S + \eta \theta Q_v + \eta Q_p - (\mu + d) C.
\end{align*}
\]

Our aim is to minimize the cost arising from the consumption of the social resources for smokers and the consumption of the medical and health resources for patients caused by smoking, as well as the costs incurred by media propaganda and smoking cessation treatment. For this end, the total cost functional is defined as
ε

S

\(0.6\)

\(0.8\)

\(1.2\)

\(1.4\)

\(1.6\)

\(2.2\)

\(2.4\)

Figure 1: The number of smokers \((S(t))\) \(\times 10^6\).

Table 1: The biological meanings and estimated values of parameters.

| Parameter | Description | Value | Source |
|-----------|-------------|-------|--------|
| \(\mu\)  | The natural death rate | \(4 \times 10^{-5}\) | [18] |
| \(\Lambda\) | The recruitment rate | 6000 | Assumed |
| \(\beta\) | The effective contact rate | \(1.3177 \times 10^{-11}\) | [26] |
| \(\omega\) | The ratio of occasional smoker class converted to smoker class | 0.03 | [14] |
| \(\gamma\) | The quit ratio of smokers | \(2.74 \times 10^{-4}\) | [18] |
| \(\delta\) | The ratio of quitters who quit smoking temporarily | 0.200 | [18] |
| \(\alpha\) | The relapse rate of temporal quitters | 0.0014 | [18] |
| \(\tau\) | The ratio of occasional smokers who develop smoking-related illnesses | 3.42 \times 10^{-4} | Assumed |
| \(\xi\) | A positive constant | 3.00 | Assumed |
| \(\eta\) | The ratio of permanent quitters who develop smoking-related illnesses | 2.74 \times 10^{-4} | Assumed |
| \(\theta\) | A positive constant | 6.00 | Assumed |
| \(d\) | The death rate due to smoking-related illnesses | \(1.37 \times 10^{-4}\) | Assumed |

subject to the state system given by (35). We choose a linear functional for the costs arising from the occasional smokers, the smokers, and the patients. \(\varepsilon_0\) and \(\varepsilon_1\) represent the costs arising from the consumption of the social resources for every occasional smoker and smoker, respectively. \(\varepsilon_2\) denotes the cost produced by the consumption of the medical and health resources for every patient caused by smoking. However, we choose a quadratic functional to represent the costs incurred by media coverage and smoking cessation treatment; such a cost function has been frequently used in [27–34]. \(\varepsilon_3\) and \(\varepsilon_4\) are cost weights associated with the controls \(u_1\) and \(u_2\), respectively. We seek to find an optimal control pair, \(u_1^*\) and \(u_2^*\), such that

\[
C_T(u_1^*, u_2^*) = \min_{\Phi} \{C_T(u_1, u_2)\},
\]

where the control set

\[
\Phi = \left\{(u_1, u_2) \in \left(L^\infty(0, t)\right)^2 : 0 \leq u_1(t) \leq u_1^{\text{max}}, 0 \leq u_2(t) \leq u_2^{\text{max}}, t \in [0, t]\right\}.
\]

Then the Hamiltonian \(H\) associated with problems (35)–(37) reads

\[
H = \varepsilon_0 L(t) + \varepsilon_1 S(t) + \varepsilon_2 C(t) + \frac{\varepsilon_3}{2} u_1(t) + \frac{\varepsilon_4}{2} u_2(t) + \frac{\varepsilon_5}{2} u_1^2(t)
\]

\[
+ \frac{\varepsilon_3}{2} u_1^2(t) + \lambda_1 \frac{dP}{dt} + \lambda_2 \frac{dL}{dt} + \lambda_3 \frac{dS}{dt} + \lambda_4 \frac{dQ_1}{dt} + \lambda_5 \frac{dQ_2}{dt} + \lambda_6 \frac{dC}{dt},
\]

where \(\lambda_j (j = 1, 2, \ldots, 6)\) are the solutions of the following equalities:

\[
\lambda_1 = \lambda_1 [\mu + \beta (1 - b_1 u_1) S] - \lambda_2 \beta (1 - b_1 u_1) S,
\]

\[
\lambda_2 = -\varepsilon_0 + \lambda_2 [\mu + \omega (1 - u_1) + \tau] - \lambda_3 \omega (1 - u_1) - \lambda_5 \tau,
\]

\[
\lambda_3 = -\varepsilon_1 + (\lambda_1 - \lambda_3) \beta (1 - u_1) + \lambda_1 \mu + \gamma (1 + u_2) + \tau \xi,
\]

\[
-\lambda_4 \gamma (1 + u_2) - \lambda_5 \gamma (1 + u_2) (1 - \delta) - \lambda_6 \tau \xi,
\]

\[
\lambda_4 = -\lambda_3 \omega (1 - u_1) + \lambda_4 [\mu + \alpha (1 - u_1) + \eta \theta] - \lambda_6 \eta \theta,
\]

\[
\lambda_5 = \lambda_5 (\mu + \eta) - \lambda_5 \eta \theta,
\]

\[
\lambda_6 = -\varepsilon_2 + \lambda_6 (\mu + d),
\]

satisfying the transversality condition.
\[ \lambda_i(t_i) = 0, \quad i = 1, \ldots, 6. \quad (41) \]

By Pontryagin’s Maximum Principle [35] and results obtained from Fleming and Rishel [36–38], we can get the following result:

\[ u_1^*(t) = \min \left\{ u_{1_{\text{max}}}^*, \max \left\{ 0, \left( \frac{\lambda_2 - \lambda_1}{b_1} b_1 S^P + \frac{\lambda_3 - \lambda_2}{\alpha} \omega L^* + \frac{\lambda_3 - \lambda_4}{\alpha Q} \right) \right\} \right\}, \]
\[ u_2^*(t) = \min \left\{ u_{2_{\text{max}}}^*, \max \left\{ 0, \left( \frac{\lambda_3 - \lambda_2}{\alpha} \right) y^S \right\} \right\}, \]

where \( \lambda_i \ (i = 1, 2, \ldots, 6) \) are the solutions of (40) and (41), and \( P^*, L^*, S^*, Q^* \) are optimal state solutions with associated optimal control variables \( (u_1^*, u_2^*) \).

**Proof.** In order to prove the existence of optimal control strategy \( u^* \) minimizing \( C_T(u) \), based on the method mentioned in [34, 36, 37], we need to verify whether the following hypotheses are met:

(H1) The control set and state variables are nonempty

(H2) The control set \( \Phi \) is closed and convex

(H3) The integrand of the objective functional \( C_T \) is convex in \( \Phi \) and satisfies

\[ \epsilon_0 L(t) + \epsilon_1 S(t) + \epsilon_3 C(t) + \frac{\epsilon_1}{2} u_1^2(t) + \frac{\epsilon_3}{2} u_2^2(t) \geq \gamma_1 \left( u_1^2(t) + u_2^2(t) \right)^{\gamma_2/2} - \gamma_3, \tag{44} \]

where \( \gamma_1, \gamma_2 > 0 \) and \( \gamma_3 > 0 \).

(H4) The right hand side of system (35) is bounded by the sum of the bounded control variables and state variables and can be written as a linear equation of control variables with coefficient depending on time and state.

From \( P(t) + L(t) + S(t) + Q_3(t) + Q_4(t) + C(t) \leq \Lambda / \mu \), we know that the solutions of state system are bounded. Furthermore, based on the result in [39], we can obtain the existence of the solution of system (35) with bounded coefficients. Hence, condition (H1) is satisfied. It is obvious that our control set \( \Phi \) is closed and convex defined by \( \Phi = \{ (u_1, u_2) \in \{ (L^\infty(0, t_f))^2 \} | 0 \leq u_1(t) \leq u_{1_{\text{max}}}, \} \)

\[ u_1^*(t) = \min \left\{ u_{1_{\text{max}}}^*, \\max \left\{ 0, \left( \frac{\lambda_2 - \lambda_1}{b_1} b_1 S^P + \frac{\lambda_3 - \lambda_2}{\alpha} \omega L^* + \frac{\lambda_3 - \lambda_4}{\alpha Q} \right) \right\} \right\}, \]
\[ u_2^*(t) = \min \left\{ u_{2_{\text{max}}}^*, \\max \left\{ 0, \left( \frac{\lambda_3 - \lambda_2}{\alpha} \right) y^S \right\} \right\}, \]

Theorem 3. There exists an optimal strategy \( u^* = (u_1^*, u_2^*) \in \Phi \) such that

\[ C_T(u_1^*, u_2^*) = \min_{(u_1, u_2) \in \Phi} C_T(u_1, u_2), \tag{42} \]

then the optimal controls \( u_1^*, u_2^* \in \Phi \) are given by

\[ 0 \leq u_1(t) \leq u_{1_{\text{max}}}, t \in [0, t_f] \], which satisfies condition (H2). Since the integrand of the objective functional is positive and quadratic in the control variables, it is convex. Notice that

\[ \epsilon_0 L(t) + \epsilon_1 S(t) + \epsilon_3 C(t) + \frac{\epsilon_1}{2} u_1^2(t), \]

\[ + \frac{\epsilon_3}{2} u_2^2(t) \geq \frac{\min \{ \epsilon_1, \epsilon_3 \} }{2} \left( u_1^2(t) + u_2^2(t) \right), \tag{45} \]

\[ \geq \gamma_1 \left( u_1^2(t) + u_2^2(t) \right)^{\gamma_2/2} - \gamma_3, \]

with \( \gamma_1 > 0, \gamma_2 = (\min \{ \epsilon_1, \epsilon_3 \} )/2 > 0 \), and \( \gamma_3 = 2 \). Hence, the condition (H3) is satisfied. By definition, each right hand side of system (35) is continuous and can be written as a linear function of control \( u = (u_1, u_2) \) with coefficients depending on time and states, which satisfies the condition (H4). Therefore, we conclude that there exists an optimal control.

Furthermore, by equating to zero the derivatives of the Hamiltonian with respect to the controls, we obtain

\[ u_1 = \left( \frac{\lambda_2 - \lambda_1}{b_1} b_1 S^P + \frac{\lambda_3 - \lambda_2}{\alpha} \omega L^* + \frac{\lambda_3 - \lambda_4}{\alpha Q} \right), \]
\[ u_2 = \left( \frac{\lambda_3 - \lambda_2}{\alpha} \right) y^S, \tag{46} \]

Using the property of the control space, we have

\[ u_1^*(t) = \min \left\{ u_{1_{\text{max}}}^*, \\max \left\{ 0, \left( \frac{\lambda_2 - \lambda_1}{b_1} b_1 S^P + \frac{\lambda_3 - \lambda_2}{\alpha} \omega L^* + \frac{\lambda_3 - \lambda_4}{\alpha Q} \right) \right\} \right\}, \]
\[ u_2^*(t) = \min \left\{ u_{2_{\text{max}}}^*, \\max \left\{ 0, \left( \frac{\lambda_3 - \lambda_2}{\alpha} \right) y^S \right\} \right\}, \tag{47} \]
5. Numerical Results and Cost-Effectiveness Analysis

In this section, numerical simulations and cost-effectiveness analysis [40] are performed to illustrate the effects of control smoking by different control strategies. We apply the parameter values listed in Table 1 to obtain numerical results for the optimal system by using a forward-backward iterative method [41]. The cost-effectiveness of alternative combinations of the two control measures will be investigated.

According to the method mentioned in [27, 29, 40] and our prior work [42], we will focus on comparing the following three control strategies. Strategy a: The combination of media coverage and smoking cessation treatment is implemented to combat smoking habit. For this case, $u_1$ and $u_2$ are defined as control variables. Strategy b: Single media coverage is performed. In this case, only $u_1$ is taken as control variable. Strategy c: Single treatment measure is carried out. In this case, only $u_2$ is seen as the control variable. Our purpose is to provide an analytical method for the strategic decision-makers. Due to the lack of the available literatures and data, as an example, we take cost coefficients $\epsilon_1 (i = 0, 1, 2, 3, 4)$ as $\epsilon_0 = 1$, $\epsilon_1 = 1$, $\epsilon_2 = 1$, $\epsilon_3 = 36$, $\epsilon_4 = 36$, and $b_1 = 0.8$, respectively. The maximums of $u_1(t)$ and $u_2(t)$ are taken as 1 and 4, respectively. The smoking-prevent equilibrium $E_a$ is served as the initial point of system (35), and the control period is taken as 20 years, i.e., $t_f = 20 \times 365 = 7300$ days (where $E_a = (1.011 \times 10^6, 6.4411 \times 10^6, 1.4693 \times 10^6, 2.6111 \times 10^6, 1.0258 \times 10^6, 1.0472 \times 10^7)$).

5.1. Strategy a: The Combination of Media Coverage and Smoking Cessation Treatment. For this strategy, corresponding optimal control variables $u_1^*(t)$, $u_2^*(t)$ and optimal state variables $S^*(t)$, $C^*(t)$ are depicted in Figures 3(a)–3(d), respectively.

Figures 3(a) and 3(b) tell us that media coverage intensity and treatment intensity almost always take their maximum and then subsequently reduce to zero. From Figures 3(c) and 3(d), we know that adopting optimal combined control strategies $u_1^*(t)$, $u_2^*(t)$ can significantly reduce the numbers of smokers and patients with smoking-related illnesses. In order to more clearly show the efficacy of strategy a, the efficacy function of smokers averted by strategy $a$ is defined as

$$E_{aS} = \frac{S(0) - S_a^*(t)}{S(0)},$$

where $S(0)$ is the initial number of smokers and $S_a^*(t)$ is the corresponding optimal state associated with optimal control strategy $a$. Efficacy function of smokers $E_{aS}^*(t)$ is depicted in Figure 4(a), which indicates that taking the optimal combined control strategy $a$ can reduce the number of smokers be highest up to more than 98%. Similarly, the efficacy function of patients with smoking-related illnesses averted by strategy $a$ is defined as

$$E_{aC} = \frac{C(0) - C_a^*(t)}{C(0)},$$

where $C(0)$ represents the initial number of patients with smoking-related illnesses and $C_a^*(t)$ is the corresponding optimal state associated with optimal control strategy $a$. The corresponding plot is shown in Figure 4(b), from which we can know that taking the optimal control measures $u_1^*(t)$, $u_2^*(t)$ can make decrements of patients be highest up to more than 60%. In a word, optimal strategy $a$ is very effective in controlling smoking.

To investigate the cost-effectiveness of different control strategies, the total occasional smokers averted by the optimal strategy $a$ during the time period $t_f$ is firstly defined as

$$A_{aS} = t_f S(0) - \int_0^{t_f} S_a^*(t) dt,$$

where $S_a^*(t)$ is optimal state associated with the optimal strategy $a$ and $S(0)$ is the initial number of occasional smokers. Similarly, the total smokers and patients with smoking-related illness averted by the optimal strategy $a$ during the time period $t_f$ are, respectively, defined as

$$A_{aS} = t_f S(0) - \int_0^{t_f} S_a^*(t) dt,$$

$$A_{aC} = t_f C(0) - \int_0^{t_f} C_a^*(t) dt,$$

where $S_a^*(t)$ and $C_a^*(t)$ are optimal states associated with the optimal control of strategy $a$, and $S(0)$ and $C(0)$ are the initial numbers of smokers and patients, respectively. We expect that the numbers of occasional smokers and smokers are as less as possible. Especially, we further expect that the numbers of smokers and patients is very effective.

For strategy $a$, we can, respectively, calculate the values of $A_{aS}$, $A_{aS}$, $A_{aC}$, $TA_a$, and $C_{Ta}$ (see Table 2).

5.2. Strategies b and c: Single Media Coverage and Single Smoking Cessation Treatment. For single media convergence strategy, we take $u_1$ as the control variable to minimize the objective functional $C_f (36)$ and take $u_2 = 0$. Similarly, for single smoking cessation treatment strategy, we take $u_2$ as the control variable and set $u_1 = 0$. The optimal control variables of $u_1^*(t)$ and $u_2^*(t)$ for strategies b and c are shown in Figures 5(a) and 5(b), respectively. Corresponding optimal state variables $S^*(t)$ and $P^*(t)$ are depicted in Figures 5(c) and 5(d), respectively.
Similarly, the efficacy functions of smokers and patients averted for strategy $k$ ($k = b$ or $c$) are also, respectively, defined as

$$E_{kS} = \frac{S(0) - S^*_k(t)}{S(0)},$$

$$E_{kC} = \frac{C(0) - C^*_k(t)}{C(0)}, \quad (k = b \text{ or } c).$$

The corresponding time series of efficacy functions are depicted in Figures 6(a) and 6(b), respectively.

The results of the strategy $b$ are denoted by the blue dotted lines, while the results of the strategy $c$ are represented by the red solid lines. From Figures 5(a), 5(c), 5(d), 6(a), and 6(b), we know that taking single high-intensity media coverage can effectively combat smoking behavior. Similarly, Figures 5(b)–5(d) tell us that single treatment measure can also obviously reduce the numbers of smokers and patients with smoking-related illnesses. In comparison, single optimal media coverage measure is more effective than single treatment strategy in controlling smoking and reducing the number of patients with smoking-related illnesses. Furthermore, for single media coverage strategy $b$ and single smoking cessation strategy $c$, the values of $A_{kL}$, $A_{kS}$, $A_{kC}$, $T_{Ak}$, and $C_{Tk}$ ($k = b$ or $c$) are, respectively, calculated and listed in Table 2.

5.3. Cost-Effectiveness Analysis. In this subsection, the cost-effectiveness of the three alternative strategies is investigated by the incremental cost-effectiveness ratio mentioned in [27–29, 40]. The differences between the costs and health
outcomes of different control strategies are compared by this ratio, which is used to investigate the additional cost per additional health outcome. Based on the method mentioned in [27–29, 40], we rank the strategies in increasing order of effectiveness for the total cases (including occasional smokers, smokers, and patients) averted by strategy $k$ ($k = a, b, c$) and list them in Table 3.

Next, we define and calculate the ICERs as follows:

$$\text{ICER}_k = \frac{C_{T_k} - C_{T_{Ta}}} {TA_k - TA_a} = 5.7229 \times 10^{10} - 5.7229 \times 10^{10} - 1.3131 \times 10^{10} - 1.0139 \times 10^{10} = -3.0034.$$  

(54)

Comparing ICER$_b$ with ICER$_c$, reveals a cost-saving of 3.0034 for strategy $b$ over strategy $c$, which indicates that strategy $b$ is more inexpensive and more effective than strategy $c$. Hence, the single smoking cessation strategy is ruled out from the set of alternatives strategies. We rule out strategy $b$, which is more costly and less effective than strategy $c$.

Hence, we can get the following values of the ICER:

\[
\text{ICER}_b = \frac{C_{T_b}} {TA_b} = 5.7229 \times 10^{10} = 4.7470,
\]

\[
\text{ICER}_a = \frac{C_{T_a} - C_{T_b}} {TA_a - TA_b} = 5.1856 \times 10^{10} - 5.3703 \times 10^{10} - 1.1929 \times 10^{10} - 1.1313 \times 10^{10} = -0.2315.
\]

(55)

From above calculations, we know that strategy $b$ is more costly and less effective than strategy $a$. Therefore, strategy $b$ is excluded. Consequently, strategy $a$, combining of mass media and smoking cessation treatment, is the most cost-effective among the three strategies considered.

### 6. Further Discussion and Conclusion

In this paper, we apply an example to investigate the effects of media coverage and smoking cessation treatment on controlling smoking. Firstly, we give the concrete form of the basic reproduction number $R_0$ and discuss the existence and stabilities of equilibria. Secondly, from the estimated parameter values, we obtain the basic reproduction numbers $R_0$.
smoking behavior. Finally, from the numerical results and cost-effectiveness analysis, we conclude that the combination of media coverage and smoking cessation treatment is the most cost-effective strategy. Although we have investigated the effects of media coverage and smoking cessation treatment in controlling smoking, we still do not consider the impact of second-hand smoke on nonsmokers. We will use the real data about tobacco in China to model the parameters and discuss the impact of second-hand smoke on individuals, society, and economy in our future work.

Appendix

A. Proof of $b_1 b_2 b_3 - b_1^2 - b_1^2 b_4 > 0$

Proof. For the sake of convenience, we let $x = bc - \alpha \gamma \delta$. Note that $bc - \alpha \gamma \delta > 0$, so $x > 0$.

Since

$$b_1 = \mu + \beta S_* + a + b + c,$$
$$b_2 = (\mu + \beta S_*)(a + b + c) + (bc - \alpha \gamma \delta) + (ab - \omega \beta P_*) + ac,$$
$$b_3 = (\mu + \beta S_*)((bc - \alpha \gamma \delta) + (ab - \omega \beta P_*) + ac) + \beta S_\omega \beta P_*,$$
$$b_4 = \beta S_* \beta \omega P_* c,$$

we can easily obtain

$$ab - \omega \beta P_* = \frac{\alpha \gamma \delta a}{c},$$
$$\beta S_* = \mu (R_0 - 1),$$
$$\mu + \beta S_* = \mu R_0,$$
$$\beta \omega P_* c = ax,$$
$$\beta \omega P_* = \frac{ax}{c}.$$

Hence, we rewrite $b_1, b_2, b_3, b_4$ as follows:

Table 3: Incremental cost-effectiveness ratio in increasing order of total cases averted.

| Strategy $k$ | Total cases averted $TA$ | Total cost $C_T$ | ICER |
|--------------|--------------------------|-----------------|------|
| No strategy  | 0                        | 0               | -    |
| Strategy c   | $1.0139 \times 10^{10}$  | $5.7229 \times 10^{10}$ | 5.6444 |
| Strategy b   | $1.1313 \times 10^{10}$  | $5.3703 \times 10^{10}$ | -3.0034 |
| Strategy a   | $1.1929 \times 10^{10}$  | $5.1856 \times 10^{10}$ | -0.2315 |
where

\[ d_i = (a + b + c)(x + ac + \frac{ay\delta a}{c})^2, \]

\[ d_2 = (a + b + c)^2(x + ac + \frac{ay\delta a}{c}), \]

\[ d_3 = (a + b + c)(x + ac + \frac{ay\delta a}{c}). \]

\[ d_4 = x^2 + \frac{ax(c^2 + ay\delta a + a^2(c^2 + 2c^2\alpha y\delta a + \alpha y\delta(x + ay\delta)))}{c}. \]

\[ d_5 = 2c^2(b + c)^2x + c(2c^2 + x + 2ay\delta)(b^2 + c^2 + 3x + 2ay\delta)a \]

\[ + (4c^4 + x^2 + c^2(x + 4ay\delta + b(c(4c^2 + x + 4ay\delta)a^2 + c(2c^2 + x + 2ay\delta)a)^3, \]

\[ d_6 = \frac{1}{c}(3c(b + c)x + a^2(b(c + 3c^2 + 2ay\delta) + a(b^3 + 6bc^2 + 3c^2 + 2b\alpha y\delta)), \]

\[ d_7 = \frac{1}{c}(aay\delta(2ab + b^2 + 3ay\delta) + a(ab + b^2 + 6ay\delta)x + 2ax^2) + a^2(ab + 4ay\delta) \]

\[ + (2a^2 + b^2)x + (a^3 + 2ay\delta) + (3a + 2b)x)c + (2a^2 + x)c^2 + ac^3, \]

\[ d_8 = \frac{1}{c}(3c(b + c)x + a^2(2x + 3c^2 + 3ay\delta) + a(3c^3 + 6bc^2 + 2bx + 3by\delta)), \]

\[ d_9 = (b + c)(x + ab + ac + a^2). \]

Obviously \(d_i > 0, \quad i = 1, \ldots, 9\). Note that \(\mathcal{R}_0 > 1\); hence, \(b_1b_2b_3 - b_3^2 - b_1^2b_4 > 0\). □

The third additive compound matrix \(A^{[3]}\) for a matrix \(A = (a_{ij})_{4 \times 4}\) is given by:

\[ b_1 = \mu(\mathcal{R}_0 + a + b + c), \]

\[ b_2 = \mu(\mathcal{R}_0)(a + b + c) + x + \frac{ay\delta a}{c} + ac, \]

\[ b_3 = \mu(\mathcal{R}_0)(x + \frac{ay\delta a}{c} + ac) + \mu(\mathcal{R}_0 - 1)\frac{ax}{c}, \]

\[ b_4 = \mu(\mathcal{R}_0 - 1)ax. \]

In the following, we will calculate \(b_1b_2b_3 - b_3^2 - b_1^2b_4\):

\[ b_1b_2b_3 - b_3^2 - b_1^2b_4 = (\mu(\mathcal{R}_0 + a + b + c)(\mu(\mathcal{R}_0)(a + b + c) + x + \frac{ay\delta a}{c} + ac)(\mu(\mathcal{R}_0)(x + \frac{ay\delta a}{c} + ac) + \mu(\mathcal{R}_0 - 1)\frac{ax}{c}) \]

\[ - (\mu(\mathcal{R}_0)(x + \frac{ay\delta a}{c} + ac) + \mu(\mathcal{R}_0 - 1)\frac{ax}{c})^2 - \mu(\mathcal{R}_0 + a + b + c)^2\mu(\mathcal{R}_0 - 1)ax \]

\[ = d_1\mu + d_2\mu^2 + d_3\mu^3 + (a + b + c)d_4\mu + \frac{1}{c^2}d_5\mu^2 + d_6\mu^3)(\mathcal{R}_0 - 1) + (d_7\mu^2 + d_8\mu^3)(\mathcal{R}_0 - 1)^2 + d_9\mu^3(\mathcal{R}_0 - 1)^3, \]

\(\text{(A.5)}\)

**B. The Third Additive Compound Matrix**
Data Availability

In this paper, partial parameter values are cited from the previous literatures which are listed in our references. Due to the lack of the available literatures and data, the other parameter values are based on some reasonable assumptions (see details in Section 3.3). All of the Matlab codes which are related to this paper can be provided at any time.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

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\[ A^{[3]} = \begin{bmatrix} a_{11} + a_{22} + a_{33} & a_{34} & -a_{24} & a_{14} \\ a_{43} & a_{11} + a_{22} + a_{44} & a_{23} & -a_{13} \\ -a_{42} & a_{32} & a_{11} + a_{33} + a_{44} & a_{12} \\ a_{41} & -a_{31} & a_{21} & a_{22} + a_{33} + a_{44} \end{bmatrix}. \] (B.1)

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