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Backward bifurcation and optimal control in a co-infection model for SARS-CoV-2 and ZIKV

Andrew Omame\textsuperscript{a,b,}\textsuperscript{*}, Mujahid Abbas\textsuperscript{c,d}, Chibueze P. Onyenegecha\textsuperscript{e}

\textsuperscript{a} Department of Mathematics, Federal University of Technology, Owerri, Nigeria
\textsuperscript{b} Abdus Salam School of Mathematical Sciences, Government College University Katchery Road, Lahore 54000, Pakistan
\textsuperscript{c} Department of Mathematics, Government College University Katchery Road, Lahore 54000, Pakistan
\textsuperscript{d} Department of Medical Research, China Medical University Hospital, China Medical University, Taichung 40402, Taiwan
\textsuperscript{e} Department of Physics, Federal University of Technology, Owerri, Nigeria

\begin{abstract}
In co-infection models for two diseases, it is mostly claimed that, the dynamical behavior of the sub-models usually predict or drive the behavior of the complete models. However, under a certain assumption such as, allowing incident co-infection with both diseases, we have a different observation. In this paper, a new mathematical model for SARS-CoV-2 and Zika co-dynamics is presented which incorporates incident co-infection by susceptible individuals. It is worth mentioning that the assumption is missing in many existing co-infection models. We shall discuss the impact of this assumption on the dynamics of a co-infection model. The model also captures sexual transmission of Zika virus. The positivity and boundedness of solution of the proposed model are studied, in addition to the local asymptotic stability analysis. The model is shown to exhibit backward bifurcation caused by the disease-induced death rates and parameters associated with susceptibility to a second infection by those singly infected. Using Lyapunov functions, the disease free and endemic equilibria are shown to be globally asymptotically stable for $R_0, 1$, respectively. To manage the co-circulation of both infections effectively, under an endemic setting, time dependent controls in the form of SARS-CoV-2, Zika and co-infection prevention strategies are incorporated into the model. The simulations show that SARS-CoV-2 prevention could greatly reduce the burden of co-infections with Zika. Furthermore, it is also shown that prevention controls for Zika can significantly decrease the burden of co-infections with SARS-CoV-2.
\end{abstract}

Introduction

Arbovirus diseases (ARBOD) transmitted by \textit{Aedes aegypti}, such as zika, dengue and chikungunya and the concurrent circulation of these diseases are of major public health concerns in tropical and subtropical regions. The Coronavirus pandemic caused by the “severe acute respiratory syndrome coronavirus 2” (SARS-CoV-2) has posed serious health challenges in countries with overlapping epidemics, consequently increasing the burden on public health system [1]. This is why, SARS-CoV-2 and arboviruses (ARBOD) epidemics co-occurrence has become a matter of great concern to government and health agencies in tropical regions of the world. Indeed, the resemblance in clinical symptoms of Zika and SARS-CoV-2, especially at the early stages of infection is a great challenge which makes appropriate diagnosis very difficult. Hence, the delay in the administration of an appropriate treatment leads to increase in the spread of infection. [2,3]. Wrong diagnosis can result in lack of the proper care of the right disease and leads to worst health conditions [1,4]. Rosario and Siqueira [5], in a recent study, also observed that arboviral infections could have life-threatening implications, such as Guillain-Barré syndrome (GBS), encephalitis, myelitis and others.

Mathematical modeling has become an important tool for studying the dynamics of infectious diseases [6–12]. Several models have been developed to study the dynamics of SARS-CoV-2 [13–17]. Atangana [13] developed and analyzed a fractal-fractional model for SARS-CoV-2 to assess the impact of lockdown prior to the advent of vaccination, and showed that effective lockdown strategy was very appropriate to contain the spread of the disease at the onset of the pandemic. Also, Khan and Atangana [14] modeled the dynamics of SARS-CoV-2 with quarantine and isolation. They analyzed the dynamical behavior of the disease by describing the interactions among the bats and unknown hosts. Kolebaje and co-authors [15] modeled the dynamics of COVID-19 in some African countries using a real data. They estimated the

\* Corresponding author at: Department of Mathematics, Federal University of Technology, Owerri, Nigeria.

\begin{flushleft}
E-mail address: andrew.omame@futo.edu.ng (A. Omame).
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https://doi.org/10.1016/j.rinp.2022.105481

Received 11 February 2022; Received in revised form 27 March 2022; Accepted 2 April 2022
Available online 9 April 2022

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basic reproduction numbers for some countries and also presented how the disease could be controlled. In another study, Bonyah and co-workers [16] investigated a fractional optimal control model for COVID-19. They highlighted the importance of different control strategies in mitigating the spread of the disease. Moreover, the stability and optimal analysis for a COVID-19 model with quarantine and media awareness were discussed by the authors in [17].

Numerous mathematical studies have investigated the dynamics of SARS-CoV-2 and its co-infection with other diseases such as dengue [26], HIV [27], diabetes [28–31], tuberculosis [32,33] and malaria [34–36]. Most of the co-infection models in the literature do not include the assumption that susceptible individuals can get incident co-infection with the two diseases (an assumption which is possible for some diseases, and yet always ignored). Since there has not been any model yet to study the co-infection between SARS-CoV-2 and Zika virus, we therefore consider a robust novel mathematical model for the co-interactions between these two diseases, capturing incident co-infection by susceptible individuals. We shall also examine how this assumption could influence the dynamics of a co-infection model.

The major contributions of the paper are highlighted as follows:

i. The positivity and boundedness of solution of the model are discussed.

ii. The model presented herein is qualitatively analyzed for the occurrence of backward bifurcation.

iii. Using Lyapunov functions, the stability of both the disease free and endemic equilibria are examined, when $R_0 < 1$ and $R_0 > 1$, respectively.

iv. Time dependent controls are incorporated into the model and analyzed via the Pontryagin’s principle.

v. The entire model is simulated to examine the impact of various optimal control strategies on the dynamics of SARS-CoV-2, Zika virus and their co-infections.

Model formulation

At any time $t$, the total human population $N_h(t)$ consists of the following epidemiological states: Susceptible humans $S_h(t)$, infectious humans with SARS-CoV-2 $K_{C}^h(t)$, infectious humans with Zika virus $K_{Z}^h(t)$, humans co-infected with SARS-CoV-2 and Zika virus $K_{CZ}^h(t)$, with $R(t), K_{C}^h(t)$, $K_{Z}^h(t)$, $K_{CZ}^h(t)$ denoting infected population recovered from SARS-CoV-2 and Zika virus, respectively. The total vector population, at any time $t$, $N_v(t)$ consists of the following states: $S_v(t), K_{C}^v(t)$, $K_{Z}^v(t)$, $K_{CZ}^v(t)$, denoting susceptible vectors and vectors infected with Zika virus, respectively. Susceptible humans catch SARS-CoV-2 at the rate $\beta_h K_{C}^h/N_h$. Individuals in this state may catch zika virus either from infected humans or vectors at the rate $\beta_h K_{Z}^v/N_v$, and each infected individual with SARS-CoV-2 gives rise to $1$ new infected individual with SARS-CoV-2 during its infectious period with probability $\beta_h K_{C}^h/N_h$, and each infected individual with Zika gives rise to $1$ new infected individual with Zika during its infectious period with probability $\beta_h K_{Z}^v/N_v$. The death rates due to SARS-CoV-2, Zika or co-infection are denoted by $\mu_h, \mu_v$, respectively. Likewise, those infected with zika virus can get infected with SARS-CoV-2 at the rate $\beta_v K_{Z}^v/N_v$. Human–human transmission of Zika has been investigated in the literature (see, for example [22]). It is also assumed that the natural death rate for each epidemiological group is $\mu_h, \mu_v$.

### Description of parameters in the model (1).

| Parameter | Description | Value | References |
|-----------|-------------|-------|------------|
| $\eta_C$  | SARS-CoV-2 disease-induced death rate | 0.015/day | [18] |
| $\eta_Z$  | Zika disease-induced death rate | 0.001 | [19] |
| $\zeta_C$ | SARS-CoV-2 recovery rate | 1/7 | [20, 21] |
| $\zeta_Z$ | Zika recovery rate | 0.09 – 0.15 | [22] |
| $\eta_{CZ}$ | Co-infected disease-induced death rate | 0.015/day | Assumed |
| $\zeta_{CZ}$ | Co-infected recovery rate | 1/7/day | Assumed |
| $\lambda_h$ | Human recruitment rate | $\frac{100000}{\pi}$ per day | [23] |
| $\lambda_v$ | Vector recruitment rate | 20,000 per day | [19] |
| $\beta_1$ | Contact rate for SARS-CoV-2 infection | 0.5944 | [24] |
| $\beta_2$ | Contact rate for Zika infection (human to human) | 0.0100 | [22] |
| $\beta_3$ | Contact rate for Zika infection (vector to human) | 0.43 | [23] |
| $\beta_4$ | Contact rate for Zika infection (human to vector) | 0.60 – 0.75 | [22] |
| $\mu_h$ | Human natural death rate | $\frac{1}{7}$ | [25] |
| $\mu_v$ | Vector removal rate | $\frac{1}{7}$ per day | [19] |
| $\omega_1, \omega_2$ | Modification parameters | 1.0 | Assumed |

### Analysis of the model

We shall now analyze the model qualitatively (1) without considering the controls. We begin with the following:

#### Positivity of solutions

For the model (1) to be epidemiologically meaningful, it is appropriate to show that all its state variables are non-negative over time. We prove the results below:
Theorem 1. Let the initial data be $S_t(0) \geq 0, K_t^h(0) \geq 0, K_t^v(0) \geq 0, K_t^h(0) \geq 0, R(0) \geq 0, S_v(0) \geq 0, K_v^v(0) \geq 0$.

Then the solutions $(S_t, K_t^h, K_t^v, R_t, S_v, K_v^v)$ of the model (1) are non-negative for all time $t > 0$.

Proof. See Appendix A "Proof of Theorem 1".

boundedness

Theorem 2. The closed set $Q = Q^h \times Q^v$, with

$$Q^h = \left \{ (S_h, K_h^h, K_h^v, R_h) \in \mathbb{R}_+^4 : S_h + K_h^h + K_h^v + K_h^v \geq 0, R \leq \frac{A_h}{\mu_h} \right \},$$

$$Q^v = \left \{ (S_v, K_v^v) \in \mathbb{R}_+^2 : S_v + K_v^v \geq \frac{A_v}{\mu_v} \right \}.$$

is positively invariant with respect to the model (1).

Proof. Adding all the equations corresponding to the human components of the system (1), we have

$$\frac{dN_h}{dt} = A_h - \mu_h N_h(t) - \eta C K_h^v + \eta h K_v^h + \eta v C K_v^v.$$  \hspace{1cm} (2)

It follows from (2) that

$$A_h - (\mu_h + 3) \mu_h \leq \frac{dN_h}{dt} \leq A_h - \mu_h N_h,$$

where $\eta = \min\{\eta_v, \eta_h, \eta_C\}$.

which can be re-written as

$$\frac{dN_h}{dt} \leq A_h - \mu_h N_h.$$  \hspace{1cm} (3)

By applying the comparison theorem [37] and simplifying, we obtain that

$$N_h(t) \leq \frac{A_h}{\mu_h}.$$  \hspace{1cm} (4)

Therefore, the total human population, $N_h(t) \leq \frac{A_h}{\mu_h}$ as $t \to \infty$. Following the arguments similar to those given above, the total vector population, $N_v(t) \leq \frac{A_v}{\mu_v}$. Hence, the system (1) has the solution in $Q$. Thus, the given system is positively invariant.

The basic reproduction number of the model

By setting the right-hand sides of the equations in the model (1) to zero, we obtain the disease free equilibrium (DFE) of the model (1) evaluated at the disease-free equilibrium, $H_0$, and is given by:

$$R_0 = \rho(FV^{-1}) = \max\{R_{OC}, R_{OC}, R_{OCZ}\},$$

where $R_{OC}$, $R_{OCZ}$, and $R_{OCZ}$ are the associated reproduction numbers for SARS-CoV-2, Zika and co-infection of both diseases, respectively and are given by

$$R_{OC} = \frac{\beta_1}{G_1}, \hspace{0.5cm} R_{OCZ} = 1 + \frac{\beta_1}{G_1} \frac{1}{2} \left( \frac{\beta_2}{G_2} + \frac{\beta_3}{G_3} \right)^2.$$  \hspace{1cm} (6)

For the sake of simplicity, reproduction number associated with the human-to-human Zika transmission is denoted by $R_{OCZ}^h = \frac{\beta_2}{G_2}$, and the reproduction number associated with the vector-to-human-to-vector Zika transmission denotes $R_{OCZ}^v = \sqrt{\frac{\beta_2}{G_2} + \frac{\beta_3}{G_3}}$. Thus, the Zika associated reproduction number can be re-written as

$$R_{OCZ} = \frac{1}{2} \left( R_{OCZ}^h + \sqrt{R_{OCZ}^h + 4R_{OCZ}^v} \right).$$

Local asymptotic stability of the disease free equilibrium (DFE) of the model

Theorem 3. The DFE, $H_0$, of the model (1) is locally asymptotically stable (LAS) if $R_0 < 1$, and unstable if $R_0 > 1$.

Proof. The local stability of the model (1) is analyzed by the Jacobian matrix of the system (1) evaluated at the disease-free equilibrium, $H_0$, and is given by

$$\begin{bmatrix} -\mu_h & -\beta_1 & -\beta_2 & -\beta_3 & 0 & 0 & 0 \\ 0 & -\beta_1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\beta_2 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\beta_3 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\mu_v & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\mu_v \\ 0 & 0 & 0 & 0 & 0 & 0 & -\mu_v \end{bmatrix}$$  \hspace{1cm} (7)

The eigenvalues are given by

$$p_1 = -\mu_h, \hspace{0.5cm} p_2 = -\mu_v \hspace{0.5cm} \text{with multiplicity 2},$$

whereas, the remaining eigenvalues are the solutions of the equations given by

$$p^2 + \left( G_2 + 2 \mu_2 + \frac{\beta_3 S_v^c}{N_h} \right) p + \mu_v G_2 (1 - R_{OCZ}^v - R_{OCZ}) = 0.$$  \hspace{1cm} (8)

Applying the Routh Hurwitz criterion, the roots of equations in (8) have negative real parts if and only if $R_{OC} < 1$ and $R_{OC} < 1$. Thus, the DFE, $H_0$ is locally asymptotically stable if $R_0 = \max\{R_{OC}, R_{OCZ}, R_{OCZ}\} < 1$.

Endemic equilibrium points of the model

Suppose the reproduction number $R_0 = \max\{R_{OC}, R_{OCZ}, R_{OCZ}\} > 1$.

Also, let the factors playing a significant role in the disease transmission for the proposed model at steady state be denoted by

$$\lambda_C^h = \frac{\beta_1 K_h^h}{N_h}, \hspace{0.5cm} \lambda_Z^h = \frac{\beta_2 K_h^v + \beta_3 K_h^h}{N_h}, \hspace{0.5cm} \lambda_{CZ}^h = \frac{\beta_3 K_h^h}{N_h}.$$  \hspace{1cm} (9)

Then the model (1) will have multiple endemic equilibria $E^* = (S^*_h, K_h^h, K_h^v, K_h^v, R^*_h, S^*_v, K_v^v)$, where
The model (1) can be re-presented in the following form

\[
\begin{align*}
\frac{dx_1}{dt} &= A_b - (\beta_1 x_2 + (\beta_2 x_3 + \beta_0 x_4) + \mu_b) x_1 \\
\frac{dx_2}{dt} &= \beta_1 x_2 x_1 - (\zeta_C + \mu_b) x_2 \\
\frac{dx_3}{dt} &= \beta_2 x_3 x_1 - (\zeta_C + \mu_b) x_3 - \alpha x_2 x_3 x_5 \\
\frac{dx_4}{dt} &= \beta_1 x_2 x_1 + (\beta_2 x_3 + \beta_0 x_4) x_2 + 2 \alpha x_2 x_3 x_5 - (\zeta_C + \mu_b) x_4 \\
\frac{dx_5}{dt} &= \beta_3 x_2 x_1 + (\beta_2 x_3 + \beta_0 x_4) x_2 + 2 \alpha x_2 x_3 x_5 - (\zeta_C + \mu_b) x_5 \\
\text{Consider the case when } R_0 &= \max(R_{OC}, R_{GZ}, R_{OCZ}) = 1, \text{ if the contact rate } \beta_1 \text{ (say) is chosen as a bifurcation parameter, then solving for } \beta_1 = \beta_1^* \text{ from } R_0 = 1 \text{ we have } \beta_1 = \beta_1^* = G_3 \\
\text{Similarly, for } R_0 &= \max(R_{OC}, R_{GZ}, R_{OCZ}) = 1, \text{ we have } \beta_1 = G_3. \\
\text{Evaluating the Jacobian of the system (11) at the DFE, } J(H_0), \text{ we obtain:}
\end{align*}
\]

\[J(H_0) = \begin{pmatrix}
-\mu_b & -\beta_1 x_1' & -\beta_1 x_1' & -\beta_1 x_1' & 0 & 0 & -\beta_1 x_1' \\
0 & \beta_1 x_1' - G_1 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & \beta_2 x_1' - G_2 & \zeta_C & 0 & 0 & 0 \\
0 & 0 & 0 & \beta_3 x_1' - G_3 & 0 & 0 & 0 \\
0 & 0 & -\beta_1 x_1' & -\beta_1 x_1' & 0 & -\mu_b & 0 \\
0 & 0 & -\beta_1 x_1' & -\beta_1 x_1' & 0 & -\mu_b & 0
\end{pmatrix}
\]

Using the approach in [39], the matrix \( J(H_0) \) has a right eigenvector associated with the zero eigenvalue of \( J(H_0) \) given by \( \varphi = [\varphi_1, \varphi_2, \varphi_3, \ldots, \varphi_m]^T \), where the components are:

\[
\begin{align*}
\varphi_1 &= -1 \frac{1}{\mu} \begin{pmatrix} \beta_1 x_1' & \beta_1 x_2' & \beta_1 x_3' & \beta_1 x_4' \end{pmatrix} \\
\varphi_2 &= \frac{\beta_1 x_1'}{G_1} \\
\varphi_3 &= \frac{\beta_2 x_1'}{G_2} \\
\varphi_4 &= \frac{\beta_3 x_1'}{G_3} \\
\varphi_5 &= \frac{1}{\mu} \begin{pmatrix} \zeta_C x_2' & \zeta_C x_3' \end{pmatrix} \\
\varphi_6 &= \frac{1}{\mu} \begin{pmatrix} \beta_1 x_1' (\varphi_3 + \varphi_4) \end{pmatrix}
\end{align*}
\]

The non-zero components of the left eigenvector of \( J(H_0)^* \) satisfying \( \varphi \delta = 1 \) are

\[
\begin{align*}
\delta_1 &= \frac{\beta_1 x_1'}{G_1} \quad \delta_2 = \delta_3 = 0, \quad \delta_4 = \frac{\beta_1 x_1'}{G_3} \quad \delta_5 = \frac{\beta_1 x_1'}{\mu}.
\end{align*}
\]

Using Theorem 4.1 in [39] and computing the non-zero partial derivatives of \( f(x) \) at the disease free equilibrium, \( (H_0) \), the associated bifurcation coefficients are defined below

\[
\begin{align*}
a &= \sum_{k,i,j=1} \delta_k \varphi_k \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0) \quad \text{and} \quad b = \sum_{k,i,j=1} \delta_k \varphi_k \frac{\partial^2 f_k}{\partial x_i \partial \beta_j}(0,0),
\end{align*}
\]

where,

\[
\begin{align*}
a &= 2 \begin{pmatrix} \beta_1 x_1' & -\beta_1 x_1' & \beta_1 x_1' & 0 \end{pmatrix} \\
\beta_1 x_1' + \beta_2 x_2' + \beta_0 x_3' + 2 \beta_2 x_1' \delta_3 \\
-2 \beta_1 x_1' \varphi_2 \varphi_3 \delta_3 + 2 \beta_2 x_1' \varphi_2 \varphi_3 \delta_3 + 2 \alpha x_2 \beta_1 x_1' \varphi_2 \varphi_3 \delta_3 + 2 \alpha x_2 \beta_1 x_1' \varphi_2 \varphi_3 \delta_3 \\
+ 2 \beta_1 x_1' \varphi_2 \varphi_3 \delta_3 + 2 \beta_2 x_1' \varphi_2 \varphi_3 \delta_3 + 2 \alpha x_2 \beta_1 x_1' \varphi_2 \varphi_3 \delta_3 + 2 \alpha x_2 \beta_1 x_1' \varphi_2 \varphi_3 \delta_3
\end{align*}
\]

is positive.

**Proof.** Suppose

\[H_e = \begin{pmatrix} S_{x_1} & K_{x_2} & K_{x_3} & K_{x_4} & K_{x_5} & K_{x_6} & K_{x_7} & \ldots \end{pmatrix}^T \]

denote an arbitrary endemic equilibrium of the model. By the following change of variables,

\[S = x_1, R = x_2, x_3, x_4, x_5, x_6, x_7, \ldots\]
positive which indicates the occurrence of backward bifurcation. However, if we set the parameters associated with the susceptibility to infection with a second disease by individuals infected with single infection $a_1 = a_2 = 0$, then the co-efficient satisfies

$$a = 2(\beta_1 \varphi_2 \delta_2 + \beta_2 \varphi_1 \delta_3 + \beta_3 \varphi_2 \delta_3 + \beta_4 \varphi_3 \delta_4) \varphi_1 + 2\beta_3 (\varphi_1 + \varphi_2) \delta_1 \varphi_3 < 0 \text{ (since } \varphi_1 < 0, \varphi_3 < 0),$$

which rules out the possibility of backward bifurcation in the co-infection model. Thus, it is concluded that, human disease-induced death rates and terms associated with susceptibility to additional infection by singly infected individuals can induce backward bifurcation in the co-infection model for two diseases. Therefore, it is observed that, in addition to disease induced death rates (which induced bifurcation in the sub-model), parameters associated with infection with a second disease cause backward bifurcation in the complete model. Hence, by allowing incident co-infection with both diseases, the dynamics of the sub-model does not always drive or influence the dynamics of the complete co-infection model.

Global asymptotic stability of the disease-free equilibrium of the model (1) for a special case

**Theorem 5.** In the absence of infection with a second disease by singly infected individuals (that is, $a_1 = a_2 = 0$), the DFE of the model (1) given by $Q_0$, is GAS in $Q$ provided that $R_0 \leq 1$.

**Proof.** See Appendix B “Proof of Theorem 5”

The epidemiological implication of Theorem 5 is; if those already infected with a single disease do not get infected with a second disease, then both SARS-CoV-2 and Zika can be eliminated from the population provided that the threshold quantity, $R_0 < 1$, regardless of the initial sizes of the sub-populations.

Global asymptotic stability of endemic equilibrium of the model (1) for a special case

**Theorem 6.** In the absence of infection with a second disease by singly infected individuals (that is, $a_1 = a_2 = 0$), the endemic equilibrium $Q_*$, of the model (1) with $\gamma_2 = \gamma_3 = \gamma_{CZ} = 0$ is globally asymptotically stable (GAS) in $Q \backslash Q_0$ with $Q_0 = Q^h_0 \times Q^v_0$ whenever $R_0 < 1$, where

$$Q^h_0 = \left\{ (S_h , {K^h_C} , {K^h_CZ} , {K^h_CZ2} , R) \in Q^h : {K^h_C} = {K^h_CZ} = 0 \right\}$$

$$Q^v_0 = \left\{ (S_v , {K^v_C}) \in Q^v : {K^v_C} = 0 \right\}$$

**Proof.** See Appendix C “Proof of Theorem 6”

The epidemiological significance of Theorem 6 is; if those already infected with a single infection do not get infected with a second disease, and if diseases induced death is negligible, then both SARS-CoV-2 and HBV will persist in the population provided that the threshold quantity, $R_0 > 1$.

Optimal control analysis

It was observed in the preceding sections that the occurrence of backward bifurcation in the model (1) makes the effective control of both diseases difficult in the population. The aim of this section is to incorporate the time dependent controls into the model (1) to obtain the optimal interventions for the elimination of the co-infections. They are defined as follows: $\theta_1(t)$: SARS-CoV-2 prevention control, $\theta_3(t)$: Zika prevention control, $\theta_3(t)$: Control against incident co-infection, and $\theta_4(t)$: Control against infection with a second disease, and the optimal control model is given by:

$$\frac{dS_h}{dt} = A_h - \left( (1 - \theta_1) \frac{\beta_1 K^h_C}{N_h} + (1 - \theta_2) \frac{\beta_2 K^h_CZ}{N_h} \right) S_h + (1 - \theta_1) \frac{\beta_1 K^h_CZ2}{N_h} S_h$$

$$\frac{dK^h_C}{dt} = (1 - \theta_1) \frac{\beta_1 K^h_C}{N_h} S_h - \left( \gamma_2 + \gamma_{CZ} + \mu_h \right) K^h_C$$

$$\frac{dK^h_CZ}{dt} = (1 - \theta_1) \frac{\beta_1 K^h_CZ}{N_h} S_h - \left( \gamma_2 + \gamma_{CZ} + \mu_h \right) K^h_CZ$$

$$\frac{dK^h_CZ2}{dt} = (1 - \theta_1) \frac{\beta_1 K^h_CZ2}{N_h} S_h - \left( \gamma_2 + \gamma_{CZ} + \mu_h \right) K^h_CZ2$$

$$\frac{dK^h_CZ3}{dt} = (1 - \theta_1) \frac{\beta_1 K^h_CZ3}{N_h} S_h - \left( \gamma_2 + \gamma_{CZ} + \mu_h \right) K^h_CZ3$$

$$\frac{dK^h_CZ4}{dt} = (1 - \theta_1) \frac{\beta_1 K^h_CZ4}{N_h} S_h - \left( \gamma_2 + \gamma_{CZ} + \mu_h \right) K^h_CZ4$$

$$...$$

$$\frac{dR}{dt} = \xi_2 K^h_CZ + \gamma_{CZ} K^h_CZ2 - \mu_R R$$

$$\frac{dS_v}{dt} = A_v - \left( (1 - \theta_1) \frac{\beta_2 K^v_C}{N_h} + \mu_c \right) S_v$$

$$\frac{dK^v_C}{dt} = (1 - \theta_2) \frac{\beta_2 K^v_C}{N_h} S_v - \left( \gamma_2 + \gamma_{CZ} + \mu_h \right) K^v_C$$

subject to the initial conditions

$$S_{h0} = S_0(0), \quad K^h_{C0} = K^h_C(0), \quad K^h_{CZ0} = K^h_{CZ}(0), \quad K^h_{CZ20} = K^h_{CZ2}(0), \quad R_0 = R(0), \quad S_{v0} = S_0(0), \quad K^v_{C0} = K^v_C(0).$$

Let us consider the following objective function

$$J \left[ \theta_1, \theta_2, \theta_3, \theta_4 \right] = \int_0^T \left[ K^h_C(t) + K^v_C(t) + K^h_{CZ}(t) + S_v(t) + K^v_{CZ}(t) \right. + \alpha_1 \frac{\beta_1 K^h_C}{N_h} + \alpha_2 \frac{\beta_2 K^v_C}{N_h} + \beta_1 K^h_CZ + \beta_2 K^v_CZ \right] dt,$$
To prove Theorem 7, we proceed as follows:

\[ f(t, x, \theta) = \left( 1 - \theta_3 \right) \frac{\beta_h K_h}{N_h} S_h + \alpha_5 (1 - \theta_4) \frac{\beta_z K_z}{N_h} K_z^h \]

with \( \phi(t, x) \) is given in Box II.

As the parameters and variables of the model are positive, we have

\[ \| f(t, x, \theta) \| \leq \| \theta(t, x) \| + \| \phi(t, x) \| \| \theta \| \]

\[ \leq a + b \| \theta \|, \quad \text{where } a > 0, b > 0. \]

(iii) The optimal control problem's Lagrangian is given by

\[ L = K_C(t) + K_w(t) + \lambda(t) + S_i(t) + \frac{1}{2} \sum_{i=1}^{4} \xi_i \theta_i^2. \]
\[
\phi(t, x) = \begin{pmatrix}
\frac{\beta_1^0 K_0^h S_h}{\lambda_h x_h} & \frac{\beta_1^0 K_0^h + \beta_2^0 K_0^L x_h}{\lambda_h x_h} & \frac{\beta_2^0 K_0^L z}{\lambda_h x_h} & 0 \\
0 & -\frac{\beta_1^0 K_0^h + \beta_2^0 K_0^L z}{\lambda_h x_h} & 0 & a_1 - \frac{\beta_2^0 K_0^L z}{\lambda_h x_h} \\
0 & 0 & -\frac{\beta_1^0 K_0^h + \beta_2^0 K_0^L z}{\lambda_h x_h} & \frac{\beta_2^0 K_0^L z}{\lambda_h x_h} - a_2 \\
\frac{\beta_1^0 K_0^h + \beta_2^0 K_0^L z}{\lambda_h x_h} & 0 & 0 & 0
\end{pmatrix}
\]

Box II.

and hence convexity of \( L \).

(iv.) There exists constants \( m_1, m_2 \) and \( m_3 \) such that, \( L \geq m_1 |\theta|^m - m_2, \) \( m_1 > 0, m_2 > 0, m_3 > 1 \) We now establish the bound on \( L \). Note that \( z_0 \theta_1^2 \leq z_0 \). As \( \theta_1 \in [0, 1] \), \( z_0 \theta_1^2 \leq z_0 \). Now,

\[
L \geq \frac{\beta_1^0}{2} \theta_1^2 + \frac{\beta_1^0}{2} \theta_2^2 + \frac{\beta_1^0}{2} \theta_3^2 + \frac{\beta_1^0}{2} + \frac{\beta_2^0}{2} \theta_4^2 - \frac{\beta_2^0}{2} \theta_5^2 \\
\geq \min \left\{ \frac{\beta_1^0}{2} \theta_1^2 + \frac{\beta_1^0}{2} \theta_2^2 + \frac{\beta_1^0}{2} \theta_3^2 + \frac{\beta_1^0}{2} + \frac{\beta_2^0}{2} \theta_4^2 - \frac{\beta_2^0}{2} \theta_5^2 \right\}
\]

Hence,

\[
L \geq m_1 |\theta|^m - m_2, \quad \text{where,} \quad m_1 = \min \left\{ \frac{\beta_1^0}{2} \frac{\beta_1^0}{2} \frac{\beta_1^0}{2} \frac{\beta_1^0}{2} + \frac{\beta_2^0}{2} \theta_4^2 - \frac{\beta_2^0}{2} \right\} > 0,
\]

\( m_2 = \frac{z_0}{2} > 0 \) and \( m_3 > 1 \). \( \square \)

Theorem 8. Suppose the set \( \theta = \{\theta_1, \theta_2, \theta_3, \theta_4\} \) minimizes \( J \) over \( U \), then adjoint variables \( \alpha_1, \alpha_2, \ldots, \alpha_7 \), satisfy the adjoint equations

\[
\alpha_i(t_j) = 0, \quad \text{where,} \quad i = S, K_0^h, K_0^L, K_0^L, R, S, K_0^L.
\]

Furthermore,

\[
\alpha_i(t_j) = 0
\]

Principle \[43\] is applied to obtain the following:

\[
\begin{align*}
\frac{d\alpha_1}{dt} &= \frac{dX}{\partial S_0}, \\
\frac{d\alpha_2}{dt} &= \frac{dX}{\partial K_0^h}, \\
\frac{d\alpha_3}{dt} &= \frac{dX}{\partial K_0^L}, \\
\frac{d\alpha_4}{dt} &= \frac{dX}{\partial K_0^L}, \\
\frac{d\alpha_5}{dt} &= \frac{dX}{\partial S_0}, \\
\frac{d\alpha_6}{dt} &= \frac{dX}{\partial S_0}, \\
\frac{d\alpha_7}{dt} &= \frac{dX}{\partial S_0}.
\end{align*}
\]

On the interior of the set, where \( 0 < \theta_j < 1 \), \( \forall \ (j = 1, \ldots, 4) \), we have

\[
\begin{align*}
0 &= \frac{d\alpha_1}{dt} = \xi_1 N \theta_1^* - \beta_1^0 S_h(\theta_2 - \theta_1), \\
0 &= \frac{d\alpha_2}{dt} = \xi_2 N \theta_2^* - \{\beta_1^0 K_0^h S_h(\theta_3 - \theta_2) + \beta_2^0 (K_0^h + K_0^L) S_h(\theta_4 - \theta_3)\}, \\
0 &= \frac{d\alpha_3}{dt} = \xi_3 N \theta_3^* - \beta_1 K_0^L S_h(\theta_4 - \theta_3), \\
0 &= \frac{d\alpha_4}{dt} = \xi_4 N \theta_4^* - \{\beta_1^0 K_0^h S_h(\theta_3 - \theta_2) + \beta_2^0 K_0^L S_h(\theta_4 - \theta_3)\}.
\end{align*}
\]

Therefore,

\[
\begin{align*}
\theta_1^* &= \frac{\beta_1^0 S_h(\theta_2 - \theta_1)}{\xi_1 N}, \\
\theta_2^* &= \frac{\beta_1^0 K_0^h S_h(\theta_3 - \theta_2) + \beta_2^0 (K_0^h + K_0^L) S_h(\theta_4 - \theta_3)}{\xi_2 N}, \\
\theta_3^* &= \frac{\beta_1^0 K_0^L S_h(\theta_4 - \theta_3)}{\xi_3 N}, \\
\theta_4^* &= \frac{\beta_1^0 K_0^L S_h(\theta_3 - \theta_2) + \beta_2^0 K_0^L S_h(\theta_4 - \theta_3)}{\xi_4 N}, \\
\theta_5^* &= \frac{\alpha_1(\theta_1)}{\xi_1 N}, \\
\theta_6^* &= \frac{\alpha_2(\theta_2)}{\xi_2 N}, \\
\theta_7^* &= \frac{\alpha_3(\theta_3)}{\xi_3 N}, \\
\theta_8^* &= \frac{\alpha_4(\theta_4)}{\xi_4 N}.
\end{align*}
\]

Proof of Theorem 8. Considering \( U^* = (\theta_1^*, \theta_2^*, \theta_3^*, \theta_4^*) \) and the associated solutions \( S_0, K_0^h, K_0^L, K_0^L, R, S, K_0^L \), Pontryagin’s Maximum
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and $74.9$ respectively [23,25]. The initial conditions used for the sim-

tion strategy, for $\theta_1 \neq 0$, $\theta_2 \neq 0$, $\beta_1 = 0.2441$, $\beta_2 = 0.02441$, $\beta_3 = 0.200$, $\beta_4 = 0.18$, $\beta_5' = 0.501$, so that $R_0 = \max(\mathcal{R}_\text{SARS-CoV-2}, \mathcal{R}_\text{Zika}) = 1.1938 > 1$.

\begin{equation}
\times \left( -\beta_1 K_C^{\beta_1}(0) - \beta_2 K_C^{\beta_2}(0) + \beta_1 K_C^{\beta_1}(0) - \beta_2 K_C^{\beta_2}(0) \right) \right) \right) \right) \right)
\end{equation}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig1.png}
\caption{Impact of SARS-CoV-2 prevention ($\theta_1$) on individuals in $K_C^{\beta_1}$ and $K_C^{\beta_2}$ epidemiological classes. Here, $\beta_1 = 0.2441$, $\beta_2 = 0.02441$, $\beta_3 = 0.200$, $\beta_4 = 0.18$, $\beta_5' = 0.501$, so that $R_0 = \max(\mathcal{R}_\text{SARS-CoV-2}, \mathcal{R}_\text{Zika}) = 1.1938 > 1$.}
\end{figure}

Numerical simulations

In this section, simulations of the control system (15) are carried out. This is done with MATLAB using the forward backward sweep by Runge Kutta method. The quadratic cost functions $\frac{1}{2} \omega_1 \beta_1^2 + \frac{1}{2} \omega_2 \beta_2^2 + \frac{1}{2} \omega_3 \beta_3^2$ and $\frac{1}{2} \omega_4 \beta_4^2$ are used. The weight constants are assumed as: $\omega_1 = 25$, $\omega_2 = 20$, $\omega_3 = 35$ and $\omega_4 = 45$.

In the subsequent sections, we investigate the impact of various control strategies on the co-dynamics of both diseases and their co-infection. For the demographic parameters, $A_k$ and $B_k$, we obtained their values based on the total population and life expectancy of Espirito Santo state, Brazil (a country with co-endemicity of both SARS-CoV-2 and zika virus), which are approximately given by 4,108,508 and 74.9 respectively [23,25]. The initial conditions used for the simulations are set as follows: $S_0(0) = 3,600,000; I_C^{\beta_1}(0) = 800; I_C^{\beta_2}(0) = 24; I_C^{\beta_3}(0) = 100; R(0) = 100; S_0(0) = 4000; I_C^{\beta_4}(0) = 600$.

\textbf{Strategy A: Impact of SARS-CoV-2 prevention control ($\theta_1 \neq 0$)}

The simulations of the optimal control system (15) when the strategy that prevents SARS-CoV-2 ($\theta_1 \neq 0$) is implemented, are depicted in Figs. 1(a) and 1(b), respectively. On implementation of this intervention strategy, for $\beta_1 = 0.2441$, $\beta_2 = 0.02441$, $\beta_3 = 0.200$, $\beta_4 = 0.18$, $\beta_5' = 0.501$, so that $R_0 = \max(\mathcal{R}_\text{SARS-CoV-2}, \mathcal{R}_\text{Zika}) = 1.1938 > 1$, we observe a significant decrease in the total number of individuals infected with SARS-CoV-2, as expected (shown in Fig. 1(a)). Interestingly, this strategy has high positive population level impact on co-infected cases, as observed in Fig. 2(b). It is important to note that zika prevention strategy averts more co-infection cases than the SARS-prevention strategy. Equally, this strategy causes great reduction in infected vector populations as observed in Fig. 2(c). The control profiles for this strategy are depicted by Fig. 2(d). It is observed that the control has very high effect against Zika transmission.

\textbf{Strategy B: Impact of Zika prevention controls ($\theta_2 \neq 0$)}

The simulations of the optimal control system (15) when the strategy that prevents Zika transmission (both human and vectors) ($\theta_2 \neq 0$) is implemented, are depicted in Figs. 2(a), 2(b), 2(c), respectively. Implementation of this intervention strategy, for $\beta_1 = 0.2441$, $\beta_2 = 0.02441$, $\beta_3 = 0.200$, $\beta_4 = 0.18$, $\beta_5' = 0.501$, so that $R_0 = \max(\mathcal{R}_\text{SARS-CoV-2}, \mathcal{R}_\text{Zika}) = 1.1938 > 1$ shows a significant decrease in the total number of individuals infected with Zika virus, as expected (shown in Fig. 2(a)). Also, this strategy has high positive population level impact on co-infected cases, as observed in Fig. 2(b). It is interesting to note that zika prevention strategy averts more co-infection cases than the SARS-prevention strategy. Equally, this strategy causes great reduction in infected vector populations as observed in Fig. 2(c). The control profiles for this strategy are depicted by Fig. 2(d). It is observed that the control has very high effect against Zika transmission.

\textbf{Strategy C: Impact of control against co-infections with both diseases ($\theta_1 \neq 0, \theta_2 \neq 0$)}

The simulations of system (15) when the strategy that prevents incident co-infection with SARS-CoV-2 and Zika virus ($\theta_1 \neq 0$) is implemented, are depicted in Figs. 3(a) and 3(b). Implementation of this intervention strategy, for $\beta_1 = 0.2441$, $\beta_2 = 0.02441$, $\beta_3 = 0.200$, $\beta_4 = 0.18$, $\beta_5' = 0.501$, so that $R_0 = \max(\mathcal{R}_\text{SARS-CoV-2}, \mathcal{R}_\text{Zika}) = 1.1938 > 1$ indicates a significant decrease in the total number of individuals co-infected with SARS-CoV-2 and Zika virus as depicted by Fig. 3(a). Thus, to avert co-infection cases in the population, it is not enough to prevent new single cases. Efforts must also be made to prevent individuals from getting infected with concurrent infections. This control strategy also caused a great reduction of infected vector population, as shown in Fig. 3(b). Also, the simulation of the system (15) when the strategy that prevents infection with a second disease by those already infected, is depicted by Fig. 3(c). It is observed that a good number of co-infected cases is averted when this strategy is strictly put in place. The control profiles for prevention of incident co-infections and prevention of an additional infection by singly infected individuals, are presented in Figs. 3(d) and 3(e). It is observed that, the control strategy against incident co-infections attains its peak value nearly after 50 days into the simulation period and throughout maintains this value. Moreover, the control against infection with a second disease, was at its peak throughout the simulation period.
Fig. 2. Impact of Zika prevention ($\theta_1$) on individuals in $\mathcal{K}_Z^0$ and $\mathcal{K}_{CZ}^0$, and vectors in $\mathcal{K}_Z^0$ epidemiological class. Here, $\beta_1 = 0.2441, \beta_2 = 0.02441, \beta_3 = 0.200, \beta_4 = 0.18, \beta_1' = 0.501$, so that $R_0 = \max(R_{CC}, R_{CZ}, R_{ZC}) = 1.1938 > 1$.

Fig. 3. Impact of control against incident co-infections $\theta_3$ and $\theta_4$ on individuals in $\mathcal{K}_{CZ}^0$ and $\mathcal{K}_{ZC}^0$, and vectors in $\mathcal{K}_Z^0$ epidemiological class. Here, $\beta_1 = 0.2441, \beta_2 = 0.02441, \beta_3 = 0.200, \beta_4 = 0.18, \beta_1' = 0.501$, so that $R_0 = \max(R_{CC}, R_{CZ}, R_{ZC}) = 1.1938 > 1$. 
Conclusion

In this paper, a new mathematical model for SARS-CoV-2 and Zika co-dynamics was presented, incorporating incident co-infection by susceptible individuals which is not common in the existing models. We discussed the impact of this assumption on the dynamics of a co-infection model. The model also incorporated sexual transmission of Zika. The positivity and boundedness of solution of the developed model was investigated, in addition to local asymptotic stability analysis. The model was shown to exhibit backward bifurcation, caused by disease induced death rates and parameters associated with susceptibility to a second infection by those already infected. Employing the Lyapunov functions, the disease free and endemic equilibria were discussed. The Lyapunov function was shown to globally asymptotically stable for $R_0 < 1$ and $R_0 > 1$, respectively. To manage the co-circulation of both infections in an effective manner, under an endemic setting, time dependent controls in the form of SARS-CoV-2, Zika and co-infection prevention strategies were incorporated into the model. The simulations showed that SARS-CoV-2 prevention could greatly reduce the burden of co-infections with Zika. Furthermore, it was shown that prevention controls for Zika can significantly reduce the burden of co-infections with SARS-CoV-2. We expect that the findings of this paper will open new avenues of research in this direction.

The model proposed in this paper focused only on SARS-CoV-2 and Zika co-infection, without vaccination or re-infection either with single or both diseases. Incorporating vaccination for SARS-CoV-2 and re-infection for both diseases, one could obtain an extension of the model. Also, the emergence of different variants of SARS-CoV-2 attracts further studies on their co-infections with other diseases, such as Zika, dengue, TB, influenza, Malaria and others. One could therefore, consider multistrain of SARS-CoV-2 and co-infection with Zika virus. Also, more investigations could be carried out to the mathematical (stochastic, agent based modeling, within/intra-host) and epidemiological dynamics of SARS-CoV-2 and Zika co-infection. The current research was not a case study because of insufficient data and information about the co-infection of both diseases. For instance, little is known about infection acquired cross-immunity between both diseases. Not much information is available to answer the question: whether the current available vaccines against SARS-CoV-2 could have any impact on the dynamics of Zika virus. Thus, further studies with more reliable data and detailed information about the co-infection of both diseases is viable.

Appendix A: Proof of Theorem 1

Let $t_1 = \sup\{t > 0 : S_h(t) > 0, K_C^b(0) > 0, K_C^{bN}(0) > 0, R(0) > 0, S_c(t) > 0, L_C^b(0) > 0\}$, Moreover from $[0, t_1]$. Thus, $t_1 > 0$.

Suppose further, $\lambda_C = \frac{\beta_h K_C^b}{N_h}, \lambda_z = \frac{(\beta_z K_z^b + \beta_C K_C^b)}{N_h}, \lambda_{CZ} = \frac{\beta_{CZ}}{N_h}$, then the first model equation can be written as:

$$\frac{dS_h}{dt} = A_h - (\lambda_C + \lambda_z + \lambda_{CZ} + \mu)S_h,$$

(29)

Applying the integrating factor method on (29), we obtain

$$\frac{d}{dt} \left\{ S_h(t) \exp \left[ \int_0^t (\lambda_C(u) + \lambda_z(u) + \lambda_{CZ}(u))du + \mu t \right] \right\} = A_h \exp \left[ \int_0^t (\lambda_C(u) + \lambda_z(u) + \lambda_{CZ}(u))du + \mu t \right]
$$

and

$$S_h(t_1) \exp \left[ \int_0^{t_1} (\lambda_C(u) + \lambda_z(u) + \lambda_{CZ}(u))du + \mu(t_1) \right] = S_h(0) \exp \left[ \int_0^{t_1} (\lambda_C(u) + \lambda_z(u) + \lambda_{CZ}(u))du + \mu t \right] dx,$$

with,

$$S_h(t_1) = S_h(0) \exp \left[ \int_0^{t_1} (\lambda_C(u) + \lambda_z(u) + \lambda_{CZ}(u))du - \mu t_1 \right] + \exp \left[ \int_0^{t_1} (\lambda_C(u) + \lambda_z(u) + \lambda_{CZ}(u))du - \mu t_1 \right] \times A_h \exp \left[ \int_0^{t_1} (\lambda_C(u) + \lambda_z(u) + \lambda_{CZ}(u))du + \mu t \right] dx > 0.$$ 

Similarly, it can be shown that:

$$K_C^b(0) > 0, K_C^{bN}(0) > 0, K_{CZ}^b(0) > 0, R(0) > 0, S_c(0) > 0, K_C^b(0) > 0.$$

Appendix B: Proof of Theorem 5

Consider the Lyapunov function

$$E_1 = \ln \left[ \left( S_h - S_h^0 \right) + \frac{K_C^b}{N_h} + \frac{K_C^{bN}}{N_h} + \frac{R}{N_c} + \left( S_c - S_c^0 \right) + K_C^Z \right]$$

$$+ \frac{1}{G_1} K_C^b + \frac{1}{G_2} K_C^Z + \frac{1}{G_3} K_C + \frac{\beta_C}{\mu_G} K_C Z,$$

with Lyapunov derivative

$$E_1 = \frac{1}{\left( S_h - S_h^0 \right) + \frac{K_C^b}{N_h} + \frac{K_C^{bN}}{N_h} + \frac{R}{N_c} + \left( S_c - S_c^0 \right) + K_C^Z} \times \left( A_h - \left( \frac{\beta_h K_C^b}{N_h} + \frac{(\beta_z K_z^b + \beta_C K_C^b)}{N_h} + \frac{\beta_{CZ}}{N_h} \right) S_h \right)
$$

$$+ \frac{1}{G_1} \frac{K_C^b}{N_h} S_h - \left( \eta_C + \zeta_C + \mu_C \right) K_C + \frac{1}{G_2} K_C Z$$

$$- \left( \eta_z + \zeta_z + \mu_z \right) K_C Z$$

$$+ \frac{1}{G_3} \frac{\beta_{CZ}}{N_h} S_h$$

$$- \left( \eta_{CZ} + \zeta_{CZ} + \mu_{CZ} \right) K_C Z$$

$$+ \frac{1}{G_1} \frac{K_C^b}{N_h} S_h - \left( \eta_C + \zeta_C + \mu_C \right) K_C Z$$

$$- \mu_C R + A_h - \left( \frac{\beta_C}{\mu_G} K_C Z + \frac{\beta_{CZ}}{N_h} \right) S_h + \frac{1}{G_2} \frac{(K_C^b + K_C^{bN})}{N_h} S_h$$

$$- \mu_z K_C Z$$

$$+ \frac{1}{G_1} \frac{K_C^b}{N_h} S_h - \frac{1}{G_2} S_h - \left( \eta_z + \zeta_z + \mu_z \right) K_C Z$$

$$+ \frac{1}{G_2} \frac{(\beta_z K_z^b + \beta_{CZ})}{N_h} S_h - \left( \eta_z + \zeta_z + \mu_z \right) K_C Z$$

$$+ \frac{1}{G_3} \frac{\beta_{CZ}}{N_h} S_h - \left( \eta_C + \zeta_C + \mu_C \right) K_C Z.$$
Appendix C: Proof of Theorem 6

Substituting the derivatives in (1) into $\dot{v}^2$, and

\[ + (A_\nu - \mu_\nu(S_\nu + k^N_C k^N_Z + R) + A_\epsilon - \mu_\epsilon(S_\epsilon + k^N_Z) \]

- $\eta C k^N_C + \eta C k^N_Z + \eta C k^N_C = 0 + \left( \frac{\beta_1}{\mathcal{G}_1} - 1 \right) k^N_C \]

+ \left( \frac{\beta_1}{\mathcal{G}_1} \right) k^N_C \]

+ $\frac{\beta_2}{\mathcal{G}_2} \left( \frac{\beta_2^2 s^2}{\mu_\nu \mathcal{G}_2 N^2} - 1 \right) k^N_C + \left( \frac{\beta_1}{\mathcal{G}_1} \right) k^N_C \]

= $\frac{(\eta C)^2 + \eta C k^N_C + \eta C k^N_Z + R + (S_\nu - S_\epsilon) + k^N_Z}{\mathcal{G}_1} \]

\[ \text{ Simplifying further (noting that } S_\nu + k^N_C + k^N_Z + k^N_C + R \leq \frac{(S_\nu)}{\mathcal{G}_1} \text{ and } \frac{(S_\epsilon)}{\mathcal{G}_1} \text{, we have} \]

$\mathcal{L}_1 \leq \left( \frac{(S_\nu - S_\epsilon) + k^N_C + k^N_Z + R + (S_\nu - S_\epsilon) + k^N_Z}{\mathcal{G}_1} \right) \]

+ $\frac{(R_{oc})}{\mathcal{G}_1} k^N_C \]

+ $\frac{(R_{oc})}{\mathcal{G}_2} k^N_C \]

Since all the model parameters and variables are non-negative, it follows that $\mathcal{L}_1 < 0$ for $R_{oc} = \max[R_{oc}, R_{oc} - R_{oc} C] \leq 1$. Hence, $\mathcal{L}_1$ is a Lyapunov function on $Q$. Thus, the DFE is globally asymptotically stable [44].

Appendix C: Proof of Theorem 6

Consider the model (1) with $\eta C = \eta = 0$ (with $k^N_C = \frac{S_\nu}{\mathcal{G}_1}$, $\beta_1 = \frac{\beta_1}{\mathcal{G}_1}$, $\beta_2 = \frac{\beta_2}{\mathcal{G}_2}$, $\beta_3 = \frac{\beta_3}{\mathcal{G}_3}$, $\beta_4 = \frac{\beta_4}{\mathcal{G}_4}$, and $R_{oc} > 1$, so that the associated unique endemic equilibrium exists. Also, consider the non-linear Lyapunov function:

$\mathcal{L}_2 = \mu(S_\nu - s_\nu)^2 + \left( \frac{k^N_C}{K^N_C} \right) + \left( 1 - \frac{k^N_C}{K^N_C} \right) k^N_C \]

\[ \text{Substituting the derivatives in (1) into } \mathcal{L}_2, \text{ we have} \]

$\mathcal{L}_2 = \mu \left( S_\nu - s_\nu \right) - \left( \frac{k^N_C}{K^N_C} \right) + \left( 1 - \frac{k^N_C}{K^N_C} \right) k^N_C \]

\[ + \left( 1 - \frac{k^N_C}{K^N_C} \right) k^N_C \]

\[ + \left( 1 - \frac{k^N_C}{K^N_C} \right) k^N_C \]

\[ + \mu \left( 1 - \frac{k^N_C}{K^N_C} \right) \left( \frac{\beta_2}{\mathcal{G}_2} \right) \]
\[ \frac{\mu - (K_C^b \beta_1 + K_M^b \beta_1^M) (\theta - 1)}{(K_C^b + K_M^b + K_M^C + R + S_h)} \]

\[ \phi_1' = \phi_1 \left( \frac{(K_C^b \beta_1 + K_M^b \beta_1^M) (\theta - 1)}{(K_C^b + K_M^b + K_M^C + R + S_h)} \right) \]

\[ - S_h (K_C^b \beta_1 + K_M^b \beta_1^M) (\theta - 1) \]

\[ + \frac{K_M^b \beta_1 (\theta - 1)}{(K_C^b + K_M^b + K_M^C + R + S_h)} \]

\[ + \frac{K_C^b \beta_1 (\theta - 1)}{(K_C^b + K_M^b + K_M^C + R + S_h)} \]

\[ + \frac{K_M^b \beta_1 (\theta - 1)}{(K_C^b + K_M^b + K_M^C + R + S_h)} \]

\[ + \frac{K_C^b \beta_1 (\theta - 1)}{(K_C^b + K_M^b + K_M^C + R + S_h)} \]

\[ - \frac{k_C^b S_h \beta_1 (\theta - 1)}{(K_C^b + K_M^b + K_M^C + R + S_h)} \]

\[ - \frac{k_C^b S_h \beta_1 (\theta - 1)}{(K_C^b + K_M^b + K_M^C + R + S_h)} \]

\[ - \frac{k_C^b S_h \beta_1 (\theta - 1)}{(K_C^b + K_M^b + K_M^C + R + S_h)} \]

\[ + \frac{k_C^b S_h \beta_1 (\theta - 1)}{(K_C^b + K_M^b + K_M^C + R + S_h)} \]

\[ - \frac{k_C^b S_h \beta_1 (\theta - 1)}{(K_C^b + K_M^b + K_M^C + R + S_h)} \]

\[ + \frac{k_C^b S_h \beta_1 (\theta - 1)}{(K_C^b + K_M^b + K_M^C + R + S_h)} \]

\[ + \frac{k_C^b S_h \beta_1 (\theta - 1)}{(K_C^b + K_M^b + K_M^C + R + S_h)} \]

\[ + \phi_1 \left( \frac{(K_C^b \beta_1 + K_M^b \beta_1^M) (\theta - 1)}{(K_C^b + K_M^b + K_M^C + R + S_h)} \right) \]

\[ + \phi_1 \left( \frac{(K_C^b \beta_1 + K_M^b \beta_1^M) (\theta - 1)}{(K_C^b + K_M^b + K_M^C + R + S_h)} \right) \]

\[ + \phi_1 \left( \frac{(K_C^b \beta_1 + K_M^b \beta_1^M) (\theta - 1)}{(K_C^b + K_M^b + K_M^C + R + S_h)} \right) \]

\[ + \phi_1 \left( \frac{(K_C^b \beta_1 + K_M^b \beta_1^M) (\theta - 1)}{(K_C^b + K_M^b + K_M^C + R + S_h)} \right) \]

\[ + \phi_1 \left( \frac{(K_C^b \beta_1 + K_M^b \beta_1^M) (\theta - 1)}{(K_C^b + K_M^b + K_M^C + R + S_h)} \right) \]

Thus, \( L_2 \leq 0 \) for \( R_0 > 1 \). Hence, \( L_2 \) is a Lyapunov function in \( D \setminus D_0 \) and we conclude that the GAS of EEP is globally asymptotically stable for \( R_0 > 1 \).
\[
\begin{align*}
&+ S_i \beta_i^2 \phi_i \left( \theta_i - 1 \right) \left( \mathcal{K}_C^{0b} + \mathcal{K}_Z^{0b} \right) \\
&\left( \mathcal{K}_C^{0b} + \mathcal{K}_C^{0b} + \mathcal{K}_Z^{0b} + R + S_h \right) \\
&- S_i \beta_i^2 \phi_i \left( \theta_i - 1 \right) \left( \mathcal{K}_C^{0b} + \mathcal{K}_Z^{0b} \right) \\
&\left( \mathcal{K}_C^{0b} + \mathcal{K}_C^{0b} + \mathcal{K}_Z^{0b} + R + S_h \right) \\
&+ \phi_i \left( \theta_i - 1 \right) \left( \mathcal{K}_C^{0b} + \mathcal{K}_Z^{0b} \right) \\
&\left( \mathcal{K}_C^{0b} + \mathcal{K}_C^{0b} + \mathcal{K}_Z^{0b} + R + S_h \right) \\
&\phi_i = \phi_1 \left( \eta_1 + \mu_h + \zeta_1 + \frac{S_h \beta_2 \left( \theta_2 - 1 \right)}{\left( \mathcal{K}_C^{0b} + \mathcal{K}_Z^{0b} + \mathcal{K}_Z^{0b} + R + S_h \right)} \right)
\end{align*}
\]
\[
\begin{align*}
\phi'_e &= \phi_e - \phi_e \left( \frac{K_C S_b \beta_1 (\theta_1 - 1)}{(K_C + K_C Z + K_Z^2 + R + S_b)^2} \right) \\
&+ \frac{K_C + K_C Z + K_Z^2 + R + S_b}{(K_C + K_C Z + K_Z^2 + R + S_b)^2} - 1 \\
\phi_s' &= \phi_s - \phi_s \left( \frac{S_b \left( K_C \beta_2 + K_C Z \beta_2 + (\theta_2 - 1) \left( K_C + K_C Z + K_Z^2 + R + S_b \right)^2 \right)}{\left( K_C + K_C Z + K_Z^2 + R + S_b \right)^2} \right) \\
&+ \frac{K_C + K_C Z + K_Z^2 + R + S_b}{(K_C + K_C Z + K_Z^2 + R + S_b)^2} - 1 \\
\phi_i' &= \phi_i - \phi_i \left( \frac{K_C \beta_1 (\theta_1 - 1)}{(K_C + K_C Z + K_Z^2 + R + S_b)^2} \right) \\
&+ \frac{K_C + K_C Z + K_Z^2 + R + S_b}{(K_C + K_C Z + K_Z^2 + R + S_b)^2} - 1 \\
\phi_z' &= \phi_z - \phi_z \left( \frac{S_b \left( K_C \beta_2 + K_C Z \beta_2 + (\theta_2 - 1) \left( K_C + K_C Z + K_Z^2 + R + S_b \right)^2 \right)}{\left( K_C + K_C Z + K_Z^2 + R + S_b \right)^2} \right) \\
&+ \frac{K_C + K_C Z + K_Z^2 + R + S_b}{(K_C + K_C Z + K_Z^2 + R + S_b)^2} - 1
\end{align*}
\]

References

[1] Vicente CR, da Silva TCC, Pereira LDA, Miranda AE. Impact of concurrent epidemics of dengue, Chikungunya, Zika, and COVID-19. J Braz Soc Trop Med 2021;5(0837-2020). http://dx.doi.org/10.1590/0037-8682-0837-2020.

[2] Ribeiro VST, Telles JP, Tuon FF. Arborival diseases and COVID-19 in Brazil: Concerns regarding climatic, sanitation, and endemic setting. J Nat Med Virol 2020;92(11):2390-1.

[3] Monitoramento dos casos de arbovíorese urbanas transmitidas pelo aedes (dengue, chikungunya e zika), semanas epidemiológicas 01 a 52. 2020. https://portalarquivos2.saude.gov.br/images/pdf/2020/janeiro/20/Boletim-epidemiologico-SVS-02-1.-pdf.

[4] Wilder-Smith A, Tissier H, Ooi EE, Coloma J, Scott TW, Gubler DJ. Preventing dengue epidemics during the COVID-19 pandemic. Am J Trop Med Hyg 2020;103(2):570–1.

[5] do Rosário MS, de Siqueira IC. Concerns about COVID-19 and arboviral (chikungunya, dengue, zika) concurrent outbreaks. Braz J Infect Dis 2020;24(6):583-4.

[6] Din A, Li Y, Yusuf A, et al. Impact of information intervention on stochastic hepatitis B model and its variable-order fractional model. Eur Phys J Spec Top 2022. http://dx.doi.org/10.11040/epj.s1733-022-00543-5.

[7] Alqahtani R, Yusuf A. Development and analysis of a seir model for Covid-19 epidemic with vaccination and nonsingular kernel. Fractals 2022;30(1):224100.

[8] Khan A, Zarin R, Ahmed I, Yusuf A, Humphries UW. Numerical and theoretical analysis of rabies model under the harmonic mean type incidence rate. Results Phys 2021;29:104652. http://dx.doi.org/10.1016/j.rinp.2021.104652.

[9] Kumar P, Erturk VS, Yusuf A, Kumar S. Fractional time-delay mathematical modelling of Oncolytic Virotherapy. Chaos Solitons Fractals 2021;150111123. http://dx.doi.org/10.1016/j.chaos.2021.111123.

[10] Omame A, Okuonghae D, Nwajeri UK. A fractional-order multi-vaccination model for COVID-19 with non-singular kernel. Alexandria Eng J 2022. http://dx.doi.org/10.1016/j.aej.2021.11.037.

[11] Omame A, Inyama SC. Stochastic model and simulation of the prevalence of measles. Int J Math Sci Eng 2014;8(1):311–23.

[12] Okuonghae D. Analysis of a stochastic mathematical model for tuberculosis with case detection. Int J Dynam Control. 2021. http://dx.doi.org/10.1007/s40435-021-00863-8.

[13] Atangana A. Modelling the spread of COVID-19 with new fractional-fractal operators: can the lockdown save mankind before vaccination? Chaos Solitons Fractals 2020;136:109860.

[14] Khan MA, Atangana A, Alzahrani E. The dynamics of COVID-19 with quarantine and isolation. Adv Differential Equations 2020;2020(1):1–22.

[15] Kolebaje OT, Vincent OR, Vincent UE, McClintock PVE. Nonlinear growth and mathematical modelling of COVID-19 in some african countries with the Atangana-Baleanu fractional. Commun Nonlinear Sci Numer Simul 2022;105:106076, derivative.

[16] Bonyah E, Sagoe AK, Devendra S, Deniz S. Fractional optimal control dynamics of coronavirus model with Mittag-Leffler law. Ecol Complex 2021;45:100880.

[17] Zhang J, Qiao Y, Zhang Y. Stability analysis and optimal control of COVID-19 with quarantine and media awareness. Math Biosci Eng 2022;19(5):4911–32. http://dx.doi.org/10.3934/mbe.20222230.

[18] Ferguson NM, Laydon D, Nedjati-Gilani G, Imai N, Ainslie K, Baguelin M, Bhatia S, Boonyasiri A, Cucunubá Z, Cuomo-Dannenburg G, et al. Impact of non-pharmaceutical interventions (npis) to reduce covid-19 mortality and healthcare demand. Vol. 16, London: Imperial College COVID-19 Response Team: 2020.

[19] Garba SM, Gumel AB, Abu Bakar MR. Backward bifurcations in Dengue transmission dynamics. Math Biosci 2008;215:11–25.

[20] Cauchemez S, Fraser C, van Kerkhove MD, Donnelly CA, Riley S, Rambaut A, et al. Middle east respiratory syndrome corona virus: quantification of the extent of the epidemic, surveillance biases, and transmissibility. Lancet Infect Dis 2014;14.

[21] Rui JChenT-M, Wang Q-P, Zhao Z-Y, Cui J-A, Yin L. A mathematical model for simulating the phase-based transmissibility of a novel coronavirus. Infect Dis Poverty 2020;9:24. http://dx.doi.org/10.1186/s40249-020-00640-3.

[22] Okuneye KO, Velasco-Hernandez ZX, Gumel AB. The unhyd Chikungunya-Dengue-Zika trinity: A theoretical analysis. J Biol Systems 2017;25(4):545-85.

[23] https://www.citypopulation.de/en/brazil/cities/espirito-santo/ (Accessed Jan 1, 2022).

[24] Lin Q, Zhao S, Gao D, Lou Y, Yang S, Musa SS, Wang MH, Cai Y, Wang W, Yang I, et al. A conceptual model for the coronavirus disease 2019 (COVID-19) outbreak in Wuhan, China with individual reaction and governmental action. Int J Infect Dis 2020;93:211-6.
[25] https://www.indexmundi.com/brazil/demographics_profile.html (Accessed Jan 1, 2022).

[26] Omame A, Rwezaura H, Diagne ML, et al. Covid-19 and dengue co-infection in Brazil: optimal control and cost-effectiveness analysis. Eur Phys J Plus 2021;136:1090. http://dx.doi.org/10.1140/epjp/s13360-021-02030-6.

[27] Omame A, Isah ME, Abbas M, Abdel-Aty A, Onyenegecha CP. A fractional order model for dual variants of COVID-19 and HIV co-infection via Atangana-Baleanu derivative. Alexandria Eng J 2022. http://dx.doi.org/10.1016/j.aej.2022.03.013.

[28] Omame A, Sene N, Nomega I, Nwakamma CJ, Nwoefor EU, Iheonu NO, Okuonghae D. Analysis of COVID-19 and comorbidity co-infection model. Optim Control Appl Methods 2021;42(6):1568–90. http://dx.doi.org/10.1002/oca.2748.

[29] Yavus Ozkose. Investigation of interactions between COVID-19 and diabetes with hereditary traits using real data: A case study in Turkey. Comput Biol Med 2021. http://dx.doi.org/10.1016/j.compbiomed.2021.105044.

[30] Omame A, Abbas M, Nwajiery UK. A fractional-order control model for diabetes COVID-19 co-dynamics with Mittag-Leffler function. Alexandria Eng J 2022;61(10):7619–35. http://dx.doi.org/10.1016/j.aej.2022.01.012.

[31] Khan MS, Samreen M, Ozair M, et al. Bifurcation analysis of a discrete-time compartmental model for hypertensive or diabetic patients exposed to COVID-19. Eur Phys J Plus 2021;136:853. http://dx.doi.org/10.1140/epjp/s13360-021-01862-6.

[32] Goudiaby MS, Gning LD, Diagne ML, Dia BM, Rwezaura H, Tchuenche JM. Optimal control analysis of a COVID-19 and tuberculosis co-dynamics model. Inform Med Unlocked 2022;26:1008492022.

[33] Omame A, Abbas M, Onyenegecha PC. A fractional-order model for COVID-19 and tuberculosis co-infection using Atangana-Baleanu derivative. Chaos Solitons Fractals 153(1):111486.

[34] Weiss DJ, Bertozzi-Villa A, Rumisha SF, Amratia P, Arambepola R, Battle KE, et al. Indirect effects of the COVID-19 pandemic on malaria intervention coverage, morbidity, and mortality in Africa: a geospatial modelling analysis. Lancet Inf Dis 2020;21:59–69.

[35] Sherrard-Smith E, Hogan AB, Hamlet A, et al. The potential public health consequences of COVID-19 on malaria in Africa. Nat Med 2020;26:1411–6.

[36] Tchoumi SY, Diagne ML, Rwezaura H, Tchuenche JM. Malaria and COVID-19 co-dynamics: A mathematical model and optimal control. Appl Math Model 2021;99:294–327.

[37] Lahshikamthanam S, Leela S, Martynyuk AA. Stability analysis of nonlinear systems. New York: Marcel Dekker, Inc; 1989.

[38] van den Driessche P, Watmough J. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Math Biosci 2002;180(1):29–48.

[39] Castillo-Chavez C, Song B. Dynamical models of tuberculosis and their applications. Math Biosci Eng 2004;1:361–404.

[40] Mtsi E, Rwezaura H, Tchuenche JM. A mathematical analysis of malaria and tuberculosis co-dynamics. Discrete Contin Dyn Syst B 2009;12(4):827–64.

[41] Nwankwo A, Okuonghae D. Mathematical analysis of the transmission dynamics of HIV syphilis co-infection in the presence of treatment for syphilis. Bull Math Biol 2018;80(3):437–92.

[42] Fleming WH. Deterministic and stochastic optimal control. New York: Springer; 1975.

[43] Pontryagin L, Boltyanskii V, Gamkrelidze R, Mishchenko E. The mathematical theory of optimal control process, Vol. 4. New York/London: John Wiley & Sons; 1963.

[44] LaSalle JP. The stability of dynamical systems. Regional conferences series in applied mathematics, Philadelphia: SIAM; 1976.