Advances in Differential Equations and Control Processes 2026, 33(2), 4021.
https://doi.org/10.59400/adecp4021

Article

Within-host dynamics of ZIKV-CHIKV co-infection: Stability analysis and effective therapeutic strategies

Ahmed Elaiw* , **Zainab Alkhudhari, Aatef Hobiny**

Department of Mathematics, Faculty of Science, King Abdulaziz University, P. O. Box 80203, Jeddah 21589, Saudi Arabia

*** Corresponding author:** Ahmed Elaiw, aelaiwksu.edu.sa@kau.edu.sa

CITATION

Elaiw A, Alkhudhari Z, Hobiny A. Within-host dynamics of ZIKV-CHIKV co-infection: Stability analysis and effective therapeutic strategies. Advances in Differential Equations and Control Processes. 2026; 33(2): 4021. https://doi.org/10.59400/adecp4021

ARTICLE INFO

Received: 9 February 2026
Revised: 13 April 2026
Accepted: 16 April 2026
Available online: 6 May 2026

Abstract: In this paper, we develop a mathematical model that describes the within-host co-dynamics of two arboviruses, Zika virus (ZIKV) and Chikungunya virus (CHIKV). The model is also modified to investigate the impact of various treatment strategies. The model incorporates four cell types: uninfected target cells, latently infected cells, actively infected cells, and antibodies. The analysis establishes that all solutions remain nonnegative and bounded over time. It further reveals the presence of four distinct steady states: the disease-free steady state, the ZIKV-only steady state, the CHIKV-only steady state, and the coexistence steady state representing co-infection. The next-generation matrix technique was applied to determine the reproduction numbers for the ZIKV-only model, the CHIKV-only model, and the ZIKV-CHIKV co-infection model (denoted by R_Z^L, R_C^L and $R_0^L = \max\{R_Z^L, R_C^L\}$, respectively) as well as the invasion reproduction numbers $R_Z^{L,inv}$ and $R_C^{L,inv}$ which determine whether a virus can successfully invade an existing infection state. We conducted a mathematical analysis to determine the existence of equilibrium points and to establish the criteria for their global stability. Global stability is verified through the application of suitably constructed Lyapunov functions. The effects of four therapeutic strategies are included: (i) antiviral therapy that prevents viral infection of target cells, (ii) antiviral therapy that suppresses viral production, (iii) immune-stimulating treatment, and (iv) therapy that increases the rate of antibody circulation. Simulations show antivirals outperform immune-boosting strategies in clearing co-infection, while combining both offers synergy by suppressing replication and enhancing host defenses. The proposed model, along with the theoretical analysis, is new and offers a useful framework for studying viral co-infections.

Keywords: within-host model; ZIKV-CHIKV co-infection; immune response; antiviral therapy; global stability; basic reproduction number; invasion reproduction number; Lyapunov function

1. Introduction

Zika and Chikungunya are viral diseases transmitted by mosquitoes, caused by the Zika virus (ZIKV) and Chikungunya virus (CHIKV), respectively. These re-emerging arboviruses are primarily found in tropical and subtropical regions, where environmental and climatic conditions favor the proliferation of Aedes mosquito vectors, including Aedes aegypti and Aedes albopictus. Their reappearance and rapid spread have become a major global health concern, largely driven by factors such as increased international travel, accelerated urbanization, and climate change [1]. Both infections are associated with serious complications: ZIKV can cause neurological

disorders and congenital abnormalities, while CHIKV often leads to severe and persistent musculoskeletal symptoms, highlighting their significant public health impact [2]. In recent years, outbreaks of ZIKV and CHIKV have increased worldwide, contributing substantially to disease burden through elevated morbidity and, in some cases, mortality. According to Puntasecca et al. [3], between 2010 and 2019, CHIKV and ZIKV were responsible for an estimated annual loss of more than 106,000 and 44,000 disability-adjusted life years (DALYs), respectively. ZIKV, a member of the Flaviviridae family and the Flavivirus genus, is primarily transmitted by Aedes aegypti and Aedes albopictus mosquitoes [4]. In addition to vector-borne transmission, ZIKV can spread between humans through horizontal transmission (e.g., sexual contact) and vertical transmission (from mother to fetus during pregnancy). Moreover, infected humans can transmit the virus to susceptible mosquitoes when bitten, thereby sustaining the transmission cycle [5]. Zika virus (ZIKV) was first identified in 1947 in rhesus monkeys in the Zika Forest of Uganda, and human infections were documented in 1952 [6]. ZIKV was initially identified in Brazil in early 2015 [7], after which it rapidly expanded, with local transmission documented in over 86 countries and territories by 2018. Due to the extensive spread of this emerging public health threat, healthcare professionals need to be able to recognize the various clinical manifestations associated with ZIKV infection [8]. CHIKV is an RNA virus belonging to the Alphavirus genus of the Togaviridae family [9]. Like ZIKV, CHIKV is also primarily transmitted by Aedes mosquitoes. CHIKV was initially identified in 1952 on the Makonde Plateau in Africa [10]. From the 1960s through the 1980s, a number of outbreaks were recorded across several countries in both Asia and Africa. In contrast to dengue, which can be fatal in severe cases, chikungunya infections are rarely associated with mortality, although they can cause debilitating symptoms [11]. Since its re-emergence in 2004, CHIKV has caused increasingly extensive and severe outbreaks, particularly throughout the Indian Ocean islands and the Americas [12]. The clinical presentations of Chikungunya and Zika fevers closely resemble one another, commonly featuring symptoms such as fever, joint pain, muscle aches, skin rash, and eye inflammation [13]. Both viruses are also capable of leading to serious complications, including long-lasting joint pain and neurological issues [13]. Moreover, ZIKV infection during pregnancy has been linked to fetal complications, most notably congenital Zika syndrome [14]. Although both viruses produce similar early symptoms, with some differences, a notable distinction lies in the duration of illness: ZIKV infections typically resolve within two weeks, while CHIKV infections can result in prolonged joint pain and arthritis that may last for a year or longer [15].

In regions where viruses with similar transmission routes are widespread, individuals may acquire co-infections involving two or more pathogens. Viral infections lead to complex interactions that can influence replication dynamics and disease progression, and they often play a key role in determining suitable treatment strategies for managing co-infections [16]. Several studies have identified instances of concurrent infections with ZIKV and CHIKV [8, 15–19]. ZIKV-CHIKV coinfection cases have been documented in multiple countries, including Haiti, Colombia, Brazil, Nicaragua, Ecuador, and Mexico [17]. According to a meta-analysis, the

overall prevalence of CHIKV coinfection among individuals infected with ZIKV was estimated at 1%, with regional variations, higher in North America (2.8%) and considerably lower in Asia (0.1%) [16].

Mathematical models for infectious disease transmission are essential tools for understanding how diseases spread within populations, particularly during viral outbreaks such as COVID-19 [20, 21]. These models support the development of control strategies and assist in guiding public health policies. Considerable attention has been given to modeling single-pathogen infections, especially those related to Zika virus [5, 22–26]. Likewise, Chikungunya virus has been extensively studied through mathematical modeling [27–31].

Within-host mathematical models that describe the interactions among viruses, target cells, and immune cells have attracted considerable research interest. These models play a crucial role in deepening our understanding of viral dynamics within the host. It also provides insight into intracellular processes that are difficult to investigate experimentally in vitro. Moreover, such modeling enables the prediction of disease progression and supports the development of effective antiviral therapies and vaccines. Osuna et al. [32] and Best et al. [33] constructed a mathematical model for ZIKV infection as:

$$\begin{aligned}
\frac{dX}{dt} &= -\beta_Z X V_Z, \\
\frac{dY_Z^L}{dt} &= \beta_Z X V_Z - \eta_Z Y_Z^L, \\
\frac{dY_Z^A}{dt} &= \eta_Z Y_Z^L - a_Z Y_Z^A, \\
\frac{dV_Z}{dt} &= k_Z Y_Z^A - c_Z V_Z.
\end{aligned}$$

Here, X denotes the concentration of uninfected cells, which become infected upon contact with free ZIKV V_Z. The infection rate is given by the mass-action term $\beta_Z X V_Z$. Infected cells first enter a latent or eclipse stage Y_Z^L, during which they do not yet produce viral particles. These cells transition to a virus-producing state Y_Z^A at a rate $\eta_Z Y_Z^L$, where $1/\eta_Z$ represents the average duration of the eclipse phase. The actively infected cells are removed at rate a_Z, accounting for cytopathic effects caused by ZIKV. Each productively infected cell releases virus at a rate $k_Z Y_Z^A$, while free viral particles are eliminated from the system at a rate $c_Z V_Z$. In the study by Osuna et al. [32], a well-established target cell-limited framework was adapted to fit Zika virus data from non-pregnant monkeys. Building on this work, Best et al. [33] investigated the effects of antiviral treatments on ZIKV within-host dynamics using the same model from Osuna et al., which was identified through model selection as the most suitable for non-pregnant hosts. Later, Best and Perelson [34] developed more sophisticated within-host ZIKV models by explicitly incorporating immune responses into the viral dynamics. In their approach, interferon-α (IFNα) concentrations or natural killer (NK) cell activity were introduced as time-dependent components influencing the course of infection. Tuncer and Martcheva [35] formulated both within-host and within-vector models for ZIKV, addressing cases in pregnant and non-pregnant hosts. Their work was

driven by available empirical data and validated against experimental observations from monkey studies. Best et al. [36] developed mathematical models for ZIKV infection that account for the innate immune response and include mechanisms through which the virus interferes with or suppresses this immune activity.

The initial ZIKV within-host model did not incorporate the generation of target cells or account for the natural death rates of uninfected and latently infected cells. Nonetheless, this foundational model has been widely used to study ZIKV infection dynamics. Tang et al. [37] extended this framework by including both the recruitment and death rates of target cells. In their model, the dynamics of the uninfected target cell population X were described by:

$$\frac{dX}{dt} = \lambda - dX - \beta_Z X V_Z,$$

where λ is the constant rate of target cell generation, and dX represents the natural death rate of target cells.

Advancements have also been made in understanding the within-host dynamics of CHIKV through mathematical modeling. A within-host model for CHIKV dynamics that incorporates both the natural turnover of susceptible target cells (through recruitment and death processes) and the contribution of the antibody-mediated immune response is formulated [38]. The system is expressed as follows:

$$\begin{aligned}
\frac{dX}{dt} &= \lambda - dX - \beta_C X V_C, \\
\frac{dY_C^A}{dt} &= \beta_C X V_C - a_C Y_C^A, \\
\frac{dV_C}{dt} &= k_C Y_C^A - c_C V_C - r_C V_C W_C, \\
\frac{dW_C}{dt} &= \gamma_C + q_C V_C W_C - \mu_C W_C.
\end{aligned}$$

Here the subscript refers to CHIKV, W_C represents CHIKV-specific antibodies concentration. Antibodies are produced at a basal rate γ_C, further stimulated by viral presence at rate $q_C V_C W_C$ and decay at rate $\mu_C W_C$. The CHIKV particles are neutralized through antibody binding at a rate $r_C V_C W_C$. Elaiw et al. [39] proposed a CHIKV infection model incorporating latently infected cells, a time delay, and a generalized incidence function. In a related study, Alade et al. [40] examined a delayed CHIKV model where the rates of production, clearance, and proliferation of all compartments, along with the incidence rate, were governed by general nonlinear expressions. Models that consider two distinct transmission mechanisms (direct CHIKV-to-cell and infected-cell-to-cell pathways) have been explored [41–45]. Stochastic CHIKV infection models were presented in the studies by Gokila and Sambath [46] and by Yu et al. [47]. A fractional-order CHIKV infection model with adaptive immune response was examined [28].

Mathematical modeling of ZIKV co-infection with other arboviruses at the population level has attracted research interest. Such a co-infection as Zika and dengue co-infection [7,48,49]. In the study by Omame et al. [50], a fractional-order framework

was proposed to study the transmission dynamics of Zika–Dengue co-infection. In this formulation, the Atangana–Baleanu operator in the Caputo's sense was utilized to capture memory and hereditary effects within the system. Isea and Karl [51] proposed a co-infection model among Zika, Chikungunya and Dengue in order to study the dynamics of the three diseases at the same time. They observed the possibility of co-infection among the three diseases based on available data. Omame et al. [52] formulated and investigated a co-dynamics model that incorporates COVID-19 together with Zika, Chikungunya, and Dengue infections. The study explored how the presence of COVID-19 influences the transmission patterns of the other three arboviruses, and conversely, how these viruses may affect COVID-19 dynamics. Both local and global stability properties of the system were examined. Building on this work, Omame and Abbas [53] extended the framework by incorporating vaccination strategies against COVID-19 and Dengue to investigate their effects on the transmission dynamics of the Zika virus. However, despite these population-level studies of co-infection dynamics among humans, to the best of our knowledge, no mathematical model has been developed to investigate the within-host co-infection dynamics of Zika and Chikungunya viruses.

The main contributions of this paper are:

- We formulate a new model that describes the within-host co-dynamics of ZIKV and CHIKV.
- The model's well-posedness is shown.
- Four threshold parameters are determined, which completely govern the existence and stability of the four steady states of the model.
- We prove the global stability of all steady states using the Lyapunov method.
- The impact of various treatment strategies is examined.
- Theoretical results are supported via numerical simulations.

2. ZIKV-CHIKV co-infection model

The mathematical model of ZIKV-CHIKV co-infection is built upon the following biological and immunological assumptions:

H1 (Population dynamics)**.** *The proposed model describes the temporal evolution of several interacting populations: the concentration of uninfected target cells $X(t)$; ZIKV-infected cells in both latent and active states, denoted by $Y_Z^L(t)$ and $Y_Z^A(t)$; CHIKV-infected cells in latent and active phases, represented by $Y_C^L(t)$ and $Y_C^A(t)$; the free viral particles of ZIKV and CHIKV, given by $V_Z(t)$ and $V_C(t)$; and finally, the antibody responses specific to ZIKV and CHIKV, expressed as $W_Z(t)$ and $W_C(t)$. Compartments X, Y_Z^L, Y_Z^A, Y_C^L, Y_C^A, V_Z, V_C, W_Z and W_C die at rates dX, $b_Z Y_Z^L$, $a_Z Y_Z^A$, $b_C Y_C^L$, $a_C Y_C^A$, $c_Z V_Z$, $c_C V_C$, $\mu_Z W_Z$, and $\mu_C W_C$, respectively.*

H2 (Target cell competition)**.** *ZIKV and CHIKV compete for the same target cells X.*

H3 (Infection dynamics)**.** *Uninfected target cells are supplied at rate λ, and are infected by ZIKV and CHIKV with incidence terms $\beta_Z X V_Z$ and $\beta_C X V_C$, respectively (See Equation (1)).*

H4 (Infection outcomes)**.** *A fraction θ_Z of ZIKV-infected cells becomes active Y_Z^A, with the remainder $1-\theta_Z$ latent Y_Z^L; similarly, θ_C of CHIKV-infected cells becomes active Y_C^A, and $1-\theta_C$ enters latency Y_C^L (See Equations (2) and (4)).*

H5 (Latent cell activation)**.** *Latently infected cells activate at rates $\eta_Z Y_Z^L$ for ZIKV and $\eta_C Y_C^L$ for CHIKV (See Equations (2) and (4)).*

H6 (Viral production and neutralization)**.** *Free ZIKV and CHIKV virions are generated by actively infected cells Y_Z^A and Y_C^A at rates $k_Z Y_Z^A$ and $k_C Y_C^A$, respectively. These viral particles are subsequently neutralized by their corresponding antibodies W_Z and W_C at rates $r_Z V_Z W_Z$ and $r_C V_C W_C$ (See Equations (6) and (7)).*

H7 (Antibody dynamics)**.** *Virus-specific antibodies W_Z and W_C are produced at baseline rates γ_Z and γ_C, and are further stimulated by the presence of virus through the interactions $q_Z V_Z W_Z$ and $q_C V_C W_C$ (See Equations (8) and (9)).*

Based on assumptions H1–H7, the ZIKV-CHIKV co-infection model can be expressed as:

$$\frac{dX}{dt} = \lambda - dX - \beta_Z X V_Z - \beta_C X V_C, \tag{1}$$

$$\frac{dY_Z^L}{dt} = (1-\theta_Z)\beta_Z X V_Z - (\eta_Z + b_Z) Y_Z^L, \tag{2}$$

$$\frac{dY_Z^A}{dt} = \theta_Z \beta_Z X V_Z + \eta_Z Y_Z^L - a_Z Y_Z^A, \tag{3}$$

$$\frac{dY_C^L}{dt} = (1-\theta_C)\beta_C X V_C - (\eta_C + b_C) Y_C^L, \tag{4}$$

$$\frac{dY_C^A}{dt} = \theta_C \beta_C X V_C + \eta_C Y_C^L - a_C Y_C^A, \tag{5}$$

$$\frac{dV_Z}{dt} = k_Z Y_Z^A - c_Z V_Z - r_Z V_Z W_Z, \tag{6}$$

$$\frac{dV_C}{dt} = k_C Y_C^A - c_C V_C - r_C V_C W_C, \tag{7}$$

$$\frac{dW_Z}{dt} = \gamma_Z + q_Z V_Z W_Z - \mu_Z W_Z, \tag{8}$$

$$\frac{dW_C}{dt} = \gamma_C + q_C V_C W_C - \mu_C W_C. \tag{9}$$

All model parameters are assumed to be strictly positive. **Figure 1** illustrates the within-host progression pathways of ZIKV and CHIKV, emphasizing their interplay and the resulting effects on immune response dynamics. The initial condition for the system is given by:

$$\begin{aligned} X(0) > 0, Y_Z^L(0) \geq 0, Y_Z^A(0) \geq 0, \\ Y_C^L(0) \geq 0, Y_C^A(0) \geq 0, \\ V_Z(0) \geq 0, V_C(0) \geq 0, \\ W_Z(0) > 0, W_C(0) > 0. \end{aligned}$$

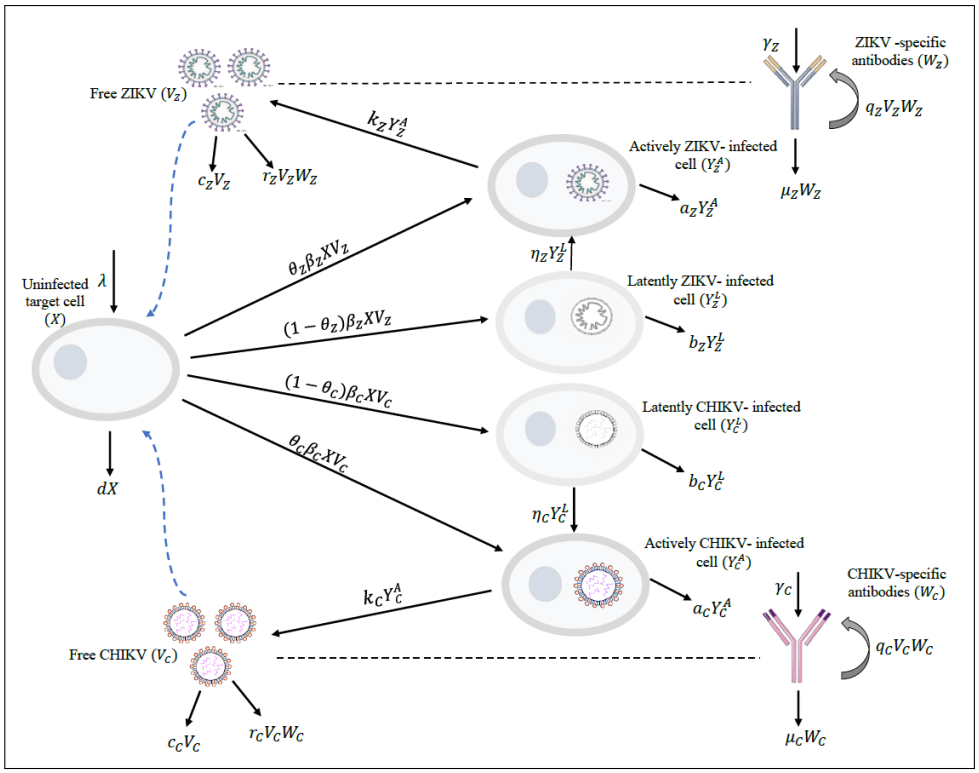


Figure 1. A schematic representation illustrating the within-host co-infection dynamics of ZIKV and CHIKV.

In what follows, we examine the fundamental and global characteristics of the model.

3. Preliminaries

This section provides preliminary findings on the model's well-posedness, together with the identification of steady states and the conditions ensuring their existence.

Model's well-posedness

It follows that the right-hand side of the system given by Equations (1)–(9) is continuous and satisfies a Lipschitz condition on the interval $[0, \iota]$, for some $\iota > 0$. Therefore, by standard results in the theory of differential equations, the Equations (1)–(9), subject to non-negative initial data, admits a unique local solution $(X(t), Y_Z^L(t), Y_Z^A(t), Y_C^L(t), Y_C^A(t), V_Z(t), V_C(t), W_Z(t), W_C(t))$ defined for $t \in [0, t_*)$, where $0 < t_* < \infty$.

Let us define $\chi_i > 0$, $i = 1, 2, ..., 5$ and $\sigma^L > 0$ as:

$$\chi_1 = \frac{\lambda}{\sigma^L} + \frac{\gamma_Z r_Z a_Z}{2\sigma^L q_Z k_Z} + \frac{\gamma_C r_C a_C}{2\sigma^L q_C k_C},$$
$$\chi_2 = \frac{2k_Z}{a_Z}\chi_1,\ \chi_3 = \frac{2k_C}{a_C}\chi_1,$$
$$\chi_4 = \frac{2q_Z k_Z}{r_Z a_Z}\chi_1,\ \chi_5 = \frac{2q_C k_C}{r_C a_C}\chi_1,$$
$$\sigma^L = \min\{d, b_Z, \frac{a_Z}{2}, b_C, \frac{a_C}{2}, c_Z, c_C, \mu_Z, \mu_C\}.$$

Lemma 1. *Under the initial condition of Equation (2), the solutions of Equations (1)–(9) are nonnegative and remain bounded for all* $t \geq 0$.

Proof.

$$\begin{aligned}
\frac{dX}{dt}|_{X=0} &= \lambda > 0,\\
\frac{dY_Z^L}{dt}|_{Y_Z^L=0} &= (1-\theta_Z)\beta_Z X V_Z \geq 0 \ \text{ for } \ X, V_Z \geq 0,\\
\frac{dY_Z^A}{dt}|_{Y_Z^A=0} &= \theta_Z\beta_Z X V_Z + \eta_Z Y_Z^L \geq 0 \ \text{ for } \ X, V_Z, Y_Z^L \geq 0,\\
\frac{dY_C^L}{dt}|_{Y_C^L=0} &= (1-\theta_C)\beta_C X V_C \geq 0 \ \text{ for } \ X, V_C \geq 0,\\
\frac{dY_C^A}{dt}|_{Y_C^A=0} &= \theta_C\beta_C X V_C + \eta_C Y_C^L \geq 0 \ \text{ for } \ X, V_C, Y_C^L \geq 0,\\
\frac{dV_Z}{dt}|_{V_Z=0} &= k_Z Y_Z^A \geq 0 \ \text{ for } Y_Z^A \geq 0,\\
\frac{dV_C}{dt}|_{V_C=0} &= k_C Y_C^A \geq 0 \ \text{ for } Y_C^A \geq 0,\\
\frac{dW_Z}{dt}|_{W_Z=0} &= \gamma_Z > 0,\\
\frac{dW_C}{dt}|_{W_C=0} &= \gamma_C > 0.
\end{aligned}$$

Thus, all solutions of Equations (1)–(9) with initial $(X(0), Y_Z^L(0), Y_Z^A(0), Y_C^L(0), Y_C^A(0), V_Z(0), V_C(0), W_Z(0), W_C(0)) \in \mathbb{R}^9_{\geq 0}$ satisfy $(X(t), Y_Z^L(t), Y_Z^A(t), Y_C^L(t), Y_C^A(t), V_Z(t), V_C(t), W_Z(t), W_C(t)) \in \mathbb{R}^9_{\geq 0}$ [54]. Define $T^L(t)$ as:

$$T^L = X + Y_Z^L + Y_Z^A + Y_C^L + Y_C^A + \tfrac{a_Z}{2k_Z}V_Z + \tfrac{a_C}{2k_C}V_C + \tfrac{a_Z r_Z}{2q_Z k_Z}W_Z + \tfrac{a_C r_C}{2q_C k_C}W_C,$$

then

$$\begin{aligned}
\frac{dT^L}{dt} = \frac{dX}{dt} + \frac{dY_Z^L}{dt} + \frac{dY_Z^A}{dt} + \frac{dY_C^L}{dt} + \frac{dY_C^A}{dt} + \frac{a_Z}{2k_Z}\frac{dV_Z}{dt}\\
+\frac{a_C}{2k_C}\frac{dV_C}{dt} + \frac{a_Z r_Z}{2q_Z k_Z}\frac{dW_Z}{dt} + \frac{a_C r_C}{2q_C k_C}\frac{dW_C}{dt}.
\end{aligned}$$

Using Equations (1)–(9) we get

$$\begin{aligned}
\frac{dT^L}{dt} &= \lambda - dX - \beta_Z X V_Z - \beta_C X V_C + (1-\theta_Z)\beta_Z X V_Z - b_Z Y_Z^L - \eta_Z Y_Z^L + \theta_Z\beta_Z X V_Z\\
&\quad - a_Z Y_Z^A + \eta_Z Y_Z^L + (1-\theta_C)\beta_C X V_C - b_C Y_C^L - \eta_C Y_C^L + \theta_C\beta_C X V_C - a_C Y_C^A\\
&\quad + \eta_C Y_C^L + \frac{a_Z}{2k_Z}(k_Z Y_Z^A - c_Z V_Z - r_Z V_Z W_Z) + \frac{a_C}{2k_C}(k_C Y_C^A - c_C V_C - r_C V_C W_C)\\
&\quad + \frac{a_Z r_Z}{2q_Z k_Z}(\gamma_Z + q_Z V_Z W_Z - \mu_Z W_Z) + \frac{a_C r_C}{2q_C k_C}(\gamma_C + q_C V_C W_C - \mu_C W_C)\\
&= \lambda - dX - b_Z Y_Z^L - \frac{a_Z}{2}Y_Z^A - b_C Y_C^L - \frac{a_C}{2}Y_C^A - \frac{a_Z c_Z}{2k_Z}V_Z - \frac{a_C c_C}{2k_C}V_C\\
&\quad + \frac{a_Z r_Z \gamma_Z}{2q_Z k_Z} - \frac{a_Z r_Z \mu_Z}{2q_Z k_Z}W_Z + \frac{a_C r_C \gamma_C}{2q_C k_C} - \frac{a_C r_C \mu_C}{2q_C k_C}W_C\\
&\leq \lambda + \frac{a_Z r_Z \gamma_Z}{2q_Z k_Z} + \frac{a_C r_C \gamma_C}{2q_C k_C} - \sigma^L T^L.
\end{aligned}$$

Thus, $T^L(t) \leq \chi_1$ when $T^L(0) \leq \chi_1$. This implies that $0 \leq X, Y_Z^L, Y_Z^A, Y_C^L, Y_C^A \leq \chi_1$, $0 \leq V_Z \leq \chi_2$, $0 \leq V_C \leq \chi_3$, $0 \leq W_Z \leq \chi_4$, and $0 \leq W_C \leq \chi_5$ if $0 \leq$

$X(0)+Y_Z^L(0)+Y_Z^A(0)+Y_C^L(0)+Y_C^A(0)+\frac{a_Z}{2k_Z}V_Z(0)+\frac{a_C}{2k_C}V_C(0)+\frac{a_Z r_Z}{2q_Z k_Z}W_Z(0)+\frac{a_C r_C}{2q_C k_C}W_C(0) \leq \chi_1$.

So we define a region Ω^L as:

$$\Omega^L = \Big\{(X, Y_Z^L, Y_Z^A, Y_C^L, Y_C^A, V_Z, V_C, W_Z, W_C) \in \mathbb{R}^9_{\geq 0} : \\ 0 \leq X, Y_Z^L, Y_Z^A, Y_C^L, Y_C^A \leq \chi_1, \quad 0 \leq V_Z \leq \chi_2, \quad 0 \leq V_C \leq \chi_3, \\ 0 \leq W_Z \leq \chi_4, \quad 0 \leq W_C \leq \chi_5\Big\}.$$

Lemma 1 shows that the biologically feasible region is positively invariant for the Equations (1)–(9). □

4. The basic reproduction numbers

The basic reproduction number represents the average number of new infections generated by a single infected cell during its infectious period, assuming that all target cells are initially uninfected. It is evaluated at the disease-free steady state. The basic reproduction number R_0^L for the ZIKV-CHIKV co-infection system is derived using the next-generation matrix approach introduced by Driessche and Watmough [55].

4.1. The basic reproduction number for ZIKV-only infection

The ZIKV-only infection model is obtained by setting $Y_C^L = Y_C^A = V_C = 0$ in Equations (1)–(9), which yields the following reduced model:

$$\frac{dX}{dt} = \lambda - dX - \beta_Z X V_Z, \tag{10}$$
$$\frac{dY_Z^L}{dt} = (1-\theta_Z)\beta_Z X V_Z - (\eta_Z + b_Z)Y_Z^L, \tag{11}$$
$$\frac{dY_Z^A}{dt} = \theta_Z \beta_Z X V_Z + \eta_Z Y_Z^L - a_Z Y_Z^A, \tag{12}$$
$$\frac{dV_Z}{dt} = k_Z Y_Z^A - c_Z V_Z - r_Z V_Z W_Z, \tag{13}$$
$$\frac{dW_Z}{dt} = \gamma_Z + q_Z V_Z W_Z - \mu_Z W_Z, \tag{14}$$
$$\frac{dW_C}{dt} = \gamma_C - \mu_C W_C. \tag{15}$$

The disease-free steady state of Equations (10)–(15) is given by $SS^0 = (X^0, 0, 0, 0, W_Z^0, W_C^0)$, where $X^0 = \frac{\lambda}{d}$, $W_Z^0 = \frac{\gamma_Z}{\mu_Z}$ and $W_C^0 = \frac{\gamma_C}{\mu_C}$. The basic reproduction number for the ZIKV-only infection, R_Z^L, is defined as the spectral radius (i.e., the dominant eigenvalue) of the next-generation matrix $\rho(\mathbb{F}_Z \mathbb{V}_Z^{-1})$, where $\mathbb{F}_Z$ represents the infection matrix and $\mathbb{V}_Z$ denotes the transition matrix derived from system [55].

We define the matrices $\mathcal{F}_Z$ and $\mathcal{V}_Z$, which represent the new infection terms and the remaining transition terms, respectively, as:

$$\mathcal{F}_Z = \begin{bmatrix} (1-\theta_Z)\beta_Z X V_Z \\ \theta_Z \beta_Z X V_Z \\ 0 \end{bmatrix}, \ \mathcal{V}_Z = \begin{bmatrix} (\eta_Z + b_Z)Y_Z^L \\ -\eta_Z Y_Z^L + a_Z Y_Z^A \\ -k_Z Y_Z^A + c_Z V_Z + r_Z V_Z W_Z \end{bmatrix}.$$

The Jacobians of the matrices $\mathcal{F}_Z$ and $\mathcal{V}_Z$ evaluated at the disease-free steady state of Equations (10)–(15) are given by:

$$\mathbb{F}_Z = \begin{bmatrix} 0 & 0 & (1-\theta_Z)\beta_Z X^0 \\ 0 & 0 & \theta_Z \beta_Z X^0 \\ 0 & 0 & 0 \end{bmatrix}, \ \mathbb{V}_Z = \begin{bmatrix} \eta_Z + b_Z & 0 & 0 \\ -\eta_Z & a_Z & 0 \\ 0 & -k_Z & c_Z + r_Z W_Z^0 \end{bmatrix}.$$

Hence, the basic reproduction number for the ZIKV-only infection is given by:

$$R_Z^L = \rho(\mathbb{F}_Z \mathbb{V}_Z^{-1}) = \frac{k_Z \beta_Z \lambda \mu_Z (b_Z \theta_Z + \eta_Z)}{a_Z d (b_Z + \eta_Z)(r_Z \gamma_Z + c_Z \mu_Z)}.$$

4.2. The basic reproduction number for CHIKV-only infection

Similarly, the CHIKV infection model is obtained by setting $Y_Z^L = Y_Z^A = V_Z = 0$ in Equations (1)–(9) leading to the following reduced model:

$$\frac{dX}{dt} = \lambda - dX - \beta_Z X V_Z - \beta_C X V_C, \tag{16}$$

$$\frac{dY_C^L}{dt} = (1-\theta_C)\beta_C X V_C - (\eta_C + b_C) Y_C^L, \tag{17}$$

$$\frac{dY_C^A}{dt} = \theta_C \beta_C X V_C + \eta_C Y_C^L - a_C Y_C^A, \tag{18}$$

$$\frac{dV_C}{dt} = k_C Y_C^A - c_C V_C - r_C V_C W_C, \tag{19}$$

$$\frac{dW_Z}{dt} = \gamma_Z + q_Z V_Z W_Z - \mu_Z W_Z, \tag{20}$$

$$\frac{dW_C}{dt} = \gamma_C + q_C V_C W_C - \mu_C W_C. \tag{21}$$

Using the same procedure as for the ZIKV case, the basic reproduction number, R_C^L, for CHIKV is derived via the next-generation matrix approach. Accordingly, the matrices $\mathcal{F}_C$ and $\mathcal{V}_C$ are defined as follows:

$$\mathcal{F}_C = \begin{bmatrix} (1-\theta_C)\beta_C X V_C \\ \theta_C \beta_C X V_C \\ 0 \end{bmatrix}, \ \mathcal{V}_C = \begin{bmatrix} (\eta_C + b_C) Y_C^L \\ -\eta_C Y_C^L + a_C Y_C^A \\ -k_C Y_C^A + c_C V_C + r_C V_C W_C \end{bmatrix}.$$

The Jacobians of the matrices $\mathcal{F}_C$ and $\mathcal{V}_C$ evaluated at the disease-free steady state of Equations (16)–(21) SS^0 are given by:

$$\mathbb{F}_C = \begin{bmatrix} 0 & 0 & (1-\theta_C)\beta_C X^0 \\ 0 & 0 & \theta_C \beta_C X^0 \\ 0 & 0 & 0 \end{bmatrix}, \mathbb{V}_C = \begin{bmatrix} \eta_C + b_C & 0 & 0 \\ -\eta_C & a_C & 0 \\ 0 & -k_C & c_C + r_C W_C^0 \end{bmatrix}.$$

Hence

$$R_C^L = \rho(\mathbb{F}_C \mathbb{V}_C^{-1}) = \frac{k_C \beta_C \lambda \mu_C (b_C \theta_C + \eta_C)}{a_C d (b_C + \eta_C)(r_C \gamma_C + c_C \mu_C)}.$$

4.3. The basic reproduction number for ZIKV-CHIKV co-infection

For the co-infection model of Equations (1)–(9), we calculate the basic reproduction number R_0^L as $R_0^L = \rho(\mathbb{F}_0 \mathbb{V}_0^{-1})$ where

$$\mathbb{F}_0 = \begin{bmatrix} 0 & 0 & 0 & 0 & (1-\theta_Z)\beta_Z X^0 & 0 \\ 0 & 0 & 0 & 0 & \theta_Z\beta_Z X^0 & 0 \\ 0 & 0 & 0 & 0 & 0 & (1-\theta_C)\beta_C X^0 \\ 0 & 0 & 0 & 0 & 0 & \theta_C\beta_C X^0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix} \text{ and}$$

$$\mathbb{V}_0 = \begin{bmatrix} \eta_Z + b_Z & 0 & 0 & 0 & 0 & 0 \\ -\eta_Z & a_Z & 0 & 0 & 0 & 0 \\ 0 & 0 & \eta_C + b_C & 0 & 0 & 0 \\ 0 & 0 & -\eta_C & a_C & 0 & 0 \\ 0 & -k_Z & 0 & 0 & c_Z + r_Z W_Z^0 & 0 \\ 0 & 0 & 0 & -k_C & 0 & c_C + r_C W_C^0 \end{bmatrix}.$$

The basic reproduction number for the co-infection model is:

$$\begin{aligned} R_0^L &= \rho(\mathbb{F}_0\mathbb{V}_0^{-1}) \\ &= \max\left\{ \frac{k_Z\beta_Z\lambda\mu_Z(b_Z\theta_Z + \eta_Z)}{a_Z d(b_Z+\eta_Z)(r_Z\gamma_Z + c_Z\mu_Z)}, \frac{k_C\beta_C\lambda\mu_C(b_C\theta_C + \eta_C)}{a_C d(b_C+\eta_C)(r_C\gamma_C + c_C\mu_C)} \right\} \\ &= \max\{R_Z^L, R_C^L\}. \end{aligned}$$

5. The invasion reproduction numbers

In between-host dynamics, the invasion reproduction number quantifies the ability of a new disease to invade a population in which another disease is already at an endemic steady state [56, 57]. In within-host viral dynamics, it measures the ability of a new virus to invade a host in which another virus has already established an infected steady state [58].

5.1. Invasion of ZIKV into a CHIKV-resident host

Assume that CHIKV is resident at the CHIKV mono-infection steady state $\overline{SS} = (\overline{X}, 0, 0, \overline{Y}_C^L, \overline{Y}_C^A, 0, \overline{V}_C, \overline{W}_Z, \overline{W}_C)$, where

$$\begin{aligned} &\overline{X} = \frac{\lambda}{d + \beta_C\overline{V}_C},\ \overline{Y}_Z^L = 0,\ \overline{Y}_Z^A = 0,\ \overline{Y}_C^L = \frac{(1-\theta_C)\beta_C \digamma_4 \lambda \overline{V}_C}{(\eta_C + b_C)(d + \beta_C\overline{V}_C)}, \\ &\overline{Y}_C^A = \frac{\rho_C\beta_C\lambda\overline{V}_C}{a_C(\eta_C + b_C)(d + \beta_C\overline{V}_C)}, \\ &\overline{W}_Z = \frac{\gamma_Z}{\mu_Z} \text{ and } \overline{W}_C = \frac{\gamma_C}{\mu_C - q_C\overline{V}_C} > 0 \text{ where } \overline{V}_C \in \left(0, \frac{\mu_C}{q_C}\right). \end{aligned}$$

The invasion reproduction number of ZIKV is derived by considering Equations (10)–(15) and evaluating the Jacobian matrices of $\mathcal{F}_Z$ and $\mathcal{V}_Z$ at the steady state $\overline{SS}$, yielding

$$\mathbb{F}_Z^{L,inv} = \begin{bmatrix} 0 & 0 & (1-\theta_Z)\beta_Z\overline{X} \\ 0 & 0 & \theta_Z\beta_Z\overline{X} \\ 0 & 0 & 0 \end{bmatrix}, \mathbb{V}_Z^{L,inv} = \begin{bmatrix} \eta_Z + b_Z & 0 & 0 \\ -\eta_Z & a_Z & 0 \\ 0 & -k_Z & c_Z + r_Z\overline{W}_Z \end{bmatrix}.$$

Thus, the invasion reproduction number of ZIKV is given by

$$R_Z^{L,inv} = \rho\left(\mathbb{F}_Z^{inv}\mathbb{V}_Z^{inv-1}\right) = \frac{k_Z\beta_Z\rho_Z\overline{X}}{a_Z(\eta_Z+b_Z)(c_Z+r_Z\overline{W}_Z)} = \frac{k_Z\beta_Z\lambda\mu_Z\rho_Z}{a_Z d(\eta_Z+b_Z)(r_Z\gamma_Z+c_Z\mu_Z)\left(1+\frac{\beta_C}{d}\overline{V}_C\right)}.$$

5.2. Invasion of CHIKV into a ZIKV-resident host

Assume that ZIKV is resident at the ZIKV-only infection steady state $SS^* = (X^*, Y_Z^*, 0, V_Z^*, 0, W_Z^*, W_C^*)$, where

$$X^* = \frac{\lambda}{d+\beta_Z V_Z^*},\ Y_Z^{L*} = \frac{(1-\theta_Z)\beta_Z\lambda V_Z^*}{(\eta_Z+b_Z)(d+\beta_Z V_Z^*)},\ Y_Z^{A*} = \frac{\rho_Z\beta_Z\lambda V_Z^*}{a_Z(\eta_Z+b_Z)(d+\beta_Z V_Z^*)},$$
$$Y_C^{L*} = 0,\ Y_C^{A*} = 0,\ W_Z^* = \frac{\gamma_Z}{\mu_Z - q_Z V_Z^*} \text{ and } W_C^* = \frac{\gamma_C}{\mu_C} \text{ where } V_Z^* \in \left(0, \frac{\mu_Z}{q_Z}\right).$$

Considering Equations (16)–(21), the corresponding next-generation matrices for CHIKV invading a ZIKV-resident host are given by

$$\mathbb{F}_C^{inv} = \begin{bmatrix} 0 & 0 & (1-\theta_C)\beta_C X^* \\ 0 & 0 & \theta_C\beta_C X^* \\ 0 & 0 & 0 \end{bmatrix}, \mathbb{V}_C^{inv} = \begin{bmatrix} \eta_C+b_C & 0 & 0 \\ -\eta_C & a_C & 0 \\ 0 & -k_C & c_C+r_C W_C^* \end{bmatrix}.$$

Hence, the invasion reproduction number of CHIKV is

$$R_C^{L,inv} = \rho\left(\mathbb{F}_C^{inv}\mathbb{V}_C^{inv-1}\right) = \frac{k_C\beta_C\rho_C X^*}{a_C(\eta_C+b_C)(c_C+r_C W_C^*)} = \frac{k_C\beta_C\lambda\mu_C\rho_C}{a_C d(\eta_C+b_C)(r_C\gamma_C+c_C\mu_C)\left(1+\frac{\beta_Z}{d}V_Z^*\right)}.$$

6. Existence and global stability of equilibria

We investigate the existence of steady states for the model defined by Equations (1)–(9). The basic reproduction number R_0^L for the ZIKV-CHIKV co-infection system is given by

$$R_0^L = \max\{R_Z^L, R_C^L\},$$

where,

$$R_Z^L = \frac{k_Z\beta_Z\lambda\mu_Z(\eta_Z+b_Z\theta_Z)}{a_Z d(\eta_Z+b_Z)(r_Z\gamma_Z+c_Z\mu_Z)},$$
$$R_C^L = \frac{k_C\beta_C\lambda\mu_C(\eta_C+b_C\theta_C)}{a_C d(\eta_C+b_C)(r_C\gamma_C+c_C\mu_C)}.$$

It should be noted that R_Z^L corresponds to the basic reproduction number associated with ZIKV-only infection, whereas R_C^L represents that of CHIKV-only infection.

Furthermore, the invasion reproduction numbers $R_Z^{L,inv}$ and $R_C^{L,inv}$, which describe the ability of one virus to invade when the other is already at endemic steady

state, are derived for Equations (1)–(9). Specifically, they are given by

$$R_Z^{L,inv} = \frac{k_Z\beta_Z\lambda\mu_Z(\eta_Z + b_Z\theta_Z)}{a_Z d(\eta_Z + b_Z)(r_Z\gamma_Z + c_Z\mu_Z)\left(1 + \frac{\beta_C}{d}\overline{V}_C\right)} = \frac{R_Z^L}{1 + \frac{\beta_C}{d}\overline{V}_C},$$
$$R_C^{L,inv} = \frac{k_C\beta_C\lambda\mu_C(\eta_C + b_C\theta_C)}{a_C d(\eta_C + b_C)(r_C\gamma_C + c_C\mu_C)\left(1 + \frac{\beta_Z}{d}V_Z^*\right)} = \frac{R_C^L}{1 + \frac{\beta_Z}{d}V_Z^*}.$$

Clearly,

$$R_Z^{L,inv} = \frac{R_Z^L}{1 + \frac{\beta_C}{d}\overline{V}_C} < R_Z^L,$$
$$R_C^{L,inv} = \frac{R_C^L}{1 + \frac{\beta_Z}{d}V_Z^*} < R_C^L.$$

6.1. Existence of steady states

Define $X^0 = \frac{\lambda}{d}$, $W_Z^0 = \frac{\gamma_Z}{\mu_Z}$ and $W_C^0 = \frac{\gamma_C}{\mu_C}$. As a result, we can derive the following key finding concerning the existence of steady states for the system outlined by Equations (1)–(9).

Lemma 2. *(i) The disease-free steady state always exists and is given by* $SS^0 = (X^0, 0, 0, 0, 0, 0, 0, W_Z^0, W_C^0)$,

(ii) if $R_Z^L > 1$, *then, in addition to* SS^0, *there exists a ZIKV-only steady state* $SS^* = (X^*, Y_Z^{L*}, Y_Z^{A*}, 0, 0, V_Z^*, 0, W_Z^*, W_C^*)$,

(iii) if $R_C^L > 1$, *then, in addition to* SS^0, *there exists a CHIKV-only steady state* $\overline{SS} = (\overline{X}, 0, 0, \overline{Y}_C^L, \overline{Y}_C^A, 0, \overline{V}_C, \overline{W}_Z, \overline{W}_C)$,

(iv) if $R_Z^{L,inv} > 1$ *and* $R_C^{L,inv} > 1$, *then the system admits the steady states* SS^0, SS^* *and* $\overline{SS}$ *as well as a coexistence (co-infection) steady state of the form* $\widetilde{SS} = (\widetilde{X}, \widetilde{Y}_Z^L, \widetilde{Y}_Z^A, \widetilde{Y}_C^L, \widetilde{Y}_C^A, \widetilde{V}_Z, \widetilde{V}_C, \widetilde{W}_Z, \widetilde{W}_C)$.

Proof. Let the right-hand sides of Equations (1)–(9) be set equal to zero.

$$0 = \lambda - dX - \beta_Z X V_Z - \beta_C X V_C, \tag{22}$$
$$0 = (1 - \theta_Z)\beta_Z X V_Z - (\eta_Z + b_Z)Y_Z^L, \tag{23}$$
$$0 = \theta_Z\beta_Z X V_Z + \eta_Z Y_Z^L - a_Z Y_Z^A, \tag{24}$$
$$0 = (1 - \theta_C)\beta_C X V_C - (\eta_C + b_C)Y_C^L, \tag{25}$$
$$0 = \theta_C\beta_C X V_C + \eta_C Y_C^L - a_C Y_C^A, \tag{26}$$
$$0 = k_Z Y_Z^A - c_Z V_Z - r_Z V_Z W_Z, \tag{27}$$
$$0 = k_C Y_C^A - c_C V_C - r_C V_C W_C, \tag{28}$$
$$0 = \gamma_Z + q_Z V_Z W_Z - \mu_Z W_Z, \tag{29}$$
$$0 = \gamma_C + q_C V_C W_C - \mu_C W_C. \tag{30}$$

From Equations (22)–(30) we have

$$
\begin{aligned}
X &= \frac{\lambda}{d+\beta_Z V_Z+\beta_C V_C},\ Y_Z^L = \frac{(1-\theta_Z)\beta_Z\lambda V_Z}{(\eta_Z+b_Z)(d+\beta_Z V_Z+\beta_C V_C)},\\
Y_Z^A &= \frac{(\eta_Z+b_Z\theta_Z)\beta_Z\lambda V_Z}{a_Z(\eta_Z+b_Z)(d+\beta_Z V_Z+\beta_C V_C)},\ Y_C^L = \frac{(1-\theta_C)\beta_C\lambda V_C}{(\eta_C+b_C)(d+\beta_Z V_Z+\beta_C V_C)},\\
Y_C^A &= \frac{(\eta_C+b_C\theta_C)\beta_C\lambda V_C}{a_C(\eta_C+b_C)(d+\beta_Z V_Z+\beta_C V_C)},\ W_Z = \frac{\gamma_Z}{\mu_Z-q_Z V_Z} \text{ and } W_C = \frac{\gamma_C}{\mu_C-q_C V_C}.
\end{aligned} \tag{31}
$$

We note that $W_Z > 0$ and $W_C > 0$, when $V_Z \in \left[0, \frac{\mu_Z}{q_Z}\right)$ and $V_C \in \left[0, \frac{\mu_C}{q_C}\right)$ respectively.

Substituting in Equations (27) and (28) we obtain

$$
\left(\frac{k_Z\beta_Z\lambda(\eta_Z+b_Z\theta_Z)}{a_Z(\eta_Z+b_Z)(d+\beta_Z V_Z+\beta_C V_C)}+\frac{r_Z\gamma_Z}{q_Z V_Z-\mu_Z}-c_Z\right)V_Z = 0, \tag{32}
$$

$$
\left(\frac{k_C\beta_C\lambda(\eta_C+b_C\theta_C)}{a_C(\eta_C+b_C)(d+\beta_Z V_Z+\beta_C V_C)}+\frac{r_C\gamma_C}{q_C V_C-\mu_C}-c_C\right)V_C = 0. \tag{33}
$$

Equations (32) and (33) admit four possible cases:

Case (I) $V_Z = 0$ and $V_C = 0$ corresponding to the disease-free steady state $SS^0 = (X^0, 0, 0, 0, 0, 0, 0, W_Z^0, W_C^0)$.

Case (II) $V_Z \neq 0$ and $V_C = 0$, so from Equation (32) we get

$$
\frac{k_Z\beta_Z\lambda(\eta_Z+b_Z\theta_Z)}{a_Z(\eta_Z+b_Z)(d+\beta_Z V_Z)}-c_Z-\frac{r_Z\gamma_Z}{\mu_Z-q_Z V_Z} = 0,
$$

which gives

$$
\frac{A_Z^L V_Z^2+B_Z^L V_Z+C_Z^L}{q_Z V_Z-\mu_Z} = 0, \tag{34}
$$

where

$$
\begin{aligned}
A_Z^L &= a_Z\beta_Z c_Z q_Z(\eta_Z+b_Z),\\
B_Z^L &= a_Z d c_Z q_Z(\eta_Z+b_Z)-k_Z\beta_Z\lambda q_Z(\eta_Z+b_Z\theta_Z)-a_Z\beta_Z(\eta_Z+b_Z)(r_Z\gamma_Z+c_Z\mu_Z),\\
C_Z^L &= k_Z\beta_Z\lambda\mu_Z(\eta_Z+b_Z\theta_Z)-a_Z d(\eta_Z+b_Z)(r_Z\gamma_Z+c_Z\mu_Z).
\end{aligned}
$$

Define

$$
H^{L*}(V_Z) = \frac{A_Z^L V_Z^2+B_Z^L V_Z+C_Z^L}{q_Z V_Z-\mu_Z},\ \text{ where } V_Z \in \left[0, \frac{\mu_Z}{q_Z}\right).
$$

We get

$$
\begin{aligned}
H^{L*}(0) &= -\frac{C_Z^L}{\mu_Z} = \frac{a_Z d(\eta_Z+b_Z)(r_Z\gamma_Z+c_Z\mu_Z)-k_Z\beta_Z\lambda\mu_Z(\eta_Z+b_Z\theta_Z)}{\mu_Z}\\
&= \frac{a_Z d(\eta_Z+b_Z)(r_Z\gamma_Z+c_Z\mu_Z)}{\mu_Z}\left(1-R_Z^L\right).
\end{aligned}
$$

We have $H^{L*}(0) < 0$ if $R_Z^L > 1$. Moreover

$$
\lim_{V_Z\to\left(\frac{\mu_Z}{q_Z}\right)^-} H^{L*}(V_Z) = \infty,
$$

then there exists $V_Z^* \in \left(0, \frac{\mu_Z}{q_Z}\right)$ such that $H^{L*}(V_Z^*) = 0$. If $R_Z^L > 1$, then

$$\begin{aligned}
&\Rightarrow \frac{k_Z\beta_Z\lambda\mu_Z(\eta_Z + b_Z\theta_Z)}{a_Z d(\eta_Z + b_Z)(r_Z\gamma_Z + c_Z\mu_Z)} > 1 \\
&\Rightarrow k_Z\beta_Z\lambda\mu_Z(\eta_Z + b_Z\theta_Z) > a_Z d(\eta_Z + b_Z)(r_Z\gamma_Z + c_Z\mu_Z) > a_Z d c_Z\mu_Z(\eta_Z + b_Z) \\
&\Rightarrow k_Z\beta_Z\lambda q_Z(\eta_Z + b_Z\theta_Z) > a_Z d c_Z q_Z(\eta_Z + b_Z),
\end{aligned}$$

which implies that $B_Z^L < 0$. Moreover

$$C_Z^L = k_Z\beta_Z\lambda\mu_Z(\eta_Z + b_Z\theta_Z) - a_Z d(\eta_Z + b_Z)(r_Z\gamma_Z + c_Z\mu_Z) > 0 \text{ if } R_Z^L > 1.$$

Therefore, two positive solutions exist as:

$$V_Z^{\pm} = \frac{-B_Z^L \pm \sqrt{\left(B_Z^L\right)^2 - 4A_Z^L C_Z^L}}{2A_Z^L}.$$

We have

$$\lim_{V_Z \to \left(\frac{\mu_Z}{q_Z}\right)^+} H^{L*}(V_Z) = -\infty,$$
$$\lim_{V_Z \to \infty} H^{L*}(V_Z) = \infty.$$

Then

$$V_Z^- \in \left(0, \frac{\mu_Z}{q_Z}\right) \text{ and } V_Z^+ \in \left(\frac{\mu_Z}{q_Z}, \infty\right).$$

Then we take

$$V_Z^* = \frac{-B_Z^L - \sqrt{\left(B_Z^L\right)^2 - 4A_Z^L C_Z^L}}{2A_Z^L}.$$

Hence

$$\begin{aligned}
&X^* = \frac{X^0}{1 + \frac{\beta_Z}{d}V_Z^*} > 0,\ Y_Z^{L*} = \frac{(1-\theta_Z)\beta_Z X^0 V_Z^*}{(\eta_Z + b_Z)(1 + \frac{\beta_Z}{d}V_Z^*)} > 0, \\
&Y_Z^{A*} = \frac{(\eta_Z + b_Z\theta_Z)\beta_Z X^0 V_Z^*}{a_Z(\eta_Z + b_Z)(1 + \frac{\beta_Z}{d}V_Z^*)} > 0, \\
&Y_C^{L*} = 0,\ Y_C^{A*} = 0,\ W_Z^* = \frac{\gamma_Z}{\mu_Z - q_Z V_Z^*} > 0 \text{ and } W_C^* = \frac{\gamma_C}{\mu_C} > 0.
\end{aligned}$$

Consequently, a ZIKV-only infection steady state

$$SS^* = (X^*, Y_Z^{L*}, Y_Z^{A*}, 0, 0, V_Z^*, 0, W_Z^*, W_C^*) \tag{35}$$

exists whenever $R_Z^L > 1$.

Case (III) $V_Z = 0$ and $V_C \neq 0$, hence $\overline{Y}_Z^L = 0$, $\overline{Y}_Z^A = 0$. Equation (33) reduces to

$$\frac{(\eta_C + b_C\theta_C)k_C\beta_C\lambda}{a_C(d + \beta_C V_C)(\eta_C + b_C)} - c_C + \frac{r_C\gamma_C}{q_C V_C - \mu_C} = 0,$$

which gives

$$\frac{A_C^L V_C^2 + B_C^L V_C + C_C^L}{q_C V_C - \mu_C} = 0, \tag{36}$$

where

$$A_C^L = a_C c_C q_C \beta_C(\eta_C + b_C),$$
$$B_C^L = a_C d c_C q_C \beta_C(\eta_C + b_C) - k_C \lambda q_C \beta_C(\eta_C + \theta_C b_C) - \beta_C a_C(\gamma_C r_C + \mu_C c_C)(\eta_C + b_C),$$
$$C_C^L = k_C \lambda \mu_C \beta_C(\eta_C + \theta_C b_C) - d a_C(\gamma_C r_C + \mu_C c_C)(\eta_C + b_C).$$

We define a continuous function $\overline{H}^L$ as:

$$\overline{H}^L(V_C) = \frac{A_C^L V_C^2 + B_C^L V_C + C_C^L}{q_C V_C - \mu_C}, \text{ where } V_C \in \left[0, \frac{\mu_C}{q_C}\right).$$

We get

$$\begin{aligned}\overline{H}^L(0) &= -\frac{C_C^L}{\mu_C} = \frac{a_C d(\eta_C + b_C)(r_C\gamma_C + c_C\mu_C) - k_C\beta_C\lambda\mu_C(\eta_C + b_C\theta_C)}{\mu_C} \\ &= \frac{a_C d(\eta_C + b_C)(r_C\gamma_C + c_C\mu_C)}{\mu_C}\left(1 - R_C^L\right).\end{aligned}$$

We have $\overline{H}^L(0) < 0$ if $R_C^L > 1$. Moreover

$$\lim_{V_C \to \left(\frac{\mu_C}{q_C}\right)^-} \overline{H}^L(V_C) = \infty,$$

then there exists $\overline{V}_C \in \left(0, \frac{\mu_C}{q_C}\right)$ such that $\overline{H}^L(\overline{V}_C) = 0$. Clearly, if $R_C^L > 1$, then

$$C_C^L = k_C\beta_C\lambda\mu_C(\eta_C + b_C\theta_C) - a_C d(\eta_C + b_C)(r_C\gamma_C + c_C\mu_C) > 0.$$

Moreover,

$$k_C\beta_C\lambda q_C(\eta_C + b_C\theta_C) > a_C d c_C q_C(\eta_C + b_C).$$

Thus $B_C^L < 0$, which implies the existence of two positive solutions:

$$V_C^{\pm} = \frac{-B_C^L \pm \sqrt{\left(B_C^L\right)^2 - 4A_C^L C_C^L}}{2A_C^L}.$$

We have

$$\lim_{V_C \to \left(\frac{\mu_C}{q_C}\right)^+} \overline{H}^L(V_C) = -\infty, \text{ and } \lim_{V_C \to \infty} \overline{H}^L(V_C) = \infty.$$

Then

$$V_C^- \in \left(0, \frac{\mu_C}{q_C}\right) \text{ and } V_C^+ \in \left(\frac{\mu_C}{q_C}, \infty\right).$$

Then we take

$$\overline{V}_C = \frac{-B_C^L - \sqrt{\left(B_C^L\right)^2 - 4A_C^L C_C^L}}{2A_C^L}.$$

Hence

$$\overline{X} = \frac{X^0}{1 + \frac{\beta_C}{d}\overline{V}_C} > 0, \ \overline{Y}_C^L = \frac{\beta_C(1 - \theta_C)X^0\overline{V}_C}{(\eta_C + b_C)(1 + \frac{\beta_C}{d}\overline{V}_C)} > 0,$$

$$\overline{Y}_C^A = \frac{\beta_C(\eta_C + b_C\theta_C)X^0\overline{V}_C}{a_C(\eta_C + b_C)(1 + \frac{\beta_C}{d}\overline{V}_C)} > 0,\ \overline{W}_Z = \frac{\gamma_Z}{\mu_Z} > 0 \text{ and } \overline{W}_C = \frac{\gamma_C}{\mu_C - q_C\overline{V}_C} > 0.$$

Hence, a CHIKV-only infection steady state exists, $\overline{SS} = (\overline{X}, 0, 0, \overline{Y}_C^L, \overline{Y}_C^A, 0, \overline{V}_C, \overline{W}_Z, \overline{W}_C)$ when $R_C^L > 1$.

Case (IV) When $V_Z \neq 0$ and $V_C \neq 0$, Equations (32) and (33) leading to the following:

$$\frac{k_Z\beta_Z\lambda(\eta_Z + b_Z\theta_Z)}{a_Z(\eta_Z + b_Z)(d + \beta_Z V_Z + \beta_C V_C)} - c_Z + \frac{r_Z\gamma_Z}{q_Z V_Z - \mu_Z} = 0, \tag{37}$$

$$\frac{k_C\beta_C\lambda(\eta_C + b_C\theta_C)}{a_C(\eta_C + b_C)(d + \beta_Z V_Z + \beta_C V_C)} - c_C + \frac{r_C\gamma_C}{q_C V_C - \mu_C} = 0. \tag{38}$$

We solve Equations (37) and (38) by applying the isocline method [59]. Define

$$f_1^L(V_Z, V_C) = \frac{k_Z\beta_Z\lambda(\eta_Z + b_Z\theta_Z)}{a_Z(\eta_Z + b_Z)(d + \beta_Z V_Z + \beta_C V_C)} - c_Z + \frac{r_Z\gamma_Z}{q_Z V_Z - \mu_Z} = 0,$$
$$V_Z \in \left[0, \frac{\mu_Z}{q_Z}\right). \tag{39}$$

$$f_2^L(V_Z, V_C) = \frac{k_C\beta_C\lambda(\eta_C + b_C\theta_C)}{a_C(b_C + \eta_C)(d + \beta_Z V_Z + \beta_C V_C)} - c_C + \frac{r_C\gamma_C}{q_C V_C - \mu_C} = 0,$$
$$V_C \in \left[0, \frac{\mu_C}{q_C}\right). \tag{40}$$

From Equation (39), we observe the following:

(a) For $V_Z = 0$, we obtain

$$\frac{k_Z\beta_Z\lambda(\eta_Z + b_Z\theta_Z)}{a_Z(\eta_Z + b_Z)(d + \beta_C V_C)} - c_Z - \frac{r_Z\gamma_Z}{\mu_Z} = 0,$$

$$\Rightarrow V_C = \frac{d}{\beta_C}\left(\frac{k_Z\beta_Z\lambda\mu_Z(\eta_Z + b_Z\theta_Z)}{a_Z d(\eta_Z + b_Z)(r_Z\gamma_Z + c_Z\mu_Z)} - 1\right) = \frac{d}{\beta_C}(R_Z^L - 1) =: \widehat{V}_C.$$

This value is positive whenever $R_Z^L > 1$.

(b) For $V_C = 0$, we have

$$\frac{k_Z\beta_Z\lambda(\eta_Z + b_Z\theta_Z)}{a_Z(\eta_Z + b_Z)(d + \beta_Z V_Z)} - c_Z + \frac{r_Z\gamma_Z}{q_Z V_Z - \mu_Z} = 0.$$

From Equation (34), it follows that

$$V_Z = V_Z^* = \frac{-B_Z^L - \sqrt{(B_Z^L)^2 - 4A_Z^L C_Z^L}}{2A_Z^L}.$$

(c)

$$\frac{dV_C}{dV_Z} = -\frac{\partial f_1^L/\partial V_Z}{\partial f_1^L/\partial V_C}$$
$$= -\frac{k_Z\beta_Z^2\lambda(\eta_Z + b_Z\theta_Z)(q_Z V_Z - \mu_Z)^2 + a_Z q_Z r_Z\gamma_Z(\eta_Z + b_Z)(d + \beta_Z V_Z + \beta_C V_C)^2}{k_Z\beta_Z\beta_C\lambda(\eta_Z + b_Z\theta_Z)(q_Z V_Z - \mu_Z)^2} < 0,\ V_Z \in \left(0, \frac{\mu_Z}{q_Z}\right).$$

It follows that V_C is a decreasing function of V_Z. Hence, the isocline $f_Z^L(V_Z, V_C)$

intersects the V_Z-axis at $V_Z = V_Z^*$ and the V_C-axis at $V_C = \widehat{V}_C = \frac{d}{\beta_C}(R_Z^L - 1)$.

Now, from Equation (40), we obtain the following:

(d) For $V_C = 0$, we have

$$\frac{k_C\beta_C\lambda(\eta_C + b_C\theta_C)}{a_C(\eta_C + b_C)(d + \beta_Z V_Z)} - c_C - \frac{r_C\gamma_C}{\mu_C} = 0,$$

$$\Longrightarrow V_Z = \frac{d}{\beta_Z}(R_C^L - 1) =: \widehat{V}_Z.$$

This quantity is positive whenever $R_C^L > 1$.

(e) For $V_Z = 0$, we obtain

$$\frac{(\eta_C + b_C\theta_C)k_C\beta_C\lambda}{a_C(\eta_C + b_C)(d + \beta_C V_C)} - c_C + \frac{r_C\gamma_C}{q_C V_C - \mu_C} = 0.$$

From Equation (36), it follows that

$$V_C = \overline{V}_C = \frac{-B_C^L - \sqrt{\left(B_C^L\right)^2 - 4A_C^L C_C^L}}{2A_C^L}.$$

(f)

$$\frac{dV_C}{dV_Z} = -\frac{\partial f_2^L/\partial V_Z}{\partial f_2^L/\partial V_C}$$

$$= -\frac{k_C\beta_Z\beta_C\lambda(\eta_C + b_C\theta_C)(q_C V_C - \mu_C)^2}{a_C q_C r_C\gamma_C(\eta_C + b_C)(d + \beta_Z V_Z + \beta_C V_C)^2 + k_C\beta_C^2\lambda(\eta_C + b_C\theta_C)(q_C V_C - \mu_C)^2} < 0,\ V_C \in \left(0, \frac{\mu_C}{q_C}\right).$$

Then V_C is decreasing function of V_Z. Consequently, the isocline $f_2^L(V_Z, V_C)$ intersects the V_C-axis at $V_C = \overline{V}_C$ and the V_Z-axis at $V_Z = \widehat{V}_Z = \frac{d}{\beta_Z}(R_C^L - 1)$.

The above analysis shows that the two Equations (39) and (40) intersect at a point $(\widetilde{V}_Z, \widetilde{V}_C)$, where $\widetilde{V}_Z \in \left(0, \frac{\mu_Z}{q_Z}\right)$, $\widetilde{V}_C \in \left(0, \frac{\mu_C}{q_C}\right)$ if

$$\widehat{V}_Z > V_Z^* \Longrightarrow R_C^L > 1 + \frac{\beta_Z}{d}V_Z^* \Longrightarrow R_C^{L,inv} > 1,$$
$$\widehat{V}_C > \overline{V}_C \Longrightarrow R_Z^L > 1 + \frac{\beta_C}{d}\overline{V}_C \Longrightarrow R_Z^{L,inv} > 1.$$

Hence

$$\widetilde{X} = \frac{\lambda}{d + \beta_Z\widetilde{V}_Z + \beta_C\widetilde{V}_C} > 0,$$
$$\widetilde{Y}_Z^L = \frac{(1-\theta_Z)\beta_Z\lambda\widetilde{V}_Z}{(\eta_Z + b_Z)(d + \beta_Z\widetilde{V}_Z + \beta_C\widetilde{V}_C)} > 0,$$
$$\widetilde{Y}_Z^A = \frac{(\eta_Z + b_Z\theta_Z)\beta_Z\lambda\widetilde{V}_Z}{(\eta_Z + b_Z)(d + \beta_Z\widetilde{V}_Z + \beta_C\widetilde{V}_C)} > 0,$$
$$\widetilde{Y}_C^L = \frac{(1-\theta_C)\beta_C\lambda\widetilde{V}_C}{(\eta_C + b_C)(d + \beta_Z\widetilde{V}_Z + \beta_C\widetilde{V}_C)} > 0,$$
$$\widetilde{Y}_C^A = \frac{(\eta_C + b_C\theta_C)\beta_C\lambda\widetilde{V}_C}{a_C(b_C + \eta_C)(d + \beta_Z\widetilde{V}_Z + \beta_C\widetilde{V}_C)} > 0,$$

$$\widetilde{W}_Z = \frac{\gamma_Z}{\mu_Z - q_Z \widetilde{V}_Z} > 0,$$
$$\widetilde{W}_C = \frac{\gamma_C}{\mu_C - q_C \widetilde{V}_C} > 0.$$

Thus, the ZIKV–CHIKV co-infection steady state $\widetilde{SS} = (\widetilde{X}, \widetilde{Y}_Z^L, \widetilde{Y}_Z^A, \widetilde{Y}_C^L, \widetilde{Y}_C^A, \widetilde{V}_Z, \widetilde{V}_C, \widetilde{W}_Z, \widetilde{W}_C)$ exists whenever $R_Z^{L,inv} > 1$ and $R_C^{L,inv} > 1$. □

6.2. Global stability analysis

In this section, we adopt the Lyapunov functional technique introduced by Korobeinikov [60] to establish the global asymptotic stability of all steady states. Let $\Theta_i^L(X, Y_Z^L, Y_Z^A, Y_C^L, Y_C^A, V_Z, V_C, W_Z, W_C)$ be a Lyapunove function and denotes $\widetilde{\Gamma}_j^L$ be the largest invariant subset of

$$\widetilde{\Gamma}_j^L = \{(X, Y_Z^L, Y_Z^A, Y_C^L, Y_C^A, V_Z, V_C, W_Z, W_C) : \frac{d\Theta_j^L}{dt} = 0\}, j = 0, 1, 2, 3.$$

We also employ the arithmetic mean-geometric mean inequality:

$$\left(\prod_{i=1}^{n} \varkappa_i\right)^{\frac{1}{n}} \leq \frac{1}{n}\sum_{i=1}^{n} \varkappa_i, \varkappa_i \geq 0, i = 1, 2, ..., n. \tag{41}$$

Theorem 1. *The disease-free steady state $SS^0 = (X^0, 0, 0, 0, 0, 0, 0, W_Z^0, W_C^0)$ is globally asymptotically stable if $R_0^L \leq 1$, otherwise, it becomes unstable.*

Proof. Define $\Theta_0^L(X, Y_Z^L, Y_Z^A, Y_C^L, Y_C^A, V_Z, V_C, W_Z, W_C)$ as:

$$\begin{aligned}\Theta_0^L = {} & X^0\left(\frac{X}{X^0} - 1 - \ln\frac{X}{X^0}\right) + \frac{\eta_Z}{\eta_Z + \theta_Z b_Z} Y_Z^L + \frac{\eta_Z + b_Z}{\eta_Z + \theta_Z b_Z} Y_Z^A + \frac{\eta_C}{\eta_C + \theta_C b_C} Y_C^L \\ & + \frac{\eta_C + b_C}{\eta_C + \theta_C b_C} Y_C^A + \frac{a_Z(\eta_Z + b_Z)}{k_Z(\eta_Z + \theta_Z b_Z)} V_Z + \frac{a_C(\eta_C + b_C)}{k_C(\eta_C + \theta_C b_C)} V_C \\ & + \frac{a_Z r_Z(\eta_Z + b_Z)}{k_Z q_Z(\eta_Z + \theta_Z b_Z)} W_Z^0\left(\frac{W_Z}{W_Z^0} - 1 - \ln\frac{W_Z}{W_Z^0}\right) \\ & + \frac{a_C r_C(\eta_C + b_C)}{k_C q_C(\eta_C + \theta_C b_C)} W_C^0\left(\frac{W_C}{W_C^0} - 1 - \ln\frac{W_C}{W_C^0}\right).\end{aligned}$$

We observe that $\Theta_0^L(X, Y_Z^L, Y_Z^A, Y_C^L, Y_C^A, V_Z, V_C, W_Z, W_C) > 0$ for all $(X, Y_Z^L, Y_Z^A, Y_C^L, Y_C^A, V_Z, V_C, W_Z, W_C) > 0$ and $\Theta_0^L(X^0, 0, 0, 0, 0, 0, 0, W_Z^0, W_C^0) = 0$. Calculating $\frac{d\Theta_0^L}{dt}$ along the solutions of Equations (1)–(9) as:

$$\begin{aligned}\frac{d\Theta_0^L}{dt} = {} & \left(1 - \frac{X^0}{X}\right)\frac{dX}{dt} + \frac{\eta_Z}{\eta_Z + \theta_Z b_Z}\frac{dY_Z^L}{dt} + \frac{\eta_Z + b_Z}{\eta_Z + \theta_Z b_Z}\frac{dY_Z^A}{dt} + \frac{\eta_C}{\eta_C + \theta_C b_C}\frac{dY_C^L}{dt} \\ & + \frac{\eta_C + b_C}{\eta_C + \theta_C b_C}\frac{dY_C^A}{dt} + \frac{a_Z(\eta_Z + b_Z)}{k_Z(\eta_Z + \theta_Z b_Z)}\frac{dV_Z}{dt} + \frac{a_C(\eta_C + b_C)}{k_C(\eta_C + \theta_C b_C)}\frac{dV_C}{dt} \\ & + \frac{a_Z r_Z(\eta_Z + b_Z)}{k_Z q_Z(\eta_Z + \theta_Z b_Z)}\left(1 - \frac{W_Z^0}{W_Z}\right)\frac{dW_Z}{dt} + \frac{a_C r_C(\eta_C + b_C)}{k_C q_C(\eta_C + \theta_C b_C)}\left(1 - \frac{W_C^0}{W_C}\right)\frac{dW_C}{dt}\end{aligned}$$

Substituting from Equations (1)–(9) we get

$$\begin{aligned}\frac{d\Theta_0^L}{dt} &= \left(1-\frac{X^0}{X}\right)(\lambda - dX - \beta_Z X V_Z - \beta_C X V_C)\\ &+ \frac{\eta_Z}{\eta_Z+\theta_Z b_Z}((1-\theta_Z)\beta_Z X V_Z - (\eta_Z+b_Z)Y_Z^L)\\ &+ \frac{\eta_Z+b_Z}{\eta_Z+\theta_Z b_Z}(\theta_Z\beta_Z X V_Z - a_Z Y_Z^A + \eta_Z Y_Z^L)\\ &+ \frac{\eta_C}{\eta_C+\theta_C b_C}((1-\theta_C)\beta_C X V_C - (\eta_C+b_C)Y_C^L)\\ &+ \frac{\eta_C+b_C}{\eta_C+\theta_C b_C}(\theta_C\beta_C X V_C - a_C Y_C^A + \eta_C Y_C^L)\\ &+ \frac{a_Z(\eta_Z+b_Z)}{k_Z(\eta_Z+\theta_Z b_Z)}(k_Z Y_Z^A - c_Z V_Z - r_Z V_Z W_Z)\\ &+ \frac{a_C(\eta_C+b_C)}{k_C(\eta_C+\theta_C b_C)}(k_C Y_C^A - c_C V_C - r_C V_C W_C)\\ &+ \frac{a_Z r_Z(\eta_Z+b_Z)}{k_Z q_Z(\eta_Z+\theta_Z b_Z)}\left(1-\frac{W_Z^0}{W_Z}\right)\\ &\times(\gamma_Z + q_Z V_Z W_Z - \mu_Z W_Z)\\ &+ \frac{a_C r_C(\eta_C+b_C)}{k_C q_C(\eta_C+\theta_C b_C)}\left(1-\frac{W_C^0}{W_C}\right)(\gamma_C + q_C V_C W_C - \mu_C W_C).\end{aligned}$$

Collecting terms we obtain

$$\begin{aligned}\frac{d\Theta_0^L}{dt} &= \left(1-\frac{X^0}{X}\right)(\lambda - dX) + \beta_Z X^0 V_Z + \beta_C X^0 V_C - \frac{a_Z c_Z(\eta_Z+b_Z)}{k_Z(\eta_Z+\theta_Z b_Z)}V_Z\\ &- \frac{a_C c_C(\eta_C+b_C)}{k_C(\eta_C+\theta_C b_C)}V_C\\ &+ \frac{a_Z r_Z(\eta_Z+b_Z)}{k_Z q_Z(\eta_Z+\theta_Z b_Z)}\left(1-\frac{W_Z^0}{W_Z}\right)(\gamma_Z - \mu_Z W_Z) - \frac{a_Z r_Z(\eta_Z+b_Z)}{k_Z(\eta_Z+\theta_Z b_Z)}V_Z W_Z^0\\ &+ \frac{a_C r_C(\eta_C+b_C)}{k_C q_C(\eta_C+\theta_C b_C)}\left(1-\frac{W_C^0}{W_C}\right)(\gamma_C - \mu_C W_C) - \frac{a_C r_C(\eta_C+b_C)}{k_C(\eta_C+\theta_C b_C)}V_C W_C^0.\end{aligned}$$

Using $(\lambda, \gamma_Z, \gamma_C) = (dX^0, \mu_Z W_Z^0, \mu_C W_C^0)$, we obtain

$$\begin{aligned}\frac{d\Theta_0^L}{dt} &= -\frac{d(X-X^0)^2}{X} - \frac{a_Z r_Z \mu_Z(\eta_Z+b_Z)}{k_Z q_Z(\eta_Z+\theta_Z b_Z)}\frac{(W_Z-W_Z^0)^2}{W_Z}\\ &- \frac{a_C r_C \mu_C(\eta_C+b_C)}{k_C q_C(\eta_C+\theta_C b_C)}\frac{(W_C-W_C^0)^2}{W_C}\\ &+ \frac{a_Z(\eta_Z+b_Z)(c_Z\mu_Z + r_Z\gamma_Z)}{k_Z\mu_Z(\eta_Z+\theta_Z b_Z)}\left(\frac{\beta_Z k_Z \mu_Z X^0(\eta_Z+\theta_Z b_Z)}{a_Z(\eta_Z+b_Z)(c_Z\mu_Z+r_Z\gamma_Z)} - 1\right)V_Z\\ &+ \frac{a_C(\eta_C+b_C)(c_C\mu_C + r_C\gamma_C)}{k_C\mu_C(\eta_C+\theta_C b_C)}\left(\frac{\beta_C k_C \mu_C X^0(\eta_C+\theta_C b_C)}{a_C(\eta_C+b_C)(c_C\mu_C+r_C\gamma_C)} - 1\right)V_C\\ &= -\frac{d(X-X^0)^2}{X} - \frac{a_Z r_Z \mu_Z(\eta_Z+b_Z)}{k_Z q_Z(\eta_Z+\theta_Z b_Z)}\frac{(W_Z-W_Z^0)^2}{W_Z}\\ &- \frac{a_C r_C \mu_C(\eta_C+b_C)}{k_C q_C(\eta_C+\theta_C b_C)}\frac{(W_C-W_C^0)^2}{W_C}\\ &+ \frac{a_Z(\eta_Z+b_Z)(c_Z\mu_Z + r_Z\gamma_Z)}{k_Z\mu_Z(\eta_Z+\theta_Z b_Z)}\left(R_Z^L - 1\right)V_Z\\ &+ \frac{a_C(\eta_C+b_C)(c_C\mu_C + r_C\gamma_C)}{k_C\mu_C(\eta_C+\theta_C b_C)}\left(R_C^L - 1\right)V_C.\end{aligned}$$

If $R_Z^L \le 1$ and $R_C^L \le 1$, then $\frac{d\Theta_0^L}{dt} \le 0, \forall \left(X, Y_Z^L, Y_Z^A, Y_C^L, Y_C^A, V_Z, V_C, W_Z, W_C\right) >$

0. Moreover, $\frac{d\Theta_0^L}{dt} = 0$ when $(X, W_Z, W_C) = (X^0, W_Z^0, W_C^0)$ and $(R_Z^L - 1)V_Z = (R_C^L - 1)V_C = 0$. The solutions of system Equations (1)–(9) converge to $\widetilde{\Gamma}_0^L$ [61]. The set has elements satisfying $(X, W_Z, W_C) = (X^0, W_Z^0, W_C^0)$,

$$(R_Z^L - 1)V_Z = 0 \text{ and } (R_C^L - 1)V_C = 0. \tag{42}$$

There are four cases:

(i) $R_Z^L = 1$ and $R_C^L = 1$. Then from Equation (1) we get

$$0 = \frac{dX}{dt} = \lambda - dX^0 - \beta_Z X^0 V_Z - \beta_C X^0 V_C \Longrightarrow (\beta_Z V_Z + \beta_C V_C)X^0 = 0 \tag{43}$$
$$\Longrightarrow V_Z(t) = 0,\ V_C(t) = 0 \text{ for any } t,$$

and then $\frac{dV_Z}{dt} = \frac{dV_C}{dt} = 0$. From Equations (6) and (7), we find that

$$0 = \frac{dV_Z}{dt} = k_Z Y_Z^A(t) \Rightarrow Y_Z^A(t) = 0 \text{ for any } t, \tag{44}$$
$$0 = \frac{dV_C}{dt} = k_C Y_C^A(t) \Rightarrow Y_C^A(t) = 0 \text{ for any } t, \tag{45}$$

so $\frac{dY_Z^A}{dt} = \frac{dY_C^A}{dt} = 0$. From Equations (3) and (5), we find that

$$0 = \frac{dY_Z^A}{dt} = \eta_Z Y_Z^L \Rightarrow Y_Z^L(t) = 0 \text{ for any } t, \tag{46}$$
$$0 = \frac{dY_C^A}{dt} = \eta_C Y_C^L \Rightarrow Y_C^L(t) = 0 \text{ for any } t. \tag{47}$$

Thus $\widetilde{\Gamma}_0^L = \{SS^0\}$.

(ii) $R_Z^L < 1$ and $R_C^L < 1$. Then from Equation (42) we have $V_Z = V_C = 0$ and Equations (44) and (45) indicate $Y_Z^A = 0$ and $Y_C^A = 0$. From Equations (46) and (47) we get $Y_Z^L = 0$ and $Y_C^L = 0$ and hence $\widetilde{\Gamma}_0^L = \{SS^0\}$.

(iii) $R_Z^L = 1$ and $R_C^L < 1$. Then from Equation (42) we get $V_C = 0$ and from Equation (43) we obtain $V_Z = 0$. Equations (44)– (47) imply that $Y_Z^A = Y_C^A = Y_Z^L = Y_C^L = 0$. Thus $\widetilde{\Gamma}_0^L = \{SS^0\}$.

(iv) $R_Z^L < 1$ and $R_C^L = 1$. Then from Equation (42) we obtain $V_Z = 0$ and from Equation (43) we get $V_C = 0$. Equations (44)–(47) indicate $Y_Z^A = Y_C^A = Y_Z^L = Y_C^L = 0$. Thus $\widetilde{\Gamma}_0^L = \{SS^0\}$.

By applying LaSalle's invariant principle as formulated in Khalil's study [62], it follows that SS^0 is globally asymptotically stable.

To establish the instability of SS^0 when $R_Z^L > 1$ and/or $R_C^L > 1$, we examine the characteristic equation obtained by linearizing Equations (1)–(9) about SS^0. The resulting characteristic polynomial is given by:

$$(d+\xi)(\mu_Z+\xi)(\mu_C+\xi)\left(\xi^3 + \hat{D}_2^L\xi^2 + \hat{D}_1^L\xi + \hat{D}_0^L\right)\left(\xi^3 + \hat{E}_2^L\xi^2 + \hat{E}_1^L\xi + \hat{E}_0^L\right) = 0, \tag{48}$$

where ξ is the eigenvalue and

$$\hat{D}_2^L = a_Z + b_Z + c_Z + \eta_Z + r_Z W_Z^0,$$

$$\begin{aligned}
\hat{D}_1^L &= a_Z(\eta_Z + b_Z) + a_Z c_Z + c_Z(\eta_Z + b_Z) + a_Z r_Z W_Z^0 \\
&\quad + (\eta_Z + b_Z) r_Z W_Z^0 - \theta_Z \beta_Z k_Z X^0, \\
\hat{D}_0^L &= a_Z(\eta_Z + b_Z)(c_Z + r_Z W_Z^0) - \beta_Z k_Z X^0(\eta_Z + \theta_Z b_Z) \\
&= -\frac{a_Z(\eta_Z + b_Z)(c_Z \mu_Z + r_Z \gamma_Z)}{\mu_Z} \left(R_Z^L - 1\right), \\
\hat{E}_2^L &= a_C + b_C + c_C + \eta_C + r_C W_C^0, \\
\hat{E}_1^L &= a_C(\eta_C + b_C) + a_C c_C + c_C(\eta_C + b_C) + a_C r_C W_C^0 \\
&\quad + (\eta_C + b_C) r_C W_C^0 - \theta_C \beta_C k_C X^0, \\
\hat{E}_0^L &= a_C(\eta_C + b_C)(c_C + r_C W_C^0) - \beta_C k_C X^0(\eta_C + \theta_C b_C) \\
&= -\frac{a_C(\eta_C + b_C)(c_C \mu_C + r_C \gamma_C)}{\mu_C} \left(R_C^L - 1\right).
\end{aligned}$$

It is evident that if $R_0^L > 1$, then $\hat{D}_0^L < 0$ and/or $\hat{E}_0^L < 0$. Consequently, Equation (48) admits at least one positive root, implying that SS^0 is unstable. □

Theorem 2. *The ZIKV-only infection steady state* $SS^* = (X^*, Y_Z^{L*}, Y_Z^{A*}, 0, 0, V_Z^*, 0, W_Z^*, W_C^*)$ *is globally asymptotically stable if* $R_Z^L > 1$ *and* $R_C^{L,inv} \leq 1$. *Furthermore,* SS^* *is unstable when* $R_C^{L,inv} > 1$.

Proof. Define $\Theta_1^L(X, Y_Z^L, Y_Z^A, Y_C^L, Y_C^A, V_Z, V_C, W_Z, W_C)$ as:

$$\begin{aligned}
\Theta_1^L &= X^* \left(\frac{X}{X^*} - 1 - \ln \frac{X}{X^*}\right) + \frac{\eta_Z}{\eta_Z + \theta_Z b_Z} Y_Z^{L*} \left(\frac{Y_Z^L}{Y_Z^{L*}} - 1 - \ln \frac{Y_Z^L}{Y_Z^{L*}}\right) \\
&\quad + \frac{\eta_Z + b_Z}{\eta_Z + \theta_Z b_Z} Y_Z^{A*} \left(\frac{Y_Z^A}{Y_Z^{A*}} - 1 - \ln \frac{Y_Z^A}{Y_Z^{A*}}\right) + \frac{\eta_C}{\eta_C + \theta_C b_C} Y_C^L + \frac{\eta_C + b_C}{\eta_C + \theta_C b_C} Y_C^A \\
&\quad + \frac{a_Z(\eta_Z + b_Z)}{k_Z(\eta_Z + \theta_Z b_Z)} V_Z^* \left(\frac{V_Z}{V_Z^*} - 1 - \ln \frac{V_Z}{V_Z^*}\right) + \frac{a_C(\eta_C + b_C)}{k_C(\eta_C + \theta_C b_C)} V_C \\
&\quad + \frac{a_Z r_Z(\eta_Z + b_Z)}{k_Z q_Z(\eta_Z + \theta_Z b_Z)} W_Z^* \left(\frac{W_Z}{W_Z^*} - 1 - \ln \frac{W_Z}{W_Z^*}\right) \\
&\quad + \frac{a_C r_C(\eta_C + b_C)}{k_C q_C(\eta_C + \theta_C b_C)} W_C^* \left(\frac{W_C}{W_C^*} - 1 - \ln \frac{W_C}{W_C^*}\right).
\end{aligned}$$

We observe that $\Theta_1^L(X, Y_Z^L, Y_Z^A, Y_C^L, Y_C^A, V_Z, V_C, W_Z, W_C) > 0$ for all $(X, Y_Z^L, Y_Z^A, Y_C^L, Y_C^A, V_Z, V_C, W_Z, W_C) > 0$ and $\Theta_1^L(X^*, Y_Z^{L*}, Y_Z^{A*}, 0, 0, V_Z^*, 0, W_Z^*, W_C^*) = 0$. Calculating $\frac{d\Theta_1^L}{dt}$ along the solutions of Equations (1)–(9) as:

$$\begin{aligned}
\frac{d\Theta_1^L}{dt} &= \left(1 - \frac{X^*}{X}\right) \frac{dX}{dt} + \frac{\eta_Z}{\eta_Z + \theta_Z b_Z} \left(1 - \frac{Y_Z^{L*}}{Y_Z^L}\right) \frac{dY_Z^L}{dt} \\
&\quad + \frac{\eta_Z + b_Z}{\eta_Z + \theta_Z b_Z} \left(1 - \frac{Y_Z^{A*}}{Y_Z^A}\right) \frac{dY_Z^A}{dt} + \frac{\eta_C}{\eta_C + \theta_C b_C} \frac{dY_C^L}{dt} \\
&\quad + \frac{\eta_C + b_C}{\eta_C + \theta_C b_C} \frac{dY_C^A}{dt} + \frac{a_Z(\eta_Z + b_Z)}{k_Z(\eta_Z + \theta_Z b_Z)} \left(1 - \frac{V_Z^*}{V_Z}\right) \frac{dV_Z}{dt} + \frac{a_C(\eta_C + b_C)}{k_C(\eta_C + \theta_C b_C)} \frac{dV_C}{dt} \\
&\quad + \frac{a_Z r_Z(\eta_Z + b_Z)}{k_Z q_Z(\eta_Z + \theta_Z b_Z)} \left(1 - \frac{W_Z^*}{W_Z}\right) \frac{dW_Z}{dt} + \frac{a_C r_C(\eta_C + b_C)}{k_C q_C(\eta_C + \theta_C b_C)} \left(1 - \frac{W_C^*}{W_C}\right) \frac{dW_C}{dt}
\end{aligned}$$

Substituting from Equations (1)–(9) and collecting terms we get

$$\begin{aligned}\frac{d\Theta_1^L}{dt} &= \left(1-\frac{X^*}{X}\right)(\lambda - dX)\\ &+ \left(\beta_Z X^* - \frac{a_Z c_Z(\eta_Z+b_Z)}{k_Z(\eta_Z+\theta_Z b_Z)} - \frac{a_Z r_Z(\eta_Z+b_Z)}{k_Z(\eta_Z+\theta_Z b_Z)} W_Z^*\right) V_Z\\ &+ \left(\beta_C X^* - \frac{a_C c_C(\eta_C+b_C)}{k_C(\eta_C+\theta_C b_C)} - \frac{a_C r_C(\eta_C+b_C)}{k_C(\eta_C+\theta_C b_C)} W_C^*\right) V_C\\ &- \frac{\eta_Z(1-\theta_Z)\beta_Z}{\eta_Z+\theta_Z b_Z} X V_Z \frac{Y_Z^{L*}}{Y_Z^L}\\ &+ \frac{\eta_Z(\eta_Z+b_Z)}{\eta_Z+\theta_Z b_Z} Y_Z^{L*} - \frac{(\eta_Z+b_Z)\theta_Z\beta_Z}{\eta_Z+\theta_Z b_Z} X V_Z \frac{Y_Z^{A*}}{Y_Z^A} + \frac{a_Z(\eta_Z+b_Z)}{\eta_Z+\theta_Z b_Z} Y_Z^{A*}\\ &- \frac{\eta_Z(\eta_Z+b_Z)}{\eta_Z+\theta_Z b_Z} Y_Z^L \frac{Y_Z^{A*}}{Y_Z^A} - \frac{a_Z(\eta_Z+b_Z)}{\eta_Z+\theta_Z b_Z} Y_Z^A \frac{V_Z^*}{V_Z} + \frac{a_Z c_Z(\eta_Z+b_Z)}{k_Z(\eta_Z+\theta_Z b_Z)} V_Z^*\\ &+ \frac{a_Z r_Z(\eta_Z+b_Z)}{k_Z(\eta_Z+\theta_Z b_Z)} V_Z^* W_Z + \frac{a_Z r_Z(\eta_Z+b_Z)}{k_Z q_Z(\eta_Z+\theta_Z b_Z)}\left(1-\frac{W_Z^*}{W_Z}\right)(\gamma_Z - \mu_Z W_Z)\\ &+ \frac{a_C r_C(\eta_C+b_C)}{k_C q_C(\eta_C+\theta_C b_C)}\left(1-\frac{W_C^*}{W_C}\right)(\gamma_C - \mu_C W_C).\end{aligned}$$

Using the steady state conditions

$$\begin{aligned}\lambda &= dX^* + \beta_Z X^* V_Z^*,\\ (1-\theta_Z)\beta_Z X^* V_Z^* &= (b_Z+\eta_Z) Y_Z^{L*},\\ a_Z Y_Z^{A*} &= \theta_Z\beta_Z X^* V_Z^* + \eta_Z Y_Z^{L*},\\ k_Z Y_Z^{A*} &= c_Z V_Z^* + r_Z V_Z^* W_Z^*,\\ \gamma_Z &= \mu_Z W_Z^* - q_Z V_Z^* W_Z^*,\\ \gamma_C &= \mu_C W_C^*.\end{aligned}$$

We obtain

$$\begin{aligned}\frac{d\Theta_1^L}{dt} &= -\frac{d(X-X^*)^2}{X}\\ &+ \frac{\eta_Z(1-\theta_Z)}{\eta_Z+\theta_Z b_Z}\beta_Z X^* V_Z^*\left[4 - \frac{X^*}{X} - \frac{X V_Z Y_Z^{L*}}{X^* V_Z^* Y_Z^L} - \frac{Y_Z^L Y_Z^{A*}}{Y_Z^{L*} Y_Z^A} - \frac{Y_Z^A V_Z^*}{Y_Z^{A*} V_Z}\right]\\ &+ \frac{\theta_Z(\eta_Z+b_Z)}{\eta_Z+\theta_Z b_Z}\beta_Z X^* V_Z^*\left[3 - \frac{X^*}{X} - \frac{X V_Z Y_Z^{A*}}{X^* V_Z^* Y_Z^A} - \frac{Y_Z^A V_Z^*}{Y_Z^{A*} V_Z}\right]\\ &+ \frac{a_C d(\eta_C+b_C)(c_C\mu_C + r_C\gamma_C)}{k_C\lambda\mu_C(\eta_C+\theta_C b_C)} X^*\left(R_C^L - 1 - R_Z^{L*}\right) V_C\\ &- \frac{a_Z r_Z \mu_Z(\eta_Z+b_Z)}{k_Z q_Z(\eta_Z+\theta_Z b_Z)}\frac{(W_Z - W_Z^*)^2}{W_Z} - \frac{a_C r_C \mu_C(\eta_C+b_C)}{k_C q_C(\eta_C+\theta_C b_C)}\frac{(W_C - W_C^*)^2}{W_C}\\ &+ \frac{a_Z r_Z(\eta_Z+b_Z)}{k_Z(\eta_Z+\theta_Z b_Z)} V_Z^*\frac{(W_Z - W_Z^*)^2}{W_Z}.\end{aligned}$$

From steady state conditions of SS^*, we have $V_Z^* - \frac{\mu_Z}{q_Z} = -\frac{\gamma_Z}{q_Z W_Z^*}$. It follows that

$$\begin{aligned}\frac{d\Theta_1^L}{dt} &= -\frac{d(X-X^*)^2}{X}\\ &+ \frac{\eta_Z(1-\theta_Z)}{\eta_Z+\theta_Z b_Z}\beta_Z X^* V_Z^*\left[4 - \frac{X^*}{X} - \frac{X V_Z Y_Z^{L*}}{X^* V_Z^* Y_Z^L} - \frac{Y_Z^L Y_Z^{A*}}{Y_Z^{L*} Y_Z^A} - \frac{Y_Z^A V_Z^*}{Y_Z^{A*} V_Z}\right]\\ &+ \frac{\theta_Z(\eta_Z+b_Z)}{\eta_Z+\theta_Z b_Z}\beta_Z X^* V_Z^*\left[3 - \frac{X^*}{X} - \frac{X V_Z Y_Z^{A*}}{X^* V_Z^* Y_Z^A} - \frac{Y_Z^A V_Z^*}{Y_Z^{A*} V_Z}\right]\\ &+ \frac{a_C(\eta_C+b_C)(c_C\mu_C + r_C\gamma_C)}{k_C\mu_C(\eta_C+\theta_C b_C)}\left(R_C^{L,inv} - 1\right) V_C\\ &- \frac{a_Z r_Z \gamma_Z(\eta_Z+b_Z)}{k_Z q_Z(\eta_Z+\theta_Z b_Z)}\frac{(W_Z - W_Z^*)^2}{W_Z^* W_Z} - \frac{a_C r_C \mu_C(\eta_C+b_C)}{k_C q_C(\eta_C+\theta_C b_C)}\frac{(W_C - W_C^*)^2}{W_C}.\end{aligned}$$

Applying Equation (41) we obtain

$$\frac{X^*}{X} + \frac{XV_Z Y_Z^{L*}}{X^* V_Z^* Y_Z^L} + \frac{Y_Z^L Y_Z^{A*}}{Y_Z^{L*} Y_Z^A} + \frac{Y_Z^A V_Z^*}{Y_Z^{A*} V_Z} \geq 4.$$

Consequently, if $R_C^{L,inv} \leq 1$, then $\frac{d\Theta_1^L}{dt} \leq 0$, for all $(X, Y_Z^L, Y_Z^A, Y_C^L, Y_C^A, V_Z, V_C, W_Z, W_C) > 0$. Moreover, $\frac{d\Theta_1^L}{dt} = 0$ when $X = X^*$, $Y_Z^L = Y_Z^{L*}$, $Y_Z^A = Y_Z^{A*}$, $V_Z = V_Z^*$, $W_Z = W_Z^*$, $W_C = W_C^*$ and $\left(R_C^{L,inv} - 1\right) V_C = 0$. The solutions of Equations (1)–(9) approach $\widetilde{\Gamma}_1^L$ as $t \to \infty$. This set consists of elements for which $X = X^*$, $Y_Z^L = Y_Z^{L*}$, $Y_Z^A = Y_Z^{A*}$, $V_Z = V_Z^*$, $W_Z = W_Z^*$, $W_C = W_C^*$ and

$$\left(R_C^{L,inv} - 1\right) V_C = 0. \tag{49}$$

We have two cases:
(i) When $R_C^{L,inv} < 1$, Equation (49) implies that $V_C = 0$. Substituting this into Equation (7) yields:

$$0 = \frac{dV_C}{dt} = k_C Y_C^A(t) \Rightarrow Y_C^A(t) = 0 \text{ for any t.} \tag{50}$$

From Equation (5) we have

$$0 = \frac{dY_C^A}{dt} = \eta_C Y_C^L(t) \Rightarrow Y_C^L(t) = 0 \text{ for any t.} \tag{51}$$

Hence $\widetilde{\Gamma}_1^L = \{SS^*\}$.

(ii) When $R_C^{L,inv} = 1$, it follows from Equation (1) that

$$0 = \frac{dX}{dt} = \lambda - dX^* - \beta_Z X^* V_Z^* - \beta_C X^* V_C \Rightarrow V_C(t) = 0 \text{ for any t.}$$

Using Equations (50) and (51) we obtain $Y_C^A = Y_C^L = 0$. Therefore, $\widetilde{\Gamma}_1^L = \{SS^*\}$. By applying LaSalle's invariant principle, it follows that SS^* is globally asymptotically stable.

To assess the instability of SS^* when $R_C^{L,inv} > 1$, we derive the characteristic equation at SS^* by evaluating the Jacobian matrix of the system, which yields:

$$\begin{aligned}
&(\mu_C + \xi)\left(\xi^3 + \hat{F}_2^L \xi^2 + \hat{F}_1^L \xi + \hat{F}_0^L\right)[q_Z r_Z V_Z^* W_Z^* (a_Z + \xi)(d + \beta_Z V_Z^* + \xi)(b_Z + \eta_Z + \xi) \\
&- (q_Z V_Z^* - \mu_Z - \xi)((a_Z + \xi)(c_Z + r_Z W_Z^* + \xi)(d + \beta_Z V_Z^* + \xi)(\eta_Z + b_Z + \xi) \\
&- k_Z \beta_Z X^* (d + \xi) + (\eta_Z + \theta_Z (b_Z + \xi)))] \\
&= 0,
\end{aligned} \tag{52}$$

where the coefficients $\hat{F}_2^L$, $\hat{F}_1^L$ and $\hat{F}_0^L$ are defined as:

$$\begin{aligned}
\hat{F}_2^L &= a_C + b_C + c_C + \eta_C + r_C W_C^*, \\
\hat{F}_1^L &= a_C(\eta_C + b_C) + a_C c_C + c_C(\eta_C + b_C) + a_C r_C W_C^* \\
&\quad + (\eta_C + b_C) r_C W_C^* - \theta_C \beta_C k_C X^*, \\
\hat{F}_0^L &= a_C(\eta_C + b_C)(c_C + r_C W_C^*) - \beta_C k_C X^* (\eta_C \theta_C + b_C) \\
&= -\frac{a_C(\eta_C + b_C)(r_C \gamma_C + c_C \mu_C)}{\mu_C}\left(R_C^{L,inv} - 1\right).
\end{aligned}$$

If $R_C^{L,inv} > 1,$ then $\hat{F}_0^L < 0$, and hence, Equation (52) has a positive root and hence SS^* is unstable. □

Theorem 3. *The CHIKV-only infection steady state* $\overline{SS} = (\overline{X}, 0, 0, \overline{Y}_C^L, \overline{Y}_C^A, 0, \overline{V}_C, \overline{W}_Z, \overline{W}_C)$ *is globally asymptotically stable if* $R_C^L > 1$ *and* $R_Z^{L,inv} \leq 1$. *Furthermore,* $\overline{SS}$ *is unstable. when* $R_Z^{L,inv} > 1$.

Proof. Define $\Theta_2^L(X, Y_Z^L, Y_Z^A, Y_C^L, Y_C^A, V_Z, V_C, W_Z, W_C)$ as:

$$\begin{aligned}
\Theta_2^L &= \overline{X}\left(\frac{X}{\overline{X}} - 1 - \ln\frac{X}{\overline{X}}\right) + \frac{\eta_Z}{\eta_Z + \theta_Z b_Z} Y_Z^L + \frac{\eta_Z + b_Z}{\eta_Z + \theta_Z b_Z} Y_Z^A \\
&+ \frac{\eta_C}{\eta_C + \theta_C b_C} \overline{Y}_C^L \left(\frac{Y_C^L}{\overline{Y}_C^L} - 1 - \ln\frac{Y_C^L}{\overline{Y}_C^L}\right) \\
&+ \frac{\eta_C + b_C}{\eta_C + \theta_C b_C} \overline{Y}_C^A \left(\frac{Y_C^A}{\overline{Y}_C^A} - 1 - \ln\frac{Y_C^A}{\overline{Y}_C^A}\right) + \frac{a_Z(\eta_Z + b_Z)}{k_Z(\eta_Z + \theta_Z b_Z)} V_Z \\
&+ \frac{a_C(\eta_C + b_C)}{k_C(\eta_C + \theta_C b_C)} \overline{V}_C \left(\frac{V_C}{\overline{V}_C} - 1 - \ln\frac{V_C}{\overline{V}_C}\right) \\
&+ \frac{a_Z r_Z(\eta_Z + b_Z)}{k_Z q_Z(\eta_Z + \theta_Z b_Z)} \overline{W}_Z \left(\frac{W_Z}{\overline{W}_Z} - 1 - \ln\frac{W_Z}{\overline{W}_Z}\right) \\
&+ \frac{a_C r_C(\eta_C + b_C)}{k_C q_C(\eta_C + \theta_C b_C)} \overline{W}_C \left(\frac{W_C}{\overline{W}_C} - 1 - \ln\frac{W_C}{\overline{W}_C}\right).
\end{aligned}$$

Calculating $\frac{d\Theta_2^L}{dt}$ along the solutions of Equations (1)–(9) as:

$$\begin{aligned}
\frac{d\Theta_2^L}{dt} &= \left(1 - \frac{\overline{X}}{X}\right)\frac{dX}{dt} + \frac{\eta_Z}{\eta_Z + \theta_Z b_Z}\frac{dY_Z^L}{dt} + \frac{\eta_Z + b_Z}{\eta_Z + \theta_Z b_Z}\frac{dY_Z^A}{dt} \\
&+ \frac{\eta_C}{\eta_C + \theta_C b_C}\left(1 - \frac{\overline{Y}_C^L}{Y_C^L}\right)\frac{dY_C^L}{dt} + \frac{\eta_C + b_C}{\eta_C + \theta_C b_C}\left(1 - \frac{\overline{Y}_C^A}{Y_C^A}\right)\frac{dY_C^A}{dt} \\
&+ \frac{a_Z(\eta_Z + b_Z)}{k_Z(\eta_Z + \theta_Z b_Z)}\frac{dV_Z}{dt} + \frac{a_C(\eta_C + b_C)}{k_C(\eta_C + \theta_C b_C)}\left(1 - \frac{\overline{V}_C}{V_C}\right)\frac{dV_C}{dt} \\
&+ \frac{a_Z r_Z(\eta_Z + b_Z)}{k_Z q_Z(\eta_Z + \theta_Z b_Z)}\left(1 - \frac{\overline{W}_Z}{W_Z}\right)\frac{dW_Z}{dt} + \frac{a_C r_C(\eta_C + b_C)}{k_C q_C(\eta_C + \theta_C b_C)}\left(1 - \frac{\overline{W}_C}{W_C}\right)\frac{dW_C}{dt}.
\end{aligned}$$

Substituting from Equations (1)–(9) and collecting terms we obtain

$$\begin{aligned}
\frac{d\Theta_2^L}{dt} &= \left(1 - \frac{\overline{X}}{X}\right)(\lambda - dX) + \left(\beta_Z \overline{X} - \frac{a_Z c_Z(\eta_Z + b_Z)}{k_Z(\eta_Z + \theta_Z b_Z)} - \frac{a_Z r_Z(\eta_Z + b_Z)}{k_Z(\eta_Z + \theta_Z b_Z)}\overline{W}_Z\right) V_Z \\
&+ \left(\beta_C \overline{X} - \frac{a_C c_C(\eta_C + b_C)}{k_C(\eta_C + \theta_C b_C)} - \frac{a_C r_C(\eta_C + b_C)}{k_C(\eta_C + \theta_C b_C)}\overline{W}_C\right) V_C \\
&- \frac{\eta_C(1 - \theta_C)\beta_C}{\eta_C + \theta_C b_C} X V_C \frac{\overline{Y}_C^L}{Y_C^L} + \frac{\eta_C(\eta_C + b_C)}{\eta_C + \theta_C b_C}\overline{Y}_C^L \\
&- \frac{(\eta_C + b_C)\theta_C \beta_C}{\eta_C + \theta_C b_C} X V_C \frac{\overline{Y}_C^A}{Y_C^A} + \frac{a_C(\eta_C + b_C)}{\eta_C + \theta_C b_C}\overline{Y}_C^A - \frac{\eta_C(\eta_C + b_C)}{\eta_C + \theta_C b_C} Y_C^L \frac{\overline{Y}_C^A}{Y_C^A} \\
&- \frac{a_C(\eta_C + b_C)}{\eta_C + \theta_C b_C} Y_C^A \frac{\overline{V}_C}{V_C} + \frac{a_C c_C(\eta_C + b_C)}{k_C(\eta_C + \theta_C b_C)}\overline{V}_C + \frac{a_C r_C(\eta_C + b_C)}{k_C(\eta_C + \theta_C b_C)}\overline{V}_C W_C \\
&+ \frac{a_Z r_Z(\eta_Z + b_Z)}{k_Z q_Z(\eta_Z + \theta_Z b_Z)}\left(1 - \frac{\overline{W}_Z}{W_Z}\right)(\gamma_Z - \mu_Z W_Z) \\
&+ \frac{a_C r_C(\eta_C + b_C)}{k_C q_C(\eta_C + \theta_C b_C)}\left(1 - \frac{\overline{W}_C}{W_C}\right)(\gamma_C - \mu_C W_C).
\end{aligned}$$

Applying the steady state conditions

$$\begin{aligned}
\lambda - d\overline{X} &= \beta_C \overline{X}\,\overline{V}_C,\\
(1-\theta_C)\beta_C \overline{X}\,\overline{V}_C &= (\eta_C + b_C)\overline{Y}_C^L,\\
\theta_C\beta_C \overline{X}\,\overline{V}_C + \eta_C \overline{Y}_C^L &= a_C \overline{Y}_C^A,\\
c_C\overline{V}_C + r_C\overline{W}_C\,\overline{V}_C &= k_C\overline{Y}_C^A,\\
\gamma_Z &= \mu_Z \overline{W}_Z,\\
\gamma_C + q_C\overline{W}_C\overline{V}_C &= \mu_C\overline{W}_C,
\end{aligned}$$

we get

$$\begin{aligned}
\frac{d\Theta_2^L}{dt} =& -\frac{d(X-\overline{X})^2}{X}\\
&+ \frac{\eta_C(1-\theta_C)}{\eta_C+\theta_C b_C}\beta_C\overline{X}\overline{V}_C\left[4 - \frac{\overline{X}}{X} - \frac{XV_C\overline{Y}_C^L}{\overline{X}\overline{V}_C Y_C} - \frac{Y_C^L\overline{Y}_C^A}{\overline{Y}_C^L Y_C^A} - \frac{Y_C^A\overline{V}_C}{\overline{Y}_C^A V_C}\right]\\
&+ \frac{\theta_C(\eta_C+b_C)}{\eta_C+\theta_C b_C}\beta_C\overline{X}\overline{V}_C\left[3 - \frac{\overline{X}}{X} - \frac{XV_C\overline{Y}_C^A}{\overline{X}\overline{V}_C Y_C^A} - \frac{Y_C^A\overline{V}_C}{\overline{Y}_C^A V_C}\right]\\
&+ \frac{a_Z(\eta_Z+b_Z)(c_Z\mu_Z + r_Z\gamma_Z)}{k_Z\mu_Z(\eta_Z+\theta_Z b_Z)}\left(R_Z^{L,inv}-1\right)V_Z\\
&- \frac{a_Z r_Z\mu_Z(\eta_Z+b_Z)}{k_Z q_Z(\eta_Z+\theta_Z b_Z)}\frac{(W_Z-\overline{W}_Z)^2}{W_Z} - \frac{a_C r_C\mu_C(\eta_C+b_C)}{k_C q_C(\eta_C+\theta_C b_C)}\frac{(W_C-\overline{W}_C)^2}{W_C}\\
&+ \frac{a_C r_C(\eta_C+b_C)}{k_C(\eta_C+\theta_C b_C)}\overline{V}_C\frac{(W_C-\overline{W}_C)^2}{W_C}.
\end{aligned}$$

From Equilibrium conditions of $\overline{SS}$, we have $\overline{V}_C - \frac{\mu_C}{q_C} = -\frac{\gamma_C}{q_C\overline{W}_C}$. It follows that

$$\begin{aligned}
\frac{d\Theta_2^L}{dt} =& -\frac{d(X-\overline{X})^2}{X}\\
&+ \frac{\eta_C(1-\theta_C)}{\eta_C+\theta_C b_C}\beta_C\overline{X}\overline{V}_C\left[4 - \frac{\overline{X}}{X} - \frac{XV_C\overline{Y}_C^L}{\overline{X}\overline{V}_C Y_C} - \frac{Y_C^L\overline{Y}_C^A}{\overline{Y}_C^L Y_C^A} - \frac{Y_C^A\overline{V}_C}{\overline{Y}_C^A V_C}\right]\\
&+ \frac{\theta_C(\eta_C+b_C)}{\eta_C+\theta_C b_C}\beta_C\overline{X}\overline{V}_C\left[3 - \frac{\overline{X}}{X} - \frac{XV_C\overline{Y}_C^A}{\overline{X}\overline{V}_C Y_C^A} - \frac{Y_C^A\overline{V}_C}{\overline{Y}_C^A V_C}\right]\\
&+ \frac{a_Z(\eta_Z+b_Z)(c_Z\mu_Z + r_Z\gamma_Z)}{k_Z\mu_Z(\eta_Z+\theta_Z b_Z)}\left(R_Z^{L,inv}-1\right)V_Z\\
&- \frac{a_Z r_Z\mu_Z(\eta_Z+b_Z)}{k_Z q_Z(\eta_Z+\theta_Z b_Z)}\frac{(W_Z-\overline{W}_Z)^2}{W_Z} - \frac{a_C r_C\gamma_C(\eta_C+b_C)}{k_C q_C(\eta_C+\theta_C b_C)}\frac{(W_C-\overline{W}_C)^2}{\overline{W}_C W_C}.
\end{aligned}$$

Consequenty, if $R_Z^{L,inv} \leq 1$, using Equation (40), we get $\frac{d\Theta_2^L}{dt} \leq 0$, where $\frac{d\Theta_2^L}{dt} = 0$ occurs at $(X, Y_C^L, Y_C^A, V_C, W_Z, W_C) = (\overline{X}, \overline{Y}_C^L, \overline{Y}_C^A, \overline{V}_C, \overline{W}_Z, \overline{W}_C)$ and $\left(R_Z^{L,inv}-1\right)V_Z = 0$. The solutions of the model converge to $\widetilde{\Gamma}_2^L$ which contains elements with $(X, Y_C^L, Y_C^A, V_C, W_Z, W_C) = (\overline{X}, \overline{Y}_C^L, \overline{Y}_C^A, \overline{V}_C, \overline{W}_Z, \overline{W}_C)$ and

$$\left(R_Z^{L,inv}-1\right)V_Z = 0. \tag{53}$$

We have two cases:

(i) If $R_Z^{L,inv} < 1$, then Equation (53) implies that $V_Z = 0$ and from Equation (6) we get

$$0 = \frac{dV_Z}{dt} = k_Z Y_Z^A \Rightarrow Y_Z^A(t) = 0 \text{ for any } t. \tag{54}$$

From Equation (3) we have

$$0 = \frac{dY_Z^A}{dt} = \eta_Z Y_Z^L \Rightarrow Y_Z^L(t) = 0 \text{ for any } t. \tag{55}$$

Hence $\widetilde{\Gamma}_2^L = \{\overline{SS}\}$.

(ii) When $R_Z^{L,inv} = 1$, Equation (1) gives

$$\lambda - dX + \beta_Z \overline{X} V_Z + \beta_C \overline{X} \overline{V}_C = 0 \Rightarrow V_Z(t) = 0 \text{ for any } t.$$

From Equations (54) and (55) we have $Y_Z^A = Y_Z^L = 0$. Hence $\widetilde{\Gamma}_2^L = \{\overline{SS}\}$. LaSalle's invariant principle shows that $\overline{SS}$ is globally asymptotically stable.

To investigate the instability of $\overline{SS}$ when $R_Z^{L,inv} > 1$, we derive the characteristic equation at $\overline{SS}$ by evaluating the Jacobian matrix of the system, leading to:

$$\begin{aligned}\det(J(\overline{SS}) - \xi I) = (\mu_Z + \xi)\left(\xi^3 + \hat{G}_2^L \xi^2 + \hat{G}_1^L \xi + \hat{G}_0^L\right)[(r_C q_C \overline{W}_C \overline{V}_C (a_C + \xi)(\beta_C \overline{V}_C + d + \xi) \\ \times (b_C + \eta_C + \xi) - (q_C \overline{V}_C - \mu_C - \xi)((a_C + \xi)(c_C + r_C \overline{W}_C + \xi)(\beta_C \overline{V}_C + d + \xi) \\ \times (\eta_C + b_C + \xi) - k_C \beta_C \overline{X}(d + \xi) + (\eta_C + \theta_C(b_C + \xi)))] \\ = 0,\end{aligned} \tag{56}$$

where the coefficients $\hat{G}_2^L, \hat{G}_1^L$ and $\hat{G}_0^L$ are defined as:

$$\begin{aligned}\hat{G}_2^L &= a_Z + b_Z + c_Z + \eta_Z + r_Z \overline{W}_Z, \\ \hat{G}_1^L &= a_Z(\eta_Z + b_Z) + a_Z c_Z + c_Z(b_Z + \eta_Z) + a_Z r_Z \overline{W}_Z \\ &\quad + (\eta_Z + b_Z) r_Z \overline{W}_Z - \beta_Z k_Z \overline{X}, \\ \hat{G}_0^L &= -\frac{a_Z(\eta_Z + b_Z)(c_Z \mu_Z + r_Z \gamma_Z)}{\mu_Z}\left(R_Z^{L,inv} - 1\right).\end{aligned}$$

If $R_Z^{L,inv} > 1$, then $\hat{G}_0^L < 0$, and hence, Equation (56) has a positive root and hence $\overline{SS}$ is unstable. □

Theorem 4. *The ZIKV-CHIKV co-infection steady state* $\widetilde{SS} = \left(\widetilde{X}, \widetilde{Y}_Z^L, \widetilde{Y}_Z^A, \widetilde{Y}_C^L, \widetilde{Y}_C^A, \widetilde{V}_Z, \widetilde{V}_C, \widetilde{W}_Z, \widetilde{W}_C\right)$ *is globally asymptotically stable if* $R_Z^{L,inv} > 1$ *and* $R_C^{L,inv} > 1$.

Proof. Define $\Theta_3^L(X, Y_Z^L, Y_Z^A, Y_C^L, Y_C^A, V_Z, V_C, W_Z, W_C)$ as:

$$\begin{aligned}\Theta_3^L &= \widetilde{X}\left(\frac{X}{\widetilde{X}} - 1 - \ln\frac{X}{\widetilde{X}}\right) + \frac{\eta_Z}{\eta_Z + \theta_Z b_Z}\widetilde{Y}_Z^L\left(\frac{Y_Z^L}{\widetilde{Y}_Z^L} - 1 - \ln\frac{Y_Z^L}{\widetilde{Y}_Z^L}\right) \\ &\quad + \frac{\eta_Z + b_Z}{\eta_Z + \theta_Z b_Z}\widetilde{Y}_Z^A\left(\frac{Y_Z^A}{\widetilde{Y}_Z^A} - 1 - \ln\frac{Y_Z^A}{\widetilde{Y}_Z^A}\right) \\ &\quad + \frac{\eta_C}{\eta_C + \theta_C b_C}\widetilde{Y}_C^L\left(\frac{Y_C^L}{\widetilde{Y}_C^L} - 1 - \ln\frac{Y_C^L}{\widetilde{Y}_C^L}\right) + \frac{\eta_C + b_C}{\eta_C + \theta_C b_C}\widetilde{Y}_C^A\left(\frac{Y_C^A}{\widetilde{Y}_C^A} - 1 - \ln\frac{Y_C^A}{\widetilde{Y}_C^A}\right) \\ &\quad + \frac{a_Z(\eta_Z + b_Z)}{k_Z(\eta_Z + \theta_Z b_Z)}\widetilde{V}_Z\left(\frac{V_Z}{\widetilde{V}_Z} - 1 - \ln\frac{V_Z}{\widetilde{V}_Z}\right) + \frac{a_C(\eta_C + b_C)}{k_C(\eta_C + \theta_C b_C)}\widetilde{V}_C\left(\frac{V_C}{\widetilde{V}_C} - 1 - \ln\frac{V_C}{\widetilde{V}_C}\right) \\ &\quad + \frac{a_Z r_Z(\eta_Z + b_Z)}{k_Z q_Z(\eta_Z + \theta_Z b_Z)}\widetilde{W}_Z\left(\frac{W_Z}{\widetilde{W}_Z} - 1 - \ln\frac{W_Z}{\widetilde{W}_Z}\right) \\ &\quad + \frac{a_C r_C(\eta_C + b_C)}{k_C q_C(\eta_C + \theta_C b_C)}\widetilde{W}_C\left(\frac{W_C}{\widetilde{W}_C} - 1 - \ln\frac{W_C}{\widetilde{W}_C}\right).\end{aligned}$$

We observe that $\Theta_3^L(X, Y_Z^L, Y_Z^A, Y_C^L, Y_C^A, V_Z, V_C, W_Z, W_C) > 0$ for all $(X, Y_Z^L, Y_Z^A,$

$Y_C^L, Y_C^A, V_Z, V_C, W_Z, W_C) > 0$ and $\Theta_3^L(\widetilde{X}, \widetilde{Y}_Z^L, \widetilde{Y}_Z^A, \widetilde{Y}_C^L, \widetilde{Y}_C^A, \widetilde{V}_Z, \widetilde{V}_C, \widetilde{W}_Z, \widetilde{W}_C) = 0$. Calculating $\frac{d\Theta_3^L}{dt}$ along the solutions of Equations (1)–(9) as:

$$\begin{aligned}\frac{d\Theta_3^L}{dt} &= \left(1-\frac{\widetilde{X}}{X}\right)\frac{dX}{dt} + \frac{\eta_Z}{\eta_Z+\theta_Z b_Z}\left(1-\frac{\widetilde{Y}_Z^L}{Y_Z^L}\right)\frac{dY_Z^L}{dt} + \frac{\eta_Z+b_Z}{\eta_Z+\theta_Z b_Z}\left(1-\frac{\widetilde{Y}_Z^A}{Y_Z^A}\right)\frac{dY_Z^A}{dt}\\ &+ \frac{\eta_C}{\eta_C+\theta_C b_C}\left(1-\frac{\widetilde{Y}_C^L}{Y_C^L}\right)\frac{dY_C^L}{dt} + \frac{\eta_C+b_C}{\eta_C+\theta_C b_C}\left(1-\frac{\widetilde{Y}_C^A}{Y_C^A}\right)\frac{dY_C^A}{dt}\\ &+ \frac{a_Z(\eta_Z+b_Z)}{k_Z(\eta_Z+\theta_Z b_Z)}\left(1-\frac{\widetilde{V}_Z}{V_Z}\right)\frac{dV_Z}{dt} + \frac{a_C(\eta_C+b_C)}{k_C(\eta_C+\theta_C b_C)}\left(1-\frac{\widetilde{V}_C}{V_C}\right)\frac{dV_C}{dt}\\ &+ \frac{a_Z r_Z(\eta_Z+b_Z)}{k_Z q_Z(\eta_Z+\theta_Z b_Z)}\left(1-\frac{\widetilde{W}_Z}{W_Z}\right)\frac{dW_Z}{dt} + \frac{a_C r_C(\eta_C+b_C)}{k_C q_C(\eta_C+\theta_C b_C)}\left(1-\frac{\widetilde{W}_C}{W_C}\right)\frac{dW_C}{dt}.\end{aligned}$$

Substituting from Equations (1)–(9) and collecting terms we obtain

$$\begin{aligned}\frac{d\Theta_3^L}{dt} &= \left(1-\frac{\widetilde{X}}{X}\right)(\lambda - dX) + \left(\beta_Z\widetilde{X} - \frac{a_Z c_Z(\eta_Z+b_Z)}{k_Z(\eta_Z+\theta_Z b_Z)} - \frac{a_Z r_Z(\eta_Z+b_Z)}{k_Z(\eta_Z+\theta_Z b_Z)}\widetilde{W}_Z\right)V_Z\\ &+ \left(\beta_C\widetilde{X} - \frac{a_C c_C(\eta_C+b_C)}{k_C(\eta_C+\theta_C b_C)} - \frac{r_C a_C(\eta_C+b_C)}{k_C(\eta_C+\theta_C b_C)}\widetilde{W}_C\right)V_C\\ &- \frac{\eta_Z(1-\theta_Z)\beta_Z}{\eta_Z+\theta_Z b_Z}XV_Z\frac{\widetilde{Y}_Z^L}{Y_Z^L}\\ &- \frac{\eta_C(1-\theta_C)\beta_C}{\eta_C+\theta_C b_C}XV_C\frac{\widetilde{Y}_C^L}{Y_C^L} + \frac{\eta_Z(\eta_Z+b_Z)}{\eta_Z+\theta_Z b_Z}\widetilde{Y}_Z^L + \frac{\eta_C(\eta_C+b_C)}{\eta_C+\theta_C b_C}\widetilde{Y}_C^L\\ &- \frac{(\eta_Z+b_Z)\theta_Z\beta_Z}{\eta_Z+\theta_Z b_Z}XV_Z\frac{\widetilde{Y}_Z^A}{Y_Z^A} - \frac{(\eta_C+b_C)\theta_C\beta_C}{\eta_C+\theta_C b_C}XV_C\frac{\widetilde{Y}_C^A}{Y_C^A} + \frac{a_Z(\eta_Z+b_Z)}{\eta_Z+\theta_Z b_Z}\widetilde{Y}_Z^A\\ &+ \frac{a_C(\eta_C+b_C)}{\eta_C+\theta_C b_C}\widetilde{Y}_C^A - \frac{\eta_Z(\eta_Z+b_Z)}{\eta_Z+\theta_Z b_Z}Y_Z^L\frac{\widetilde{Y}_Z^A}{Y_Z^A} - \frac{\eta_C(\eta_C+b_C)}{\eta_C+\theta_C b_C}Y_C^L\frac{\widetilde{Y}_C^A}{Y_C^A}\\ &- \frac{a_Z(\eta_Z+b_Z)}{\eta_Z+\theta_Z b_Z}Y_Z^A\frac{\widetilde{V}_Z}{V_Z} - \frac{a_C(\eta_C+b_C)}{\eta_C+\theta_C b_C}Y_C^A\frac{\widetilde{V}_C}{V_C}\\ &+ \frac{a_Z c_Z(\eta_Z+b_Z)}{k_Z(\eta_Z+\theta_Z b_Z)}\widetilde{V}_Z + \frac{a_C c_C(\eta_C+b_C)}{k_C(\eta_C+\theta_C b_C)}\widetilde{V}_C\\ &+ \frac{a_Z r_Z(\eta_Z+b_Z)}{k_Z q_Z(\eta_Z+\theta_Z b_Z)}\left(1-\frac{\widetilde{W}_Z}{W_Z}\right)(\gamma_Z - \mu_Z W_Z) + \frac{a_Z r_Z(\eta_Z+b_Z)}{k_Z(\eta_Z+\theta_Z b_Z)}\widetilde{V}_Z W_Z\\ &+ \frac{a_C r_C(\eta_C+b_C)}{k_C q_C(\eta_C+\theta_C b_C)}\left(1-\frac{\widetilde{W}_C}{W_C}\right)(\gamma_C - \mu_C W_C) + \frac{a_C r_C(\eta_C+b_C)}{k_C(\eta_C+\theta_C b_C)}\widetilde{V}_C W_C.\end{aligned}$$

Applying the steady state conditions

$$\begin{aligned}\lambda &= d\widetilde{X} + \beta_Z\widetilde{X}\widetilde{V}_Z + \beta_C\widetilde{X}\widetilde{V}_C,\\ (1-\theta_Z)\beta_Z\widetilde{X}\widetilde{V}_Z &= (\eta_Z+b_Z)\widetilde{Y}_Z^L,\\ a_Z\widetilde{Y}_Z^A &= \theta_Z\beta_Z\widetilde{X}\widetilde{V}_Z + \eta_Z\widetilde{Y}_Z^L,\\ (1-\theta_C)\beta_C\widetilde{X}\widetilde{V}_C &= (b_C+\eta_C)\widetilde{Y}_C^L,\\ a_C\widetilde{Y}_C^A &= \theta_C\beta_C\widetilde{X}\widetilde{V}_C + \eta_C\widetilde{Y}_C^L,\\ k_Z\widetilde{Y}_Z^A &= c_Z\widetilde{V}_Z + r_Z\widetilde{V}_Z\widetilde{W}_Z,\\ k_C\widetilde{Y}_C^A &= c_C\widetilde{V}_C + r_C\widetilde{V}_C\widetilde{W}_C,\\ \gamma_Z &= \mu_Z\widetilde{W}_Z - q_Z\widetilde{V}_Z\widetilde{W}_Z,\end{aligned}$$

$$\gamma_C = \mu_C \widetilde{W}_C - q_C \widetilde{V}_C \widetilde{W}_C,$$

we get

$$\begin{aligned}
\frac{d\Theta_3^L}{dt} = & -\frac{d(X-\widetilde{X})^2}{X} + \frac{\eta_Z(1-\theta_Z)}{\eta_Z+\theta_Z b_Z}\beta_Z \widetilde{X}\widetilde{V}_Z \left[4 - \frac{\widetilde{X}}{X} - \frac{XV_Z\widetilde{Y}_Z^L}{\widetilde{X}\widetilde{V}_Z Y_Z^L} - \frac{Y_Z^L\widetilde{Y}_Z^A}{\widetilde{Y}_Z^L Y_Z^A} - \frac{Y_Z^A\widetilde{V}_Z}{\widetilde{Y}_Z^A V_Z}\right] \\
& + \frac{\eta_C(1-\theta_C)}{\eta_C+\theta_C b_C}\beta_C \widetilde{X}\widetilde{V}_C \left[4 - \frac{\widetilde{X}}{X} - \frac{XV_C\widetilde{Y}_C^L}{\widetilde{X}\widetilde{V}_C Y_C^L} - \frac{Y_C^L\widetilde{Y}_C^A}{\widetilde{Y}_C^L Y_C^A} - \frac{Y_C^A\widetilde{V}_C}{\widetilde{Y}_C^A V_C}\right] \\
& + \frac{\theta_Z(\eta_Z+b_Z)}{\eta_Z+\theta_Z b_Z}\beta_Z \widetilde{X}\widetilde{V}_Z \left[3 - \frac{\widetilde{X}}{X} - \frac{XV_Z\widetilde{Y}_Z^A}{\widetilde{X}\widetilde{V}_Z Y_Z^A} - \frac{Y_Z^A\widetilde{V}_Z}{\widetilde{Y}_Z^A V_Z}\right] \\
& + \frac{\theta_C(\eta_C+b_C)}{\eta_C+\theta_C b_C}\beta_C \widetilde{X}\widetilde{V}_C \left[3 - \frac{\widetilde{X}}{X} - \frac{XV_C\widetilde{Y}_C^A}{\widetilde{X}\widetilde{V}_C Y_C^A} - \frac{Y_C^A\widetilde{V}_C}{\widetilde{Y}_C^A V_C}\right] \\
& - \frac{r_Z a_Z \mu_Z(\eta_Z+b_Z)}{k_Z q_Z(\eta_Z+\theta_Z b_Z)}\frac{(W_Z-\widetilde{W}_Z)^2}{W_Z} - \frac{r_C a_C \mu_C(\eta_C+b_C)}{k_C q_C(\eta_C+\theta_C b_C)}\frac{(W_C-\widetilde{W}_C)^2}{W_C} \\
& + \frac{a_Z r_Z(\eta_Z+b_Z)}{k_Z(\eta_Z+\theta_Z b_Z)}\widetilde{V}_Z\frac{(W_Z-\widetilde{W}_Z)^2}{W_Z} + \frac{a_C r_C(\eta_C+b_C)}{k_C(\eta_C+\theta_C b_C)}\widetilde{V}_C\frac{(W_C-\widetilde{W}_C)^2}{W_C}.
\end{aligned}$$

From the steady state conditions, we have $\widetilde{V}_Z - \frac{\mu_Z}{q_Z} = -\frac{\gamma_Z}{q_Z\widetilde{W}_Z}$ and $\widetilde{V}_C - \frac{\mu_C}{q_C} = -\frac{\gamma_C}{q_C\widetilde{W}_C}$. It follows that

$$\begin{aligned}
\frac{d\Theta_3^L}{dt} = & -\frac{d(X-\widetilde{X})^2}{X} + \frac{\eta_Z(1-\theta_Z)}{\eta_Z+\theta_Z b_Z}\beta_Z \widetilde{X}\widetilde{V}_Z \left[4 - \frac{\widetilde{X}}{X} - \frac{XV_Z\widetilde{Y}_Z^L}{\widetilde{X}\widetilde{V}_Z Y_Z^L} - \frac{Y_Z^L\widetilde{Y}_Z^A}{\widetilde{Y}_Z^L Y_Z^A} - \frac{Y_Z^A\widetilde{V}_Z}{\widetilde{Y}_Z^A V_Z}\right] \\
& + \frac{\eta_C(1-\theta_C)}{\eta_C+\theta_C b_C}\widetilde{X}\widetilde{V}_C \left[4 - \frac{\widetilde{X}}{X} - \frac{XV_C\widetilde{Y}_C^L}{\widetilde{X}\widetilde{V}_C Y_C^L} - \frac{Y_C^L\widetilde{Y}_C^A}{\widetilde{Y}_C^L Y_C^A} - \frac{Y_C^A\widetilde{V}_C}{\widetilde{Y}_C^A V_C}\right] \\
& + \frac{\theta_Z(\eta_Z+b_Z)}{\eta_Z+\theta_Z b_Z}\beta_Z \widetilde{X}\widetilde{V}_Z \left[3 - \frac{\widetilde{X}}{X} - \frac{XV_Z\widetilde{Y}_Z^A}{\widetilde{X}\widetilde{V}_Z Y_Z^A} - \frac{Y_Z^A\widetilde{V}_Z}{\widetilde{Y}_Z^A V_Z}\right] \\
& + \frac{\theta_C(\eta_C+b_C)}{\eta_C+\theta_C b_C}\beta_C \widetilde{X}\widetilde{V}_C \left[3 - \frac{\widetilde{X}}{X} - \frac{XV_C\widetilde{Y}_C^A}{\widetilde{X}\widetilde{V}_C Y_C^A} - \frac{Y_C^A\widetilde{V}_C}{\widetilde{Y}_C^A V_C}\right] \\
& - \frac{r_Z a_Z \gamma_Z(\eta_Z+b_Z)}{k_Z q_Z(\eta_Z+\theta_Z b_Z)}\frac{(W_Z-\widetilde{W}_Z)^2}{\widetilde{W}_Z W_Z} - \frac{r_C a_C \gamma_C(\eta_C+b_C)}{k_C q_C(\eta_C+\theta_C b_C)}\frac{(W_C-\widetilde{W}_C)^2}{\widetilde{W}_C W_C}.
\end{aligned}$$

We can see from Equation (41) that, $\frac{d\Theta_3^L}{dt} \leq 0$, for all $(X, Y_Z^L, Y_Z^A, Y_C^L, Y_C^A, V_Z, V_C, W_Z, W_C) > 0$. Moreover, $\frac{d\Theta_3^L}{dt} = 0$ occurs at $\widetilde{SS}$. The model's solutions converge to $\widetilde{\Gamma}_3^L = \{\widetilde{SS}\}$. LaSalle's invariant principle implies that $\widetilde{SS}$ is globally asymptotically stable. □

Table 1 provides an overview of the existence and global stability conditions for each steady state of the Equations (1)–(9).

Table 1. Criteria for existence and global stability of steady staes of Equations (1)–(9).

Steady state	**Existence conditions**	**Stability conditions**
$EQ^0 = (X^0, 0, 0, 0, 0, 0, 0, W_Z^0, W_C^0)$	–	$R_Z^L \leq 1$ and $R_C^L \leq 1$
$EQ^* = (X^*, Y_Z^{L*}, Y_Z^{A*}, 0, 0, V_Z^*, 0, W_Z^*, W_Z^*)$	$R_Z^L > 1$	$R_Z^L > 1$ and $R_C^{L,inv} \leq 1$
$\overline{EQ} = (\overline{X}, 0, 0, \overline{Y}_C^L, \overline{Y}_C^A, 0, \overline{V}_C, \overline{W}_Z, \overline{W}_C)$	$R_C^L > 1$	$R_C^L > 1$ and $R_Z^{L,inv} \leq 1$
$\widetilde{EQ} = (\widetilde{X}, \widetilde{Y}_Z^L, \widetilde{Y}_Z^A, \widetilde{Y}_C^L, \widetilde{Y}_C^A, \widetilde{V}_Z, \widetilde{V}_C, \widetilde{W}_Z, \widetilde{W}_C)$	$R_Z^{L,inv} > 1$ and $R_C^{L,inv} > 1$	$R_Z^{L,inv} > 1$ and $R_C^{L,inv} > 1$

7. Co-infection model with different treatment strategies

In the context of within-host dynamics of viral co-infections, developing effective therapeutic strategies is crucial for minimizing disease severity and limiting viral spread. The model considered here addresses the co-infection of ZIKV and CHIKV, under the impact of different treatment strategies. To study the impact of different treatment strategies through mathematical modeling, we consider four approaches, each targeting infection through a distinct mechanism. These strategies include: (1) blocking viral entry into healthy cells, (2) inhibiting viral replication within infected cells, (3) enhancing antibody production, and (4) increasing the rate of natural antibody production. The mathematical formulation of each strategy allows us to assess its effectiveness in reducing viral replication and stabilizing the disease-free state. In the following sections, we describe the modifications introduced by each treatment to the basic system.

7.1. Strategy I: Antiviral treatment for blocking viral infection

One of the most direct and biologically intuitive antiviral strategies involves preventing the virus from successfully infecting healthy target cells. This can be achieved through pharmacological agents that block viral entry into host cells, thereby reducing the effective infection rate. In the context of within-host mathematical modeling [63], this strategy is incorporated by reducing the infection transmission parameters β_Z and β_C using treatment controls u_Z and u_C, respectively. This results in the following modifications to the original system of Equations (1)–(9):

$$\frac{dX}{dt} = \lambda - dX - (1-u_Z)\beta_Z X V_Z - (1-u_C)\beta_C X V_C, \tag{57}$$

$$\frac{dY_Z^L}{dt} = (1-\theta_Z)(1-u_Z)\beta_Z X V_Z - (\eta_Z + b_Z)Y_Z^L, \tag{58}$$

$$\frac{dY_Z^A}{dt} = \theta_Z(1-u_Z)\beta_Z X V_Z + \eta_Z Y_Z^L - a_Z Y_Z^A, \tag{59}$$

$$\frac{dY_C^L}{dt} = (1-\theta_C)(1-u_C)\beta_C X V_C - (\eta_C + b_C)Y_C^L, \tag{60}$$

$$\frac{dY_C^A}{dt} = \theta_C(1-u_C)\beta_C X V_C + \eta_C Y_C^L - a_C Y_C^A, \tag{61}$$

$$\frac{dV_Z}{dt} = k_Z Y_Z^A - c_Z V_Z - r_Z V_Z W_Z, \tag{62}$$

$$\frac{dV_C}{dt} = k_C Y_C^A - c_C V_C - r_C V_C W_C, \tag{63}$$

$$\frac{dW_Z}{dt} = \gamma_Z + q_Z V_Z W_Z - \mu_Z W_Z, \tag{64}$$

$$\frac{dW_C}{dt} = \gamma_C + q_C V_C W_C - \mu_C W_C. \tag{65}$$

Where u_Z, $u_C \in [0,1]$ are antiviral efficacy against ZIKV and CHIKV, respectively. The effect of antiviral treatment manifests in the basic reproduction numbers for

Equations (57)–(65) as:

$$R_Z^L(u_Z) = \frac{k_Z(1-u_Z)\beta_Z\lambda\mu_Z(\eta_Z + b_Z\theta_Z)}{a_Z d(\eta_Z + b_Z)(r_Z\gamma_Z + c_Z\mu_Z)},$$
$$R_C^L(u_C) = \frac{k_C(1-u_C)\beta_C\lambda\mu_C(\eta_C + b_C\theta_C)}{a_C d(\eta_C + b_C)(r_C\gamma_C + c_C\mu_C)}.$$

When all other parameters are held constant, $R_Z^L(u_Z)$ and $R_C^L(u_C)$ decrease monotonically with increasing treatment intensities u_Z and u_C, respectively. This decline highlights the role of antiviral therapy in inhibiting the infection of susceptible cells by the virus. As a result, increasing the control parameters u_Z and u_C leads to a reduction in the effective infection rates, thereby decreasing the influx of newly infected latent $\left(Y_Z^L, Y_C^L\right)$ and active $\left(Y_Z^A, Y_C^A\right)$ cells. Consequently, the viral concentration (V_Z, V_C) also diminish, as fewer infected cells are available to produce new virions. Therefore, this treatment mechanism acts as a powerful preventive strategy to limit viral spread and control the severity of ZIKV and CHIKV co-infections.

The minimum efficacy levels required to bring $R_Z^L \leq 1$ and $R_C^L \leq 1$ are calculated as:

$$u_Z^{\min} = \max\left\{1 - \frac{a_Z d(\eta_Z + b_Z)(r_Z\gamma_Z + c_Z\mu_Z)}{k_Z\beta_Z\lambda\mu_Z(\eta_Z + b_Z\theta_Z)}, 0\right\},$$
$$u_C^{\min} = \max\left\{1 - \frac{a_C d(\eta_C + b_C)(r_C\gamma_C + c_C\mu_C)}{k_C\beta_C\lambda\mu_C(\eta_C + b_C\theta_C)}, 0\right\}.$$

Corollary 1. *If $u_Z^{\min} \leq u_Z \leq 1$ and $u_C^{\min} \leq u_C \leq 1$, then the disease-free steady state SS^0 is globally asymptotically stable.*

7.2. Strategy II: Antiviral treatment for blocking viral production

One of the key antiviral strategies targeting intracellular stages of viral replication involves inhibiting the production of new virions from actively infected cells. This mechanism can be implemented through therapeutic agents that interfere with viral assembly, maturation, or release processes [64]. In within-host mathematical models, this strategy is reflected by reducing the viral production rates k_Z and k_C via treatment controls υ_Z and υ_C, respectively. Incorporating this intervention leads to the following modified version of the original Equations (1)–(9):

$$\frac{dX}{dt} = \lambda - dX - \beta_Z X V_Z - \beta_C X V_C, \tag{66}$$
$$\frac{dY_Z^L}{dt} = (1-\theta_Z)\beta_Z X V_Z - (\eta_Z + b_Z)Y_Z^L, \tag{67}$$
$$\frac{dY_Z^A}{dt} = \theta_Z\beta_Z X V_Z + \eta_Z Y_Z^L - a_Z Y_Z^A, \tag{68}$$
$$\frac{dY_C^L}{dt} = (1-\theta_C)\beta_C X V_C - (\eta_C + b_C)Y_C^L, \tag{69}$$
$$\frac{dY_C^A}{dt} = \theta_C\beta_C X V_C + \eta_C Y_C^L - a_C Y_C^A, \tag{70}$$

$$\frac{dV_Z}{dt} = (1-\upsilon_Z)k_Z Y_Z^A - c_Z V_Z - r_Z V_Z W_Z, \tag{71}$$

$$\frac{dV_C}{dt} = (1-\upsilon_C)k_C Y_C^A - c_C V_C - r_C V_C W_C, \tag{72}$$

$$\frac{dW_Z}{dt} = \gamma_Z + q_Z V_Z W_Z - \mu_Z W_Z, \tag{73}$$

$$\frac{dW_C}{dt} = \gamma_C + q_C V_C W_C - \mu_C W_C. \tag{74}$$

Where $\upsilon_Z, \upsilon_C \in [0,1]$ are efficacy of antiviral treatment in inhibiting virus production from actively infected cells with ZIKV and CHIKV, respectively.

The basic reproduction numbers corresponding to Equations (66)–(74) are expressed as:

$$R_Z^L(\upsilon_Z) = \frac{(1-\upsilon_Z)k_Z\beta_Z\lambda\mu_Z(\eta_Z + b_Z\theta_Z)}{a_Z d(\eta_Z + b_Z)(r_Z\gamma_Z + c_Z\mu_Z)},$$
$$R_C^L(\upsilon_C) = \frac{(1-\upsilon_C)k_C\beta_C\lambda\mu_C(\eta_C + b_C\theta_C)}{a_C d(\eta_C + b_C)(r_C\gamma_C + c_C\mu_C)}.$$

They are structurally identical to those derived in the first strategy (blocking infection). The key difference lies in the biological interpretation: while the first strategy reduces infection rates by limiting virus entry into target cells, the second strategy directly suppresses viral output from actively infected cells. Nevertheless, the mathematical formulation of R_Z^L and R_C^L remain unchanged. Clearly, $R_Z^L(\upsilon_Z)$ and $R_C^L(\upsilon_C)$ are strictly decreasing functions of the treatment intensities υ_Z and υ_C, respectively. Therefore as υ_Z and υ_C are increased the viral concentration (V_Z, V_C) are decreased. Strengthening this inhibitory effect can drive the reproduction numbers below or equal one, ensuring the global asymptotic stability of the disease-free steady state SS^0 and confirming the clinical potential of targeting viral production in managing coinfections.

7.3. Strategy III: Immune-enhancing therapy

The third type of therapeutic intervention aims to enhance the host's immune response against ZIKV and CHIKV by stimulating antibody production. In this approach, treatment parameters ω_Z and ω_C amplify the antibody generation rates for each virus, thereby increasing the levels of W_Z and W_C. This mechanism is incorporated into the within-host model by modifying the antibody dynamics equations, while all other equations remain consistent with the original system. The modified model equations are as follows:

$$\frac{dX}{dt} = \lambda - dX - \beta_Z X V_Z - \beta_C X V_C, \tag{75}$$

$$\frac{dY_Z^L}{dt} = (1-\theta_Z)\beta_Z X V_Z - (\eta_Z + b_Z)Y_Z^L, \tag{76}$$

$$\frac{dY_Z^A}{dt} = \theta_Z\beta_Z X V_Z + \eta_Z Y_Z^L - a_Z Y_Z^A, \tag{77}$$

$$\frac{dY_C^L}{dt} = (1-\theta_C)\beta_C X V_C - (\eta_C + b_C)Y_C^L, \tag{78}$$

$$\frac{dY_C^A}{dt} = \theta_C\beta_C X V_C + \eta_C Y_C^L - a_C Y_C^A, \tag{79}$$

$$\frac{dV_Z}{dt} = k_Z Y_Z^A - c_Z V_Z - r_Z V_Z W_Z, \tag{80}$$

$$\frac{dV_C}{dt} = k_C Y_C^A - c_C V_C - r_C V_C W_C, \tag{81}$$

$$\frac{dW_Z}{dt} = \gamma_Z + (1+\omega_Z) q_Z V_Z W_Z - \mu_Z W_Z, \tag{82}$$

$$\frac{dW_C}{dt} = \gamma_C + (1+\omega_C) q_C V_C W_C - \mu_C W_C. \tag{83}$$

Where ω_Z, $\omega_C \in [0, \omega^{\max}]$ are control parameters representing the efficacy of the immune-enhancing therapy in boosting the antibody response and $\omega^{\max}$ denotes the maximum achievable level of treatment efficacy, defined as the treatment level beyond which no further improvement in efficacy is expected [65].

The basic reproduction numbers R_Z^L and R_C^L are identical to those in the original model, showing no direct dependency on the immune-enhancing parameters. However, the immune-enhancing strategy may influence the transient dynamics by accelerating immune activation and viral clearance, which will be discussed further later in the simulation.

7.4. Strategy IV: Treatment for enhancing antibodies' flow rate

This fourth type of treatment involves enhancing the baseline production rate of antibodies by directly stimulating the immune system. Unlike the previous approaches, such as infection blocking, viral production suppression, or immune stimulation through virus interaction-this strategy augments the constitutive source term of the immune components γ_Z and γ_C, modulated by control parameters κ_Z and κ_C. This leads to an increase in baseline antibody levels W_Z and W_C. The modification within the host co-infection model under this treatment is given as:

$$\frac{dX}{dt} = \lambda - dX - \beta_Z X V_Z - \beta_C X V_C, \tag{84}$$

$$\frac{dY_Z^L}{dt} = (1-\theta_Z)\beta_Z X V_Z - (\eta_Z + b_Z) Y_Z^L, \tag{85}$$

$$\frac{dY_Z^A}{dt} = \theta_Z \beta_Z X V_Z + \eta_Z Y_Z^L - a_Z Y_Z^A, \tag{86}$$

$$\frac{dY_C^L}{dt} = (1-\theta_C)\beta_C X V_C - (\eta_C + b_C) Y_C^L, \tag{87}$$

$$\frac{dY_C^A}{dt} = \theta_C \beta_C X V_C + \eta_C Y_C^L - a_C Y_C^A, \tag{88}$$

$$\frac{dV_Z}{dt} = k_Z Y_Z^A - c_Z V_Z - r_Z V_Z W_Z, \tag{89}$$

$$\frac{dV_C}{dt} = k_C Y_C^A - c_C V_C - r_C V_C W_C, \tag{90}$$

$$\frac{dW_Z}{dt} = (1+\kappa_Z)\gamma_Z + q_Z V_Z W_Z - \mu_Z W_Z, \tag{91}$$

$$\frac{dW_C}{dt} = (1+\kappa_C)\gamma_C + q_C V_C W_C - \mu_C W_C. \tag{92}$$

Here $\kappa_Z, \kappa_C \in [0, \kappa^{\max}]$ represent the intensities of immunotherapy aimed at enhancing the natural production rates of antibodies, respectively. These parameters model the therapeutic boost applied to the baseline antibody generation, thereby amplifying the

host's immune response against ZIKV and CHIKV infections [43].

Equations (84)–(92) has a disease-free steady state $SS^0_{(84)-(92)} = (\frac{\lambda}{d}, 0, 0, 0, 0, 0, 0, \frac{(1+\kappa_Z)\gamma_Z}{\mu_Z}, \frac{(1+\kappa_C)\gamma_C}{\mu_C})$. The basic reproduction numbers corresponding to Equations (84)–(92) are expressed as:

$$R^L_Z(\kappa_Z) = \frac{k_Z\beta_Z\lambda\mu_Z(\eta_Z + b_Z\theta_Z)}{a_Z d(\eta_Z + b_Z)((1+\kappa_Z)r_Z\gamma_Z + c_Z\mu_Z)},$$
$$R^L_C(\kappa_C) = \frac{k_C\beta_C\lambda\mu_C(\eta_C + b_C\theta_C)}{a_C d(\eta_C + b_C)((1+\kappa_C)r_C\gamma_C + c_C\mu_C)}.$$

We have

$$\frac{\partial R^L_Z}{\partial \kappa_Z} = -\frac{k_Z\beta_Z\lambda\mu_Z r_Z\gamma_Z(\eta_Z + b_Z\theta_Z)}{a_Z d(\eta_Z + b_Z)((1+\kappa_Z)r_Z\gamma_Z + c_Z\mu_Z)^2},$$
$$\frac{\partial R^L_C}{\partial \kappa_C} = -\frac{k_C\beta_C\lambda\mu_C r_C\gamma_C(\eta_C + b_C\theta_C)}{a_C d(\eta_C + b_C)((1+\kappa_C)r_C\gamma_C + c_C\mu_C)^2}.$$

When all other parameters are held constant, the reproduction numbers $R^L_Z(\kappa_Z)$ and $R^L_C(\kappa_C)$ decrease monotonically as the treatment intensities κ_Z and κ_C increase. This behavior reflects the role of immunotherapy in suppressing viral replication. In particular, increasing κ_Z and κ_C enhances the antibody responses W_Z and W_C, while simultaneously lowering viral loads as well as the populations of latently and actively infected cells. Hence, strengthening the immune response through treatment constitutes an effective approach for controlling DENV-CHIKV co-infection.

Our objective is to identify the threshold levels of κ_Z and κ_C that ensure $R^L_Z \leq 1$ and $R^L_C \leq 1$. It follows that

$$R^L_Z(\kappa_Z) \leq 1 \text{ for all } \kappa_Z \in \left[\kappa_Z^{\min}, \kappa_Z^{\max}\right],$$
$$R^L_C(\kappa_C) \leq 1 \text{ for all } \kappa_C \in \left[\kappa_C^{\min}, \kappa_C^{\max}\right],$$

where the minimum efficacy levels required are given by:

$$\kappa_Z^{\min} = \max\left\{0, \frac{r_Z\gamma_Z + c_Z\mu_Z}{r_Z\gamma_Z}(R^L_Z(0) - 1)\right\},$$
$$\kappa_C^{\min} = \max\left\{0, \frac{r_C\gamma_C + c_C\mu_C}{r_C\gamma_C}(R^L_C(0) - 1)\right\}.$$

Corollary 2. *If $\kappa_Z^{\min} \leq \kappa_Z \leq \kappa_Z^{\max}$ and $\kappa_C^{\min} \leq \kappa_C \leq \kappa_C^{\max}$, then the disease-free steady state $SS^0_{(84)-(92)}$ is globally asymptotically stable.*

8. Numerical simulations

In this section, we present a series of numerical simulations aimed at validating and extending the theoretical findings. By utilizing specific parameter values, we illustrate the model's dynamic behavior under varying conditions. The analysis includes assessing the stability of steady states, and the impact of different types of treatment strategies.

8.1. Stability of steady states

The system of Equations (1)–(9) is solved numerically using the MATLAB solver ode45. The values of the model parameters used in the simulations are given as: $\lambda = 10$ cells mm^{-3} day^{-1}, $d = 0.14$ day^{-1}, $\theta_Z = 0.3$, $\theta_C = 0.3$, $\eta_Z = 0.9$ day^{-1}, $\eta_C = 0.9$ day^{-1}, $b_Z = 0.14$ day^{-1}, $b_C = 0.14$ day^{-1}, $a_Z = 0.14$ day^{-1}, $a_C = 0.4443$ day^{-1}, $k_Z = 10$ viruses cells^{-1} day^{-1}, $k_C = 4$ viruses cells^{-1} day^{-1}, $c_Z = 3.5$ day^{-1}, $c_C = 0.4418$ day^{-1}, $r_Z = 0.01$ cells^{-1} mm^3 day^{-1}, $r_C = 0.001$ cells^{-1} mm^3 day^{-1}, $\gamma_Z = 1.402$ cells day^{-1}, $\gamma_C = 1.402$ cells day^{-1}, $q_Z = 0.00219$ viruses^{-1} mm^3 day^{-1}, $q_C = 0.002$ viruses^{-1} mm^3 day^{-1}, $\mu_Z = 0.4$ day^{-1}, and $\mu_C = 0.4$ day^{-1}. Parameters β_Z and β_C are varied.

Some model parameters were chosen from published studies on CHIKV or ZIKV single infections whenever dependable estimates were available. For parameters without direct experimental measurements, values consistent with established within-host viral dynamics literature were adopted within biologically reasonable ranges. The parameter set used in the numerical experiments is mainly intended to show that the theoretical stability and threshold conditions are reflected in the simulated solutions of the model. The key qualitative findings of the study, including threshold behavior, virus persistence leading to dominance or elimination, and possible coexistence patterns, are obtained from reproduction number and invasion analysis rather than from particular numerical parameter choices. The simulation results indicate that these qualitative dynamical properties remain valid under moderate variations of parameter values. The current lack of detailed clinical data for CHIKV-ZIKV co-infection limits precise parameter calibration. Future availability of reliable patient data would allow more accurate estimation of model parameters and support comprehensive quantitative validation of the proposed framework.

To analyze the global behavior of the system, ten different sets of initial conditions were used, defined as follows:

$$\begin{aligned} X &= 50 - 3s, \;\; Y_Z^L = 1 + 2s, \\ Y_Z^A &= 1 + 2s, \;\; Y_C^L = 1 + 2s, \\ Y_C^A &= 1 + 2s, \;\; V_Z = 1 + 5s, \\ V_C &= 20 + 5s, \;\; W_Z = 6 - 0.5s, \\ W_C &= 7 - 0.6s, \\ s &= 1, 2, ..., 10. \end{aligned}$$

These initial conditions were chosen to examine whether the system's solutions converge to one of the steady states regardless of the starting values.

By selecting different values for the parameters (β_Z, β_C) while keeping all other parameters fixed, four distinct plans arise as follows:

Plan 1 (Stability of SS^0): $(\beta_Z, \beta_C) = (0.0001, 0.0001)$. With this choice, we find the basic reproduction numbers R_Z^L and R_C^L take the following values $R_Z^L = 0.1307 < 1$ and $R_C^L = 0.1308 < 1$. **Figure 2** illustrates that all trajectories, initiated from various initial conditions, tend toward the steady state

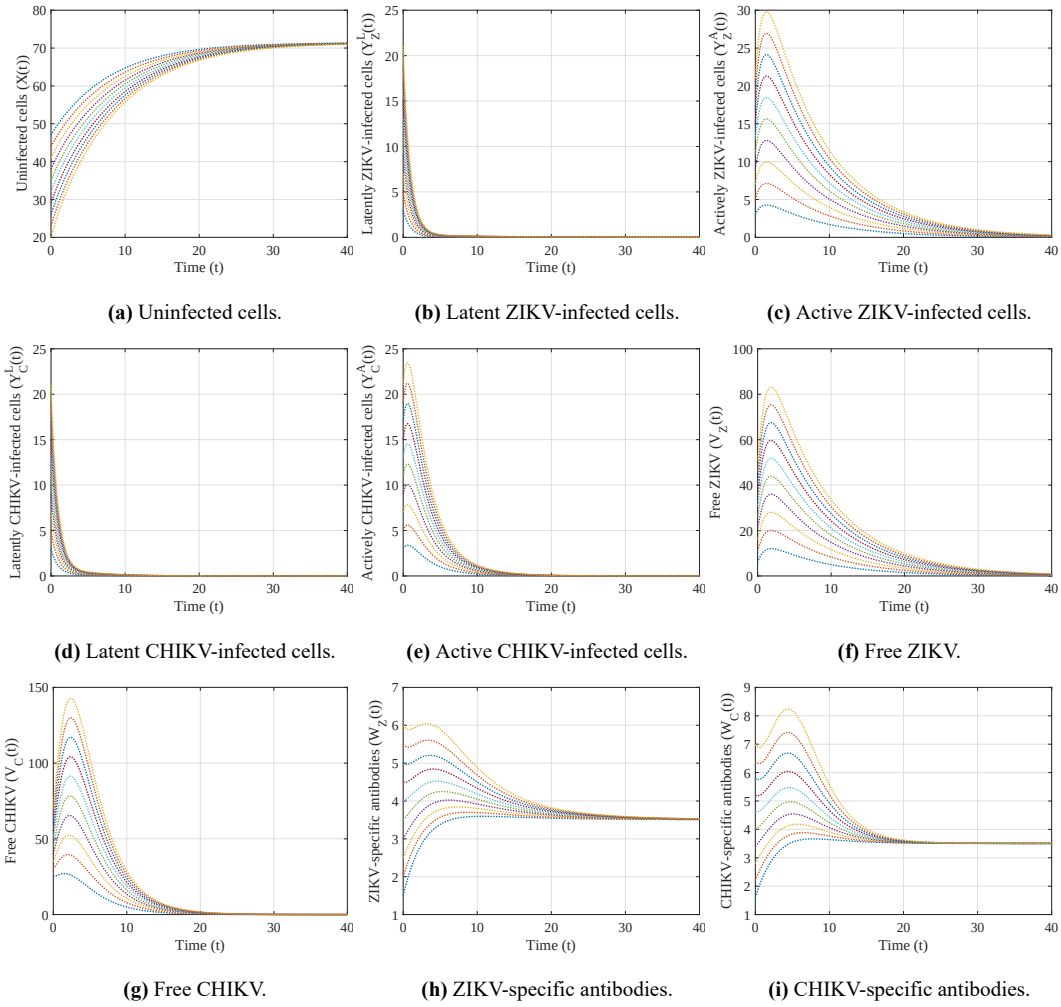
$SS^0 = (71.43, 0, 0, 0, 0, 0, 0, 3.51, 3.51)$. This convergence confirms the global asymptotic stability of SS^0, in agreement with the conclusion stated in Theorem 1. In this scenario, the system converges to the baseline steady state, where uninfected cells and virus-specific antibodies for both ZIKV and CHIKV return to their normal levels. Meanwhile, all other compartments-including infected cells and viral loads-gradually decline to zero. Consequently, the infections are completely cleared, and both viruses are eliminated from the host. This behavior indicates the existence of a stable disease-free steady state, where the immune response, whether natural or treatment-enhanced, effectively suppresses viral replication and leads to complete eradication of the pathogens.

Plan 2 (Stability of SS^*): $(\beta_Z, \beta_C) = (0.004, 0.0001)$. We obtain $R_Z^L = 5.2291 > 1$ and $R_C^{L,inv} = 0.02589 < 1$, confirming that the conditions listed in **Table 1** are satisfied. Accordingly, the steady state SS^* exists, with numerical values $SS^* = (14.13, 5.40, 58.34, 0, 0, 141.91, 0, 15.72, 3.51)$. **Figure 3** shows that solutions corresponding to different initial conditions converge to SS^*, which is consistent with Theorem 2. Under these parameter values, ZIKV remains the only persistent infection, whereas CHIKV is completely cleared. Although both viruses are present initially, the CHIKV-related components-including infected cells and viral load-decrease to zero over time. In contrast, ZIKV continues to persist, indicating that the immune response, in this setting, is not strong enough to eliminate it. This outcome reflects a clear difference in the persistence of the two viruses during co-infection, with ZIKV showing a stronger ability to sustain infection within the host.

Plan 3 (Stability of $\overline{SS}$): $(\beta_Z, \beta_C) = (0.0001, 0.004)$. For this parameter set, we obtain $R_C^L = 5.2321 > 1$ and $R_Z^{L,inv} = 0.0255 < 1$. Therefore, the conditions in **Table 1** are fulfilled, ensuring the existence of the steady state $\overline{SS}$. **Figure 4** shows that solutions corresponding to different initial conditions converge to $\overline{SS} = (13.93, 0, 0, 5.42, 16.41, 0, 144.45, 3.51, 12.62)$, in agreement with Theorem 3. Under these conditions, CHIKV persists as the only active infection, whereas ZIKV is eliminated. Although both viruses are initially present, the ZIKV-related components-including infected cells and viral load-decrease to zero over time, leading to its complete clearance from the host. In contrast, CHIKV maintains its presence, with both infected cells and free viral particles persisting over time. This result suggests that the immune response is sufficient to clear ZIKV but are less effective in eradicating CHIKV. The findings underscore the differential persistence capabilities of the two viruses during co-infection, with CHIKV exhibiting a stronger potential for long-term survival within the host, while ZIKV is successfully suppressed.

Plan 4 (Stability of $\widetilde{SS}$): $(\beta_Z, \beta_C) = (0.008, 0.008)$. We obtain $R_Z^{L,inv} = 1.0309 > 1$ and $R_C^{L,inv} = 1.0583 > 1$. Accordingly, the steady state $\widetilde{SS} = (6.87, 2.63, 25.27, 3.45, 10.46, 71.03, 93.34, 5.74, 6.57)$ is globally asymptotically stable consistent with Theorem 4. **Figure 5** shows that solutions from different initial conditions converge to this steady state. Under these conditions, both ZIKV and CHIKV persist within the host. Each virus maintains

a sustained level of replication, with their corresponding infected cells and viral loads remaining present over time. Although the immune response is active against both infections, it does not eliminate either one, leading to a long-term co-infection state. This behavior reflects the interaction between the two viruses, where neither is suppressed sufficiently, allowing their continued coexistence.

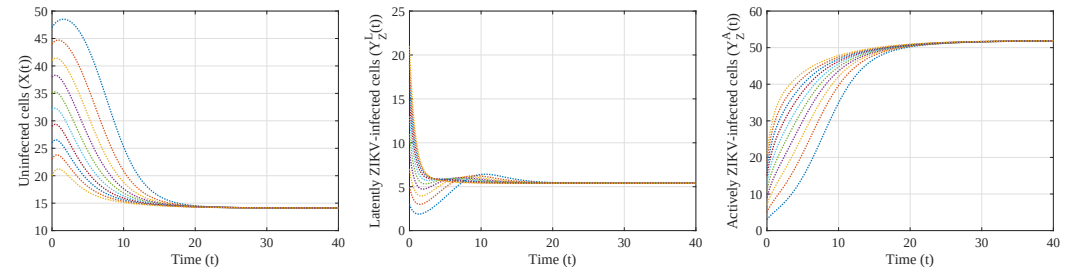


(a) Uninfected cells. **(b)** Latent ZIKV-infected cells. **(c)** Active ZIKV-infected cells.

(d) Latent CHIKV-infected cells. **(e)** Active CHIKV-infected cells. **(f)** Free ZIKV.

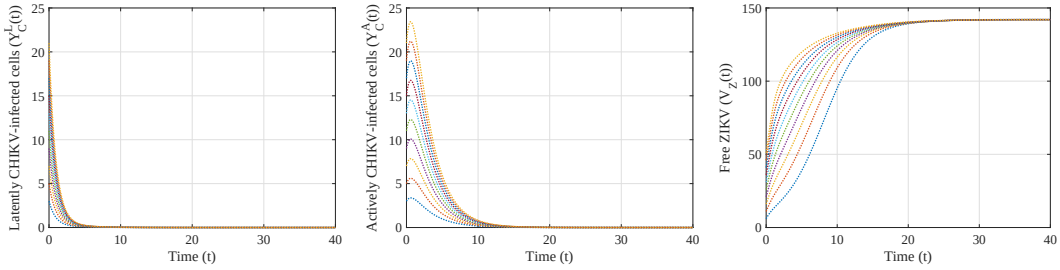
(g) Free CHIKV. **(h)** ZIKV-specific antibodies. **(i)** CHIKV-specific antibodies.

Figure 2. All trajectories of Equations (1)–(9) starting from different initial states converge to the disease-free equilibrium $EQ^0 = (71.43, 0, 0, 0, 0, 0, 0, 3.51, 3.51)$ under the conditions $R_Z^L \leq 1$ and $R_C^L \leq 1$.

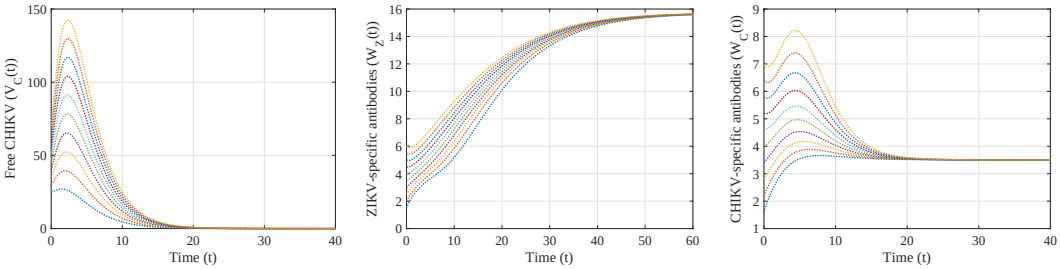


(a) Uninfected cells. **(b)** Latent ZIKV-infected cells. **(c)** Active ZIKV-infected cells.

Figure 3. *Cont.*

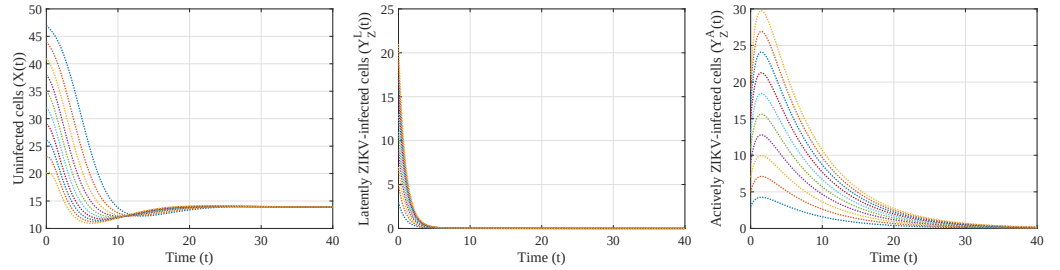


(d) Latent CHIKV-infected cells. **(e)** Active CHIKV-infected cells. **(f)** Free ZIKV.

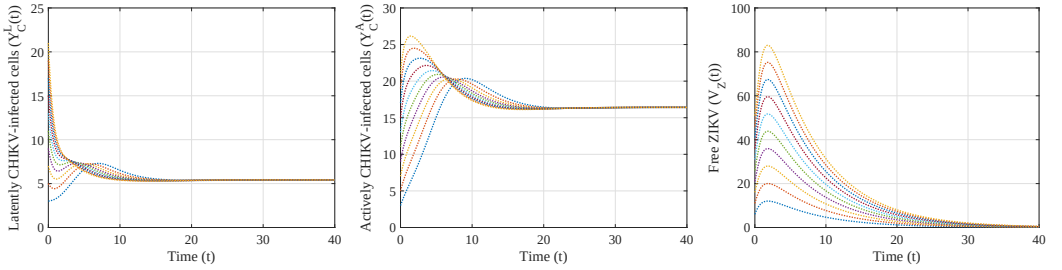


(g) Free CHIKV. **(h)** ZIKV-specific antibodies. **(i)** CHIKV-specific antibodies.

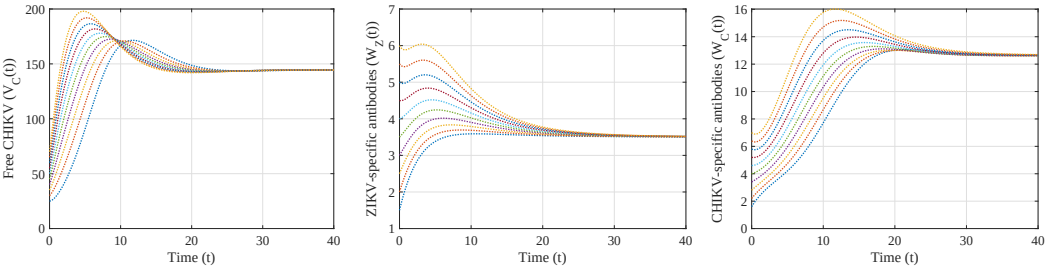
Figure 3. All trajectories of Equations (1)–(9) starting from different initial states converge to ZIKV-only infection steady state $SS^* = (14.13, 5.40, 51.90, 0, 0, 141.91, 0, 15.72, 3.51)$ under the conditions $R_Z^L > 1$ and $R_C^{L,inv} < 1$.



(a) Uninfected cells. **(b)** Latent ZIKV-infected cells. **(c)** Active ZIKV-infected cells.

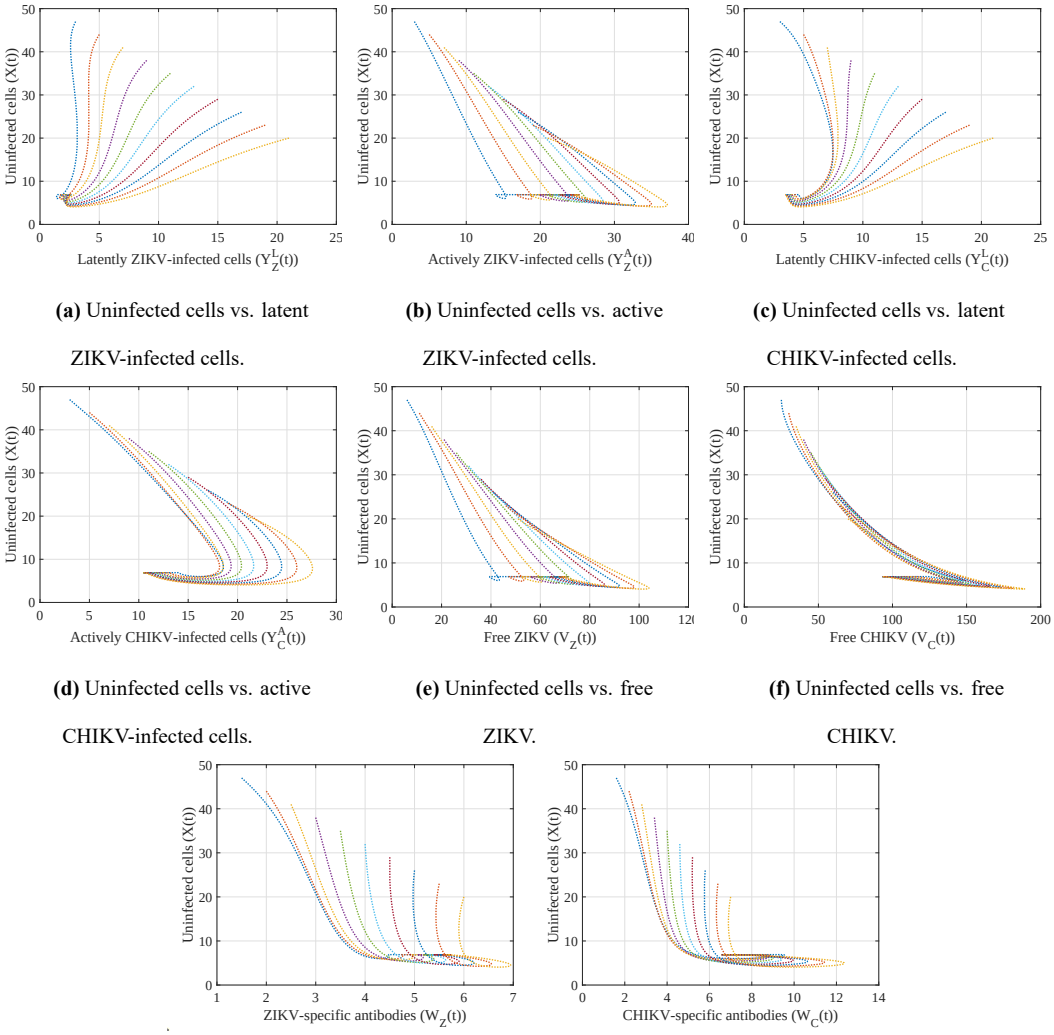


(d) Latent CHIKV-infected cells. **(e)** Active CHIKV-infected cells. **(f)** Free ZIKV.



(g) Free CHIKV. **(h)** ZIKV-specific antibodies. **(i)** CHIKV-specific antibodies.

Figure 4. All trajectories of Equations (1)–(9) starting from different initial states converge to CHIKV-only infection steady state $\overline{SS} = (13.93, 0, 0, 5.42, 16.41, 0, 144.45, 3.51, 12.62)$ under the conditions $R_C^L > 1$ and $R_Z^{L,inv} < 1$.



(a) Uninfected cells vs. latent ZIKV-infected cells. **(b)** Uninfected cells vs. active ZIKV-infected cells. **(c)** Uninfected cells vs. latent CHIKV-infected cells.

(d) Uninfected cells vs. active CHIKV-infected cells. **(e)** Uninfected cells vs. free ZIKV. **(f)** Uninfected cells vs. free CHIKV.

(g) Uninfected cells vs. ZIKV-specific antibodies. **(h)** Uninfected cells vs. CHIKV-specific antibodies.

Figure 5. Phase portraits of Equations (1)–(9) for different initial conditions showing convergence to ZIKV-CHIKV co-infection steady state $\widetilde{SS} = (6.87, 2.63, 25.27, 3.45, 10.46, 71.03, 93.34, 5.74, 6.57)$ under the conditions $R_Z^{L,inv} > 1$ and $R_C^{L,inv} > 1$.

8.2. ZIKV-CHIKV co-dynamics under different treatment strategies

To investigate the impact of different treatment strategies on the ZIKV and CHIKV co-dynamics, we conducted numerical simulations using a unified initial condition across all strategies:

$$\begin{aligned}&(X(0), Y_Z^L(0), Y_C^L(0), Y_Z^A(0), Y_C^A(0), V_Z(0), V_C(0), W_Z(0), W_C(0))\\&= (45, 9, 11, 4, 6, 25, 45, 8, 10).\end{aligned} \tag{93}$$

Each strategy is governed by a distinct system of equations tailored to the nature of the intervention. To evaluate treatment efficacy, we varied the intensity parameters u_Z,u_C,υ_Z, υ_C, ω_Z, ω_C, κ_Z and κ_C representing control levels for ZIKV and CHIKV, respectively.

For strategies I and II, which target viral infection and production mechanisms, we

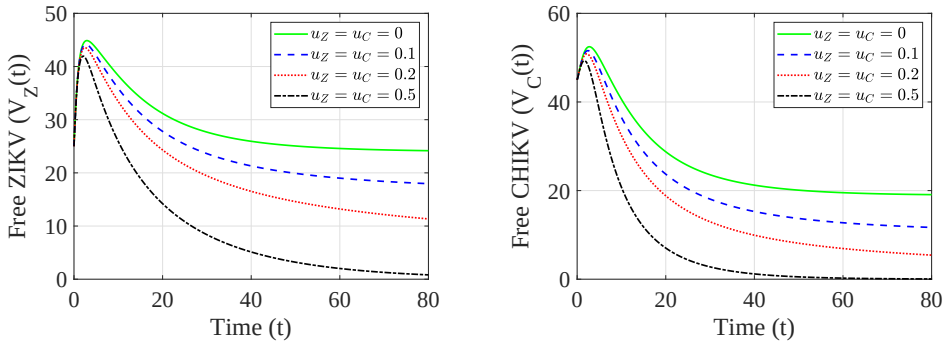
examined the following levels of control:

$$\begin{aligned} u_Z = u_C = \upsilon_Z = \upsilon_C = 0, \\ u_Z = u_C = \upsilon_Z = \upsilon_C = 0.1, \\ u_Z = u_C = \upsilon_Z = \upsilon_C = 0.2, \\ u_Z = u_C = \upsilon_Z = \upsilon_C = 0.5. \end{aligned} \tag{94}$$

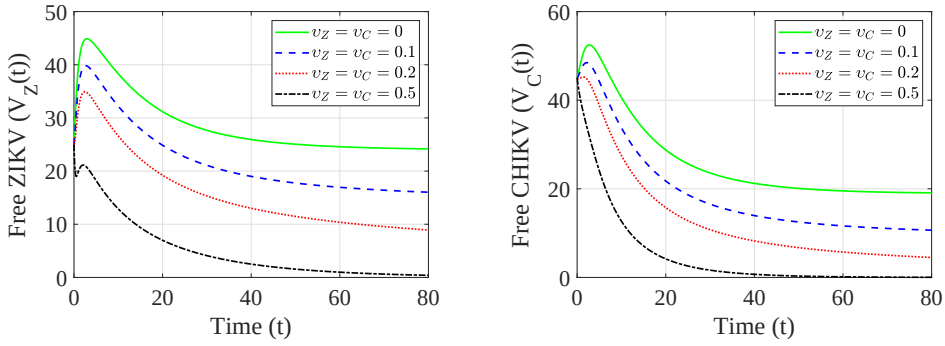
For strategies III and IV, which involve immune-enhancing interventions, we applied higher intensity levels reflecting immunomodulatory stimulation:

$$\begin{aligned} \omega_Z = \omega_C = \kappa_Z = \kappa_C = 0, \\ \omega_Z = \omega_C = \kappa_Z = \kappa_C = 10, \\ \omega_Z = \omega_C = \kappa_Z = \kappa_C = 20, \\ \omega_Z = \omega_C = \kappa_Z = \kappa_C = 50. \end{aligned} \tag{95}$$

In particular, Plan 4 is further explored by fixing $\beta_Z = \beta_C = 0.001$ and varying the treatment parameters, as shown in **Figure 6**. This simulation framework facilitates a comparative analysis of the dynamic responses under different therapeutic approaches, enabling assessment of each strategy's capacity to reduce viral load and promote infection clearance.

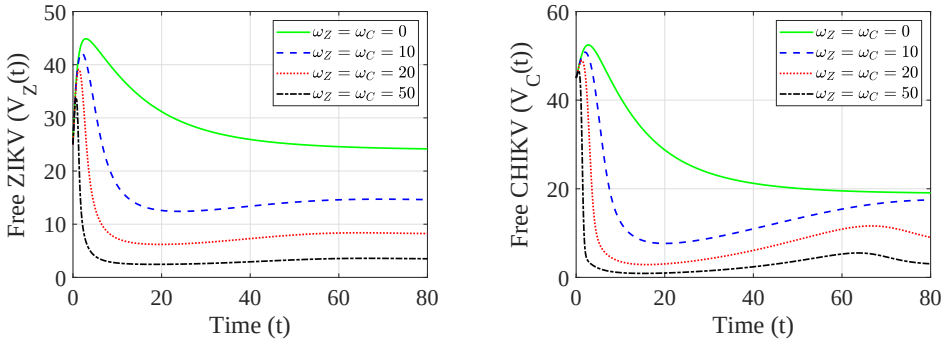


(a) Viral concentration in case of treatment strategy I.

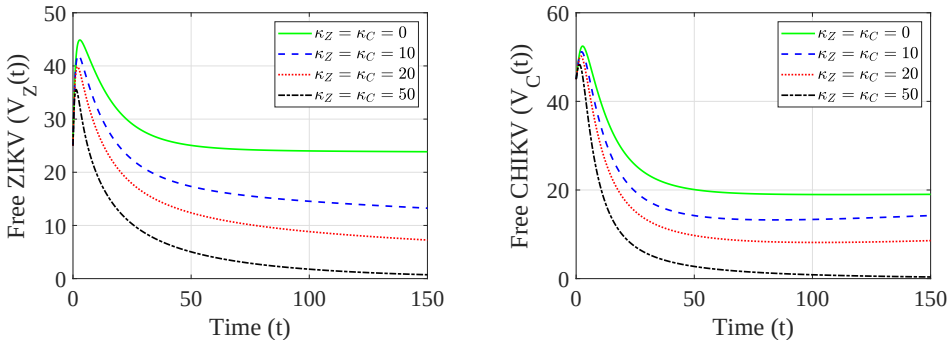


(b) Viral concentration in case of treatment strategy II.

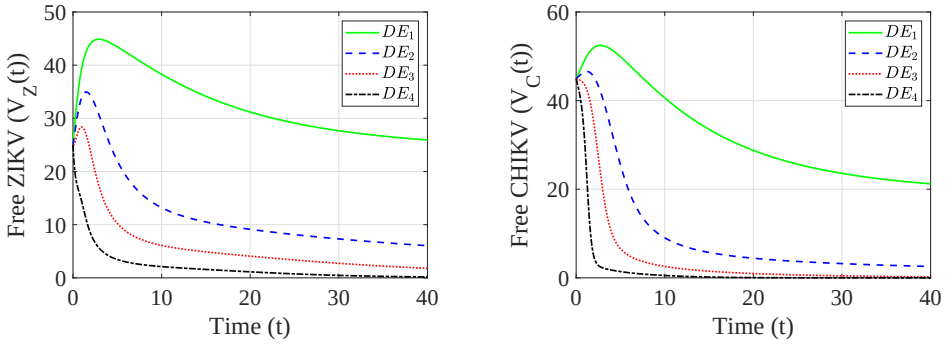
Figure 6. *Cont.*



(c) Viral concentration in case of treatment strategy III.



(d) Viral concentration in case of treatment strategy IV.



(e) Viral concentration in case of four integrated treatment strategies.

Figure 6. Effect of different treatment strategies on ZIKV and CHIKV viral concentrations during co-infection.

8.2.1. Model simulation under treatment strategy I

In this strategy, we examine the behavior of the Equations (57)–(65) under varying treatment efficacies by simulating the model using levels of efficacies u_Z and u_C in Equation (94) with initial Equation (93). **Figure 6a** shows that increasing u_Z and u_C, directly reduces the levels of free viruses (V_Z, V_C). This reduction in viral concentration subsequently leads to a decrease in latently and actively infected cells, as fewer target cells become infected. Moreover, the decline in infection burden allows for a marked increase in uninfected cells and antibody concentrations. These findings highlight the primary role of antiviral therapy in lowering viral presence, with downstream benefits for immune function and infection control, thereby supporting its effectiveness in co-infection management. It is shown in **Table 2** that, increasing the treatment parameters u_Z and u_C, will decrease the reproduction numbers R_Z^L and R_C^L. The values $R_Z^L = 1$ and $R_C^L = 1$ are reached when$u_Z \simeq 0.23505$ and $u_C \simeq 0.23549$.

Beyond this point, the infection cannot persist within the host. To examine the impact of antiviral efficacy on the system dynamics, we derived the Jacobian matrix J_u from Equations (57)–(65) and computed its eigenvalues, which determine the local stability of the equilibrium points. When there is no treatment ($u_Z = u_C = 0$), we obtain $R_Z^L(0) > 1$ and $R_C^L(0) > 1$, and only the ZIKV-CHIKV co-infection steady state $\widetilde{SS}$ will be locally stable, indicating the coexistence of ZIKV and CHIKV. At the values $u_Z = u_C = 0.1$, $\widetilde{SS}$ remains stable while other steady states are unstable. This suggests that mild antiviral is insufficient to shift the system toward eradication. At $u_Z = u_C = 0.2$, a critical transition emerges: one of the partially a CHIKV-only infection steady state $\overline{SS}$ becomes locally stable, while the full $\widetilde{SS}$ disappears. This indicates a qualitative shift in the infection dynamics, where treatment is sufficient to eliminate one virus but not both. At the critical thresholds $u_Z = 0.23505$ and $u_C = 0.23549$, where both R_Z^L and R_C^L approach 1, leading to local stability of SS^0, while all other steady states disappear. Beyond this threshold (e.g., $u_Z = u_C = 0.3$), both reproduction numbers drop below 1, confirming that sufficient suppression of viral entry effectively clears both ZIKV and CHIKV infections, as summarized in **Table 2**.

Table 2. The effect of treatment efficacies u_Z, u_C, v_Z and v_C on the associated reproduction numbers R_Z^L and R_C^L, as well as the resulting stability of steady states in case of strategies I and II.

Treatment and reproduction numbers				**Stability of steady states**			
$\boldsymbol{u_Z, v_Z}$	$\boldsymbol{R_Z^L}$	$\boldsymbol{u_C, v_C}$	$\boldsymbol{R_C^L}$	$\boldsymbol{SS^0}$	$\boldsymbol{SS^*}$	$\boldsymbol{\overline{SS}}$	$\boldsymbol{\widetilde{SS}}$
0.0	1.30727	0.0	1.30802	U	U	U	S
0.1	1.17654	0.1	1.17722	U	U	U	S
0.2	1.04582	0.2	1.04642	U	U	S	–
0.23505	1	0.23549	1	S	–	–	–
0.3	0.9151	0.3	0.9156	S	–	–	–

Note: S = stable, U = unstable; "—" indicates equilibrium does not exist.

8.2.2. Model simulation under treatment strategy II

In this strategy, we examine the dynamics of Equations (66)–(74) under varying treatment efficacies by simulating the model using levels of control v_Z and v_C in Equation (94) with initial conditions of Equation (93). As previously noted, this adjustment acts on the parameter k_Z and k_C, which governs viral release from infected cells. Although this differs from treatment strategy I, which targets the transmission parameter β_Z and β_C, both modifications result in the same expression for the basic reproduction numbers. Consequently, the values of R_Z^L and R_C^L obtained here are identical to those in strategy I, including the critical threshold where a shift to the disease-free steady state occurs, as detailed in **Table 2**. However, a notable difference arises in the behavior of the viral concentrations V_Z and V_C. Since this treatment directly inhibits viral output from infected cells rather than blocking new infections, it produces a faster and more consistent reduction in viral concentrations across increasing treatment levels as illustrated in **Figure 6b**.

8.2.3. Model simulation under treatment strategy III

In this strategy, we examine the behavior of Equations (75)–(83) under varying treatment intensities by simulating the model using levels of immune stimulation ω_Z and ω_C in Equation (95) with initial conditions of Equation (93). Based on the visual results in **Figure 6c**, this treatment strategy leads to a noticeable decline in the concentrations of both ZIKV and CHIKV as the treatment intensity ω_Z and ω_C increases. However, despite this reduction, the viral loads stabilize at positive levels even at the highest stimulation level ($\omega_Z = \omega_C = 50$), indicating that the immune-enhancing response alone is insufficient to fully clear the infection. This outcome can be attributed to the fact that the basic reproduction numbers R_Z^L and R_C^L remain above one, indicating that the immune-enhancing effect alone cannot eliminate the infection. Although these strategies reduce viral load and slow disease progression, they are not sufficient to eliminate the virus. Therefore, combining them with other interventions, such as antiviral therapies, may improve effectiveness in controlling co-infections.

8.2.4. Model simulation under treatment strategy IV

In this part, we examine the impact of treatment aimed at enhancing the antibody production rate on the co-dynamics of ZIKV and CHIKV. This is done through numerical simulations of Equations (84)–(92) using the initial conditions in Equation (93) and varying the parameters κ_Z and κ_C as specified in Equation (95). **Figure 6d** shows that as κ_Z and κ_C, both ZIKV and CHIKV concentrations are declined. This treatment approach effectively suppresses viral replication, emphasizing the role of enhancing antibody production. The local stability of the steady states was examined by evaluating the eigenvalues of the corresponding Jacobian matrix for different treatment levels (κ_Z, κ_C). When $\kappa_Z = \kappa_C = 0$, both reproduction numbers $R_Z^L(0)$ and $R_C^L(0)$ exceed unity. Under these conditions, $SS^0, SS^*$and $\overline{SS}$ are unstable, while the coexistence steady state $\widetilde{SS}$ remains stable, indicating that both viruses persist within the host. As the treatment intensities increase, the same stability pattern is initially preserved: SS^0 and SS^* remain unstable, whereas the coexistence state $\widetilde{SS}$ is stable, and one of the single-infection steady states disappears. This indicates that moderate levels of immunomodulation are not sufficient to shift the system away from endemic persistence. A transition occurs near $\kappa_Z = 39.134$ and $\kappa_C = 30.9906$, where both R_Z^L and R_C^L decrease to 1. At this threshold, SS^0 becomes locally stable, while the other steady states no longer exist, showing that viral replication has fallen below the level required for persistence. For larger treatment values (for example, $\kappa_Z = 50$ and $\kappa_C = 50$), both reproduction numbers satisfy $R_Z^L < 1$ and $R_C^L < 1$ and only SS^0 remains locally stable. This confirms that sufficiently strong enhancement of baseline antibody production can eliminate both ZIKV and CHIKV infections, as also shown in **Table 3**. The main drawbacks of this strategy are that the minimum treatment $\kappa_Z^{\min}$ and $\kappa_C^{\min}$ may exceed the $\kappa_Z^{\max}$ and $\kappa_C^{\max}$. In this case such treatment strategy will not be able to make R_Z^L and R_C^L below one and hence clearance of viruses will not be achieved.

Table 3. Influence of the treatment effectiveness parameters κ_Z and κ_C on the reproduction numbers $R_Z^L(\kappa_Z)$ and $R_C^L(\kappa_C)$, together with the corresponding stability of the steady states under strategy IV.

Treatment and reproduction numbers				**Stability of steady states**			
$\boldsymbol{\kappa_Z}$	$\boldsymbol{R_Z^L}$	$\boldsymbol{\kappa_C}$	$\boldsymbol{R_C^L}$	$\boldsymbol{SS^0}$	$\boldsymbol{SS^*}$	$\boldsymbol{\overline{SS}}$	$\boldsymbol{\widetilde{SS}}$
0.0	1.30727	0.0	1.30802	U	U	U	S
10	1.18935	10	1.21258	U	U	S	–
20	1.09094	20	1.13012	U	U	S	–
30	1.00757	30	1.05816	U	U	S	–
39.134	1	30.9906	1	S	–	–	–
40	0.93604	40	0.99482	S	–	–	–

Note: S = stable, U = unstable; "—" indicates equilibrium does not exist.

8.2.5. Model simulations under combined treatment strategies I–IV

In this scenario, we investigate the system's dynamics when all four treatment strategies (I–IV) are applied simultaneously. Under this combined therapeutic intervention, the co-infection model is reformulated as follows:

$$\begin{aligned}
\frac{dX}{dt} &= \lambda - dX - (1-u_Z)\beta_Z X V_Z - (1-u_C)\beta_C X V_C,\\
\frac{dY_Z^L}{dt} &= (1-\theta_Z)(1-u_Z)\beta_Z X V_Z - (\eta_Z + b_Z)Y_Z^L,\\
\frac{dY_Z^A}{dt} &= \theta_Z(1-u_Z)\beta_Z X V_Z + \eta_Z Y_Z^L - a_Z Y_Z^A,\\
\frac{dY_C^L}{dt} &= (1-\theta_C)(1-u_C)\beta_C X V_C - (\eta_C + b_C)Y_C^L,\\
\frac{dY_C^A}{dt} &= \theta_C(1-u_C)\beta_C X V_C + \eta_C Y_C^L - a_C Y_C^A,\\
\frac{dV_Z}{dt} &= (1-\upsilon_Z)k_Z Y_Z^A - c_Z V_Z - r_Z V_Z W_Z,\\
\frac{dV_C}{dt} &= (1-\upsilon_C)k_C Y_C^A - c_C V_C - r_C V_C W_C,\\
\frac{dW_Z}{dt} &= (1+\kappa_Z)\gamma_Z + q_Z(1+\omega_Z)V_Z W_Z - \mu_Z W_Z,\\
\frac{dW_C}{dt} &= (1+\kappa_C)\gamma_C + q_C(1+\omega_C)V_C W_C - \mu_C W_C,
\end{aligned}$$

where u_Z, u_C, υ_Z, υ_C, ω_Z, ω_C, κ_Z and κ_C represent treatment efficacy, regulating the magnitude of each therapeutic effect. The system is simulated under the combined application of treatment strategies I–IV, using varying drug efficacies as follows:

$$\begin{aligned}
&DE_1 : u_Z = u_C = \upsilon_Z = \upsilon_C = \omega_Z = \omega_C = \kappa_Z = \kappa_C = 0,\\
&DE_2 : u_Z = u_C = \upsilon_Z = \upsilon_C = 0.1,\ \omega_Z = \omega_C = \kappa_Z = \kappa_C = 10,\\
&DE_3 : u_Z = u_C = \upsilon_Z = \upsilon_C = 0.2,\ \omega_Z = \omega_C = \kappa_Z = \kappa_C = 20,\\
&DE_4 : u_Z = u_C = \upsilon_Z = \upsilon_C = 0.5;\ \omega_Z = \omega_C = \kappa_Z = \kappa_C = 50.
\end{aligned}$$

We solve the system using the initial conditions of Equation (93). As illustrated in **Figure 6e**, the combined application of treatment strategies I–IV results in a rapid and sustained reduction of viral concentrations V_Z and V_C, achieving complete clearance

in a shorter time than any single strategy alone. This outcome highlights the synergistic potential of combining antiviral and immune-enhancing interventions, providing both direct suppression of viral replication and reinforcement of host immunity.

9. Discussion and conclusion

This study has developed and carefully examined a within-host mathematical model describing the dynamics of ZIKV-CHIKV co-infection. In the analytical study, we first demonstrate the well-posedness of the proposed model. We then characterize all possible steady states of the system and derive four threshold quantities: the basic reproduction number for ZIKV infection, R_Z^L, and that for CHIKV infection, R_C^L, the invasion reproduction numbers for ZIKV infection $R_Z^{L,inv}$ and that for CHIKV infection, $R_C^{L,inv}$. The model has been extended to include the effects of four therapeutic strategies: (i) antiviral therapy that prevents viral infection of target cells, (ii) antiviral therapy that suppresses viral production, (iii) immune-stimulating treatment, and (iv) therapy that increases the rate of antibody circulation. We have studied the global threshold behavior of the co-infection model through proposing suitable Lyapunov functions:

We obtain the following results:

- The disease-free steady state SS^0 is guaranteed to exist, and it is globally asymptotically stable provided that $R_Z^L \leq 1$ and $R_C^L \leq 1$. This means that even if a small number of infected cells or viruses are introduced, the infection will eventually die out and the system will return to the healthy state. Our analysis further demonstrates that these inequalities can be realized through the implementation of appropriate therapeutic strategies. Specifically:

  1. Antiviral treatment for blocking viral infection: This mechanism reduces the probability of uninfected cells being infected by viruses. Mathematically, this is represented by modifying the infection rate constants β_Z and β_C to by $(1-u_Z)\beta_Z$ and $(1-u_C)\beta_C$, respectively.

  2. Antiviral treatment for blocking viral production: In this case, the number of viral particles produced by infected cells is reduced. This effect is incorporated in the model by replacing the viral production rates k_Z and k_C with $(1-\upsilon_Z)k_Z$ and $(1-\upsilon_C)k_C$.

  3. Treatment for enhancing the antibody flow rate: Strengthening the natural immune defense is represented by an increased rate of antibody production. In the model, this is achieved by modifying the antibody generation parameters from γ_Z and γ_C by $(1+\kappa_Z)\gamma_Z$ and $(1+\kappa_C)\gamma_C$.

  Through these interventions, the basic reproduction numbers for both ZIKV and CHIKV can be effectively reduced below unity, ensuring that the disease-free steady state remains stable.
- The ZIKV-only infection steady state SS^* exists when $R_Z^L > 1$ and it is globally asymptotically stable when $R_Z^L > 1$ and $R_C^{L,inv} \leq 1$. Biologically, this stability scenario reflects the dominance of ZIKV infection in the host, where the viral replication of ZIKV continues, but CHIKV cannot establish long-term infection.

The inequality $R_Z^L > 1$ typically holds in the absence of therapeutic interventions against ZIKV, since in that case the viral infection proceeds unchecked and successfully invades the target cell population. On the other hand, enforcing the condition $R_C^{L,inv} \leq 1$ can be achieved through the implementation of treatment strategies directed against CHIKV. These therapies act to lower its reproduction potential by incorporating treatment efficacies u_C, υ_C, κ_C.

By sufficiently applying one or more of these interventions, the effective invasion reproduction number of CHIKV can be suppressed below 1, ensuring that ZIKV persists while CHIKV is cleared from the system.

- The CHIKV-only infection steady state $\overline{SS}$ exists when $R_C^L > 1$ and it is globally asymptotically stable when $R_C^L > 1$ and $R_Z^{L,inv} \leq 1$. This case corresponds to a scenario in which CHIKV persists within the host, whereas ZIKV is completely cleared. The condition $R_C^L > 1$ may arise in the absence of effective treatment against CHIKV. In contrast, ensuring that $R_Z^{L,inv} \leq 1$ requires reducing the reproduction number associated with ZIKV. This can be achieved by implementing treatments targeting ZIKV, such as u_Z, υ_Z and κ_Z.
- The ZIKV-CHIKV co-infection steady state $\widetilde{SS}$ exists and it is globally asymptotically stable when $R_Z^{L,inv} > 1$ and $R_C^{L,inv} > 1$. This case may occur when no treatment is applied to either virus and the immune system fails to clear both infections, leading to long-term coexistence of ZIKV and CHIKV.

We performed some numerical simulations to investigate the within-host co-dynamics of ZIKV and CHIKV. We examined the stability of the four steady states by varying the infection rate parameters β_Z and β_C. Analyzing these variations provides deeper insight into the interactions between the two viruses within the host. We show that the numerical and theoretical results are consistent. To illustrate the global stability of the steady states, we solved the system using different initial conditions and showed that, for all such cases, the solutions converge to a steady state. Finally, we performed simulations under four treatment strategies. The results indicate that antiviral approaches are more effective than immune-enhancing strategies in clearing the viral co-infections. Moreover, combining both offers synergy by suppressing replication and enhancing host defenses.

Despite the theoretical insights obtained, one of the main limitations of this work lies in parameter uncertainty. Reliable parameter estimation requires clinical or experimental datasets, which are currently scarce for individuals co-infected with CHIKV and ZIKV. Although information may exist for single-virus infections, obtaining detailed measurements for dual infection cases remains challenging. Therefore, the parameter values used in this study are primarily intended for theoretical exploration. Future work will focus on refining parameter estimation using clinical observations when such data become available to improve model reliability and predictive performance.

The treatment mechanisms incorporated in this study are formulated within a simplified theoretical framework. In particular, dose-dependent pharmacological effects and potential treatment-related side effects are not considered. The

objective of this formulation is to facilitate analytical tractability and to obtain qualitative insights into the co-infection dynamics rather than to provide clinical treatment recommendations. These simplifying assumptions are adopted to focus on the mathematical properties of the model and its threshold behavior. The incorporation of more realistic pharmacological structures, including toxicity effects and pharmacokinetic–pharmacodynamic interactions, is an important direction for future research.

Author contributions: Conceptualization, AE, ZA and AH; methodology, AE; formal analysis, AE and ZA; investigation, AE; resources, AE; writing—original draft preparation, ZA; writing—review and editing, AE and AH. All authors have read and agreed to the published version of the manuscript.

Funding: This Project was funded by the Deanship of Scientific Research (DSR) at King Abdulaziz University, Jeddah, Saudi Arabia under grant No. (IPP-839-130-2025).

Institutional review board statement: Not applicable.

Informed consent statement: Not applicable.

Data availability statement: No data associated in the manuscript.

Acknowledgment: This Project was funded by the Deanship of Scientific Research (DSR) at King Abdulaziz University, Jeddah, Saudi Arabia under grant No. (IPP-839-130-2025). The authors, therefore, acknowledge with thanks DSR for technical and financial support.

Conflict of interest: The authors declare that they have no conflict of interest.

AI use statement: The authors declare that no artificial intelligence (AI) tools were used in the preparation of this manuscript.

References

1. Wei YL, Wu Z, Li RL, et al. Review of selected mosquito-borne diseases: arboviruses (dengue, chikungunya, Zika, West Nile, Japanese encephalitis, yellow fever) and parasitic diseases (malaria, lymphatic filariasis). Frontiers in Public Health. 2026; 13: 1712094. doi: 10.3389/fpubh.2025.1712094
2. Romero-Leiton JP, Acharya KR, Parmley JE, et al. Modelling the transmission of dengue, zika and chikungunya: A scoping review protocol. BMJ Open. 2023; 13(9): e074385. doi: 10.1136/bmjopen-2023-074385
3. Puntasecca CJ, King CH, LaBeaud AD. Measuring the global burden of chikungunya and Zika viruses: A systematic review. PLOS Neglected Tropical Diseases. 2021; 15(3). doi: 10.1371/journal.pntd.0009055
4. Rabe IB, Hills SL, Haussig JM, et al. A review of the recent epidemiology of zika virus infection. The American Journal of Tropical Medicine and Hygiene. 2025; 112(5): 1026–1035. doi: 10.4269/ajtmh.24-0420
5. Bessey K, Mavis M, Rebaza J, et al. Global stability analysis of a general model of Zika virus. Nonautonomous Dynamical Systems. 2019; 6(1): 18–34. doi: 10.1515/msds-2019-0002
6. Saleh FM, Bassfar Z, Mohammedsaleh ZM. Arbovirus-host epigenetic interplay: Unraveling the neurological mechanisms and therapeutic opportunities. Reviews in Medical Virology. 2026; 36(1): e70086. doi: 10.1002/rmv.70086
7. Jose SA, Raja R, Omede BI, et al. Mathematical modeling on co-infection: transmission dynamics of Zika virus and Dengue fever. Nonlinear Dynamics. 2023; 111(5): 4879–4914. doi: 10.1007/s11071-022-08063-5
8. Lobkowicz L, Ramond A, Clemente NS, et al. The frequency and clinical presentation of Zika virus coinfections: A systematic review. BMJ Global Health. 2020; 5(5): e002350. doi: 10.1136/bmjgh-2020-002350

9. Musa SS, Hussaini N, Zhao S, et al. Dynamical analysis of chikungunya and dengue co-infection model. Discrete and Continuous Dynamical Systems Series B. 2020; 25(5): 1907–1933. doi: 10.3934/dcdsb.2020009
10. Dai Y, Li Z, Zhang X, et al. Chikungunya: global epidemiology, clinical spectrum, and vector control-lessons for China from the 2025 Guangdong outbreak. Archives of Toxicology. 2026; 100: 1225–1239. doi: 10.1007/s00204-025-04273-z
11. Shoushtari M, Bakhshi H, Salehi-Vaziri M, et al. Distribution of Aedes aegypti and Aedes albopictus, and the current situation of dengue fever and chikungunya in Iran and neighboring countries: A review study. PLOS Neglected Tropical Diseases. 2026; 20(2): e0013965. doi: 10.1371/journal.pntd.0013965
12. Morrison T, Zarrella K, Sheridan R, et al. Chikungunya virus persists in joint associated macrophages and promotes chronic disease. Research Square preprint. 2025. doi: 10.21203/rs.3.rs-6917990/v1
13. Rodriguez-Morales AJ, Villamil-Gomez WE, Franco-Paredes C. The arboviral burden of disease caused by co-circulation and co-infection of dengue, chikungunya and Zika in the Americas. Travel Medicine and Infectious Disease. 2016; 14(3): 177–179. doi: 10.1016/j.tmaid.2016.05.004
14. Pierson TC, Diamond MS. The emergence of Zika virus and its new clinical syndromes. Nature. 2018; 560(7720): 573–581. doi: 10.1038/s41586-018-0446-y
15. Cherabuddi K, Iovine NM, Shah K, et al. Zika and Chikungunya virus co-infection in a traveller returning from Colombia, 2016: Virus isolation and genetic analysis. Journal of Medical Microbiology Case Reports. 2016; 3(6): e005072. doi: 10.1099/jmmcr.0.005072
16. Ahmed S, Sultana S, Kundu S, et al. Global prevalence of zika and chikungunya coinfection: A systematic review and meta-analysis. Diseases. 2024; 12(2): 31. doi: 10.3390/diseases12020031
17. Wichit S, Gumpangseth N, Hamel R, et al. Chikungunya and zika viruses: Co-circulation and the interplay between viral proteins and host factors. Pathogens. 2021; 10(4): 448. doi: 10.3390/pathogens10040448
18. Aurelio B, Kaisar MMM, Wijaya V, et al. A systematic review and meta-analysis of global DENV, CHIKV, and ZIKV co-infection. Reviews in Medical Virology. 2026; 36(2): e70108. doi: 10.1002/rmv.70108
19. Santana LMB, Moura IA, Tanaka YMR, et al. Zika virus: A review of biology, clinical impacts, and coinfections. Viruses. 2025; 17(5): 637. doi: 10.3390/v17050637
20. Guo Q, He Z. Prediction of the confirmed cases and deaths of global COVID-19 using artificial intelligence. Environmental Science and Pollution Research. 2021; 28(9): 11672–11682. doi: 10.1007/s11356-020-11930-6
21. Guo Q, Wang Z, He Z, et al. Changes in air quality from the COVID to the post-COVID era in the Beijing-Tianjin-Tangshan region in China. Aerosol and Air Quality Research. 2021; 21(12). doi: 10.4209/aaqr.210270
22. He J, Zhang GB. Propagation dynamics of a nonlocal dispersal Zika transmission model with general incidence. Mathematical Methods in the Applied Sciences. 2025; 48(3): 2886–2912. doi: 10.1002/mma.10466
23. Jia Q, Xue L, Yang J, et al. Effect of preventive measures and heterogeneity of sexual contacts on Zika virus transmission. Bulletin of Mathematical Biology. 2026; 88(4): 56. doi: 10.1007/s11538-026-01622-6
24. Zhao L, Liu Y. Propagation dynamics of a Zika virus model with diffusion and constant recruitment. Nonlinear Analysis: Real World Applications. 2026; 91: 104562. doi: 10.1016/j.nonrwa.2025.104562
25. Ding Q, Zhou S, Chen S, et al. Dynamics of a Zika epidemic model with saturated incidence in spatially heterogeneous environments. Advances in Continuous and Discrete Models. 2026; 2026: 32. doi: 10.1186/s13662-026-04077-0
26. Romero-Leiton JP, Laison EK, Alfaro R, et al. Exploring Zika's dynamics: A scoping review journey from epidemic to equations through mathematical modelling. Infectious Disease Modelling. 2025; 10(2): 536–558. doi: 10.1016/j.idm.2024.12.016
27. Jan R, Razak NNA, Boulaaras S, et al. Fractional perspective evaluation of chikungunya infection with saturated incidence functions. Alexandria Engineering Journal. 2023; 83: 35–42. doi: 10.1016/j.aej.2023.10.036
28. Chavada A, Pathak N, Khirsariya SR. Fractional-order modeling of Chikungunya virus transmission dynamics. Mathematical Methods in the Applied Sciences. 2025; 48(1): 1056–1080. doi: 10.1002/mma.10372
29. Cao Z, Shi Z, Song Z, et al. Modeling chikungunya virus infection with Black–Karasinski process: stationary distribution, probability density function, and extinction. Advances in Continuous and Discrete Models. 2025; 2025(1): 11. doi: 10.1186/s13662-025-03874-3
30. Karthik A, Ghosh M. A mathematical approach to Chikungunya transmission dynamics incorporating media awareness and optimal control. Scientific Reports. 2026. doi: 10.1038/s41598-026-40681-6
31. Wang Y, Ma H, Yan Q, et al. Modeling and control of Chikungunya with chronic infection. Infectious Disease Modelling. 2026; 11(2): 619–642. doi: 10.1016/j.idm.2025.12.002
32. Osuna CE, Lim SY, Deleage C, et al. Zika viral dynamics and shedding in rhesus and cynomolgus macaques. Nature

Medicine. 2016; 22(12): 1448. doi: 10.1038/nm.4206
33. Best K, Guedj J, Madelain V, et al. Zika plasma viral dynamics in nonhuman primates provides insights into early infection and antiviral strategies. Proceedings of the National Academy of Sciences. 2017; 114(33): 8847–8852. doi: 10.1073/pnas.1704011114
34. Best K, Perelson AS. Mathematical modeling of within-host Zika virus dynamics. Immunological Reviews. 2018; 285(1): 81–96. doi: 10.1111/imr.12687
35. Tuncer N, Martcheva M. Determining reliable parameter estimates for within-host and within-vector models of Zika virus. Journal of Biological Dynamics. 2021; 15(1): 430–454. doi: 10.1080/17513758.2021.1970261
36. Best K, Barouch DH, Guedj J, et al. Zika virus dynamics: Effects of inoculum dose, the innate immune response and viral interference. PLOS Computational Biology. 2021; 17(1): e1008564. doi: 10.1371/journal.pcbi.1008564
37. Tang B, Xiao Y, Sander B, et al. Modelling the impact of antibody-dependent enhancement on disease severity of Zika virus and dengue virus sequential and co-infection. Royal Society Open Science. 2020; 7(4): 191749. doi: 10.1098/rsos.191749
38. Wang Y, Liu X. Stability and Hopf bifurcation of a within-host chikungunya virus infection model with two delays. Mathematics and Computers in Simulation. 2017; 138: 31–48. doi: 10.1016/j.matcom.2016.12.011
39. Elaiw AM, Alade TO, Alsulami SM. Analysis of latent CHIKV dynamics models with general incidence rate and time delays. Journal of Biological Dynamics. 2018; 12(1): 700–730. doi: 10.1080/17513758.2018.1503349
40. Alade TO, Elaiw AM, Alsulami SM. Stability dynamics of a delayed generalized Chikungunya virus infection model. Journal of Applied Mathematics and Computing. 2021; 65: 575–595. doi: 10.1007/s12190-020-01405-9
41. Elaiw AM, Almalki SE, Hobiny AD. Stability of CHIKV infection models with CHIKV-monocyte and infected-monocyte saturated incidences. AIP Advances. 2019; 9(2): 025308. doi: 10.1063/1.5085804
42. Besbassi H, Hattaf K, Yousfi N. Stability and Hopf bifurcation of a generalized chikungunya virus infection model with two modes of transmission and delays. Discrete Dynamics in Nature and Society. 2020; 2020: 5908976. doi: 10.1155/2020/5908976
43. El Hajji M. Modelling and optimal control for Chikungunya disease. Theory in Biosciences. 2021; 140(1): 27–44. doi: 10.1007/s12064-020-00324-4
44. El Hajji M, Zaghdani A, Sayari S. Mathematical analysis and optimal control for chikungunya virus with two routes of infection with nonlinear incidence rate. International Journal of Biomathematics. 2022; 15(1): 2150088. doi: 10.1142/S1793524521500881
45. Alsahafi S, Woodcock S. Mathematical study for Chikungunya virus with nonlinear general incidence rate. Mathematics. 2021; 9(18): 2186. doi: 10.3390/math9182186
46. Gokila C, Sambath M. The threshold for a stochastic within-host CHIKV virus model with saturated incidence rate. International Journal of Biomathematics. 2021; 14(6): 2150042. doi: 10.1142/S179352452150042X
47. Yu F, Ullah M, Ullah S, et al. A multi-layer computational neural network approach for solving stochastic within-host chikungunya model with an adaptive immune response. International Journal of Biomathematics. 2025. doi: 10.1142/S1793524525500470
48. Bonyah E, Khan MA, Okosun KO, et al. On the co-infection of dengue fever and Zika virus. Optimal Control Applications and Methods. 2019; 40(3): 394–421. doi: 10.1002/oca.2483
49. Deolia P, Singh A, Mubayi A. Mathematical modeling of sequential Dengue–Zika infections: dynamic insights into antibody-dependent enhancement and neutralization effects. Scientific Reports. 2026. doi: 10.1038/s41598-026-44242-9
50. Iheonu NO, Nwajeri UK, Omame A. A non-integer order model for Zika and Dengue co-dynamics with cross-enhancement. Healthcare Analytics. 2023; 4: 100276. doi: 10.1016/j.health.2023.100276
51. Isea R, Karl E. A preliminary mathematical model for the dynamic transmission of dengue, chikungunya and zika. American Journal of Modern Physics and Applications. 2016; 3: 11–15. doi: 10.48550/arXiv.1606.08233
52. Omame A, Isah ME, Abbas M. An optimal control model for COVID-19, zika, dengue, and chikungunya co-dynamics with reinfection. Optimal Control Applications and Methods. 2023; 44(1): 170–204. doi: 10.1002/oca.2936
53. Omame A, Abbas M. The stability analysis of a co-circulation model for COVID-19, dengue, and zika with nonlinear incidence rates and vaccination strategies. Healthcare Analytics. 2023; 3: 100151. doi: 10.1016/j.health.2023.100151
54. Smith HL, Waltman P. The Theory of the Chemostat: Dynamics of Microbial Competition. Cambridge University Press; 1995.
55. Van den Driessche P, Watmough J. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Mathematical Biosciences. 2002; 180(1–2): 29–48. doi:

10.1016/S0025-5564(02)00108-6
56. Hussaini N, Lubuma JM, Barley K, et al. Mathematical analysis of a model for AVL-HIV co-endemicity. Mathematical Biosciences. 2016; 271: 80–95. doi: 10.1016/j.mbs.2015.10.008
57. Mitchell C, Kribs C. Invasion reproductive numbers for periodic epidemic models. Infectious Disease Modelling. 2019; 4: 124–141. doi: 10.1016/j.idm.2019.04.002
58. Ding R, Zhang L, Li HL, et al. Global dynamics on a class of HIV and Mycobacterium tuberculosis co-infection model within body. International Journal of Biomathematics. 2025: 2550016. doi: 10.1142/S1793524525500160
59. Dubey P, Dubey US, Dubey B. Modeling the dynamics of viral-host interaction during treatment of productively infected cells and free virus involving total immune response. Nonlinear Analysis: Modelling and Control. 2021; 26(4): 678–701. doi: 10.15388/namc.2021.26.21434
60. Korobeinikov A. Global properties of basic virus dynamics models. Bulletin of Mathematical Biology. 2004; 66: 879–883. doi: 10.1016/j.bulm.2004.02.001
61. Hale JK, Verduyn Lunel SM. Introduction to Functional Differential Equations. Springer; 1993. doi: 10.1007/978-1-4612-4342-7
62. Khalil HK. Nonlinear Systems, 3rd ed. Prentice Hall; 2002.
63. Tuncer N, Martcheva M. Determining reliable parameter estimates for within-host and within-vector models of Zika virus. Journal of Biological Dynamics. 2021; 15(1): 430–454. doi: 10.1080/17513758.2021.1970261
64. Saindane RA, Pathania A. Targeting key stages of the viral entry and life cycle: A comprehensive overview of the mechanisms of antiviral actions. Methods in Molecular Biology. 2025; 2927: 259–286. doi: 10.1007/978-1-0716-4546-8_15
65. Kong M, Rai SN, Bolli R. Statistical methods for selecting maximum effective dose and evaluating treatment effect when dose–response is monotonic. Statistics in Biopharmaceutical Research. 2014; 6(1): 16–29. doi: 10.1080/19466315.2013.826596