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Original article

Optimal control for a fractional tuberculosis infection model including the impact of diabetes and resistant strains

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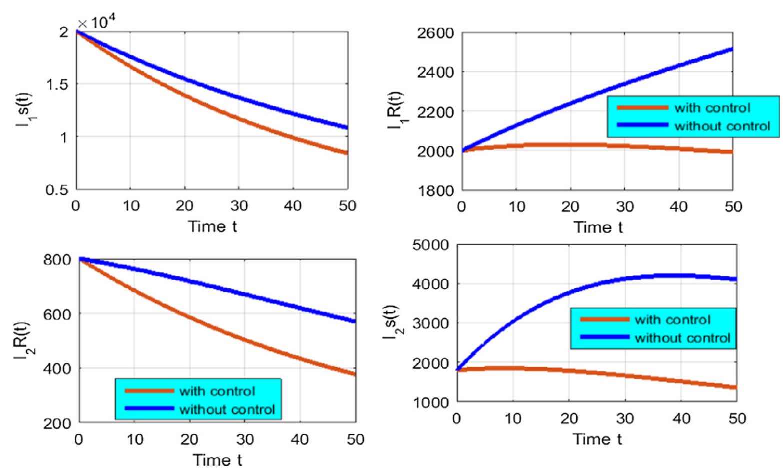
HIGHLIGHTS

- Optimal control problem for the fractional TB infection model is presented.
- The nonstandard two-step Lagrange interpolation method is presented for numerically solving the optimality system.
- Necessary and sufficient conditions that guarantee the existence and the uniqueness of the solution of the control problem are given.
- Four controls variables are proposed to minimize the cost of interventions.
- New numerical schemes for simulating fractional order optimality system with Mittag-Leffler kernel are given.

GRAPHICAL ABSTRACT



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ABSTRACT

The objective of this paper is to study the optimal control problem for the fractional tuberculosis (TB) infection model including the impact of diabetes and resistant strains. The governed model consists of 14 fractional-order (FO) equations. Four control variables are presented to minimize the cost of interventions. The fractional derivative is defined in the Atangana-Baleanu-Caputo (ABC) sense. New numerical schemes for simulating a FO optimal system with Mittag-Leffler kernels are presented. These schemes are based on the fundamental theorem of fractional calculus and Lagrange polynomial interpolation. We introduce a simple modification of the step size in the two-step Lagrange polynomial interpolation to obtain stability in a larger region. Moreover, necessary and sufficient conditions for the control problem are considered. Some numerical simulations are given to validate the theoretical results.

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Introduction

A new study suggests that millions of people with high blood sugar may be more likely to develop tuberculosis (TB) than previously expected. TB is a severe infection that is caused by bacteria in the lungs and kills many people each year, in addition to HIV/AIDS and malaria, according to the Daily Mail website [1]. In 2017, according to the World Health Organization nearly 10 million people were infected with TB [2]. Experts are concerned that a global explosion in the number of diabetes cases will put millions of people at risk [3].

Many mathematical models have been proposed to elucidate the patterns of TB [4–7], Recently, Khan et al., [8], presented a new fractional model for tuberculosis. In addition, several papers considered modeling TB with diabetes; see, for example, [9–12]. Recently, Carvalho and Pinto presented non-integer-order analysis of the impact of diabetes and resistant strains in a model of TB infection [13]. Fractional-order (FO) models provide more accurate and deeper information about the complex behaviors of various diseases than can classical integer-order models. FO systems are superior to integer-order systems due to their hereditary properties and description of memory [14–28]. Fractional optimal control problems (FOCPs) are optimal control problems associated with fractional dynamic systems. Fractional optimal control theory is a very new topic in mathematics. FOCPs may be defined in terms of different types of fractional derivatives. However, the most important types of fractional derivatives are the Riemann-Liouville and Caputo fractional derivatives [29–40]. In addition, the theory of FOCPs has been under development. Recently, some interesting real-life models of optimal control problems (OCPs) were presented elsewhere [41–52].

A new concept of differentiation was introduced in the literature whereby the kernel was converted from non-local singular to non-local and non-singular. One of the great advantages of this new kernel is its ability to portray fading memory as well as the well-defined memory of the system under investigation. A new FO derivative, based on the generalized Mittag-Leffler function as a non-local and non-singular kernel, was presented by Atangana and Baleanu [14] in 2016. The newly introduced Atangana-Beleanu derivative has been applied in the modeling of various real-world problems in different fields, as previously discussed [15–22]. This derivative, based on the Mittag-Leffler function, is more suitable for describing real-world complex problems. Numerical and analytical methods are very useful because they can play very necessary roles in characterizing the behavior of the solution of the fractional differential equations, as shown in [15–27].

To the best of our knowledge, the optimal control for a FO tuberculosis infection model that includes diabetes and resistant strains has never been explored. The main contribution of this work is to propose a class of FOCPs and develop a numerical scheme to provide an approximate solution for those FOCPs. We consider the mathematical model in Khan et al. [8], and the fractional derivative is defined here in the Atangana-Baleanu-Caputo (ABC) sense. A new generalized numerical scheme for simulating a FO optimal system with Mittag-Leffler kernels is established. These schemes are based on the fundamental theorem of fractional calculus and Lagrange polynomial interpolation. This paper was organized as follows. Fundamental relations are given in "Fundamental Relations". In "Fractional Model for TB Infection Including the Impact of Diabetes and Resistant Strains", the fractional-order model with four control variables is introduced. The proposed control problem with the optimality conditions is given in "Formulation of the Fractional Optimal Control Problem". In "Numerical Techniques for the Fractional Optimal Control Model", numerical schemes with exponential and Mittag-Leffler laws are presented. Numerical experiments are given in "Numerical Simulations". In "Conclusions", the conclusions are presented.

Fundamental relations

In the following, the basic fractional-order derivative definitions used in this paper are given.

Definition 1. The Liouville-Caputo FO derivative is defined as in [53]:

$$ {}_{a}^{C}D_t^{\alpha} g(t) = \frac{1}{\Gamma(1-\alpha)} \int_0^t (t-q)^{-\alpha} \dot{g}(q)dq, \quad 0 < \alpha \le 1. \tag{1}$$

Definition 2. The Atangana-Baleanu fractional derivative in the Liouville-Caputo sense is defined as in [14]:

$$ {}_{a}^{ABC}D_t^{\alpha} g(t) = \frac{B(\alpha)}{(1-\alpha)} \int_0^t (E_{\alpha}(-\alpha \frac{(t-q)^{\alpha}}{(1-\alpha)}) \dot{g}(q)dq\,, \tag{2}$$

where $B(\alpha) = 1 - \alpha + \frac{\alpha}{\Gamma(\alpha)}$ is the normalization function.

Definition 3. The corresponding fractional integral concerning the Atangana–Baleanu-Caputo derivative is defined as [14]

$$ {}_{a}^{ABC}I_t^{\alpha} g(t) = \frac{(1-\alpha)}{B(\alpha)} g(t) + \frac{\alpha}{B(\alpha)\Gamma(\alpha)} \int_0^t (t-q)^{\alpha-1} \dot{g}(q)dq,$$

They found that when α is zero, they recovered the initial function, and if α is 1, they obtained the ordinary integral. In addition, they computed the Laplace transform of both derivatives and obtained the following:

$$\{ {}_{0}^{ABC}D_t^{\alpha} g(t)\} = \frac{B(\alpha)G(p)p^{\alpha} - p^{\alpha-1}g(0)}{(1-\alpha)(p^{\alpha} + \frac{\alpha}{(1-\alpha)})}$$

Theorem 1. *For a function $g \in C\,[a, b]$, the following result holds* [9]:

$$|| {}_{a}^{ABC}D_t^{\alpha} g(t)|| < \frac{B(\alpha)}{(1-\alpha)} ||g(t)||, \ \ where \ \ ||g(t)|| = max_{a \le t \le b}|g(t)|,$$

Further, the Atangana–Baleanu-Caputo derivatives fulfill the Lipschitz condition [9]:

$$|| {}_{a}^{ABC}D_t^{\alpha} g_1(t) - {}_{a}^{ABC}D_t^{\alpha} g_2(t)|| < \ \varpi ||g_1(t) - g_2(t)||$$

Fractional model for TB infection including the impact of diabetes and resistant strains

In this section, we study fractional optimal control for TB infection including the impact of diabetes and resistant strains, as given in Carvalho and Pinto [13]. So that the reader can make sense of the model, Fig. 1 shows the flowchart of the model as given in Carvalho and Pinto [13]. The fractional derivative here is defined in the ABC sense. We add four control functions, u_1, u_2, u_3 and u_4, and four real positive model constants, $\omega_i, \ i = 1,2,3,4$ *and* $\omega_i \in (0,1)$. These controls are given to prevent the failure of treatment in I_{1s}, I_{1R}, I_{2s} and I_{2R}, e.g., patients' health care providers encourage them to complete the treatments by taking TB and diabetes medications regularly. This model consists of fourteen classes. Let us consider the population to be divided into diabetic (index 1) and non-diabetic

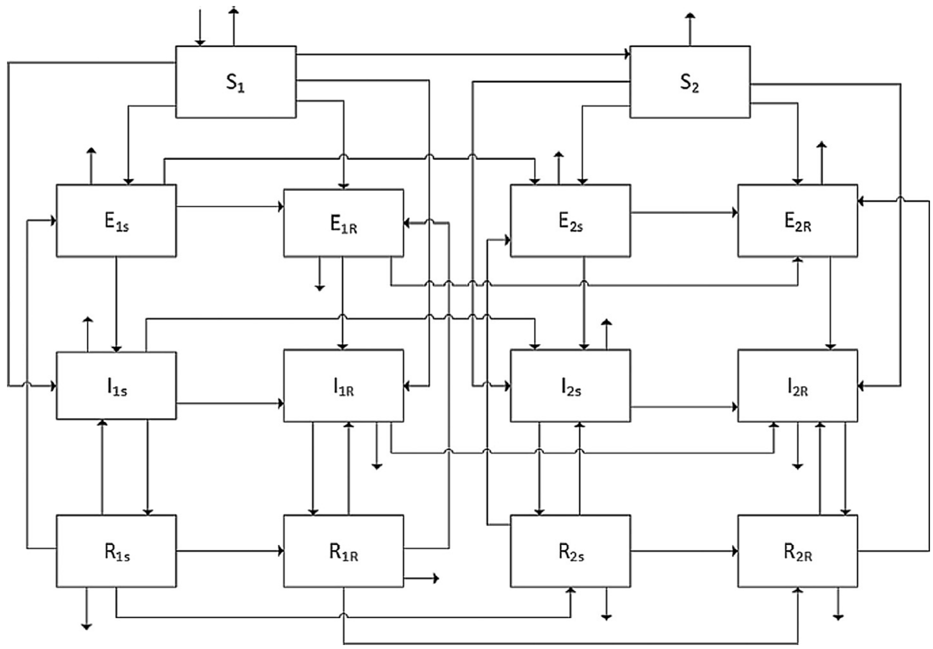

Fig. 1. Flowchart of the model [13].

(index 2). Then, we have susceptible individuals (S_2 and S_1), individuals exposed and sensitive to TB (E_{2s} and E_{1s}), individuals exposed and resistant to TB (E_{2R} and E_{1R}), individuals infected with and sensitive to TB (I_{2s} and I_{1s}), individuals infected with and resistant to TB (I_{2R} and I_{1R}), individuals recovering from and sensitivite to TB (R_{2s} and R_{1s}), and individuals recovering from and resistant to TB (R_{2R} and R_{1R}). All the parameters for the modified model in Table 1, depend on the FO because the use of the constant parameter α instead of an integer parameter can lead to better results, as one has an extra degree of freedom [40]. The main assumption of this model is that the total population N is a constant in time, i.e., the birth and death rates are equal and $d_1^\alpha = d_2^\alpha = 0$. The resulting model with four controls is given as follows:

$$ {}^{ABC}_{a}D_t^\alpha S_1 = A^\alpha - (\mu^\alpha + \alpha_D^\alpha + \lambda_T)S_1, \tag{3}$$

$$ {}^{ABC}_{a}D_t^\alpha S_2 = \alpha_D^\alpha S_1 - (\mu^\alpha + \theta\lambda_T)S_2, \tag{4}$$

$$ {}^{ABC}_{a}D_t^\alpha E_{1s} = (1-\xi)(1-P_1)\lambda_T S_1 + \sigma_{31}(1-\delta_1^\alpha R_{1s}) - (1-r_1^\alpha)(k_1^\alpha + \sigma_1\lambda_T)E_{1s} - (\xi + \alpha_D^\alpha + \mu^\alpha)E_{1s}, \tag{5}$$

$$ {}^{ABC}_{a}D_t^\alpha E_{1R} = \xi(1-P_1)\lambda_T S_1 + \xi E_{1s} + \sigma_{32}(1-\delta_1^\alpha \lambda_T R_{1R}) - (1-r_1^\alpha) \times (k_1^\alpha + \sigma_1\lambda_T)E_{1R} - (\alpha_D^\alpha + \mu^\alpha)E_{1R}, \tag{6}$$

$$ {}^{ABC}_{a}D_t^\alpha E_{2s} = (1-\xi)(1-P_2)\theta\lambda_T S_2 + \sigma_{41}\left(1-\delta_2^\alpha\right)\theta\lambda_T R_{2s} + \alpha_D^\alpha E_{1s} - (1-r_2^\alpha)(k_2^\alpha + \sigma_2\theta\lambda_T)E_{2s} - (\xi + \mu^\alpha)E_{2s}, \tag{7}$$

$$ {}^{ABC}_{a}D_t^\alpha E_{2R} = \xi(1-P_2)\theta\lambda_T S_2 + \xi E_{2s} + \sigma_{42}\left(1-\delta_2^\alpha\right)\theta\lambda_T R_{2R} + \alpha_D^\alpha E_{1R} - (1-r_2^\alpha)(k_2^\alpha + \sigma_2\theta\lambda_T)E_{2R} - \mu^\alpha E_{2R}, \tag{8}$$

$$ {}^{ABC}_{a}D_t^\alpha I_{1s} = (1-\xi)P_1\lambda_T S_1 + (1-r_1^\alpha)(k_1^\alpha + \sigma_1\lambda_T)E_{1s} + \delta_{11}^\alpha R_{1s} - (\tau_1\alpha_D^\alpha + \eta_1\xi + \gamma_{11}^\alpha + \mu^\alpha + d_1^\alpha + \omega_1 u_1)I_{1s}, \tag{9}$$

$$ {}^{ABC}_{a}D_t^\alpha I_{1R} = \xi P_1\lambda_T S_1 + (1-r_1^\alpha)(k_1^\alpha + \sigma_1\lambda_T)E_{1R} + \eta_1\xi I_{1s} + \delta_{12}^\alpha R_{1R} - (\tau_1\alpha_D^\alpha + \gamma_{12}^\alpha + \mu^\alpha + d_1^\alpha + \omega_2 u_2)I_{1R} \tag{10}$$

$$ {}^{ABC}_{a}D_t^\alpha I_{2s} = (1-\xi)P_2\theta\lambda_T S_2 + \left(1-r_2^\alpha\right)\left(k_{21}^\alpha + \sigma_2\theta\lambda_T\right)E_{2s} + \tau_1\alpha_D^\alpha I_{1s} + \delta_{21}^\alpha R_{2s} - (\eta_2\xi + \gamma_{21}^\alpha + \mu^\alpha + d_2^\alpha + \omega_3 u_3)I_{2s}, \tag{11}$$

$$ {}^{ABC}_{a}D_t^\alpha I_{2R} = \xi P_2\theta\lambda_T S_2 + (1-r_2^\alpha)(k_2^\alpha + \sigma_2\theta\lambda_T)E_{2R} + \eta_2\xi I_{2s} + \tau_1\alpha_D^\alpha I_{1R} + \delta_{22}^\alpha R_{2R} - (\gamma_{22}^\alpha + \mu^\alpha + d_2^\alpha + \omega_4 u_4)I_{2R}, \tag{12}$$

$$ {}^{ABC}_{a}D_t^\alpha R_{1s} = \gamma_{11}^\alpha I_{1s} + \omega_1 u_1 I_{1s} - \sigma_{31}(1-\delta_1^\alpha)\lambda_T R_{1s} - (\delta_{11}^\alpha + \xi + \alpha_D^\alpha + \mu^\alpha)R_{1s} \tag{13}$$

$$ {}^{ABC}_{a}D_t^\alpha R_{1R} = \gamma_{21}^\alpha I_{1R} + \omega_2 u_2 I_{1R} + \xi R_{1s} - \sigma_{32}(1-\delta_1^\alpha\lambda_T R_{1R}) - (\delta_{12}^\alpha + \alpha_D^\alpha + \mu^\alpha)R_{1R}, \tag{14}$$

$$ {}^{ABC}_{a}D_t^\alpha R_{2s} = \gamma_{21}^\alpha I_{2s} + \omega_3 u_3 I_{2s} + \alpha_D^\alpha R_{1s} - \sigma_{41}\theta(1-\delta_2^\alpha)\lambda_T R_{2s} - (\delta_{21} + \xi + \mu^\alpha)R_{2s}, \tag{15}$$

$$ {}^{ABC}_{a}D_t^\alpha R_{2R} = \gamma_{22}^\alpha I_{2R} + \omega_4 u_4 I_{2R} + \xi R_{2s} + \alpha_D R_{1R} - \sigma_{42}\theta\left(1-\delta_2^\alpha\right)\lambda_T R_{2R} - (\delta_{22}^\alpha + \mu^\alpha)R_{2R} \tag{16}$$

where

$$\lambda_T = \beta\frac{I_{1s} + \varepsilon I_{1R} + \varepsilon_1 I_{2s} + \varepsilon_2 I_{2R}}{N}$$

Control problem formulation

Let us consider the state system presented in Eqs. (3)–(16), in R^{14}, with the set of admissible control functions

$$\Omega = \{(u_1(.), u_2(.), u_3(.), u_4(.))|u_i \text{ is Lebsegue measurable on } [0,1],$$

$$0 \le u_1(.), u_2(.), u_3(.), u_4(.) \le 1, \ \forall t \in [0, T_f], \ \ i = 1,2,3,4\},$$

where T_f is the final time and $u_1(.), u_2(.), u_3(.)$ *and* $u_4(.)$ are controls functions.

Table 1
The parameters of systems (3)–(16) and their descriptions [13].

Parameter	Descriptions	Values
A^α	Recruitment rate	667685.
α_D^α	Diabetes acquisition rate	$\frac{9}{1000}yr^{-\alpha}$
β^α	Effective contact rate for TB infection	$\{5,8,9\}$
ε^α	Modification parameter	1.1
ε_1^α	Modification parameter	1.1
ε_2^α	Modification parameter	1.1
θ^α	Modification parameter	2
μ^α	Rate of natural death	$\frac{1}{53.5}yr^{-\alpha}$
ξ	Rate of TB infection among diabetic individuals	0.04
P_1	Rate of TB infection among non-diabetic individuals	0.03
P_2	Rate of TB infection among diabetic individuals	0.06
r_1^α	Non-diabetic individuals' chemoprophylaxis rate	$0yr^{-\alpha}$
r_2^α	Diabetic individuals' chemoprophylaxis rate.	$0yr^{-\alpha}$
σ_1	Non-diabetic individuals' degree of immunity	$0.75P_1$
σ_2	Diabetic individuals' degree of immunity	$0.7P_2$
k_1^α	Non-diabetic individuals' rate of endogenous reactivation	$0.00013yr^{-\alpha}$
k_2^α	Diabetic individuals' rate of endogenous reactivation	$2K_1yr^{-\alpha}$
γ_{11}^α	Non-diabetic individuals' sensitive TB infection recovery rate	$0.7372yr^{-\alpha}$
γ_{12}^α	Non-diabetic individuals' resistant TB infection recovery rate	$0.7372yr^{-\alpha}$
γ_{21}^α	Diabetic individuals' sensitive TB infection recovery rate	$0.7372yr^{-\alpha}$
γ_{22}^α	Diabetic individuals' resistant TB infection recovery rate	$0.7372yr^{-\alpha}$
d_1^α	Rate of death due to TB	$0yr^{-\alpha}$
d_2^α	Rate of death due to TB and diabetes	$0yr^{-\alpha}$
τ_1	Modification parameter	1.01
η_1	Modification parameter	1.01
η_2	Modification parameter	1.01
δ_1^α	Non-diabetic individuals of partial immunity	$0.0986yr^{-\alpha}$
δ_{11}^α	Non-diabetic individuals' partial immunity for sensitive recovered	$0.0986yr^{-\alpha}$
δ_{12}^α	Non-diabetic individuals' partial immunity after resistant recovery	$0.0986yr^{-\alpha}$
δ_2^α	Diabetic individuals' of partial immunity	$0.1yr^{-\alpha}$
δ_{21}^α	Sensitive recovered diabetic individuals' partial immunity	$0.1yr^{-\alpha}$
γ_{22}^α	Resistant recovered diabetic individuals' partial immunity	$0.1yr^{-\alpha}$
σ_{31}^α	Sensitive recovered non-diabetic individuals' degree of immunity	$0.73P_1$
σ_{32}^α	Resistant recovered non-diabetic individuals' degree of immunity	$0.73P_1$
σ_{41}^α	Sensitive recovered diabetic individuals' degree of immunity	$0.71P_2$
σ_{42}^α	Recovered diabetic individuals' degree of immunity	$0.71P_2$

The objective function is defined as follows:

$$J(u_1,u_2,u_3,u_4)=\int_0^{T_f}(I_{1s}+I_{1R}+I_{2s}+I_{2R}+\frac{B_1}{2}u_1^2(t)+\frac{B_2}{2}u_2^2(t)+\frac{B_3}{2}u_3^2(t)+\frac{B_4}{2}u_4^2(t))dt, \quad (17)$$

where B_1, B_2, B_3, and B_4 are the measure of the relative cost of the interventions associated with the controls u_1, u_2, u_3, and u_4.

Then, we find the optimal controls u_1,u_2,u_3 and u_4 that minimize the cost function

$$J(u_1,u_2,u_3,u_4)=\int_0^{T_f}\eta(S_1,S_2,E_{1s},E_{1R},E_{2s},E_{2R},I_{1s},I_{1R},I_{2s},I_{2R},R_{1s},R_{1R},R_{2s},R_{2R},u_1,u_2,u_3,u_4,t)dt, \quad (18)$$

subject to the constraint

$$ {}^{ABC}_{a}D_t^\alpha S_1=\xi_1,\ {}^{ABC}_{a}D_t^\alpha S_2=\xi_2,\ {}^{ABC}_{a}D_t^\alpha E_{1s}=\xi_3,$$

$$ {}^{ABC}_{a}D_t^\alpha E_{1R}=\xi_4,\ {}^{ABC}_{a}D_t^\alpha E_{2s}=\xi_5,\ {}^{ABC}_{a}D_t^\alpha E_{2R}=\xi_6,$$

$$ {}^{ABC}_{a}D_t^\alpha I_{1s}=\xi_7,\ {}^{ABC}_{a}D_t^\alpha I_{1R}=\xi_8,\ {}^{ABC}_{a}D_t^\alpha I_{2s}=\xi_9,$$

$$ {}^{ABC}_{a}D_t^\alpha I_{2R}=\xi_{10},\ {}^{ABC}_{a}D_t^\alpha R_{1s}=\xi_{11},\ {}^{ABC}_{a}D_t^\alpha R_{1R}=\xi_{12},$$

$$ {}^{ABC}_{a}D_t^\alpha R_{2s}=\xi_{13},\ {}^{ABC}_{a}D_t^\alpha R_{2R}=\xi_{14},$$

where

$$\xi_i=\xi(S_1,S_2,E_{1s},E_{1R},E_{2s},E_{2R},I_{1s},I_{1R},I_{2s},I_{2R},R_{1s},R_{1R},R_{2s},R_{2R},u_1,u_2,u_3,u_4,t),$$

$i=1,\dots,14$, and the following initial conditions are satisfied:

$$S_1(0)=S_{01},\ S_2(0)=S_{02},E_{1s}(0)=E_{1s0},E_{1R}(0)=E_{1R0},E_{2s}(0)=E_{2s0},$$
$$E_{2R}(0)=E_{2R0},I_{1s}(0)=I_{1s0},I_{1R}(0)=I_{1R0},I_{2s}(0)=I_{2s0},I_{2R}(0)=I_{2R0},$$
$$R_{1s}(0)=R_{1s0},R_{1R}(0)=R_{1R0},R_{2s}(0)=R_{2s0},R_{2R}(0)=R_{2R0}.$$

To define the FOCP, consider the following modified cost function [31]:

$$\tilde{J}=\int_0^{T_f}[H_a(S_1,S_2,E_{1s},E_{1R},E_{2s},E_{2R},I_{1s},I_{1R},I_{2s},I_{2R},R_{1s},R_{1R},R_{2s},R_{2R},u_j,t) -\sum_{i=1}^{14}(\lambda_i\xi_i(S_1,S_2,E_{1s},E_{1R},E_{2s},E_{2R},I_{1s},I_{1R},I_{2s},I_{2R},R_{1s},R_{1R},R_{2s},R_{2R},u_j,t)]dt, \quad (19)$$

where $j=1,2,3,4$, and $i=1,\dots,14$.

The Hamiltonian is given as follows:

$$H_a(S_1,S_2,E_{1s},E_{1R},E_{2s},E_{2R},I_{1s},I_{1R},I_{2s},I_{2R},R_{1s},R_{1R},R_{2s},R_{2R},u_j,\lambda_i,t) =\eta(S_1,S_2,E_{1s},E_{1R},E_{2s},E_{2R},I_{1s},I_{1R},I_{2s},I_{2R},R_{1s},R_{1R},R_{2s},R_{2R},u_j,t) +\sum_{i=1}^{14}\lambda_i\xi_i(S_1,S_2,E_{1s},E_{1R},E_{2s},E_{2R},I_{1s},I_{1R},I_{2s},I_{2R},R_{1s},R_{1R},R_{2s},R_{2R},u_j,t), \quad (20)$$

where, $j=1,2,3,4$, and $i=1,\dots,14$.

From Eqs. (19) and (20), the necessary and sufficient conditions for the FOCP [34–37] are as follows:

$$\begin{aligned}
&{}^{ABC}_{t}D_{t_f}^\alpha\lambda_1=\frac{\partial H_a}{\partial S_1},\ {}^{ABC}_{t}D_{t_f}^\alpha\lambda_2=\frac{\partial H_a}{\partial S_2},\\
&{}^{ABC}_{t}D_{t_f}^\alpha\lambda_3=\frac{\partial H_a}{\partial E_{1s}},\ {}^{ABC}_{t}D_{t_f}^\alpha\lambda_4=\frac{\partial H_a}{\partial E1R},\\
&{}^{ABC}_{t}D_{t_f}^\alpha\lambda_5=\frac{\partial H_a}{\partial E_{2s}},\ {}^{ABC}_{t}D_{t_f}^\alpha\lambda_6=\frac{\partial H_a}{\partial E_{2R}},\\
&{}^{ABC}_{t}D_{t_f}^\alpha\lambda_7=\frac{\partial H_a}{\partial I_{1s}},\ {}^{ABC}_{t}D_{t_f}^\alpha\lambda_8=\frac{\partial H_a}{\partial I_{1R}},\\
&{}^{ABC}_{t}D_{t_f}^\alpha\lambda_9=\frac{\partial H_a}{\partial I_{2s}},\ {}^{ABC}_{t}D_{t_f}^\alpha\lambda_{10}=\frac{\partial H_a}{\partial I_{2R}},\\
&{}^{ABC}_{t}D_{t_f}^\alpha\lambda_{11}=\frac{\partial H_a}{\partial R_{1s}},\ {}^{ABC}_{t}D_{t_f}^\alpha\lambda_{12}=\frac{\partial H_a}{\partial R_{1R}},\\
&{}^{ABC}_{t}D_{t_f}^\alpha\lambda_{13}=\frac{\partial H_a}{\partial R_{2s}},\ {}^{ABC}_{t}D_{t_f}^\alpha\lambda_{14}=\frac{\partial H_a}{\partial R_{2R}},
\end{aligned} \quad (21)$$

$$0=\frac{\partial H}{\partial u_k}, \quad (22)$$

$$ {}^{ABC}_{0}D^{\alpha}_{t}S_1=\frac{\partial H_a}{\partial\lambda_1},\ {}^{ABC}_{0}D^{\alpha}_{t}S_2=\frac{\partial H_a}{\partial\lambda_2}, $$

$$ {}^{ABC}_{0}D^{\alpha}_{t}E_{1s}=\frac{\partial H_a}{\partial\lambda_3},\ {}^{ABC}_{0}D^{\alpha}_{t}E_{1R}=\frac{\partial H_a}{\partial\lambda_4}, $$

$$ {}^{ABC}_{0}D^{\alpha}_{t}E_{2s}=\frac{\partial H_a}{\partial\lambda_5},\ {}^{ABC}_{0}D^{\alpha}_{t}E_{2R}=\frac{\partial H_a}{\partial\lambda_6}, $$

$$ {}^{ABC}_{0}D^{\alpha}_{t}I_{1s}=\frac{\partial H_a}{\partial\lambda_7},\ {}^{ABC}_{0}D^{\alpha}_{t}I_{1R}=\frac{\partial H_a}{\partial\lambda_8}, $$

$$ {}^{ABC}_{0}D^{\alpha}_{t}I_{2s}=\frac{\partial H_a}{\partial\lambda_9},\ {}^{ABC}_{0}D^{\alpha}_{t}I_{2R}=\frac{\partial H_a}{\partial\lambda_{10}}, $$

$$ {}^{ABC}_{0}D^{\alpha}_{t}R_{1s}=\frac{\partial H_a}{\partial\lambda_{11}},\ {}^{ABC}_{0}D^{\alpha}_{t}R_{1R}=\frac{\partial H_a}{\partial\lambda_{12}}, $$

$$ {}^{ABC}_{0}D^{\alpha}_{t}R_{2s}=\frac{\partial H_a}{\partial\lambda_{13}},\ {}^{ABC}_{0}D^{\alpha}_{t}R_{2R}=\frac{\partial H_a}{\partial\lambda_{14}}, $$

Moreover,

$$ \lambda_j(T_f)=0,\ \ \lambda_i,\ \ j=1,2,3,\ldots,14, \tag{23} $$

are the Lagrange multipliers. Eqs. (21) and (22) describe the necessary conditions in terms of a Hamiltonian for the optimal control problem defined above. We arrive at the following theorem:

Theorem 2. *Let S_1^*, S_2^*, E_{1R}^*, E_{1s}^*, E_{2R}^*, E_{2s}^*, I_{1R}^*, I_{1s}^*, I_{2s}^*, I_{2R}^*, R_{1R}^*, R_{1s}^*, R_{2R}^*, R_{2s}^* be the solutions of the state system and u_i^*, $i=1,\cdots,4$ be the given optimal controls. Then, there exists co-state variables $\lambda_j^*,\ j=1,\cdots,14$ satisfying the following:*

(i) Co-state equations:

$$ \begin{aligned} {}^{ABC}_{t}D^{\alpha}_{t_f}\lambda_1^* &= (-(\mu^{\alpha}+^{\alpha}_{D}+\lambda_T)\lambda_1^*+\alpha_D^{\alpha}\lambda_2+((1-\xi)(1-P_1)\lambda_T)\lambda_3^* \\ &\quad+(\xi(1-P_1)\lambda_T)\lambda_4^*+((1-\xi)P_1\lambda_T)\lambda_7^*+(\xi P_1\lambda_T)\lambda_8^*), \end{aligned} \tag{24} $$

$$ \begin{aligned} {}^{ABC}_{t}D^{\alpha}_{t_f}\lambda_2^* &= (-(\mu^{\alpha}+\theta\lambda_T)\lambda_2^*+((1-\xi)(1-P_2)\theta\lambda_T)\lambda_5^* \\ &\quad+(\xi(1-P_2)\theta\lambda_T)\lambda_6^*+(1-\xi)P_2\theta\lambda_T\lambda_9^*+\xi P_2\theta\lambda_T\lambda_{10}^*), \end{aligned} \tag{25} $$

$$ \begin{aligned} {}^{ABC}_{t}D^{\alpha}_{t_f}\lambda_3^* &= (-\lambda_3^*(1-r_1^{\alpha})(k_1^{\alpha}+\sigma_1\lambda_T)+\xi\lambda_4^*+(\alpha_D^{\alpha}E_{1s}^*)\lambda_5^* \\ &\quad+(1-r_1^{\alpha})(k_1^{\alpha}+\sigma\lambda_T)\lambda_7^*), \end{aligned} \tag{26} $$

$$ \begin{aligned} {}^{ABC}_{t}D^{\alpha}_{t_f}\lambda_4^* &= (-\lambda_4^*(1-r_1^{\alpha})(k_1^{\alpha}+\sigma_1\lambda_T)-(\alpha_D^{\alpha}+\mu^{\alpha})+\lambda_6^*\alpha_D^{\alpha} \\ &\quad+\lambda_8^*(1-r_1^{\alpha})(k_1^{\alpha}+\sigma_1\lambda_T)), \end{aligned} \tag{27} $$

$$ {}^{ABC}_{t}D^{\alpha}_{t_f}\lambda_5^*=\left(-\lambda_5^*\left(1-r_2^{\alpha}\right)\left(k_2^{\alpha}+\sigma_2\theta\lambda_T\right)+\xi\lambda_6^*+\lambda_9^*\left(1-r_2^{\alpha}\right)\left(k_2^{\alpha}+\sigma_2\theta\lambda_T\right)\right), \tag{28} $$

$$ {}^{ABC}_{t}D^{\alpha}_{t_f}\lambda_6^*=((-\lambda_6^*(1-r_2^{\alpha})(k_2^{\alpha}+\sigma_2\theta\lambda_T)+\mu^{\alpha})+\lambda_{10}^*(1-r_2^{\alpha})(k_2^{\alpha}+\sigma_2\theta\lambda_T)), \tag{29} $$

$$ \begin{aligned} {}^{ABC}_{t}D^{\alpha}_{t_f}\lambda_7^* &= (1-\frac{\beta}{N}S_1^*\lambda_1^*-\frac{\beta}{N}\theta S_2^*\lambda_2^*+(1-\xi)(1-P_1)\frac{\beta}{N}S_1^*\lambda_3^* \\ &\quad+\sigma_{31}(1-\delta_1^{\alpha})\frac{\beta}{N}R_{1s}^*\lambda_3^* \end{aligned} $$

$$ -(1-r_1^{\alpha})\frac{\beta}{N}E_{1s}^*\lambda_3^*+\xi(1-P_1)\frac{\beta}{N}S_1^*\lambda_4^*+\frac{\beta}{N}R_{1R}^*\lambda_4^*\sigma_{32}(1-\delta_1^{\alpha}) $$

$$ -(1-r_1^{\alpha})\sigma_1\frac{\beta}{N}E_{1R}^*\lambda_4^*+(1-\xi)(1-P_2)\theta\frac{\beta}{N}S_2^*\lambda_5^*+\sigma_{41}(1-\delta_2^{\alpha})\frac{\beta}{N}R_{2R}^*\lambda_5^* $$

$$ -(1-r_2^{\alpha})\sigma_2\theta\lambda_T E_{2s}\lambda_5^*+\xi(1-P_2)\theta\frac{\beta}{N}S_2^*\lambda_6^*+\frac{\beta}{N}\lambda_6^*\theta\sigma_{42} $$

$$ -(1-r_2^{\alpha})\sigma_2\theta\lambda_T E_{2R}\lambda_6^*+(1-\xi)P_1\frac{\beta}{N}S_1^*\lambda_7^*+(1-r_1^{\alpha})\sigma_1\theta\lambda_T E_{1s}\lambda_7^* $$

$$ +(\tau_1\alpha_D^{\alpha}+\eta\xi+\gamma_{11}+\mu^{\alpha}+d_1^{\alpha}+\omega_1u_1(t))\lambda_7^*+\xi P_1\frac{\beta}{N}S_1^*\lambda_8^*+(1-r_1^{\alpha}) \times\frac{\beta}{N}E_{1R}^*\lambda_8^*\sigma_1 $$

$$ +\eta_1\xi\lambda_7^*+(1-\xi)P_2\frac{\beta}{N}S_2^*\lambda_9^*\theta+\tau_1\alpha_D^{\alpha}\lambda_9^*+(1-r_2^{\alpha})\sigma_2\theta E_{2s}\frac{\beta}{N}\lambda_9^* $$

$$ +(1-r_2^{\alpha})\sigma_2\theta E_{2R}\frac{\beta}{N}\lambda_{10}^*+\xi P_2\frac{\beta}{N}S_2^*\lambda_{10}^*\theta+\gamma_{11}\lambda_{11}^*-\sigma_{31}(1-\delta_1^{\alpha})\frac{\beta}{N}R_{1s}^*\lambda_{11}^* $$

$$ +\sigma_{32}\left(1-\delta_1^{\alpha}\right)\frac{\beta}{N}R_{1R}^*\lambda_{12}^*+\sigma_{41}\left(1-\delta_2^{\alpha}\right)\frac{\beta}{N}R_{2s}^*\theta\lambda_{13}^* $$

$$ +\sigma_{42}(1-\delta_2^{\alpha})\frac{\beta}{N}R_{2R}^*\lambda_{14}^*), \tag{30} $$

$$ \begin{aligned} {}^{ABC}_{t}D^{\alpha}_{t_f}\lambda_8^* &= (1-\frac{\beta\varepsilon}{N}S_1^*\lambda_1^*-\frac{\beta\varepsilon}{N}\theta S_2^*\lambda_2^*+(1-\xi)(1-P_1)\frac{\beta\varepsilon}{N}S_1^*\lambda_3^* \\ &\quad+\sigma_{31}\left(1-\delta_1^{\alpha}\right)\frac{\beta\varepsilon}{N}R_{1s}^*\lambda_3^*-\left(1-r_1^{\alpha}\right)\frac{\beta\varepsilon}{N}E_{1s}^*\lambda_3^* \\ &\quad+\xi(1-P_1)\frac{\beta\varepsilon}{N}S_1^*\lambda_4^*+\frac{\beta\varepsilon}{N}R_{1R}^*\lambda_4^*\sigma_{32}\left(1-\delta_1^{\alpha}\right) \\ &\quad-\left(1-r_1^{\alpha}\right)\sigma_1\frac{\beta\varepsilon}{N}E_{1R}^*\lambda_4^*+(1-\xi)(1-P_2)\theta\frac{\beta\varepsilon}{N}S_2^*\lambda_5^* \\ &\quad+\sigma_{41}\left(1-\delta_2^{\alpha}\right)\frac{\beta\varepsilon}{N}R_{2R}^*\lambda_5^*-\left(1-r_2^{\alpha}\right)\sigma_2\theta\lambda_T E_{2s}\lambda_5^* \\ &\quad+\xi(1-P_2)\theta\frac{\beta\varepsilon}{N}S_2^*\lambda_6^*+\frac{\beta\varepsilon}{N}\lambda_6^*\theta\sigma_{42}-\left(1-r_2^{\alpha}\right)\sigma_2\theta\lambda_T E_{2R}^*\lambda_6^* \\ &\quad+(1-\xi)P_1\frac{\beta\varepsilon}{N}S_1^*\lambda_7^*+\left(1-r_1^{\alpha}\right)\sigma_1\theta\lambda_T E_{1s}\lambda_7^* \end{aligned} $$

$$ \begin{aligned} &+\left(\tau_1\alpha_D^{\alpha}+\gamma_{12}+\mu^{\alpha}+d^{\alpha}+\omega_2u_2(t)\right)\lambda_8^*+\xi P_1\frac{\beta\varepsilon}{N}S_1^*\lambda_8^* \\ &\quad+\left(1-r_1^{\alpha}\right)\frac{\beta\varepsilon}{N}E_{1R}^*\lambda_8^*\sigma_1+(1-\xi)P_2\frac{\beta\varepsilon}{N}S_2^*\lambda_9^*\theta+\tau_1\alpha_D^{\alpha}\lambda_9^* \\ &\quad+\left(1-r_2^{\alpha}\right)\sigma_2\theta E_{2s}^*\frac{\beta\varepsilon}{N}\lambda_9^* \end{aligned} $$

$$ \begin{aligned} &+(1-r_2^{\alpha})\sigma_2\theta E_{2R}\frac{\beta\varepsilon}{N}\lambda_{10}^*+\xi P_2\frac{\beta\varepsilon}{N}S_2^*\lambda_{10}^*\theta+\lambda_{10}^*\tau_1\alpha_D^{\alpha}+\gamma_{11}\lambda_{11}^* \\ &\quad-\sigma_{31}\left(1-\delta_1^{\alpha}\right)\frac{\beta\varepsilon}{N}R_{1s}^*\lambda_{11}^*+\sigma_{32}\left(1-\delta_1^{\alpha}\right)\frac{\beta\varepsilon}{N}R_{1R}^*\lambda_{12}^* \\ &\quad+\sigma_{41}\left(1-\delta_2^{\alpha}\right)\frac{\beta\varepsilon}{N}R_{2s}^*\theta\lambda_{13}^*+ \end{aligned} $$

$$ \sigma_{42}(1-\delta_2^{\alpha})\frac{\beta\varepsilon}{N}R_{2R}^*\lambda_{14}^*), \tag{31} $$

$$ \begin{aligned} {}^{ABC}_{t}D^{\alpha}_{t_f}\lambda_9^* &= (1-\frac{\beta\varepsilon_1}{N}S_1^*\lambda_1^*-\frac{\beta\varepsilon_1}{N}\theta S_2^*\lambda_2^*+(1-\xi)(1-P_1)\frac{\beta\varepsilon_1}{N}S_1^*\lambda_3^* \\ &\quad+\sigma_{31}(1-\delta_1^{\alpha})\frac{\beta\varepsilon_1}{N}R_{1s}^*\lambda_3^*-(1-r_1^{\alpha})\frac{\beta\varepsilon_1}{N}E_{1s}^*\lambda_3^* \\ &\quad+\xi(1-P_1)\frac{\beta\varepsilon_1}{N}S_1^*\lambda_4^*+\frac{\beta\varepsilon_1}{N}R_{1R}^*\lambda_4^*\sigma_{32}(1-\delta_1^{\alpha}) \\ &\quad-(1-r_1^{\alpha})\sigma_1\frac{\beta\varepsilon_1}{N}E_{1R}^*\lambda_4^*+(1-\xi)(1-P_2)\theta\frac{\beta\varepsilon_1}{N}S_2^*\lambda_5^* \\ &\quad+\sigma_{41}(1-\delta_2^{\alpha})\frac{\beta\varepsilon_1}{N}R_{2R}^*\lambda_5^*-(1-r_2^{\alpha})\sigma_2\theta\lambda_T E_{2s}\lambda_5^* \end{aligned} $$

$$+\xi(1-P_2)\theta\frac{\beta\varepsilon_1}{N}S_2^*\lambda_6^*+\frac{\beta\varepsilon_1}{N}\lambda_6^*\theta\sigma_{42}-(1-r_2^\alpha)\sigma_2\theta\lambda_T E_{2R}\lambda_6^*+$$

$$(1-\xi)P_1\frac{\beta\varepsilon_1}{N}S_1^*\lambda_7^*+(1-r_1^\alpha)\sigma_1\theta\lambda_T E_{1s}\lambda_7^*+\xi P_1\frac{\beta\varepsilon_1}{N}S_1^*\lambda_8^*+$$

$$(1-r_1^\alpha)\frac{\beta\varepsilon_1}{N}E_{1R}^*\lambda_8^*\sigma_1+(1-\xi)P_2\frac{\beta\varepsilon_1}{N}S_2^*\lambda_9^*\theta+\tau_1\alpha_D^\alpha\lambda_9^*$$
$$+(\eta_2\xi+\gamma_{21}+\mu^\alpha+d_2^\alpha+\omega_3u_3(t))\lambda_9^*+(1-r_2^\alpha)\sigma_2\theta E_{2s}^*\frac{\beta\varepsilon_1}{N}\lambda_9^*$$
$$+(1-r_2^\alpha)\sigma_2\theta E_{2R}^*\frac{\beta\varepsilon_1}{N}\lambda_{10}^*+\xi P_2\frac{\beta\varepsilon_1}{N}S_2^*\lambda_{10}^*\theta+\lambda_{10}^*\tau_1\alpha_D^\alpha$$
$$-\sigma_{31}(1-\delta_1^\alpha)\frac{\beta\varepsilon_1}{N}R_{1s}^*\lambda_{11}^*+\sigma_{32}(1-\delta_1^\alpha)\frac{\beta\varepsilon_1}{N}R_{1R}^*\lambda_{12}^*$$

$$+\sigma_{41}(1-\delta_2^\alpha)\frac{\beta\varepsilon_1}{N}R_{2s}^*\theta\lambda_{13}^*+\sigma_{42}(1-\delta_2^\alpha)\frac{\beta\varepsilon_1}{N}R_{2R}^*\lambda_{14}^*),\tag{32}$$

$$^{ABC}_{t}D^\alpha_{t_f}\lambda_{10}^*=(1-\frac{\beta\varepsilon_2}{N}S_1^*\lambda_1^*-\frac{\beta\varepsilon_2}{N}\theta S_2^*\lambda_2^*+(1-\xi)(1-P_1)\frac{\beta\varepsilon_2}{N}S_1^*\lambda_3^*$$

$$+\sigma_{31}(1-\delta_1^\alpha)\frac{\beta\varepsilon_2}{N}R_{1s}^*\lambda_3^*-(1-r_1^\alpha)\frac{\beta\varepsilon_2}{N}E_{1s}\lambda_3^*+\xi(1-P_1)\frac{\beta\varepsilon_2}{N}S_1^*\lambda_4^*$$

$$+\frac{\beta\varepsilon_2}{N}R_{1R}^*\lambda_4^*\sigma_{32}(1-\delta_1^\alpha)-(1-r_1^\alpha)\sigma_1\frac{\beta\varepsilon_2}{N}E_{1R}^*\lambda_4^*$$
$$+(1-\xi)(1-P_2)\theta\frac{\beta\varepsilon_2}{N}S_2^*\lambda_5^*+\sigma_{41}(1-\delta_2^\alpha)\frac{\beta\varepsilon_2}{N}R_{2R}^*\lambda_5^*$$
$$-(1-r_2^\alpha)\sigma_2\theta\lambda_T E_{2s}^*\lambda_5^*+\xi(1-P_2)\theta\frac{\beta\varepsilon_1}{N}S_2^*\lambda_6^*+\frac{\beta\varepsilon_2}{N}\lambda_6^*\theta\sigma_{42}$$
$$-(1-r_2^\alpha)\sigma_2\theta\lambda_T E_{2R}^*\lambda_6^*+(1-\xi)P_1\frac{\beta\varepsilon_2}{N}S_1^*\lambda_7^*$$

$$+(1-r_1^\alpha)\sigma_1\theta\lambda_T E_{1s}^*\lambda_7^*+\xi P_1\frac{\beta\varepsilon_1}{N}S_1^*\lambda_8^*+(1-r_1^\alpha)\frac{\beta\varepsilon_1}{N}E_{1R}^*\lambda_8^*\sigma_1$$

$$+(1-\xi)P_2\frac{\beta\varepsilon_2}{N}S_2^*+\tau_1\alpha_D^\alpha\lambda_9^*+(1-r_2^\alpha)\sigma_2\theta E_{2s}^*\frac{\beta\varepsilon_2}{N}\lambda_9^*$$

$$+(1-r_2^\alpha)\sigma_2\theta E_{2R}^*\frac{\beta\varepsilon_2}{N}\lambda_{10}^*+(\gamma_{22}+\mu^\alpha+d_2^\alpha+\omega_4u_4^*(t))\lambda_{10}^*+\xi P_2$$
$$\times\frac{\beta\varepsilon_2}{N}S_2^*\lambda_{10}^*\theta$$

$$-\sigma_{31}(1-\delta_1^\alpha)\frac{\beta\varepsilon_2}{N}R_{1s}^*\lambda_{11}^*+\sigma_{32}(1-\delta_1^\alpha)\frac{\beta\varepsilon_2}{N}R_{1R}^*\lambda_{12}^*$$

$$+\sigma_{41}(1-\delta_2^\alpha)\frac{\beta\varepsilon_2}{N}R_{2s}^*\theta\lambda_{13}^*+\sigma_{42}(1-\delta_2^\alpha)\frac{\beta\varepsilon_2}{N}R_{2R}^*\lambda_{14}^*),\tag{33}$$

$$^{ABC}_{t}D^\alpha_{t_f}\lambda_{11}^*=(\sigma_{31}(1-\delta_1^\alpha)\lambda_T\lambda_3^*+\sigma_{32}(1-\delta_1^\alpha)\lambda_T\lambda_4^*+\delta_{11}^\alpha\lambda_7^*$$
$$+\sigma_{31}(1-\delta_1^\alpha)\lambda_T\lambda_{11}^*-\lambda_{11}^*(\delta_{11}^\alpha+\xi+\alpha_D^\alpha+\mu^\alpha)$$
$$+\omega_1u_1^*\lambda_{11}^*-\xi\lambda_{12}+\alpha_D^\alpha\lambda_{13}),\tag{34}$$

$$^{ABC}_{t}D^\alpha_{t_f}\lambda_{12}^*=(\sigma_{32}(1-\delta_1^\alpha)\lambda_T\lambda_4^*+\delta_{12}^\alpha\lambda_8^*-\lambda_{11}^*(\delta_{12}^\alpha+\omega_2u_2^*\lambda_{12}^*$$
$$+\alpha_D^\alpha+\mu^\alpha)+\alpha_D^\alpha\lambda_{14}^*),\tag{35}$$

$$^{ABC}_{t}D^\alpha_{t_f}\lambda_{13}^*=(\sigma_{41}(1-\delta_2^\alpha)\theta\lambda_T\lambda_5^*+\lambda_9^*\delta_{21}+\omega_3u_3^*\lambda_{13}^*-\lambda_{13}^*(\delta_{12}^\alpha$$
$$+\xi+\mu^\alpha)+\lambda_{14}^*\xi),\tag{36}$$

$$^{ABC}_{t}D^\alpha_{t_f}\lambda_{14}^*=(\sigma_{42}(1-\delta_2^\alpha)\theta\lambda_T\lambda_6^*+\delta_{22}\lambda_{10}^*+\sigma_{42}(1-\delta_2^\alpha)\theta\lambda_T\lambda_{14}^*$$
$$-(\delta_{22}^\alpha+\mu^\alpha)\lambda_{14}^*+u_4^*\lambda_{14}^*)\tag{37}$$

(ii) Transversality conditions:

$$\lambda_j^*(T_f)=0,\ \ j=1,2,...,14.\tag{38}$$

(iii) Optimality conditions:

$$H_a(S_1^*,S_2^*,E_{1s}^*,E_{1R}^*,E_{2s}^*,E_{2R}^*,I_{1s}^*,I_{1R}^*,I_{2s}^*,I_{2R}^*,R_{2s}^*,R_{2R}^*,u_1^*,u_2^*,u_3^*,u_4^*,\lambda_j)$$
$$=\min_{0\le u_1^*,u_2^*,u_3^*,u_4^*\le 1}H((S_1^*,S_2^*,E_{1s}^*,E_{1R}^*,E_{2s}^*,E_{2R}^*,I_{1s}^*,I_{1R}^*,I_{2s}^*,I_{2R}^*,R_{2s}^*,R_{2R}^*,u_1^*,u_2^*,u_3^*,u_4^*,\lambda_j),\tag{39}$$

$$u_1^*=\min\{1,\max\{0,\frac{(\omega_1I_{1s}^*)(\lambda_{11}^*-\lambda_7^*)}{B_1}\}\},\tag{40}$$

$$u_2^*=\min\{1,\max\{0,\frac{(\omega_2I_{1R}^*)(\lambda_{12}^*-\lambda_8^*)}{B_2}\}\}.\tag{41}$$

$$u_3^*=\min\{1,\max\{0,\frac{(\omega_3I_{2s}^*)(\lambda_{13}^*-\lambda_9^*)}{B_3}\}\},\tag{42}$$

$$u_4^*=\min\{1,\max\{0,\frac{(\omega_4I_{2R}^*)(\lambda_{14}^*-\lambda_{10}^*)}{B_4}\}\}.\tag{43}$$

Proof. We find the co-state system Eqs. (24)–(37), from Eq. (21), where

$$H_a^*=I_{1s}^*+I_{1R}^*+I_{2s}^*+I_{2R}^*+\frac{B_1}{2}u_1^2(t)+\frac{B_2}{2}u_2^2(t)+\frac{B_3}{2}u_3^2(t)$$
$$+\frac{B_4}{2}u_4^2(t)+\lambda_{1_a}^{*^{ABC}}D_t^\alpha S_1^*+\lambda_{2_a}^{*^{ABC}}D_t^\alpha S_2^*+\lambda_{3_a}^{*^{ABC}}D_t^\alpha E_{1s}^*$$
$$+\lambda_{4_a}^{*^{ABC}}D_t^\alpha E_{1R}^*+\lambda_{5_a}^{*^{ABC}}D_t^\alpha E_{2s}^*+\lambda_{6_a}^{*^{ABC}}D_t^\alpha E_{2R}^*+\lambda_{7_{ABC}}^{*^c}D_t^\alpha I_{1s}^*$$
$$+\lambda_{8_a}^{*^{ABC}}D_t^\alpha I_{1R}^*+\lambda_{9_a}^{*^{ABC}}D_t^\alpha I_{2s}^*+\lambda_{10_a}^{*^{ABC}}D_t^\alpha I_{2R}^*s+\lambda_{11_a}^{*^{ABC}}R_{1s_t}^\alpha$$
$$+\lambda_{12_a}^{*^{ABC}}D_t^\alpha R_{1R}^*+\lambda_{13_a}^{*^{ABC}}D_t^\alpha R_{2s}^*+\lambda_{14_a}^{*^{ABC}}D_t^\alpha R_{2R}^*,\tag{44}$$

is the Hamiltonian. Moreover, the condition in Eq. (23)*also* holds, and the optimal control characterization in Eqs. (40)–(43) can be derived from Eq. (22). #

Substituting u_i^*, i = 1,2,...,4 in (3)-(16), we can obtain the following state system:

$$^{ABc}_{a}D_t^\alpha S_1^*=A^\alpha-(\mu^\alpha+\alpha_D^\alpha+\lambda_T)S_1^*,\tag{45}$$

$$^{ABC}_{a}D_t^\alpha S_2^*=\alpha_D^\alpha S_1-(\mu^\alpha+\theta\lambda_T)S_2^*,\tag{46}$$

$$^{ABC}_{a}D_t^\alpha E_{1s}^*=(1-\xi)(1-P_1)\lambda_T S_1^*+\sigma_{31}(1-\delta_1^\alpha R_{1s}^*)$$
$$-(1-r_1^\alpha)(k_1^\alpha+\sigma_1\lambda_T)E_{1s}^*-(\xi+\alpha_D^\alpha+\mu^\alpha)E_{1s}^*,\tag{47}$$

$$^{ABC}_{a}D_t^\alpha E_{1R}^*=\xi(1-P_1)\lambda_T S_1^*+\xi E_{1s}^*+\sigma_{32}(1-\delta_1^\alpha\lambda_T R_{1R}^*)-(1$$
$$-r_1^\alpha)(k_1^\alpha+\sigma_1\lambda_T)E_{1R}^*-(\alpha_D^\alpha+\mu^\alpha)E_{1R}^*,\tag{48}$$

$$^{ABC}_{a}D_t^\alpha E_{2s}^*=(1-\xi)(1-P_2)\theta\lambda_T S_2+\sigma_{41}(1-\delta_2^\alpha)\theta\lambda_T R_{2s}^*+\alpha_D^\alpha E_{1s}^*$$
$$-(1-r_2^\alpha)(k_2^\alpha+\sigma_2\theta\lambda_T)E_{2s}^*\xi+\mu^\alpha)E_{2s}^*,\tag{49}$$

$$^{ABC}_{a}D_t^\alpha E_{2R}^*=\xi(1-P_2)\theta\lambda_T S_2^*+\xi E_{2s}^*+\sigma_{42}(1-\delta_2^\alpha)\theta\lambda_T R_{2R}^*$$
$$+\alpha_D^\alpha E_{1R}^*-(1-r_2^\alpha)(k_2^\alpha+\sigma_2\theta\lambda_T)E_{2R}^*-\mu^\alpha E_{2R}^*,\tag{50}$$

$$^{ABC}_{a}D_t^\alpha I_{1s}^*=(1-\xi)P_1\lambda_T S_1^*+(1-r_1^\alpha)(k_1^\alpha+\sigma_1\lambda_T)E_{1s}^*+\delta_{11}^\alpha R_{1s}^*$$
$$-(\tau_1\alpha_D^\alpha+\eta_1\xi+\gamma_{11}^\alpha+\mu^\alpha+d_1^\alpha+\omega_1u_1^*)I_{1s}^*,\tag{51}$$

$$^{ABC}_{a}D_t^\alpha I_{1R}^*=\xi P_1\lambda_T S_1^*+(1-r_1^\alpha)(k_1^\alpha+\sigma_1\lambda_T)E_{1R}^*+\eta_1\xi I_{1s}^*+\delta_{12}^\alpha R_{1R}^*$$
$$-(\tau_1\alpha_D^\alpha+\gamma_{12}^\alpha+\mu^\alpha+d_1^\alpha+\omega_2u_2)I_{1R}^*\tag{52}$$

$$ {}_{a}^{ABC}D_t^{\alpha} I_{2s}^* = (1-\xi)P_2\theta\lambda_T S_2^* + \left(1-r_2^\alpha\right)\left(k_{21}^\alpha+\sigma_2\theta\lambda_T\right)E_{2s}^* + \tau_1\alpha_D^\alpha I_{1s}^* + \delta_{21}^\alpha R_{2s} - \left(\eta_2\xi+\gamma_{21}^\alpha+\mu^\alpha+d_2^\alpha+\omega_3 u_3\right)I_{2s}^*, \tag{53} $$

$$ {}_{a}^{ABC}D_t^{\alpha} I_{2R}^* = \xi P_2\theta\lambda_T S_2^* + \left(1-r_2^\alpha\right)\left(k_2^\alpha+\sigma_2\theta\lambda_T\right)E_{2R}^* + \eta_2\xi I_{2s}^* + \tau_1\alpha_D^\alpha I_{1R} + \delta_{22}^\alpha R_{2R} - \left(\gamma_{22}^\alpha+\mu^\alpha+d_2^\alpha+\omega_4 u_4^*\right)I_{2R}^*, \tag{54} $$

$$ {}_{a}^{ABC}D_t^{\alpha} R_{1s}^* = \gamma_{11}^\alpha I_{1s}^* + \omega_1 u_1^* I_{1s}^* - \sigma_{31}\left(1-\delta_1^\alpha\right)\lambda_T R_{1s}^* - \left(\delta_{11}^\alpha+\xi+\alpha_D^\alpha+\mu^\alpha\right)R_{1s}^* \tag{55} $$

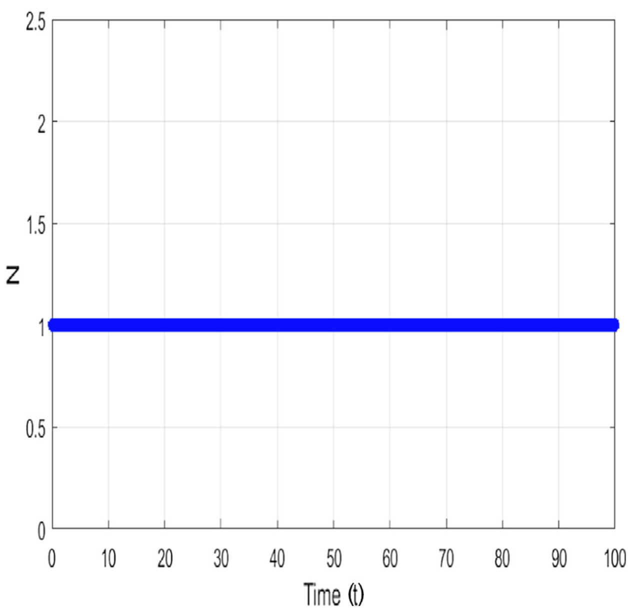

Fig. 2. Numerical simulations of $(S_1+S_2+I_{1s}+I_{1R}+I_{2s}+I_{2R}+E_{1s}+E_{1R}+E_{2s}+E_{2R}+R_{1s}+R_{1R}+R_{2s}+R_{2R})/N$ and $\alpha=1$ with control cases using *NS2LIM*.

$$ {}_{a}^{ABC}D_t^{\alpha} R_{1R}^* = \gamma_{21}^\alpha I_{1R}^* + \omega_2 u_2^* I_{1R}^* + \xi R_{1s} - \sigma_{32}\left(1-\delta_1^\alpha\lambda_T R_{1R}^*\right) - \left(\delta_{12}^\alpha+\alpha_D^\alpha+\mu^\alpha\right)R_{1R}^*, \tag{56} $$

$$ {}_{a}^{ABC}D_t^{\alpha} R_{2s}^* = \gamma_{21}^\alpha I_{2s}^* + \omega_3 u_3^* I_{2s}^* + \alpha_D^\alpha R_{1s}^* - \sigma_{41}\theta\left(1-\delta_2^\alpha\right)\lambda_T R_{2s}^* - \left(\delta_{21}+\xi+\mu^\alpha\right)R_{2s}^*, \tag{57} $$

$$ {}_{a}^{ABC}D_t^{\alpha} R_{2R}^* = \gamma_{22}^\alpha I_{2R}^* + \omega_4 u_4 I_{2R}^* + \xi R_{2s}^* + \alpha_D R_{1R}^* - \sigma_{42}\theta\left(1-\delta_2^\alpha\right)\lambda_T R_{2R}^* - \left(\delta_{22}^\alpha+\mu^\alpha\right)R_{2R}^*. \tag{58} $$

Numerical techniques for the fractional optimal control model

Let us consider the following general initial value problem:

$$ {}_{a}^{ABC}D^{\alpha} y(t) = g(t, y(t)), \quad y(0) = y_0. \tag{59} $$

Applying the fundamental theorem of FC to Eq. (59), we obtain

$$ y(t) - y(0) = \frac{1-\alpha}{B(\alpha)} g(t, y(t)) + \frac{\alpha}{\Gamma(\alpha)B(\alpha)} \int_0^t g(\theta, y(\theta))(t-\theta)^{\alpha-1} d\theta, \tag{60} $$

where $B(\alpha) = 1-\alpha+\frac{\alpha}{\Gamma(\alpha)}$ is a normalization function, and at t_{n+1}, we have

$$ y_{n+1} - y_0 = \frac{\Gamma(\alpha)(1-\alpha)}{\Gamma(\alpha)(1-\alpha)+\alpha} g(t_n, y(t_n)) + \frac{\alpha}{\Gamma(\alpha)+\alpha(1-\Gamma(\alpha)} \times \sum_{m=0}^{n} \int_{t_m}^{t_{m+1}} g \cdot (t_{n+1}-\theta)^{\alpha-1} d\theta, \tag{61} $$

Now, $g(\theta, y(\theta))$ will be approximated in an interval $[t_k, t_{k+1}]$ using a two-step Lagrange interpolation method. The two-step Lagrange polynomial interpolation is given as follows [22]:

$$ P = \frac{g(t_m, y_m)}{h}(\theta - t_{m-1}) - \frac{g(t_{m-1}, y_{m-1})}{h}(\theta - t_m). \tag{62} $$

Eq. (62), is replaced in Eq. (61), and by performing the same steps in [22], we obtain

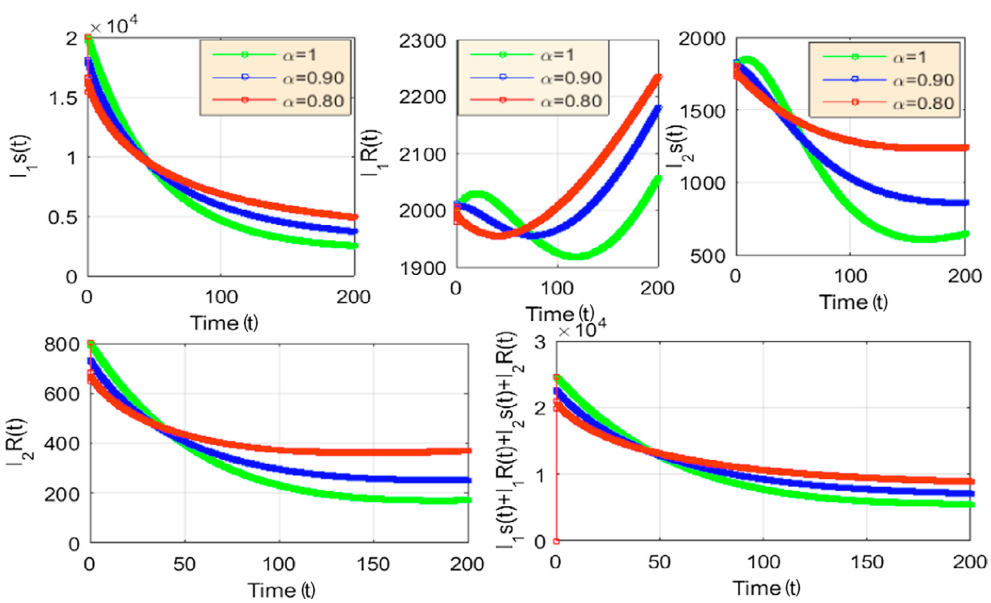

Fig. 3. Numerical simulations of I_{1s}, I_{1R}, I_{2s} and I_{2R} under different values of α with control cases using *NS2LIM*.

$$y_{n+1}-y_0=\frac{\Gamma(\alpha)(1-\alpha)}{\Gamma(\alpha)(1-\alpha)+\alpha}g(t_n,y(t_n))+\frac{1}{(\alpha+1)(1-\alpha)\Gamma(\alpha)+\alpha}$$
$$\times\sum_{m=0}^{n}h^{\alpha}g(t_m,y(t_m))(n+1-m)^{\alpha}$$
$$(n-m+2+\alpha)-(n-m)^{\alpha}(n-m+2+2\alpha)$$
$$-h^{\alpha}g(t_{m-1}),y(t_{m-1}))(n+1-m)^{\alpha+1}$$
$$(n-m+2+\alpha)-(n-m)^{\alpha}(n-m+1+\alpha), \tag{63}$$

To obtain high stability, we present a simple modification in Eq. (63). This modification is to replace the step size h *with* $\phi(h)$ such that

$$\phi(h)=h+O\left(h^2\right).\ \ 0<\phi(h)\le 1.$$

For more details, see [54]. Then, the new scheme is called the nonstandard two-step Lagrange interpolation method (NS2LIM) and is given as follows:

$$y_{n+1}-y_0=\frac{\Gamma(\alpha)(1-\alpha)}{\Gamma(\alpha)(1-\alpha)+\alpha}g(t_n,y(t_n))+\frac{1}{(\alpha+1)(1-\alpha)\Gamma(\alpha)+\alpha}$$
$$\times\sum_{m=0}^{n}\phi(h)^{\alpha}g(t_m,y(t_m))$$
$$(n+1-m)^{\alpha}(n-m+2+\alpha)-(n-m)^{\alpha}(n-m+2+2\alpha)$$
$$-\phi(h)^{\alpha}g(t_{m-1},y(t_{m-1}))$$
$$(n+1-m)^{\alpha+1}(n-m+2+\alpha)-(n-m)^{\alpha}(n-m+1+\alpha). \tag{64}$$

Then, we use the new scheme in Eq. (64) to numerically solve the state system in Eqs. (45)–(58), and we use the implicit finite difference method to solve the co-state system Eqs. (24)–(37) with the transversality conditions in Eq. (38).

Numerical simulations

In this section, we present two new schemes in Eqs. (63) and (64) to numerically simulate the fractional- order optimal system in Eqs. (45)–(58) and Eqs. (24)–(37) with the transversality condition in Eq. (38) using the parameters given in Table 1 and $\phi(h)=Q(1-e^{-h})$, where Q is a positive number less than or equal to 0.01. The initial conditions are $S_1(0)=8741400$, $S_2(0)=200000$, $E_{1s}(0)=557800$, $E_{1R}(0)=7800$, $E_{2s}(0)=4500$, $E_{2R}(0)=3000$, $I_{1s}(0)=20000$, $I_{1R}(0)=2000$, $I_{2s}(0)=1800$, $I_{2R}(0)=800$, $R_{1s}(0)=8000$, $R_{1R}(0)=800$, $R_{2s}(0)=200$, $andR_{2R}(0)=100$. For computational purposes, we use MATLAB on a computer with the 64-bit Windows 7 operating system and 4 GB of RAM. We now show some numerical aspects of the simulation of the proposed model in Eqs. (3)–(16). Fig. 2 shows that the summation of all the unknown of variables in the proposed model in Eqs. (3)–(16) is strictly constant during the studied time in the controlled case when using the scheme in Eq. (64). This result indicates that the proposed method is efficient. Fig. 3 shows the numerical solutions of I_{1s}, I_{1R}, I_{2s} and I_{2R} using the scheme in Eq. (64) when $T_f=200$ in the controlled case. We note that the solutions for different values of α vary close to the integer-order solution, i.e., the FO model is a generalization of the integer-order model and the FOCP systems and is more suitable for describing the real world. In Figs. 4–6, we examined the numerical results of I_{1s}, I_{1R}, I_{2s} and I_{2R} in the case $\alpha=0.95,1$, and we note that there are fewer infected individuals

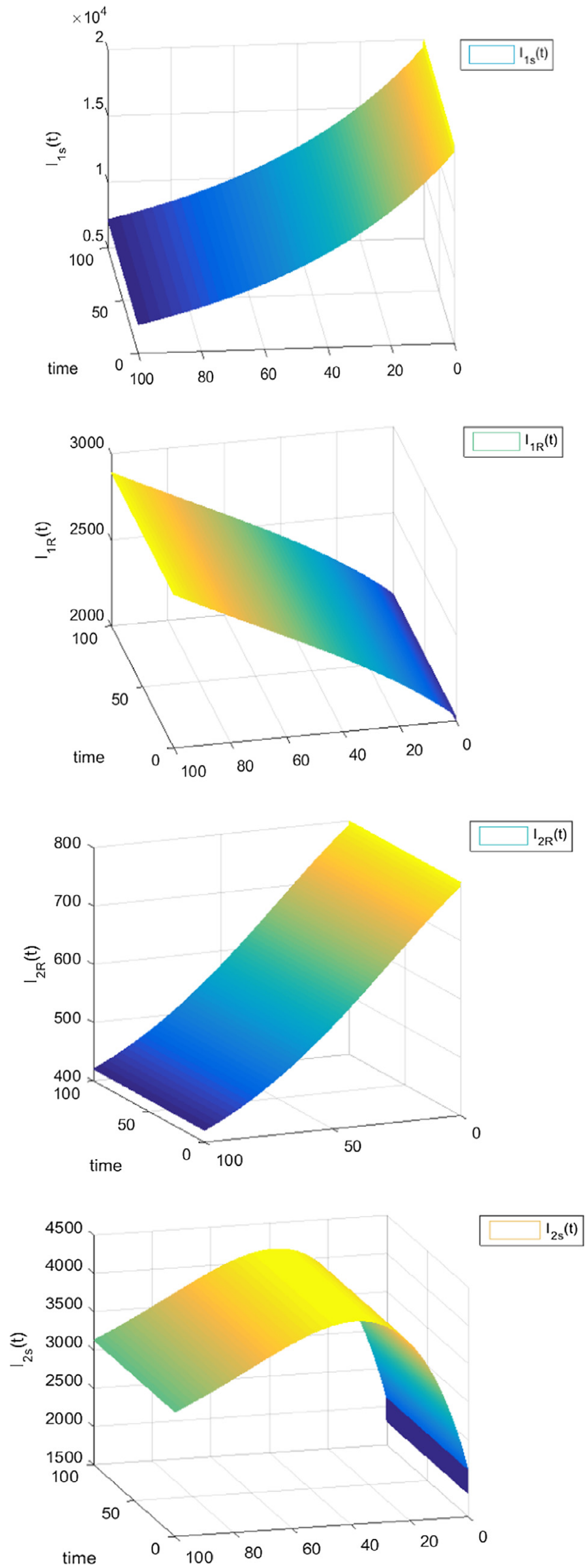

Fig. 4. Numerical simulations of I_{1s}, I_{1R}, I_{2s} and I_{2R} with $\alpha=0.95$ and $\beta=9$ without control cases using *NS2LIM*.

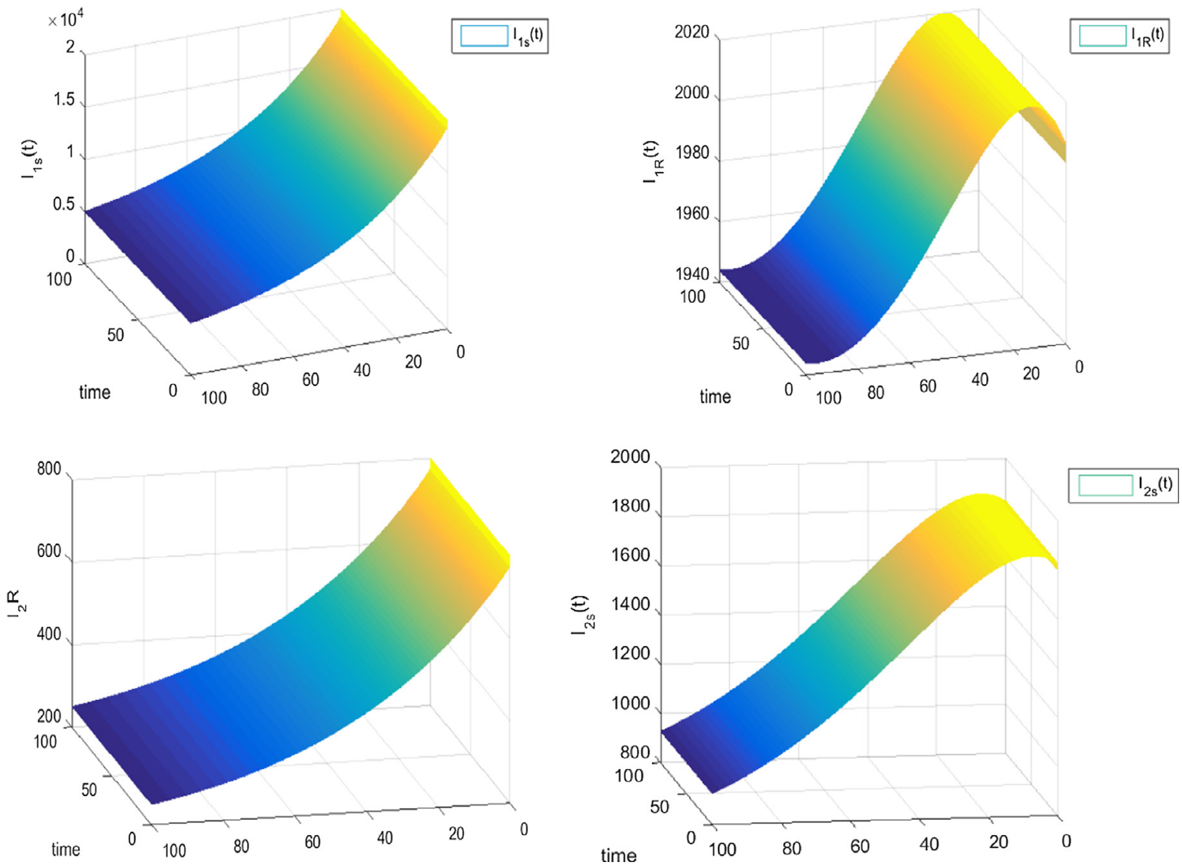

Fig. 5. Numerical simulations of I_{1s}, I_{1R}, I_{2s} and I_{2R} when $B_1 = B_2 = B_3 = B_4 = 100$ and $\alpha = 0.95$, $\beta = 9$ with control cases using *NS2LIM*.

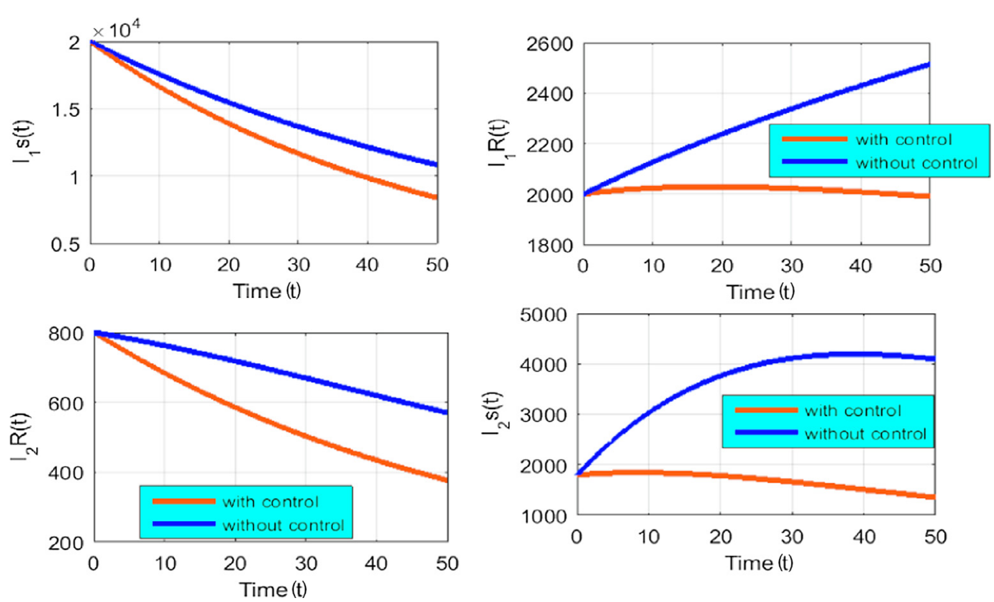

Fig. 6. Numerical simulations of I_{1s}, I_{1R}, I_{2s} and I_{2R} when $B_1 = B_3 = 5000$, $B_2 = B_4 = 100$, $\beta = 8$, and $\alpha = 1$ with and without control cases using *NS2LIM*.

in the control case. These results agree with the results given in Table 2. Fig. 7 illustrates the behaviour of relevant variables from the proposed model in Eqs. (3)–(16) for different αvalues using the scheme in Eq. (64). We note that the relevant variables change under different values of α following the same behaviour. Fig. 8 shows the behaviours of the relevant variables from the proposed model in Eqs. (3)–(16) for $\alpha = 0.8$ using the scheme in Eq. (63). We note that the relevant variables exhibit the same behaviour. Fig. 9

Table 2
Comparison of the values of the objective function system using NS2LIM and $T_f = 50$ with and without control cases.

α	$J(u_1^*, u_2^*, u_3^*, u_4^*)$ with control	$J(u_1^*, u_2^*, u_3^*, u_4^*)$ without controls
1	8.7371×10^5	1.0721×10^6
0.98	8.6240×10^5	1.0581×10^6
0.95	8.4617×10^5	1.0383×10^6
0.90	8.2138×10^5	1.0082×10^6
0.80	7.8340×10^5	9.6373×10^5
0.75	7.7330×10^5	9.5414×10^5
0.60	8.2733×10^5	1.0502×10^6

shows the behaviour of the control variables u_2 and u_3 at different values of α *and* $T_f = 200$ *using NS2LM*. We note that the control variables exhibit the same behaviour in the integer and fractional cases. Fig. 10 shows that the proposed scheme in Eq. (64) is more stable than the scheme in Eq. (63). Table 2 shows a comparison of the value of the objective function system using Eq. (64) with and without control cases when $T_f = 50$ and under different values of α. We note that the values of the objective function system with the control cases are lower than the values of the objective function system without the controls for all values of $0.6 < \alpha \leq 1$. Table 3 shows a comparison of the two proposed schemes in Eqs. (64) and (63) under different values of α with the control case. The solutions for the scheme in Eq. (64) appear to be slightly more accurate than those for the scheme in Eq. (63).

Conclusions

In this article, an optimal control for a fractional TB infection model that includes the impact of diabetes and resistant strains is presented. The fractional derivative is defined in the ABC sense. The proposed mathematical model utilizes a non-local and non-singular kernel. Four optimal control variables, u_1, u_2, u_3 and u_4, are introduced to reduce the number of individuals infected. It is concluded that the proposed fraction-order model can potentially describe more complex dynamics than can the integer model and can easily include the memory effects present in many real-world phenomena. Two numerical schemes are used: 2LIM and NS2LIM. Some figures are given to demonstrate how the fractional-order model is a generalization of the integer-order model. Moreover, we numerically compare the two methods. It is found that NS2LIM is more accurate, more efficient, more direct and more stable than 2LIM.

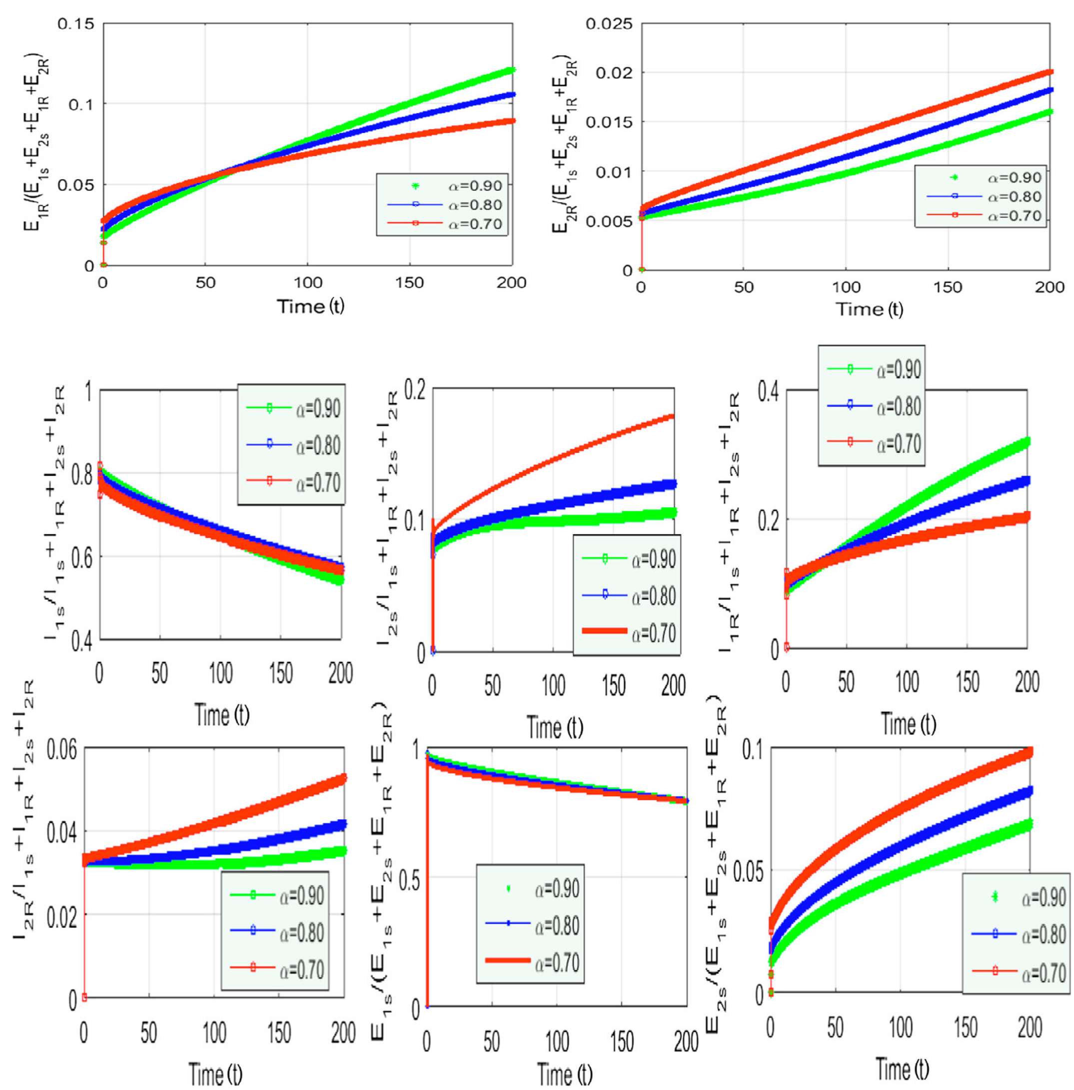

Fig. 7. Numerical simulations of the relevant variables with control cases when $B_1 = B_3 = 500$, $B_2 = B_4 = 100$ and $\beta = 5$ with different values of α using *NS2LIM*.

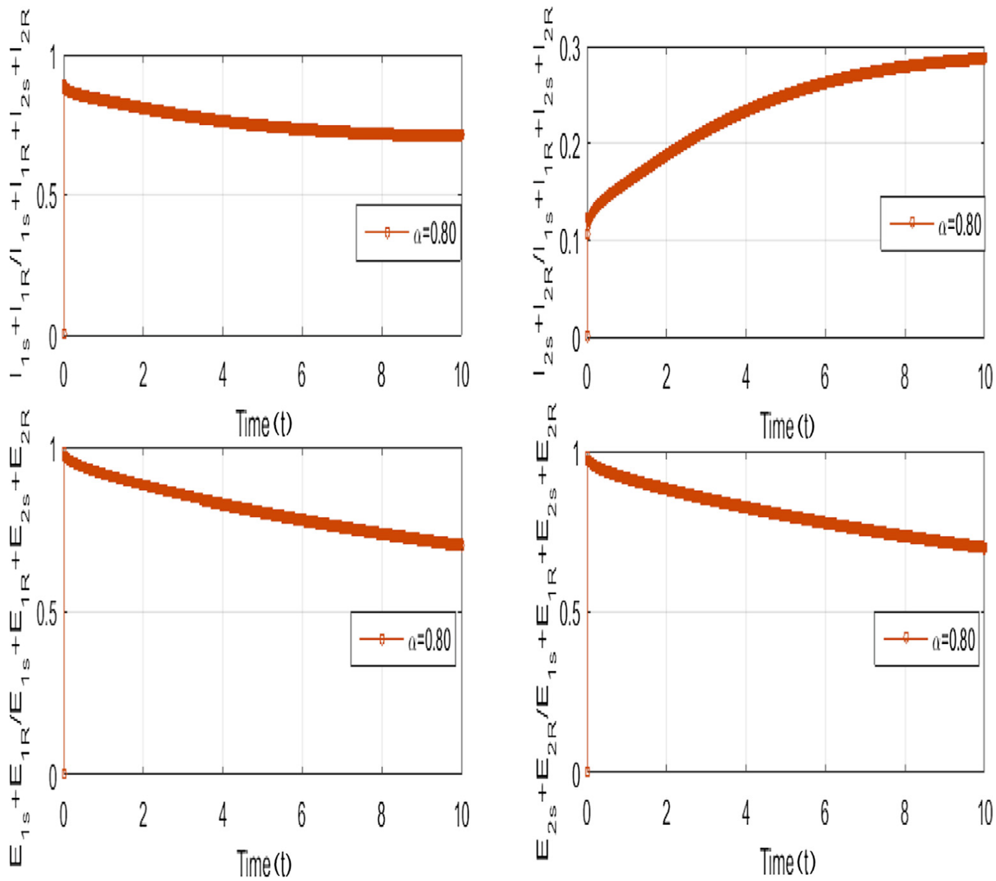

Fig. 8. Dynamics of relevant variables of the system in Eqs. (45)–(58) when $B_1 = B_2 = B_3 = B_4 = 100$ and $\beta = 5$, with control cases using 2*LIM*.

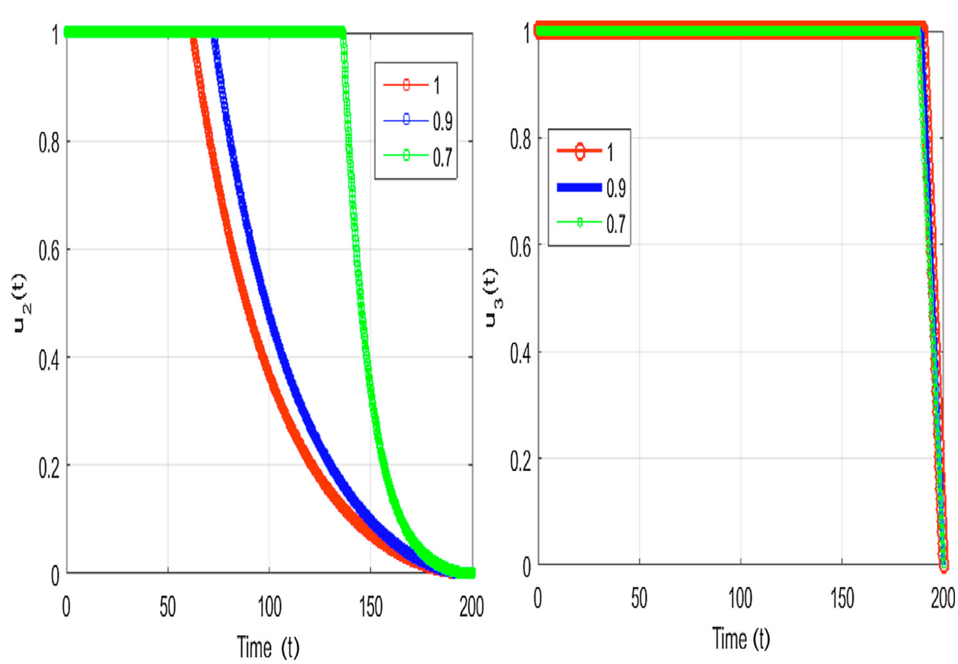

Fig. 9. Numerical simulations of the control variables using *NS2LIM*.

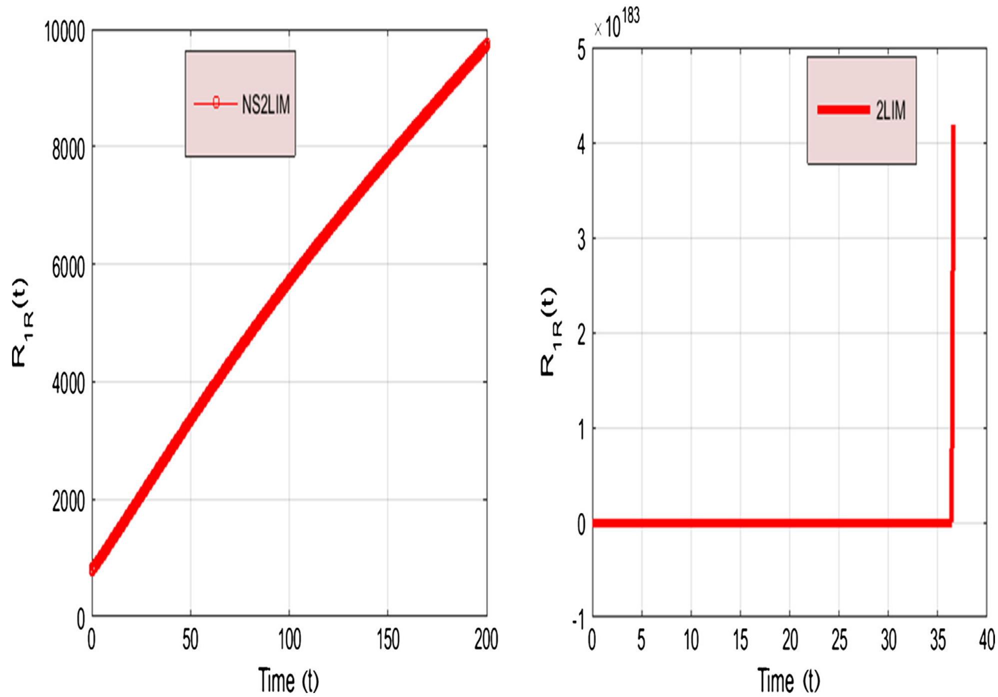

Fig. 10. Numerical simulations of R_1 when $B_1 = B_2 = B_3 = B_4 = 100$ and $\alpha = 0.9$, $h = 1$ with control case using *NS2LIM* and *2LIM*.

Table 3
Comparison of 2LIM and NS2LIM in the controlled case with $T_f = 10$, $h = 0.1$ and $\beta = 5$.

Variables	2LIM	*NS2LIM*	α
I_{1R}	6.0500×10^3	1.9694×10^3	0.8
I_{2s}	1.7822×10^3	1.5554×10^3	
I_{1R}	4.0922×10^3	1.9382×10^3	0.7
I_{2s}	3.1513×10^3	1.6662×10^3	
I_{1R}	2.9203×10^3	1.9168×10^3	0.6
I_{2s}	6.2551×10^3	2.3815×10^3	

Compliance with Ethics Requirements

This article does not contain any studies with human or animal subjects.

Conflict of interest

The authors have declared no conflict of interest.

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