Eur. Phys. J. Plus (2017) **132**: 363
DOI 10.1140/epjp/i2017-11625-3

THE EUROPEAN PHYSICAL JOURNAL PLUS

Regular Article

On the dynamics of HIV-AIDS and cryptosporidiosis

K.O. Okosun[1], M.A. Khan[2,a], E. Bonyah[1,3], and S.T. Ogunlade[4]

[1] Department of Mathematics, Vaal University of Technology, Vanderbijlpark, South Africa
[2] Department of Mathematics, City University of Science and Information Technology, Khyber Pakhtunkhwa, 2500, Pakistan
[3] Department of Mathematics and Statistics, Kumasi Technical University, Kumasi, Ghana
[4] Department of Mathematical Sciences, Federal University of Technology, Akure, Nigeria

Received: 10 June 2017 / Revised: 27 June 2017
Published online: 25 August 2017 –

Abstract. This paper seeks to examine a mathematical model for cryptosporidiosis-HIV co-infection, in order to explore their synergistic relationship in the presence of prevention and treatment. Firstly, we investigate the sub-models and their steady states properties. They are found to be locally and globally stable. Thereafter, the steady states of the co-infected model were studied and they proved to exhibit backward bifurcation phenomena. Furthermore, we incorporate time-dependent controls in the model and apply Pontryagin's maximum principle, so that we can determine the best optimal strategy to control the co-infected diseases. Finally, we present the numerical results, which show that the best strategy to control co-infection is to combine all the five controls at the same time.

1 Introduction

In Sub-Saharan Africa, diseases such as trypanosomiasis, schistosomiasis, malaria, etc., already have profound effect on the immune system and also alter the host's immune response to infections in HIV/AIDS patients. This in effect paves the way for opportunistic parasitic infections such as cryptosporidiosis, isosporiasis, microsporidiosis, etc. to attack [1, 2]. Cryptosporidium species are recognized globally as important causes of diarrhea in children and adults with major impact on chronic and life-threatening illness in immunocompromised patients, most notably those with HIV/AIDS [3, 4] especially in sub-Saharan Africa, Europe and Asia. Also, studies carried out in communities and hospitals in sub-Saharan Africa for instance have documented data on high prevalence of cryptosporidiosis in children between age 6 to 36 months. In particular, this is very obvious among malnourished or HIV positive humans [4]. A study carried out by [5] revealed that persons with compromised immune systems can suffer from life-threatening chronic cryptosporidiosis, especially when their $CD4^+$ lymphocyte counts fall $< 200\,\text{cells}/\mu\text{L}$.

In Venezuela, among HIV-infected patients, a study was done to determine the prevalence of cryptosporidiosis among the patients [6]. One of the major agents that was found to be associated with diarrhea in HIV/AIDS patients is Cryptosporidium and data evidences abound in the North-western part of Nigeria on the occurrence of this parasite among HIV patients [7]. The authors also found out that the rate is significantly higher among HIV-infected patients with diarrhea than among HIV negative with diarrhea. While in Cameroon, the authors in [8] conducted a study to determine the prevalence of intestinal parasites in HIV/AIDS patients in the Dschang-Cameroon region. In poor hygienic environment, HIV positive individuals are found to be more susceptible to co-infections with Cryptosporidium than HIV-negative humans, according to the findings in [9, 10].

Nevertheless, HIV infection has become a major health concern in the rural areas of central China and globally, which is mainly due to blood collected or supplied illegally. The co-infection of HIV and gastro-intestinal parasites (Cryptosporidium) form one of the major neglected areas all over the world [11]. Further studies have revealed that the co-infection of HIV disease and Cryptosporidium parasites often leads to deterioration of the two diseases in patients. The fact remains that the presence of parasite infection can lead to the destruction of the anti-HIV immune

[a] e-mail: altafdir@gmail.com (corresponding author)

response balance, which then eventually results to HIV viral replication and consequently accelerates the progression of patients from HIV to full blown AIDS [12, 13]. Also, in China, opportunistic parasites, such as *Cryptosporidium parvum*, *Cyclo sporacayetanesis*, *Isospora belli*, and *Microsporidium sp*, have their presence documented in patients with AIDS [14] living in villages with poor sanitation. As a result, the authors in [11, 15] carried out epidemiological studies to examine the characteristics of co-infection of HIV and intestinal parasites in a HIV/AIDS highly endemic area in China.

Therefore, the prevalence and magnitude of cryptosporidiosis parasitic infection in patients with HIV/AIDS, requires careful consideration in the developing world where poor nutrition is combined with poor hygiene and other several tropical diseases. However, to the best of our knowledge, there have been no mathematical modelling studies carried out to address this issue.

This parasitic disease called *Cryptosporidium*, is a pathogen which causes cryptosporidiosis in mammals intestines. This disease was first reported by Clarke and Tyzzer [16]. From 1976 to 1982 seven major outbreaks were recorded. In the developed economy, one of the most common waterborne diseases is cryptosporidiosis, particularly in the United States. It is mostly referred to as crypto which in Greek means hidden. The application of alcohol gels and hand sanitizers does not destroy the pathogen. In most swimming pools chlorine is applied to kill germs and this does not kill crypto. The occurrence is usually attributed to recreational and drinking purpose of water use. It is greatly transmittable if left untreated [17–19]. It can be transmitted via contact with an infected person and one can also be re-infected [20, 21]. The frequent way of transmitting the disease is normally by swallowing the organisms from food and water, or body contact with an infected individual.

The disease spread thrives more during the summer and fall and children below the age of ten years are generally affected. Another interesting thing about cryptosporidiosis is that it weakens the immune system, thereby facilitating the spread of the disease [22]. This accounts for the fact that people who have HIV/AIDS become victims of circumstances. People begin to feel the disease in their body system from 2 to 10 days after effectively getting in contact with an infected body. A study on 58 patients conducted in 1984 showed that 40 (69%) were immunocompromised and this is common with HIV/AIDS patients [17, 23, 24]. Symptoms commonly associated with the disease include dehydration, nausea, vomiting, fever and weight loss, diarrhea, stomach cramps. It is difficult and time consuming to diagnose the pathogens since they are very tiny even under the microscope and several stool tests must be carried out to confirm the pathogen.

In studies worldwide, Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS) are projected to spread at the rate of 7000 per day [25]. This is alarming and very dangerous to human existence, particularly in sub-Saharan Africa where standard health care policies are a major challenge. In the last 3 decades HIV has killed more than 30 million people [26]. One serious concern about the disease is that it affects mostly the youth who constitute the working population. The social and economic burden of HIV/AIDS cannot be quantified in many of the affected communities. Therefore, serious attention should be focussed on preventing co-infection with other pathogens in order to avoid further weakening of HIV/AIDS patients immune systems. Hence, mathematical models provide a quantitative and potentially valuable tool for this purpose.

In recent times, mathematical modelling has gained recognition as a tool for exploring the dynamics of diseases and helping in the formulation of appropriate interventions and control strategies [27]. For example, the impact of HIV prevention on the epidemic in recent years has been investigated by several researchers [28–30]. The potential effects of educational campaigns on HIV/AIDS transmission dynamics have also been extensively investigated in [31–33]. There have been other several mathematical modelling studies on HIV-AIDS and other related diseases carried out to explore the probable burden of the epidemic on the society [27, 31, 32, 34–39]. There is, however, scanty information about mathematical models on cryptosporidiosis. To the best of our knowledge there is no co-infection model on cryptosporidiosis and HIV-AIDS and, therefore, this study is to present a better insight into the co-dynamics of these diseases.

This paper presents an SIR (susceptible, infected, recovered) HIV/AIDS-cryptosporidiosis co-infection model. The paper is arranged as follows: In sect. 2, the model formulation and principles underlying assumptions are presented. The analysis of the cryptosporidiosis model only is presented in sect. 3. In sect. 4, HIV/AIDS model only is analyzed. The analysis of the co-infection model is presented in sect. 5. Section 6 is devoted to the optimal control analysis of the co-infection model. In sect. 7, the numerical results and discussions are presented. The conclusion is presented in sect. 8.

2 Mathematical model

The model sub-divides the total human population, denoted by N, into sub-populations of susceptible individuals (S), individuals with cryptosporidiosis only (I), recovered individuals from cryptosporidiosis only (R), individuals with HIV only (H), individuals with AIDS only (A), individuals with HIV-AIDS and cryptosporidiosis co-infection (C_{HI}).

So that $N = S + I + R + H + A + C_{HI}$.

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{d}t}S = \Lambda + \sigma R - \mu S - \beta_c^* S - \beta_H^* S, \\ \frac{\mathrm{d}}{\mathrm{d}t}I = \beta_c^* S - (\alpha + \mu + \psi)I - \beta_H^* I, \\ \frac{\mathrm{d}}{\mathrm{d}t}R = \alpha I - (\mu + \sigma)R - \beta_H^* R, \\ \frac{\mathrm{d}}{\mathrm{d}t}E_n = \theta I + \delta C_{HI} - \nu E_n, \\ \frac{\mathrm{d}}{\mathrm{d}t}H = \beta_H^*(S + R) - (\alpha_a + \mu + \psi_2)H - \beta_c^* H + (1 - r)\gamma C_{HI}, \\ \frac{\mathrm{d}}{\mathrm{d}t}A = \alpha_a H - (\mu + \psi_2)A - \beta_c^* A + r\gamma C_{HI}, \\ \frac{\mathrm{d}}{\mathrm{d}t}C_{HI} = \beta_c^*(H + A) + \beta_H^* I - (\mu + \gamma)C_{HI}, \end{cases} \tag{1}$$

where

$$\beta_c^* = \frac{\lambda\epsilon I}{S + I + R + H + A + C_{HI}} + \rho E_n,$$
$$\beta_H^* = \frac{\lambda_1\epsilon_1(H + A + gC_{HI})}{S + I + R + H + A + C_{HI}}.$$

Also, we have the environmental contamination denoted by E_n, the contact rate is denoted by ϵ while λ is the transmission probability. The parameter ψ, is cryptosporidiosis related death, and θ is the average contribution of each cryptosporidiosis infected individual to the environment. The rate at which crypto leaves the environment is represented by ν, and ψ_2 is for HIV/AIDS related death. The rate at which HIV infected humans move into AIDS is denoted by α_a, and the immunity waning rate is σ, while α is the recovery rate. Also, human recruitment rate is denoted by Λ, while μ is the human mortality rate and ρ is the modification parameter due to environmental treatment.

3 Model analysis

3.1 Positivity and boundedness of solutions

This section focuses on the basic properties of the solutions of the model, which are integral part of establishing the stability of the model.

Lemma 1. *The equations preserve positivity of solutions.*

Proof. In taking human population only into consideration, the vector field in the right hand of system (2) points to the direction of the boundary of $R_+^6 \backslash \{0\}$. For instance, if $A = 0$, then $A^1 = \alpha_a H + r\gamma C_{HI} \geq 0$. In a similar way the same result can be obtained for other parts (variables). For the purpose of illustration we shall dwell on human population to prove the boundedness of the solutions for the system 2. □

Lemma 2. *Each nonnegative solution of model system* 2 *is bounded in* L^1*-norm.*

Proof. By taking human population only into consideration, and let also $L^1 \in L$ of each nonnegative solution in N is expressed as $\max\{N(0), \Lambda/\mu\}$. Therefore, the norm L^1 is appropriate for the inequality $N^1 \leq \Lambda - N\mu$. Solutions based on the equation $P^1 \leq \Lambda - P\mu$ are deemed monotone increasing and bounded by Λ/μ if $P(0) \leq \Lambda/\mu$. They behave as decreasing monotone and bounded above if we have $P(0) \geq \Lambda/\mu$. By the fact that $N^1 \leq P^1$, the claims follow and in a similar manner, the rest of model variables can be established to be bounded. □

Corollary 1. *The region*

$$\Omega = \begin{cases} (S, I, R, H, A, C_{HI}) \\ \in R_+^6 : N \leq \dfrac{\Lambda}{\mu}, \\ E_n \in R_+ : E_n \leq \dfrac{\Lambda(\theta + \delta)}{\mu\nu}. \end{cases}$$

3.2 Cryptosporidiosis only model

In this section, we present the cryptosporidiosis only model.

$$\begin{cases} \dfrac{\mathrm{d}}{\mathrm{d}t}S = \Lambda + \sigma R - \mu S - \beta_c^* S, \\ \dfrac{\mathrm{d}}{\mathrm{d}t}I = \beta_c^* S - (\alpha + \mu + \psi)I, \\ \dfrac{\mathrm{d}}{\mathrm{d}t}R = \alpha I - (\mu + \sigma)R, \\ \dfrac{\mathrm{d}}{\mathrm{d}t}E_n = \theta I - \nu E_n, \end{cases} \tag{2}$$

where

$$\beta_c^* = \frac{\lambda \epsilon I}{S + I + R} + \rho E_n.$$

3.3 Stability analysis of cryptosporidiosis DFE

The cryptosporidiosis only model (2) has a disease free equilibrium (DFE), $E_c = (S^0, 0, 0, 0) = (\frac{\Lambda}{\mu}, 0, 0, 0)$. The linear stability of model (2) at E_c can be established using the next generation operator method in Driessche and Watmough [40]. It follows that the basic reproduction number of the cryptosporidiosis only model (2) denoted by $\mathcal{R}_{0c}$, can be computed as follows:

$$F = \begin{pmatrix} \lambda\epsilon & \dfrac{\rho\Lambda}{\mu} \\ 0 & 0 \end{pmatrix}, \qquad V = \begin{pmatrix} \alpha + \mu + \psi & 0 \\ -\theta & \rho \end{pmatrix}.$$

Thus, the basic reproduction number $\mathcal{R}_{0c}$ of the cryptosporidiosis only model (2) is

$$\mathcal{R}_{0c} = \frac{\theta\Lambda\rho + \lambda\mu\nu\epsilon}{\mu\nu(\alpha + \mu + \psi)}.$$

The Jacobian matrix of the cryptosporidiosis only model (2) is stable locally asymptotically if $\mathcal{R}_{0c} < 1$ and it is unstable if $\mathcal{R}_{0c} > 1$. Hence, we present the following result:

$$J_{0c} = \begin{pmatrix} -\mu & -\epsilon\lambda & \sigma & -\dfrac{\Lambda\rho}{\mu} \\ 0 & -\alpha + \epsilon\lambda - \mu - \psi & 0 & \dfrac{\Lambda\rho}{\mu} \\ 0 & \alpha & -\mu - \sigma & 0 \\ 0 & \theta & 0 & -\nu \end{pmatrix}.$$

One of the roots of the Jacobian matrix J_{0c} is $-\mu < 0$, for the remaining roots, we give the following characteristics equation:

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0,$$

where

$$\begin{aligned} a_1 &= (\alpha + \mu + \psi) + (\mu + \sigma) + \nu - \lambda\epsilon, \\ a_2 &= (\mu + \sigma)(\alpha + \mu + \nu + \psi - \lambda\epsilon) + \nu(\alpha + \mu + \psi)(1 - \mathcal{R}_{0c}), \\ a_3 &= \nu(\mu + \sigma)(\alpha + \mu + \psi)(1 - \mathcal{R}_{0c}). \end{aligned}$$

It can be easily verified that the coefficients in $a_i > 0$, for $i = 1, 2, 3$ when $\mathcal{R}_{0c} < 1$ and the condition of Routh-Hurtwiz criteria, $a_i > 0$ for $i = 1, 2, 3$ and $a_1 a_2 > a_3$. Thus, it follows from Routh-Hurtwiz criteria that the cryptosporidiosis only model (2) is stable locally asymptotically if $\mathcal{R}_{0c} < 1$.

3.4 Existence of endemic equilibrium of cryptosporidiosis

The endemic equilibrium of the cryptosporidiosis only model (2), denoted by $E_c^* = (S^*, I^*, R^*, E_n^*)$ is given by

$$\begin{cases} S^* = \dfrac{N^*\nu(\alpha+\mu+\psi)}{N^*\theta\rho + \lambda\nu\epsilon}, \\ R^* = \dfrac{\alpha I^*}{\mu+\sigma}, \\ E_n^* = \dfrac{\theta I^*}{\nu}. \end{cases}$$

3.5 The possible existence of backward bifurcation in cryptosporidiosis only model

The phenomenon of backward bifurcation can be proved by using the centre manifold theory on the cryptosporidiosis only model (2). Adopting the centre manifold theorem [41], we carry out bifurcation analysis. In order to apply the centre manifold theory, we made the following rearrangement and modification of variables in (2). First, we let $x_1 = S$, $x_2 = I$, $x_3 = R$ and $x_4 = E_n$ and $\beta_c^* = \lambda\epsilon x_2/(x_1 + x_2 + x_3) + \rho x_4$. In addition, by using the vector notation $X = (x_1, x_2, x_3, x_4)^T$, the cryptosporidiosis only model (2) can be formulated as $(\mathrm{d}X/\mathrm{d}t) = (f_1, f_2, f_3, f_4)^T$, given in the following and we choose λ as the bifurcation parameter and solve $\mathcal{R}_{0c} = 1$ which leads to

$$\begin{cases} \dfrac{\mathrm{d}x_1}{\mathrm{d}t} = \Lambda + \sigma x_3 - \mu x_1 - \beta_c^* x_1, \\ \dfrac{\mathrm{d}x_2}{\mathrm{d}t} = \beta_c^* x_1 - (\alpha+\mu+\psi)x_2, \\ \dfrac{\mathrm{d}x_3}{\mathrm{d}t} = \alpha x_2 - (\mu+\sigma)x_3, \\ \dfrac{\mathrm{d}x_4}{\mathrm{d}t} = \theta x_2 - \nu x_4, \end{cases} \tag{3}$$

where

$$\lambda = \lambda^* = \frac{\mu\nu(\alpha+\mu+\psi) - \theta\Lambda\rho}{\mu\nu\epsilon}.$$

The Jacobian matrix evaluated at disease-free equilibrium E_c with λ is

$$F = \begin{pmatrix} -\mu & -\dfrac{\mu\nu(\alpha+\mu+\psi) - \theta\Lambda\rho}{\mu\nu} & \sigma & -\dfrac{\Lambda\rho}{\mu} \\ 0 & -\alpha-\mu-\psi+\dfrac{\mu\nu(\alpha+\mu+\psi) - \theta\Lambda\rho}{\mu\nu} & 0 & \dfrac{\Lambda\rho}{\mu} \\ 0 & \alpha & -\mu-\sigma & 0 \\ 0 & \theta & 0 & -\nu \end{pmatrix}.$$

It can be simply observed that the Jacobian F of the linearized system possesses a simple zero eigenvalue and the rest of the eigenvalues have negative real parts. Therefore, the center manifold theory is appropriate to be used to analyze the dynamics of the system (3). For the case when $\mathcal{R}_{0c} = 1$, it can be shown that the Jacobian matrix F has a right eigenvector (corresponding to the zero eigenvalue), expressed as $W = (w_1, w_2, w_3, w_4)^T$ as

$$w_1 = -\frac{\alpha\mu + w_2(\mu+\sigma)(\mu+\psi)}{\mu(\mu+\sigma)}, \qquad w_2 = w_2 > 0,$$
$$w_3 = \frac{\alpha w_2}{\mu+\sigma}, \qquad w_4 = \frac{\theta w_2}{\nu}.$$

Similarly, the left eigenvector F can be computed (corresponding to the zero eigenvalue), represented as $v = (v_1, v_2, v_3, v_4)$ given by

$$v_1 = 0, \qquad v_2 = v_2 > 0,$$
$$v_3 = 0, \qquad v_4 = \frac{\Lambda\rho v_2}{\mu\nu}.$$

The computation of a is therefore based on the transformed system (3), the corresponding non-zero partial derivatives of f (evaluated at the DFE) which we require in the determination of a are given by

$$\frac{\partial^2 f_2}{\partial x_2 \partial x_2} = -\frac{2\Lambda\lambda\epsilon}{\mu},$$
$$\frac{\partial^2 f_2}{\partial x_2 \partial x_3} = -\frac{2\Lambda\lambda\epsilon\Lambda}{\mu},$$
$$\frac{\partial^2 f_2}{\partial x_1 \partial x_4} = \rho,$$
$$\frac{\partial^2 f_2}{\partial x_2 \partial \epsilon} = \frac{\lambda\Lambda}{\mu},$$
$$\frac{\partial^2 f_2}{\partial x_3 \partial \epsilon} = \frac{\lambda\Lambda}{\mu}.$$

The straight calculation of a is

$$a = -\frac{2\Lambda\lambda\epsilon v_2 w_2 \left(-\frac{\mu\rho w_2}{\Lambda\lambda\epsilon\Lambda} + w_2 + w_3\right)}{\mu}.$$

The straight calculation of b is

$$b = \frac{\lambda\Lambda v_2 (w_2 + w_3)}{\mu}.$$

The fact that coefficient b is positive shows that the sign of the coefficient a determines the local dynamics around the disease-free equilibrium for λ.

3.6 Global stability of cryptosporidiosis

In this section, we investigate the global stability of the cryptosporidiosis only model (2) at E^*_{0c}. Before proving the result, the cryptosporidiosis only model (2) has a steady state, which is

$$\begin{cases} \Lambda = -\sigma R^* + \mu S^* + \beta_c^* S^*, \\ \beta_c^* S^* = (\alpha + \mu + \psi) I^*, \\ \alpha I^* = (\mu + \sigma) R^*, \\ \theta I^* = \nu E_n^*. \end{cases}$$

Now, we state and prove the following theorem

Theorem 1. *If $\mathcal{R}_{0c} > 1$, then the endemic equilibrium of the cryptosporidiosis only model (2) at E^*_{0c} is globally asymptotically stable.*

Proof. Let us define the Lyapunov function

$$L(t) = S - S^* - S^* \log \frac{S}{S^*} + I - I^* - I^* \log \frac{I}{I^*} + \frac{\beta_c^* S^*}{\alpha I^*}\left(R - R^* - R^* \log \frac{R}{R^*}\right) + \frac{\beta_c^* S^*}{\theta I^*}\left(E_n - E_n^* - E_n^* \log \frac{E_n}{E_n^*}\right). \quad (4)$$

The time derivative of $L(t)$ is

$$L'(t) = \left(1 - \frac{S^*}{S}\right) S' + \left(1 - \frac{I^*}{I}\right) I' + \frac{\beta_c^* S^*}{\alpha I^*}\left(1 - \frac{R^*}{R}\right) R' + \frac{\beta_c^* S^*}{\theta I^*}\left(1 - \frac{E_n^*}{E_n}\right) E_n'. \quad (5)$$

Now

$$\left(1-\frac{S^*}{S}\right)S' = \left(1-\frac{S^*}{S}\right)[\Lambda+\sigma R-\mu S-\beta_c^* S]$$
$$= \left(1-\frac{S^*}{S}\right)[-\sigma R^*+\mu S^*+\beta_c^* S^*+\sigma R-\mu S-\beta_c^* S]$$
$$\leq -\sigma R^*\left(1-\frac{S^*}{S}\right)\left(1-\frac{R}{R^*}\right)+\beta_c^* S^*\left(2-\frac{S^*}{S}-\frac{S}{S^*}\right), \tag{6}$$

$$\left(1-\frac{I^*}{I}\right)I' = \left(1-\frac{I^*}{I}\right)[\beta_c^* S-(\alpha+\mu+\psi)I]$$
$$= \left(1-\frac{I^*}{I}\right)\left[\beta_c^* S-\frac{\beta_c^* S^*}{I^*}I\right]$$
$$= \beta_c^* S^*\left(1-\frac{I}{I^*}+\frac{S}{S^*}-\frac{SI^*}{IS^*}\right), \tag{7}$$

$$\frac{\beta_c^* S^*}{\alpha I^*}\left(1-\frac{R^*}{R}\right)R' = \frac{\beta_c^* S^*}{\alpha I^*}\left(1-\frac{R^*}{R}\right)[\alpha I-(\mu+\sigma)R]$$
$$= \frac{\beta_c^* S^*}{I^*}\left(1-\frac{R^*}{R}\right)\left[I-\frac{I^*}{R^*}R\right]$$
$$= \beta_c^* S^*\left(1-\frac{R}{R^*}+\frac{I}{I^*}-\frac{R^* I}{RI^*}\right) \tag{8}$$

and

$$\frac{\beta_c^* S^*}{\theta I^*}\left(1-\frac{E_n^*}{E_n}\right)E_n' = \frac{\beta_c^* S^*}{\theta I^*}\left(1-\frac{E_n^*}{E_n}\right)[\theta I-\nu E_n]$$
$$= \frac{\beta_c^* S^*}{\theta I^*}\left(1-\frac{E_n^*}{E_n}\right)[\theta I-\nu E_n]$$
$$= \beta_c^* S^*\left(1-\frac{E_n^*}{E_n}+\frac{I}{I^*}-\frac{IE_n^*}{E_n I^*}\right). \tag{9}$$

The results from (6)–(9) by substituting in (5), and simplifying, are

$$L'(t) = -\sigma R^*\left(1-\frac{S^*}{S}\right)\left(1-\frac{R}{R^*}\right)+\beta_c^* S^*\left(4-\frac{S^*}{S}-\frac{R}{R^*}-\frac{SI^*}{S^* I}-\frac{E_n}{E_n^*}-\frac{IE_n^*}{E_n I^*}-\frac{I}{I^*}\left(\frac{R}{R^*}-1\right)\right)\leq 0.$$

4 HIV/AIDS model

In this section, we present the HIV/AIDS only model:

$$\begin{cases}\dfrac{\mathrm{d}}{\mathrm{d}t}S = \Lambda-\mu S-\beta_H^* S,\\ \dfrac{\mathrm{d}}{\mathrm{d}t}H = \beta_H^* S-(\alpha_a+\mu+\psi_2)H,\\ \dfrac{\mathrm{d}}{\mathrm{d}t}A = \alpha_a H-(\mu+\psi_2)A,\end{cases} \tag{10}$$

where

$$\beta_H^* = \frac{\lambda_1\epsilon_1(H+A)}{S+H+A}.$$

4.1 Stability of the HIV/AIDS DFE

The HIV/AIDS only model (10) has a disease free equilibrium, given by

$$E_H = (S^0, 0, 0) = \left(\frac{\Lambda}{\mu}, 0, 0\right).$$

The linear stability of model (10) at E_H is established using the next generation operator method in Driessche and Watmough [40]. It follows that the basic reproduction number of the HIV/AIDS only model (10) denoted by R_{0H}, can be computed as follows:

$$F = \begin{pmatrix} \lambda_1\epsilon_1 & \lambda_1\epsilon_1 \\ 0 & 0 \end{pmatrix},$$

$$V = \begin{pmatrix} (\alpha_a + \mu + \psi_2) & 0 \\ -\alpha_a & (\mu + \psi_2) \end{pmatrix}.$$

Thus, the basic reproduction number $\mathcal{R}_{0H}$ of the HIV/AIDS only model (10) is

$$\mathcal{R}_{0H} = \frac{\lambda_1\epsilon_1}{(\mu + \psi_2)}.$$

The Jacobian matrix of the HIV/AIDS only model (10) is stable locally asymptotically if $\mathcal{R}_{0H} < 1$ and it is unstable when $\mathcal{R}_{0H} > 1$.

$$J_{0H} = \begin{pmatrix} -\mu & -\epsilon_1\lambda_1 & -\epsilon_1\lambda_1 \\ 0 & -(\mu + \alpha_a + \psi_2) + \epsilon_1\lambda_1 & \epsilon_1\lambda_1 \\ 0 & \alpha_a & -\mu - \psi_2 \end{pmatrix}.$$

The characteristics equation associated to J_{0H} is

$$(\lambda + \mu)[\lambda^2 + b_1\lambda + b_2] = 0,$$

where

$$b_1 = (\alpha_a + \mu + \psi_2) + (\mu + \psi_2)(1 - \mathcal{R}_{0H}),$$
$$b_2 = ((\mu + \psi_2)(\alpha_a + \mu + \psi_2))(1 - \mathcal{R}_{0H}).$$

One of the roots in the characteristics equation is clearly negative ($-\mu < 0$) and the other two roots can be obtained from the quadratic terms. It is obvious that the quadratic equation will give two eigenvalues with a negative real part if $\mathcal{R}_{0H} < 1$. Thus, the HIV/AIDS only model (10) at E_{H0} is stable locally asymptotically if $\mathcal{R}_{0H} < 1$.

4.2 Existence of endemic equilibrium of HIV/AIDS model

The endemic equilibrium of the HIV/AIDS only model (10) at E_{H0}, denoted by $E_H^* = (S^*, H^*, A^*)$ is given by

$$\begin{cases} S^* = \dfrac{(\alpha_a + \mu + \psi_2)H^*}{\beta_H^*}, \\ H^* = \dfrac{(\mu + \psi_2)A^*}{\alpha_a}. \end{cases}$$

4.3 Possible existence of backward bifurcation in HIV/AIDS only model

The phenomenon of backward bifurcation can be proved using the centre manifold theory on HIV/AIDS only model (10). Adopting the centre manifold theorem [41], we carry out bifurcation analysis. In order to apply the centre manifold theory, the following rearrangement and modification of variables are necessary to be made to the HIV/AIDS only model (10). First, we let $x_1 = S$, $x_2 = H$ and $x_3 = A$ and $\beta_H^* = \lambda_1\epsilon_1(x_2 + x_3)/(x_1 + x_2 + x_3)$.

In addition, by using the vector notation $X = (x_1, x_2, x_3)^T$ the HIV/AIDS only model (10) can be formulated as $(\mathrm{d}X/\mathrm{d}t) = (f_1, f_2, f_3)^T$ given in the following and we choose λ as the bifurcation parameter and solve $\mathcal{R}_{0H} = 1$ which leads to

$$\begin{cases} \dfrac{\mathrm{d}x_1}{\mathrm{d}t} = \Lambda - \mu x_1 - \beta_H^* x_1 : f_1, \\ \dfrac{\mathrm{d}x_2}{\mathrm{d}t} = \beta_H^* x_1 - (\alpha_a + \mu + \psi_2) x_2 : f_2, \\ \dfrac{\mathrm{d}x_3}{\mathrm{d}t} = \alpha_a x_2 - (\mu + \psi_2) x_3 : f_3, \end{cases} \tag{11}$$

where

$$\lambda_1 = \lambda_1^* = \frac{\mu + \psi_2}{\epsilon_1}.$$

The Jacobian matrix evaluated at disease-free equilibrium E_{0H} with λ_1 is

$$F = \begin{pmatrix} -\mu & -\mu - \psi_2 & -\mu - \psi_2 \\ 0 & -\alpha_a & \mu + \psi_2 \\ 0 & \alpha_a & -\mu - \psi_2 \end{pmatrix}.$$

It can be simply observed that the Jacobian F of the linearized system possesses a simple zero eigenvalue and the rest of the eigenvalues have negative real parts. Therefore, the centre manifold theory is appropriate to analyze the dynamics of the system (11). For the case when $R_{0H} = 1$, it can be shown that the Jacobian matrix F has a right eigenvector (corresponding to the zero eigenvalue) expressed as $W = (w_1, w_2, w_3)^T$ as

$$w_1 = -\frac{w_2(\alpha_a + \mu + \psi_2)}{\mu}, \qquad w_2 = w_2 > 0, \qquad w_3 = \frac{w_2 \alpha_a}{\mu + \psi_2}.$$

Similiarly, the left eigenvector F can be computed (corresponding to the zero eigenvalue), represented as $V = [v_1, v_2, v_3]$ given by

$$v_1 = 0, \qquad v_3 = v_2 > 0.$$

The computation of a is therefore based on the transformed system (11), the corresponding non-zero partial derivatives of f (evaluated at the DFE) which we require in the determination of a are given by

$$\frac{\partial^2 f_2}{\partial x_2 \partial x_2} = -\frac{2\lambda_1 \Lambda \epsilon_1}{\mu}, \qquad \frac{\partial^2 f_2}{\partial x_3 \partial x_3} = -\frac{2\lambda_1 \Lambda \epsilon_1}{\mu}, \qquad \frac{\partial^2 f_2}{\partial x_2 \partial x_3} = -\frac{2\lambda_1 \Lambda \epsilon_1}{\mu},$$

$$\frac{\partial^2 f_2}{\partial x_2 \partial \epsilon_1} = \frac{\lambda_1 \Lambda}{\mu}, \qquad \frac{\partial^2 f_2}{\partial x_3 \partial \epsilon_1} = \frac{\lambda_1 \Lambda}{\mu}.$$

The straight calculation of value a indicates that

$$a = -\frac{v_2(w_2 w_2 + w_3 w_2 + w_3 w_3)(2\lambda_1 \Lambda \epsilon_1)}{\mu}.$$

The computation of b is calculated as follows:

$$b = \frac{v_2(w_2 + w_3)(\lambda_1 \Lambda)}{\mu}.$$

The coefficient b is clearly positive, the sign of a is strictly negative. There exists a unique endemic equilibrium.

4.4 Global stability of HIV/AIDS model only

In this section, we investigate the global stability of HIV/AIDS only model (10) at E_{H0}^*. Having the following steady states:

$$\begin{cases} \Lambda = \mu S^* + \beta_H^* S^*, \\ \beta_H^* S^* = (\alpha_a + \mu + \psi_2) H^*, \\ \alpha_a H^* = (\mu + \psi_2) A^*, \\ \beta_H^* S^* = \dfrac{(\alpha_a + \mu + \psi_2)(\mu + \psi_2) A^*}{\alpha_a}, \end{cases}$$

we obtain the following results.

Theorem 2. *The HIV/AIDS only model* (10) *at* E^*_{H0} *is globally asymptotically stable if* $\mathcal{R}_{0H} > 1$.

Proof. We define the Lyapunov function given by

$$L(t) = S - S^* - S^* \log \frac{S}{S^*} + H - H^* - H^* \log \frac{H}{H^*} + A - A^* - A^* \log \frac{A}{A^*}. \tag{12}$$

The time derivative of $L(t)$ is

$$L'(t) = \left(1 - \frac{S^*}{S}\right) S' + \left(1 - \frac{H^*}{H}\right) H' + \left(1 - \frac{A^*}{A}\right) A'. \tag{13}$$

Here,

$$\begin{aligned}
\left(1 - \frac{S^*}{S}\right) S' &= \left(1 - \frac{S^*}{S}\right) [\Lambda - \mu S - \beta^*_H S] \\
&= \left(1 - \frac{S^*}{S}\right) [\mu S^* + \beta^*_H S^* - \mu S - \beta^*_H S] \\
&= \mu \left(1 - \frac{S^*}{S}\right) (S^* - S) + \beta^*_H S^* \left(1 - \frac{S^*}{S}\right) \left(1 - \frac{S}{S^*}\right) \\
&\leq \beta^*_H S^* \left(2 - \frac{S^*}{S} - \frac{S}{S^*}\right), \qquad (14) \\
\left(1 - \frac{H^*}{H}\right) H' &= \left(1 - \frac{H^*}{H}\right) [\beta^*_H S - (\alpha_a + \mu + \psi_2) H] \\
&= \left(1 - \frac{H^*}{H}\right) \left[\beta^*_H S - \frac{\beta^*_H S^*}{H^*} H\right] \\
&= \beta^*_H S^* \left(1 - \frac{H}{H^*} + \frac{S}{S^*} - \frac{S H^*}{H S^*}\right) \qquad (15)
\end{aligned}$$

and

$$\begin{aligned}
\frac{\beta^*_H S^*}{\alpha_a H^*} \left(1 - \frac{A^*}{A}\right) A' &= \frac{\beta^*_H S^*}{\alpha_a H^*} \left(1 - \frac{A^*}{A}\right) [\alpha_a H - (\mu + \psi_2) A] \\
&= \frac{\beta^*_H S^*}{\alpha_a H^*} \left(1 - \frac{A^*}{A}\right) \left[H - \frac{(\mu + \psi_2)}{\alpha_a} A\right] \\
&= \frac{\beta^*_H S^*}{H^*} \left(1 - \frac{A^*}{A}\right) \left[H - \frac{H^*}{A^*} A\right] \\
&= \beta^*_H S^* \left(1 - \frac{A}{A^*} + \frac{H}{H^*} - \frac{A^* H}{A H^*}\right). \qquad (16)
\end{aligned}$$

Using eqs. (14)–(16) in eq. (13), and simplifying, we obtain

$$L'(t) = \beta^*_H S^* \left(4 - \frac{A}{A^*} - \frac{S^*}{S} - \frac{S H^*}{S^* H} - \frac{A^* H}{A H^*}\right) \leq 0.$$

5 HIV-AIDS cryptosporidiosis co-infection model

The HIV-AIDS cryptosporidiosis co-infection model (1) has a DFE obtained by setting the right-hand sides of the equations in the model to zero. We have

$$E_{0HC}\left(S^0, 0, 0, 0, 0, 0\right) = \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0\right).$$

The linear stability of E_{0HC} can be established using the next generation operator method presented in Driessche and Watmough [40] on the system (1). It follows that the reproduction number of the HIV/AIDS-cryptosporidiosis co-infection model (1), denoted by $\mathcal{R}_{0Hc}$, is given by

$$F = \begin{pmatrix} \epsilon\lambda & \frac{\Lambda\rho}{\mu} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \epsilon_1\lambda_1 & \epsilon_1\lambda_1 & g\epsilon_1\lambda_1 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$V = \begin{pmatrix} \alpha+\mu+\psi & 0 & \frac{\mu\epsilon_1\lambda_1}{\Lambda} & 0 & 0 \\ -\theta & \nu & 0 & 0 & -\delta \\ 0 & 0 & \mu+\alpha_a+\psi_2 & 0 & -(1-r)\gamma \\ 0 & 0 & -\alpha_a & \mu+\psi_2 & -r\gamma \\ 0 & 0 & 0 & 0 & \gamma+\mu \end{pmatrix}.$$

So

$$\mathcal{R}_0 = \max(\mathcal{R}_{0H}, \mathcal{R}_{0c}) = \max\left\{\frac{\lambda_1\epsilon_1}{\mu+\psi_2}, \frac{\theta\Lambda\rho+\lambda\mu\nu\epsilon}{\mu\nu(\alpha+\mu+\psi)}\right\},$$

$$J_{0Hc} = \begin{pmatrix} -\mu & -\epsilon\lambda & \sigma & -\frac{\Lambda\rho}{\mu} & -\epsilon_1\lambda_1 & -\epsilon_1\lambda_1 & -g\epsilon_1\lambda_1 \\ 0 & -\alpha+\epsilon\lambda-\mu-\psi & 0 & \frac{\Lambda\rho}{\mu} & 0 & 0 & 0 \\ 0 & \alpha & -\mu-\sigma & 0 & 0 & 0 & 0 \\ 0 & \theta & 0 & -\nu & 0 & 0 & \delta \\ 0 & 0 & 0 & 0 & -\mu-\alpha_a+\epsilon_1\lambda_1-\psi_2 & \epsilon_1\lambda_1 & (1-r)\gamma+g\epsilon_1\lambda_1 \\ 0 & 0 & 0 & 0 & \alpha_a & -\mu-\psi_2 & r\gamma \\ 0 & 0 & 0 & 0 & 0 & 0 & -\gamma-\mu \end{pmatrix}.$$

The two eigenvalues $-\mu$, $-(\gamma+\mu)$ and $-(\mu+\sigma)$ are clearly negative. The remaining four eigenvalues can be computed from the following equation:

$$\lambda^4 + c_1\lambda^3 + c_2\lambda^2 + c_3\lambda + c_4 = 0, \tag{17}$$

where

$$\begin{aligned} c_1 &= \alpha_a + (\alpha+\mu+\psi) + (\gamma+\mu) + \mu + \nu - \lambda\epsilon + \psi_2 + (\mu+\psi_2)(1-\mathcal{R}_{0H}), \\ c_2 &= (\mu(\alpha+\mu+\nu+\psi) + \psi_2(\alpha+\mu+\nu+\psi) - \lambda\epsilon)(1-\mathcal{R}_{0H}) + \nu(\alpha+\mu+\psi)(1-\mathcal{R}_{0c}), \\ c_3 &= \nu(\alpha+\mu+\psi)[(\alpha_a+\mu+\psi_2) + (1-\mathcal{R}_{0H})(\mu+\psi_2)](1-\mathcal{R}_{0c}) \\ &\quad + (\alpha_a+\mu+\psi_2)(\alpha+\mu+\nu+\psi-\lambda\epsilon)(\mu+\psi_2)(1-\mathcal{R}_{0H}), \\ c_4 &= (\mu+\psi_2)(\alpha+\mu+\psi)(\alpha_a+\mu+\psi_2)(1-\mathcal{R}_{0H})(1-\mathcal{R}_{0c}). \end{aligned}$$

The eigenvalues of the characteristics equation (17) will give four eigenvalues with negative real parts if this satisfies the Routh-Hurtwiz criteria [42], such that $c_i > 0$ for $i = 1, 2, 3, 4$, with $c_1c_2c_3 > c_3^2 + c_1^2c_4$. We can easily obtain that $c_i > 0$ for $i = 1, 2, 3, 4$, when $\mathcal{R}_{0c} < 1$, $\mathcal{R}_{0H} < 1$, and $\mathcal{R}_0 < 1$. It is clear that $\mathcal{R}_0$ is the maximum of $\mathcal{R}_{0c}$ and $\mathcal{R}_{0H}$, *i.e.*, $\mathcal{R}_{0c} < \mathcal{R}_0 < 1$ and $\mathcal{R}_{0H} < \mathcal{R}_0 < 1$. Thus, it follows from [42] that the HIV-AIDS cryptosporidiosis co-infection model (1) is stable locally asymptotically at E_{0HC}.

5.1 The possible existence of backward bifurcation in co-infection of HIV-AIDS and cryptosporidiosis

The phenomenon of backward bifurcation can be shown using the concept of the centre manifold theory on system (1). Using the centre manifold theorem we undertake bifurcation analysis. Initially, we take into consideration the transmission rate $\mathcal{R}_{0c} = 1$ and $\mathcal{R}_{0H} = 1$ if and only if

$$\lambda = \lambda^* = \frac{\mu\nu(\alpha+\mu+\psi) - \theta\Lambda\rho}{\mu\nu\epsilon}$$

and

$$\lambda_1 = \lambda_1^* = \frac{\mu + \psi_2}{\epsilon_1}\,.$$

The following necessary variations of the variables are made $S = x_1$, $I = x_2$, $R = x_3$, $E_n = x_4$, $H = x_5$, $A = x_6$ and $C_{HI} = x_7$ and $N = x_1 + x_2 + x_3 + x_5 + x_6 + x_7$. Furthermore, employing vector notation $\vec{x} = (x_1, x_2, x_3, x_4, x_5, x_6, x_7)$, the HIV-AIDS cryptosporidiosis co-infection model (1) can be reformulated in the form $\mathrm{d}x/\mathrm{d}t = F\vec{x}$, with $F = (f_1, f_2, f_3, f_4, f_5, f_6, f_7)^T$ as given below

$$\begin{cases} \dfrac{\mathrm{d}x_1}{\mathrm{d}t} = \Lambda + \sigma x_3 - \mu x_1 - \beta_c^* x_1 - \beta_H^* x_1, \\ \dfrac{\mathrm{d}x_2}{\mathrm{d}t} = \beta_c^* x_1 - (\alpha + \mu + \psi) x_2 - \beta_H^* x_2, \\ \dfrac{\mathrm{d}x_3}{\mathrm{d}t} = \alpha x_2 - (\mu + \sigma) x_3 - \beta_H^* x_3, \\ \dfrac{\mathrm{d}x_4}{\mathrm{d}t} = \theta x_2 + \delta x_7 - \nu x_4, \\ \dfrac{\mathrm{d}x_5}{\mathrm{d}t} = \beta_H^*(x_1 + x_3) - (\alpha_a + \mu + \psi_2) x_5 - \beta_c^* x_5 + (1 - r)\gamma x_7, \\ \dfrac{\mathrm{d}x_6}{\mathrm{d}t} = \alpha_a x_5 - (\mu + \psi_2) x_6 - \beta_c^* x_6 + r\gamma x_7, \\ \dfrac{\mathrm{d}x_7}{\mathrm{d}t} = \beta_c^*(x_5 + x_6) + \beta_H^* x_2 - (\mu + \gamma) x_7, \end{cases} \tag{18}$$

where

$$\beta_c^* = \frac{\lambda \epsilon x_2}{x_1 + x_2 + x_3 + x_5 + x_6 + x_7} + \rho x_4,$$
$$\beta_H^* = \frac{\lambda_1 \epsilon_1 (x_5 + x_6 + g x_7)}{x_1 + x_2 + x_3 + x_5 + x_6 + x_7}\,.$$

This technique has to do with the evaluation of the Jacobian of the system (18) at the E_{0HC}, represented by J_{Hc}. This turns to be

$$J_{Hc} = \begin{pmatrix} -\mu & -J_1 & \sigma & -\dfrac{\Lambda\rho}{\mu} & -(\mu+\psi_2) & -(\mu+\psi_2) & -g\,(\mu+\psi_2) \\ 0 & J_1 - (\alpha+\mu+\psi) & 0 & \dfrac{\Lambda\rho}{\mu} & 0 & 0 & 0 \\ 0 & \alpha & -(\mu+\sigma) & 0 & 0 & 0 & 0 \\ 0 & \theta & 0 & -\nu & 0 & 0 & \delta \\ 0 & 0 & 0 & 0 & -\alpha_a & \mu+\psi_2 & (1-r)\gamma + g\,(\mu+\psi_2) \\ 0 & 0 & 0 & 0 & \alpha_a & -(\mu+\psi_2) & r\gamma \\ 0 & 0 & 0 & 0 & 0 & 0 & -(\gamma+\mu) \end{pmatrix}$$

where

$$J_1 = \frac{\mu\nu(\alpha + \mu + \epsilon) - \theta\Lambda\rho}{\mu\nu}\,.$$

J_{Hc} has a simple zero eigenvalue, with other eigenvalues having negative real parts. Hence the centre manifold theorem can be applied. We initially begin by computing the right and the left eigenvector of J_{Hc}, denoted respectively by $\vec{w} = [w_1, w_2, w_3, w_4, w_5, w_6, w_7]^T$ and $\vec{v} = [v_1, v_2, v_3, v_4, v_5, v_6, v_7]$. The following result is then obtained:

$$w_1 = -\frac{w_6(\mu + \psi_2)(\alpha_a + \mu + \psi_2)}{\mu\alpha_a}\,, \qquad w_2 = w_3 = w_4 = w_7 = 0, \qquad w_6 = w_6 > 0,$$
$$w_5 = \frac{w_6(\mu + \psi_2)}{\alpha_a}$$

and

$$v_1 = v_2 = v_3 = v_4 = 0, \qquad v_6 = v_5, \qquad v_5 = v_5 > 0, \qquad v_7 = \frac{v_5(\gamma + g\mu + g\psi_2)}{\gamma + \mu}.$$

The straight calculation of value a indicates that

$$a = -\frac{v_5\mu\lambda_1\epsilon_1(w_1w_6 + 2w_5w_5 + 2w_5w_6 + 2w_6w_5 + 2w_6w_6)}{\Lambda}.$$

The computation of b is calculated as follows:

$$b = \frac{v_5(\gamma + \mu)\epsilon_1(w_5 + w_6)}{\gamma + g(\mu + \psi_2)}.$$

The coefficient b is clearly positive, it is the sign of a that will decide about the backward bifurcation of the model.

6 Optimal control analysis

This section seeks to explore the application of Pontryagin's maximum principle to determine the necessary conditions for the optimal control of the HIV-AIDS and cryptosporidiosis co-infection. We endeavour to incorporate time dependent controls into the proposed system (19), in order to determine the best optimal strategy which can be employed to control the diseases. Thus, we have

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}S &= \Lambda + \sigma R - \mu S - (1-u_1)\beta_c^* S - (1-u_2)\beta_H^* S,\\
\frac{\mathrm{d}}{\mathrm{d}t}I &= (1-u_1)\beta_c^* S - (u_3\alpha + \mu + \psi)I - (1-u_2)\beta_H^* I,\\
\frac{\mathrm{d}}{\mathrm{d}t}R &= u_3\alpha I - (\mu + \sigma)R - (1-u_2)\beta_H^* R,\\
\frac{\mathrm{d}}{\mathrm{d}t}E_n &= \theta I + \delta C_{HI} - \nu E_n,\\
\frac{\mathrm{d}}{\mathrm{d}t}H &= (1-u_2)\beta_H^*(S+R) - (u_4\alpha_\alpha + \mu + \psi_2)H - (1-u_1)\beta_c^* H + (1-u_5 r)C_{HI},\\
\frac{\mathrm{d}}{\mathrm{d}t}A &= u_4\alpha_\alpha H - (\mu + \psi_2)A - (1-u_1)\beta_c^* A - u_5 r\gamma C_{HI},\\
\frac{\mathrm{d}}{\mathrm{d}t}C_{HI} &= (1-u_1)\beta_c^*(H + A) + (1-u_2)\beta_H^* I - (\mu + u_5\gamma)C_{HI}.
\end{aligned} \tag{19}$$

In this regard, we consider the objective functional

$$J(u_1, u_2, u_3, u_4, u_5) = \int_0^{t_f} \left[a_1 I + a_2 H + a_3 A + a_4 C_{HI} + A u_1^2 + B u_2^2 + C u_3^2 + D u_4^2 + E u_5^2\right]. \tag{20}$$

Our control problem has to do with a situation in which the number of HIVinfections, co-infections, the cryptosporidiosis infected individuals and the cost associated with the application of preventions and treatments controls $u_1(t)$, $u_2(t)$, $u_3(t)$, $u_4(t)$ and $u_5(t)$ are minimized subject to the system (19). While t_f represents the final time and the coefficients, a_1, a_2, a_3, a_4, a_5A, B, C, D, E are the balancing cost factors due to scales and importance of the ten parts of the objective function. We endeavour to obtain an optimal control, u_1^*, u_2^*, u_3^*, u_4^* and u_5^* such that where $\mathcal{U} = \{(u_1, u_2, u_3, u_4, u_5),$ such that u_1, u_2, u_3, u_4, u_5 are measurable with $0 \le u_1 \le 1,\ 0 \le u_2 \le 1,\ 0 \le u_3 \le g_2,\ 0 \le u_4 \le g_3$ and $0 \le u_5 \le g_4,$ for $t \in [0, t_f]\}$ is the control set.

1) The control $u_1(t)$ and $u_2(t)$ denote the efforts targeted at prevention of Cryptosporidiosis and HIV infections respectively.
2) The treatment control associated with Cryptosporidiosis infected individuals $u_3(t)$ satisfies $0 \leqslant u_3 \leqslant g_2$, where g_2 is the drug efficacy used for treatment of Cryptosporidiosis infected individuals.
3) The treatment control targeting on HIV/AID infected individuals $u_4(t)$ satisfies $0 \leqslant u_4 \leqslant g_3$, where g_3 is the drug efficacy used for treatment of HIV/AID infected individuals.
4) The treatment control on Cryptosporidiosis and HIV/AID infected individuals $u_5(t)$ satisfies $0 \leqslant u_5 \leqslant g_4$, where g_4 is the drug efficacy used for treatment of Cryptosporidiosis and HIV/AID infected individuals.

The critical conditions that an optimal solution must satisfy emanate from the Pontryagin's *et al.* [43] maximum principle. This principle actually transforms (1), (2) into a kind of a problem of minimizing pointwise a Hamiltonian (H), with respect to u_1, u_2, u_3 and u_4. The adjoint variable with regard to the system is denoted by λ_i, the Hamiltonian is then expressed as

$$\begin{aligned} H = {} & a_1 I + a_2 H + a_3 A + a_4 C_{HI} + A u_1^2 + B u_2^2 + C u_3^2 + D u_4^2 + E u_5^2 \\ & + \lambda_S \{\Lambda + \sigma R - \mu S - (1-u_1)\beta_c^* S - (1-u_2)\beta_H^* S\} \\ & + \lambda_I \{(1-u_1)\beta_c^* S - (u_3\alpha + \mu + \psi) I - (1-u_2)\beta_H^* I\} \\ & + \lambda_R \{u_3 \alpha I - (\mu + \sigma) R - (1-u_2)\beta_H^* R\} \\ & + \lambda_{E_n} \{\theta I + \delta C_{HI} - \nu E_n\} \\ & + \lambda_H \{(1-u_2)\beta_H^*(S+R) - (u_4\alpha_\alpha + \mu + \psi_2) H - (1-u_1)\beta_c^* H + (1-u_5 r) C_{HI}\} \\ & + \lambda_A \{u_4 \alpha_\alpha H - (\mu + \psi_2) A - (1-u_1)\beta_c^* A - u_5 r \gamma C_{HI}\} \\ & + \lambda_{C_{HI}} \{(1-u_1)\beta_c^*(H+A) + (1-u_2)\beta_H^* I - (\mu + u_5\gamma) C_{HI}\}, \end{aligned} \tag{21}$$

where λ_S, λ_I, λ_R, λ_{E_n}, λ_H, λ_A and $\lambda_{C_{HI}}$ denote the adjoint variables or co-state variables. The system of equations is attained by taking the desirable partial derivatives of the Hamiltonian (21) with regard to the associated state variable.

Theorem 3. *Given optimal controls u_1^*, u_2^*, u_3^*, u_4^*, u_5^* and solutions, S, I, R, E_n, H, A and C_{HI} of the corresponding state system* (5)–(20) *that minimize $J(u_1, u_2, u_3, u_4, u_5)$ over U. Then there exists adjoint variables λ_S, λ_I, λ_R, λ_{E_n}, λ_H, λ_A and $\lambda_{C_{HI}}$ satisfying*

$$\frac{-\mathrm{d}\lambda_i}{\mathrm{d}t} = \frac{\partial H}{\partial i}, \tag{22}$$

where $i = S, I, R, E_n, H, A, C_{HI}$ and with transversality conditions

$$\lambda_S(t_f) = \lambda_I(t_f) = \lambda_R(t_f) = \lambda_{E_n}(t_f) = \lambda(t_f) = \lambda(t_f) = \lambda_{C_{HI}}(t_f) = 0 \tag{23}$$

and

$$u_1^* = \min\left\{1, \max\left(0, \frac{\beta_c^* S[\lambda_I - \lambda_S] + \beta_c^* H[\lambda_{C_{HI}} - \lambda_H] + \beta_c^* A[\lambda_{C_{HI}} - \lambda_A]}{2A}\right)\right\}, \tag{24}$$

$$u_2^* = \min\left\{1, \max\left(0, \frac{\beta_H^* S[\lambda_H - \lambda_S] + \beta_H^* R[\lambda_H - \lambda_R] + \beta_H^* I[\lambda_{C_{HI}} - \lambda_I]}{2B}\right)\right\}, \tag{25}$$

$$u_3^* = \min\left\{1, \max\left(0, \frac{\alpha I[\lambda_I - \lambda_R]}{2C}\right)\right\}, \tag{26}$$

$$u_4^* = \min\left\{1, \max\left(0, \frac{\alpha_a H[\lambda_H - \lambda_A]}{2D}\right)\right\}, \tag{27}$$

and

$$u_5^* = \min\left\{1, \max\left(0, \frac{r C_{HI}[\lambda_H - \lambda_{C_{HI}}] + C_{HI} r \gamma \lambda_A}{2E}\right)\right\}. \tag{28}$$

Proof. Corollary 4.1 of [38] presents the existence of an optimal control as a result of the convexity of the integrand of J with respect to u_1, u_2, u_3, u_4 and u_5, a priori boundedness of the state solutions and the Lipschitz property of the state system link to the state variables. The differentiation of the Hamiltonian function computed at the optimal control leads to differential equations that govern the adjoint variables. The adjoint equations can be formulated as

$$\begin{aligned} \frac{\mathrm{d}\lambda_s}{\mathrm{d}t} = {} & (1-u_1)\left(\frac{N\lambda\varepsilon I - \lambda\varepsilon IS}{N^2}\right)(\lambda_S - \lambda_I) - \rho E_n \lambda_s + (1-u_2)\left(\frac{N\lambda_1\varepsilon(H+A+gC_{HI}) - \lambda_1\varepsilon S(H+A+gC_{HI})}{N^2}\right)(\lambda_S - \lambda_H) \\ & + \mu\lambda_S - (1-u_2)\left(\frac{I\lambda_1\varepsilon(H+A+gC_{HI})}{N^2}\right)\lambda_I - (1-u_2)\left(\frac{R\lambda_1\varepsilon(H+A+gC_{HI})}{N^2}\right)\lambda_R \\ & - (1-u_2)\left(\frac{R\lambda_1\varepsilon(H+A+gC_{HI})}{N^2}\right)\lambda_H - (1-u_1)\left(\frac{\lambda\varepsilon IH}{N^2}\right)\lambda_H \\ & - (1-u_1)\left(\frac{\lambda\varepsilon IA}{N^2}\right)\lambda_A - (1-u_1)\left(\frac{\lambda\varepsilon IH}{N^2}\right)\lambda_{C_{HI}} - (1-u_1)\left(\frac{\lambda\varepsilon IA}{N^2}\right)\lambda_{C_{HI}} \\ & - (1-u_2)\left(\frac{\lambda_1\varepsilon I(H+A+gC_{HI})}{N^2}\right)\lambda_{C_{HI}} + \mu\lambda_S, \end{aligned}$$

$$\begin{aligned}
\frac{\mathrm{d}\lambda_I}{\mathrm{d}t}=&-a_1+(1-u_1)\left(\frac{N\lambda\varepsilon S-\lambda\varepsilon IS}{N^2}\right)(\lambda_S-\lambda_I)-(1-u_2)\left(\frac{S\lambda_1\varepsilon(H+A+gC_{HI})}{N^2}\right)\lambda_S\\
&+(1-u_2)\left(\frac{N\lambda_1\varepsilon(H+A+gC_{HI})-\lambda_1\varepsilon I(H+A+gC_{HI})}{N^2}\right)\lambda_I-(1-u_2)\left(\frac{R\lambda_1\varepsilon(H+A+gC_{HI})}{N^2}\right)\lambda_R\\
&+(1-u_2)\left(\frac{S\lambda_1\varepsilon(H+A+gC_{HI})}{N^2}\right)\lambda_H+(1-u_2)\left(\frac{R\lambda_1\varepsilon(H+A+gC_{HI})}{N^2}\right)\lambda_H-(1-u_1)\left(\frac{\lambda\varepsilon H-\lambda\varepsilon IH}{N^2}\right)\lambda_H-\rho E_n\lambda_I\\
&-(1-u_1)\left(\frac{\lambda\varepsilon A-\lambda\varepsilon IA}{N^2}\right)\lambda_A-(1-u_1)\left(\frac{\lambda\varepsilon H-\lambda\varepsilon IH}{N^2}\right)\lambda_{C_{HI}}-(1-u_1)\frac{\lambda\varepsilon A-\lambda\varepsilon IA}{N^2}\lambda_{C_{HI}}\\
&-(1-u_2)\left(\frac{N\lambda_1\varepsilon(H+A+gC_{HI})-\lambda_1\varepsilon I(H+A+gC_{HI})}{N^2}\right)\lambda_{C_{HI}}+(u_3\mu+\psi)\lambda_I-\theta\lambda_{E_n}+\alpha(\lambda_I-\lambda_R),\\
\frac{\mathrm{d}\lambda_R}{\mathrm{d}t}=&(\sigma+\mu)\lambda_R-(1-u_1)\left(\frac{\lambda\varepsilon IS}{N^2}\right)\lambda_S-(1-u_2)\left(\frac{S\lambda_1\varepsilon(H+A+gC_{HI})}{N^2}\right)\lambda_S+(1-u_1)\left(\frac{\lambda\varepsilon IS}{N^2}\right)\lambda_I\\
&-(1-u_2)\left(\frac{\lambda_1I\varepsilon(H+A+gC_{HI})}{N^2}\right)\lambda_1+(1-u_2)\left(\frac{N\lambda_1\varepsilon(H+A+gC_{HI})-\lambda_1\varepsilon R(H+A+gC_{HI})}{N^2}\right)\lambda_R\\
&+(1-u_2)\left(\frac{S\lambda_1\varepsilon(H+A+gC_{HI})}{N^2}\right)\lambda_H-(1-u_2)\left(\frac{N\lambda_1\varepsilon(H+A+gC_{HI})-\lambda_1\varepsilon R(H+A+gC_{HI})}{N^2}\right)\lambda_H\\
&-(1-u_1)\left(\frac{\lambda\varepsilon IH}{N^2}\right)\lambda_{C_{HI}}-(1-u_1)\left(\frac{\lambda\varepsilon IA}{N^2}\right)\lambda_{C_{HI}}+(1-u_2)\frac{\lambda_1I\varepsilon(H+A+gC_{HI})}{N^2}\lambda_{C_{HI}},\\
\frac{\mathrm{d}\lambda_{E_n}}{\mathrm{d}t}=&\nu\lambda_E+\rho S(\lambda_S-\lambda_I)+\rho A(\lambda_A-\lambda_{C_{HI}})+\rho H(\lambda_H-\lambda_{C_{HI}}),\\
\frac{\mathrm{d}\lambda_H}{\mathrm{d}t}=&-a_2+(\mu+\psi_2)\lambda_H+u_4\alpha_a(\lambda_H-\lambda_A)-(1-u_1)\left(\frac{\lambda\varepsilon IS}{N^2}\right)\lambda_S+(1-u_2)\left(\frac{N\lambda_1\varepsilon S-\lambda_1\varepsilon S(H+A+gC_{HI})}{N^2}\right)\lambda_S\\
&+(1-u_1)\left(\frac{\lambda\varepsilon IS}{N^2}\right)\lambda_I+(1-u_2)\left(\frac{N\lambda_1\varepsilon I-\lambda_1\varepsilon I(H+A+gC_{HI})}{N^2}\right)\lambda_I\\
&+(1-u_2)\left(\frac{N\lambda_1\varepsilon R-\lambda_1\varepsilon R(H+A+gC_{HI})}{N^2}\right)\lambda_R-(1-u_2)\left(\frac{N\lambda_1\varepsilon S-\lambda_1\varepsilon S(H+A+gC_{HI})}{N^2}\right)\lambda_H\\
&-(1-u_2)\left(\frac{N\lambda_1\varepsilon R-\lambda_1\varepsilon R(H+A+gC_{HI})}{N^2}\right)\lambda_H-(1-u_1)\left(\frac{N\lambda\varepsilon I-\lambda\varepsilon IH}{N^2}\right)\lambda_H\\
&+\rho E_n\lambda_H-(1-u_1)\left(\frac{\lambda\varepsilon IA}{N^2}\right)\lambda_A+(1-u_1)\left(\frac{\lambda\varepsilon IH}{N^2}\right)\lambda_{C_{HI}}+(1-u_1)\left(\frac{\lambda\varepsilon IA}{N^2}\right)\lambda_{C_{HI}}\\
&-(1-u_2)\left(\frac{N\lambda_1\varepsilon I-\lambda_1\varepsilon I(H+A+gC_{HI})}{N^2}\right)\lambda_{C_{HI}},\\
\frac{\mathrm{d}\lambda_A}{\mathrm{d}t}=&-a_3+(\mu+\psi_2)\lambda_A-(1-u_1)\left(\frac{\lambda\varepsilon IS}{N^2}\right)\lambda_S+(1-u_2)\left(\frac{N\lambda_1\varepsilon S-\lambda_1\varepsilon S(H+A+gC_{HI})}{N^2}\right)\lambda_S\\
&+(1-u_1)\left(\frac{\lambda\varepsilon IS}{N^2}\right)\lambda_I+(1-u_2)\left(\frac{N\lambda_1\varepsilon I-\lambda_1\varepsilon I(H+A+gC_{HI})}{N^2}\right)\lambda_I\\
&+(1-u_2)\left(\frac{N\lambda_1\varepsilon R-\lambda_1\varepsilon R(H+A+gC_{HI})}{N^2}\right)\lambda_R\\
&-(1-u_2)\left(\frac{N\lambda_1\varepsilon S-\lambda_1\varepsilon S(H+A+gC_{HI})}{N^2}\right)\lambda_H+\rho E_n\lambda_A-(1-u_2)\left(\frac{N\lambda_1\varepsilon R-\lambda_1\varepsilon R(H+A+gC_{HI})}{N^2}\right)\lambda_H\\
&-(1-u_1)\left(\frac{\lambda\varepsilon IH}{N^2}\right)\lambda_H-(1-u_1)\left(\frac{\lambda\varepsilon IA}{N^2}\right)\lambda_A+(1-u_1)\left(\frac{\lambda\varepsilon IH}{N^2}\right)\lambda_{C_{HI}}\\
&+(1-u_1)\left(\frac{\lambda\varepsilon IA}{N^2}\right)\lambda_{C_{HI}}-(1-u_2)\left(\frac{N\lambda_1\varepsilon I-\lambda_1\varepsilon I(H+A+gC_{HI})}{N^2}\right)\lambda_{C_{HI}},
\end{aligned}$$

$$\begin{aligned}\frac{\mathrm{d}\lambda_{C_{HI}}}{\mathrm{d}t} =& -a_4 + u_5\gamma(\lambda_{C_{HI}} - r\lambda_A) - (1-u_1)\left(\frac{\lambda\varepsilon IS}{N^2}\right)\lambda_S + (1-u_2)\left(\frac{N\lambda_1\varepsilon gS - \lambda_1\varepsilon S(H+A+gC_{HI})}{N^2}\right)\lambda_S \\ &+(1-u_1)\left(\frac{\lambda\varepsilon IS}{N^2}\right)\lambda_I + (1-u_2)\left(\frac{N\lambda_1\varepsilon gI - \lambda_1\varepsilon I(H+A+gC_{HI})}{N^2}\right)\lambda_I \\ &+(1-u_2)\left(\frac{N\lambda_1\varepsilon gR - \lambda_1\varepsilon R(H+A+gC_{HI})}{N^2}\right)\lambda_R \\ &-(1-u_2)\left(\frac{N\lambda_1\varepsilon gS - \lambda_1\varepsilon S(H+A+gC_{HI})}{N^2}\right)\lambda_H - (1-u_2)\left(\frac{N\lambda_1\varepsilon gR - \lambda_1\varepsilon R(H+A+gC_{HI})}{N^2}\right)\lambda_H \\ &-(1-u_1)\left(\frac{\lambda\varepsilon IH}{N^2}\right)\lambda_H - (1-u_1)\left(\frac{\lambda\varepsilon IA}{N^2}\right)\lambda_A \\ &+(1-u_1)\left(\frac{\lambda\varepsilon IH}{N^2}\right)\lambda_{C_{HI}} + (1-u_1)\left(\frac{\lambda\varepsilon IA}{N^2}\right)\lambda_{C_{HI}} - (1-u_2)\left(\frac{N\lambda_1\varepsilon gI - \lambda_1\varepsilon I(H+A+gC_{HI})}{N^2}\right)\lambda_{C_{HI}} \\ &-\rho E_n\lambda_{C_{HI}(1-u_5r)\lambda_A}. \end{aligned} \tag{29}$$

Determining the values for u_1^*, u_2^*, u_3^*, u_4^* and u_5^* with respect to the constraints, the characterization (23)–(28) can be arrived at

$$0 = \frac{\partial H}{\partial u_1} = 2A - \beta_c^* S[\lambda_I - \lambda_S] - \beta_c^* H[\lambda_{C_{HI}} - \lambda_H] - \beta_c^* A[\lambda_{C_{HI}} - \lambda_A],$$

$$0 = \frac{\partial H}{\partial u_2} = 2B - \beta_H^* S[\lambda_H - \lambda_S] - \beta_H^* R[\lambda_H - \lambda_R] - \beta_H^* I[\lambda_{C_{HI}} - \lambda_I], \tag{30}$$

$$0 = \frac{\partial H}{\partial u_3} = 2C - \alpha I[\lambda_I - \lambda_R],$$

$$0 = \frac{\partial H}{\partial u_4} = 2D - \alpha_a H[\lambda_H - \lambda_A], \tag{31}$$

$$0 = \frac{\partial H}{\partial u_5} = 2E - rC_{HI}[\lambda_H - \lambda_{C_{HI}}] - C_{HI}r\gamma\lambda_A \tag{32}$$

and with transversality conditions

$$\lambda_S(t_f) = \lambda_I(t_f) = \lambda_R(t_f) = \lambda_{E_n}(t_f) = \lambda_H(t_f) = \lambda_A(t_f) = \lambda_{C_{HI}}(t_f) = 0. \tag{33}$$

We therefore obtain (see for example Lenhart and Workman [44])

$$\begin{aligned} u_1^* &= \min\left\{1, \max\left(0, \frac{\beta_c^* S[\lambda_I - \lambda_S] + \beta_c^* H[\lambda_{C_{HI}} - \lambda_H] + \beta_c^* A[\lambda_{C_{HI}} - \lambda_A]}{2A}\right)\right\}, \\ u_2^* &= \min\left\{1, \max\left(0, \frac{\beta_H^* S[\lambda_H - \lambda_S] + \beta_H^* R[\lambda_H - \lambda_R] + \beta_H^* I[\lambda_{C_{HI}} - \lambda_I]}{2B}\right)\right\}, \\ u_3^* &= \min\left\{1, \max\left(0, \frac{\alpha I[\lambda_I - \lambda_R]}{2C}\right)\right\}, \\ u_4^* &= \min\left\{1, \max\left(0, \frac{\alpha_a H[\lambda_H - \lambda_A]}{2D}\right)\right\}, \\ u_5^* &= \min\left\{1, \max\left(0, \frac{rC_{HI}[\lambda_H - \lambda_{C_{HI}}] + C_{HI}r\gamma\lambda_A}{2E}\right)\right\}, \end{aligned} \tag{34}$$

by standard control arguments dealing with the bounds on the controls, we get

$$u_i^* = \begin{cases} 0, & \text{if } \zeta_{\mathrm{i}}^* \leq 0, \\ \zeta_{\mathrm{i}}^*, & \text{if } 0 < \zeta_{\mathrm{i}}^* < 1, \\ 1, & \text{if } \zeta_{\mathrm{i}}^* \geq 1. \end{cases}$$

For $i \in 1, 2, 3, 4, 5$ and where

$$\begin{aligned} \zeta_1^* &= \min\left\{1, \max\left(0, \frac{\beta_c^* S[\lambda_I - \lambda_S] + \beta_c^* H[\lambda_{C_{HI}} - \lambda_H] + \beta_c^* A[\lambda_{C_{HI}} - \lambda_A]}{2A}\right)\right\}, \\ \zeta_2^* &= \min\left\{1, \max\left(0, \frac{\beta_H^* S[\lambda_H - \lambda_S] + \beta_H^* R[\lambda_H - \lambda_R] + \beta_H^* I[\lambda_{C_{HI}} - \lambda_I]}{2B}\right)\right\}, \\ \zeta_3^* &= \min\left\{1, \max\left(0, \frac{\alpha I[\lambda_I - \lambda_R]}{2C}\right)\right\}, \\ \zeta_4^* &= \min\left\{1, \max\left(0, \frac{\alpha_a H[\lambda_H - \lambda_A]}{2D}\right)\right\}, \\ \zeta_5^* &= \min\left\{1, \max\left(0, \frac{rC_{HI}[\lambda_H - \lambda_{C_{HI}}] + C_{HI} r\gamma\lambda_A}{2E}\right)\right\}. \end{aligned} \tag{35}$$

In the subsequent section, we explore the numerical solutions of the optimality of the proposed model and endeavour to vary the optimal controls u_1, u_2, u_3, u_4 and u_5. □

7 Numerical simulations

Here, in this section, we provide detailed discussion of the numerical solutions of the optimality system and the corresponding results of varying the optimal controls u_1, u_2, u_3, u_4 and u_5. The parameter selections, as well as giving the appropriate interpretation from various cases and the numerical simulation solutions, are obtained using MATLAB version 15.0. The optimality system, which is made up of the state system and its adjoint system, was solved to attain the optimal control solution. A fourth-order Runge-Kutta iterative scheme is applied to arrive at the solution of the optimality system. The adjoint equations were solved by employing the backward fourth-order Runge-Kutta scheme in order to obtain the current solutions of the state equations based on the transversality conditions (23). From the results arrived at, the controls were updated by using a convex combination of the previous controls and the value determined from the characterisations. This process was continued to be undertaken and the iterations were ended if the values of the unknowns at the previous iterations were very close to the ones just achieved at the current iteration [44,45]. Table 1 depicts the parameter values employed in the numerical simulation of the co-infection model. The following weight constants were taken into consideration: $A = 50$, $B = 130$, $C = 100$, $D = 200$, $E = 310$ and $a_1 = 210$, $a_2 = 380$, $a_3 = 400$, $a_4 = 260$, $a_5 = 310$.

7.1 Prevention (u_1) and treatment (u_3) of cryptosporidiosis

The cryptosporidiosis prevention control u_1 and the cryptosporidiosis treatment control u_3 are used to optimise the objective function J, at the same time the controls (u_2, u_4 and u_5) are set to zero. Figure 1(a) indicates that the number of cryptosporidiosis infected humans (I) is significantly different in optimal control cases, compared with cases without control. This control strategy has a positive effect on reducing the number of infected cryptosporidiosis humans (I). Figure 1(b) shows the environmental contamination effects and there is a substantial difference between the controlled cases and those without control. Therefore, it suggests that this strategy is capable of minimizing the environmental effect (E_n). In fig. 1(c), the cases without control are higher than the controlled cases in HIV human infection (H). A similar pattern is observed in fig. 1(d), that is, the cases without control are higher than the control scenario. It can then be inferred that controlling AIDS infection in humans (A) has nothing to do with controlling cryptosporidiosis (using prevention and treatment). Figure 1(e) depicts the effect of this strategy on the co-infected humans (C_{HI}) and there is a relatively significant difference between the cases with control and those without control. This could be attributable to cryptosporidiosis infected humans since controlling HIV-AIDS cannot be done using this control strategy.

Table 1. Description of variables and parameters of the model.

Parameter	Description	Value	Ref.
Λ	Human recruitment rate	0.005 day^{-1}	[43]
σ	Recovery rate of crypto infected individuals	0.07 day^{-1}	[46]
μ	Natural mortality rate in humans	0.00055 day^{-1}	[47]
ψ	Average contribution of crypto infected individuals to the environment	0.00095 day^{-1}	[46]
ρ	Prob. of infection thro enviro.	0.005 day^{-1}	Assumed
λ	Cryptosporidiosis transmission probability rate	0.05 day^{-1}	[46]
θ	Cryptosporidiosis infected contribution to the environment	0.7 day^{-1}	[46]
ϵ	Cryptosporidiosis contact rate	0.123 day^{-1}	[46]
ϵ_1	HIV contact rate	0.025 day^{-1}	Assumed
λ_1	HIV infection transmission probability rate	0.05 day^{-1}	[43]
α_a	Rate of progression to AIDS stage	0.000548 day^{-1}	[43]
α	Recovery rate from crypto	0.7 day^{-1}	[46]
γ	Cholera related death	0.02407 day^{-1}	[48]
ψ	Cryptosporidiosis related death	0.02407 day^{-1}	[49]
ν	Microbes mortality rate	0.033 day^{-1}	[46]
ψ_2	HIV/AIDS related death	0.00913 day^{-1}	[50]
ρ	Modification parameter	0.065 day^{-1}	Assumed
r	Rate of coinfected humans	0.08 day^{-1}	Assumed
σ	Cryptosporidiosis immunity waning rate	0.001 day^{-1}	[46]
g	Modification parameter	0.07 day^{-1}	Assumed

7.2 Prevention (u_2) and treatment (u_4) of HIV-AIDS

The HIV-AIDS prevention control u_2 and the HIV treatment control u_4 are activated to optimise the objective function J, while the rest of the controls (u_1, u_3 and u_5) are set to zero. Figure 2(a) shows that the number of cryptosporidiosis infected humans (I) is significantly different in the optimal control cases, compared to the cases without control. This strategy of controlling HIV infection in humans (H) virtually has no effect on cryptosporidiosis infected humans (I). This is anticipated, because controlling each disease requires entirely different strategies. Figure 2(b) depicts that the case without control is higher than the controlled case. The dynamics of controlling HIV is different compared with controlling environmental contamination effect E_n. Figure 2(c) indicates that there is a vast difference between the controlled case and those without control. The control strategy appears to be effective when dealing with HIV infected humans (H). A similar pattern can be seen in fig. 2(d) since it requires the same strategy to reduce the number of infected humans with AIDS (A). Figure 2(e) shows co-infected humans (C_{HI}) and there is little difference between the controlled cases and those without control. This strategy is effective in minimizing the co-infected humans.

7.3 Cryptosporidiosis and HIV-AIDS preventions (u_1) and (u_2) only

The cryptosporidiosis and HIV-AIDS prevention control u_1 and the control u_2 are employed to optimize the objective function J at the same time as the other controls (treatments) ($u_3, u_4 u_5$) are to zero.

In fig. 3(a), there is a substantial significant difference between the controlled case and the case without control for cryptosporidiosis infected humans (I). Similarly, in fig. 3(b), the result shows no difference. The strategy is effective to minimize both cryptosporidiosis and environmental contamination effect. There is a positive impact of this strategy on controlling HIV (H) as shown in fig. 3(c). Thus, the controlled case and the case without control are significantly different. The situation in fig. 3(c) is not different from fig. 3(d). This is because the mechanisms required to minimize the spread of HIV and AIDS are very similar. The co-infected humans (C_{CH}) as shown depict that there is a substantial difference between the controlled case and the case without control. This strategy is effective in dealing with HIV-AIDS related disease using prevention strategy during the intervention.

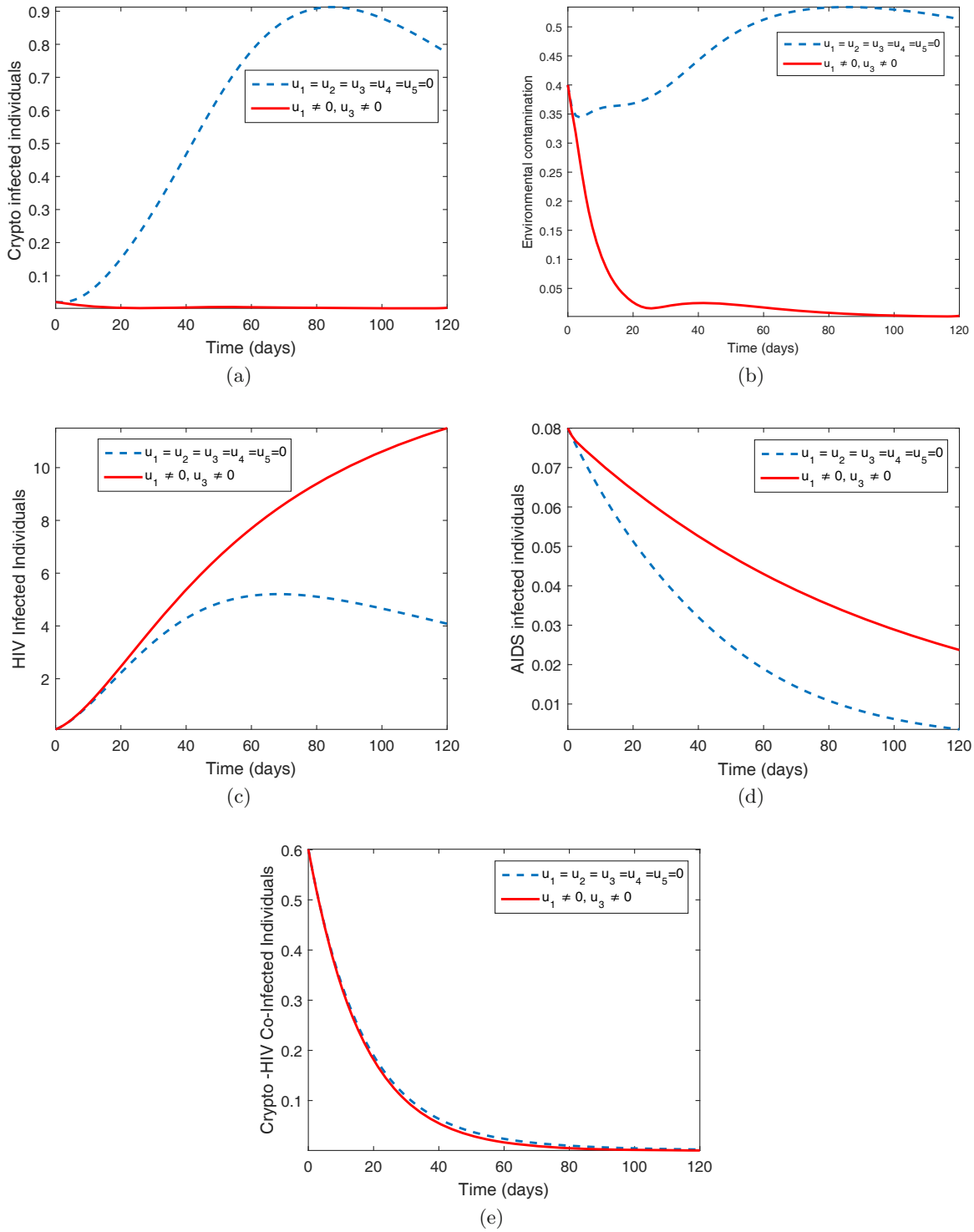

Fig. 1. Simulations of the model showing the effect of cryptosporidiosis prevention and treatment only on transmission.

7.4 Cryptosporidiosis and HIV-AIDS treatments (u_3) and (u_4) only

The cryptosporidiosis and HIV-AIDS treatment controls u_3 and u_4 are explored to optimize the objective function J while other controls which have something to do with prevention mechanisms (u_1, u_2 and u_5) are set to zero. Figure 4(a) indicates that there is a vast difference between the controlled case and the case without control in the spread of cryptosporidiosis (I). There is a relatively little difference between the controlled environmental contamination effect (E_n) and the case without control as shown in fig. 4(b). It is obvious in fig. 4(c) that the controlled case and the case

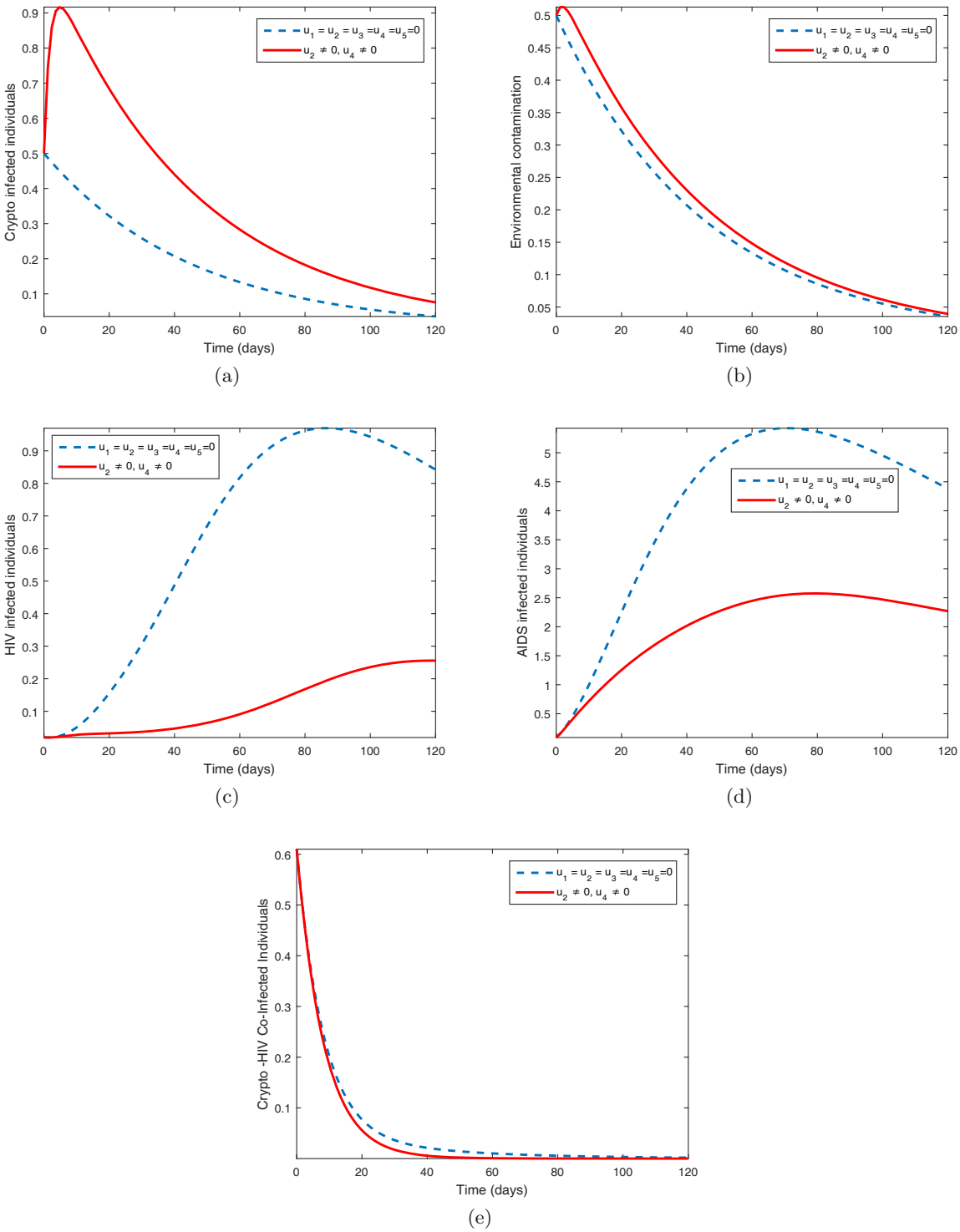

Fig. 2. Simulations of the model showing the effect of HIV prevention and treatment only on transmission.

without control are significantly different. The negative effect of this strategy in controlling HIV is anticipated since there is prescribed treatment for this disease. In fig. 4(d), a similar pattern is observed and is not surprising because there is no cure for AIDS (A). In order to effectively control AIDS (A) there is a need for a more robust strategy to achieve such a goal. There is virtually no difference between the controlled case for co-infected humans (C_{HI}) and the case without control as shown in fig. 4(e). The dynamics of the two diseases are entirely different and therefore this strategy is not effective in controlling the two diseases at the same time.

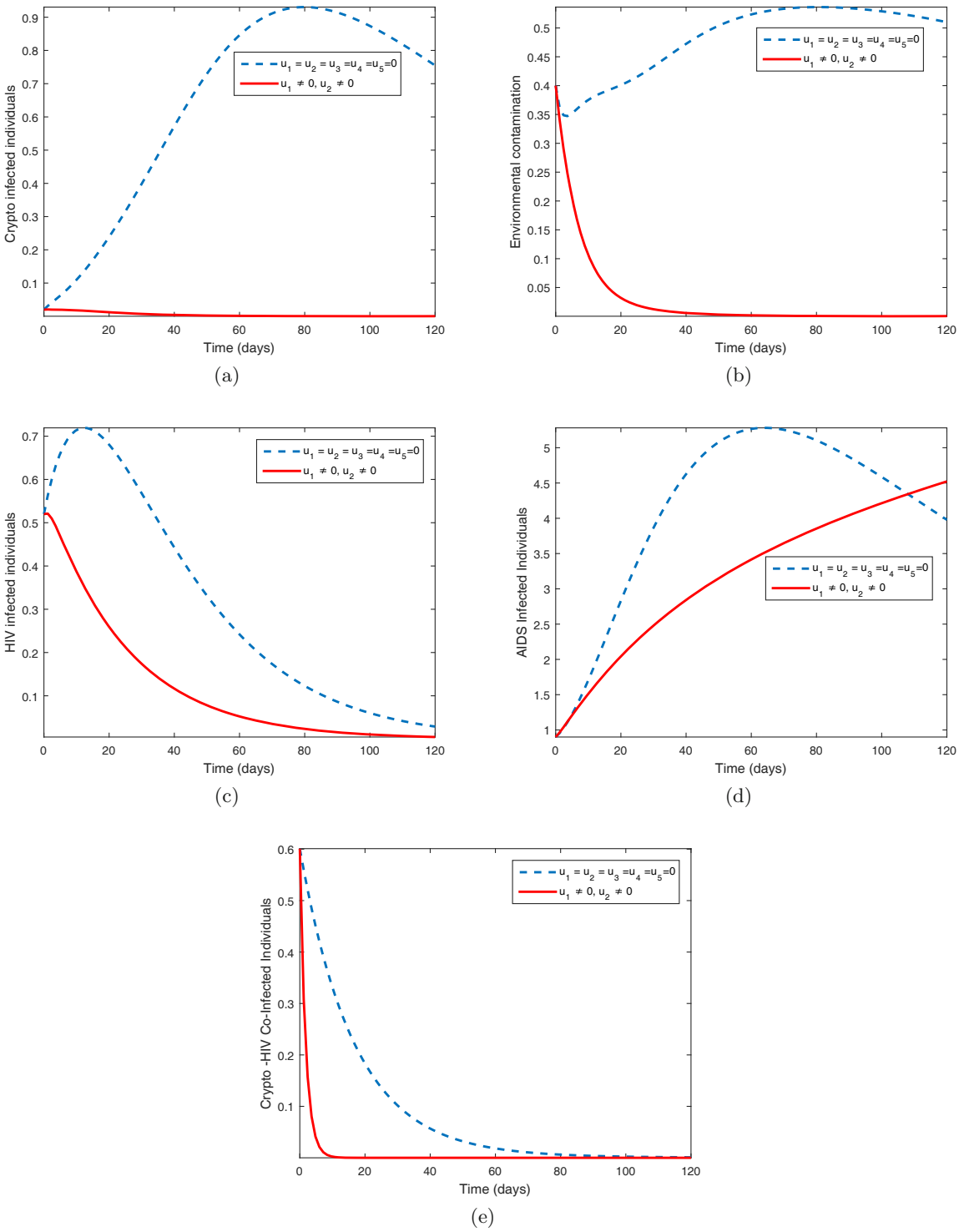

Fig. 3. Simulations of the model showing the effect of cryptosporidiosis-HIV prevention only on transmission.

7.5 HIV-AIDS and cryptosporidiosis preventions with treatments $(u_1, u_2, u_3, u_4, u_5)$

In this strategy, all the controls are used $(u_1, u_2, u_3, u_4, u_5)$ in oder to optimize the objective function J. In other words, the preventions and treatments of cryptosporidiosis and HIV-AIDS are optimized. It is clearly seen in fig. 5(a) that there is a vast significant difference between the controlled case and the case without control in the spread of cryptosporidiosis (I). A similar pattern can be observed in fig. 5(b). The positive effect is attributable to the

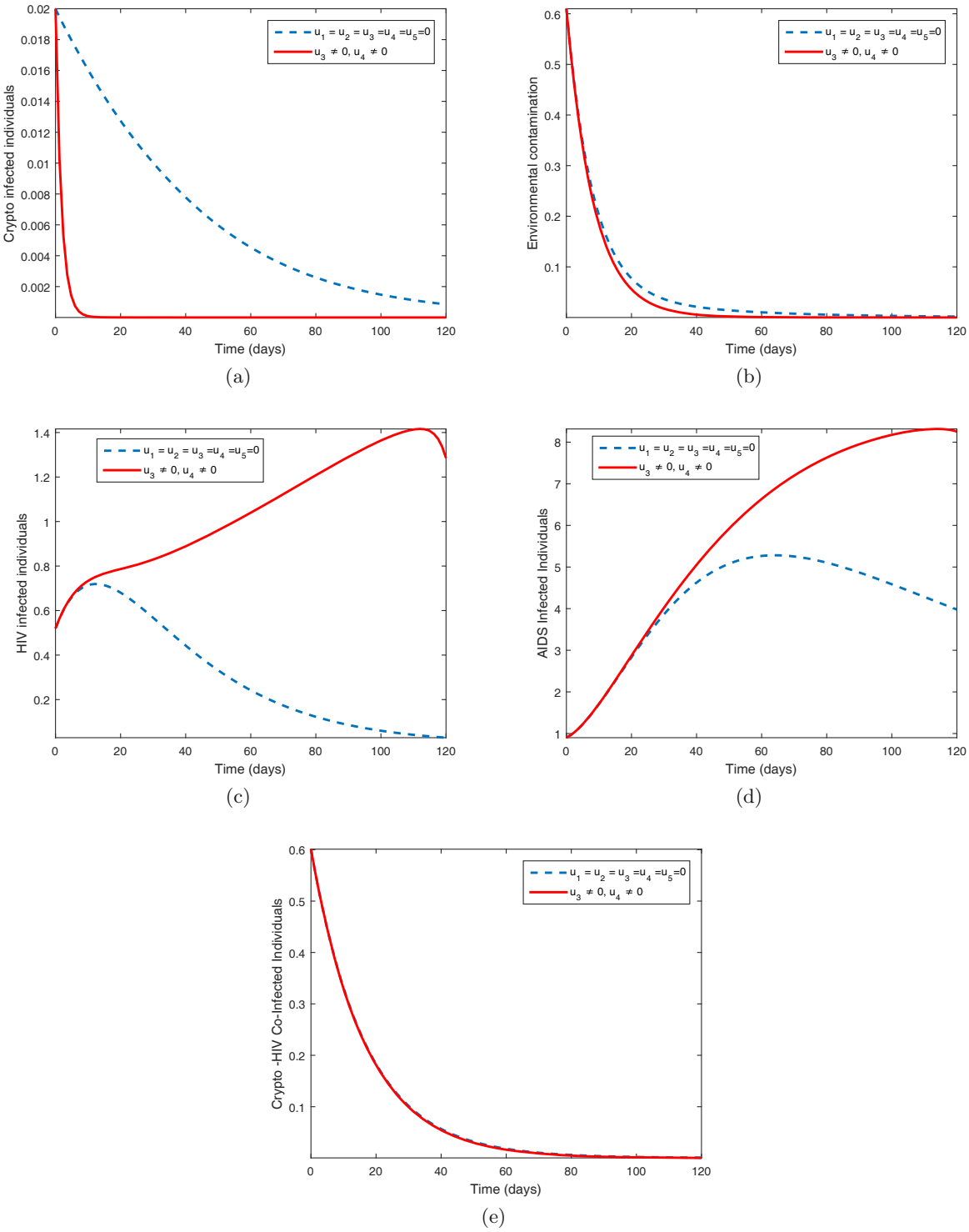

Fig. 4. Simulations of the model showing the effect of cryptosporidiosis-HIV treatment only on transmission.

effectiveness of this strategy. There is a substantial difference in the controlled case and the case without control in fig. 5(c) and a similar situation can be seen in fig. 5(d). The strategy for controlling HIV and AIDS is more effective in combining both preventive and treatment mechanisms. There is a positive effect on minimizing the number of co-infected individuals as shown in fig. 5(d). This is clearly because of the combination of both preventive and treatment mechanism same time.

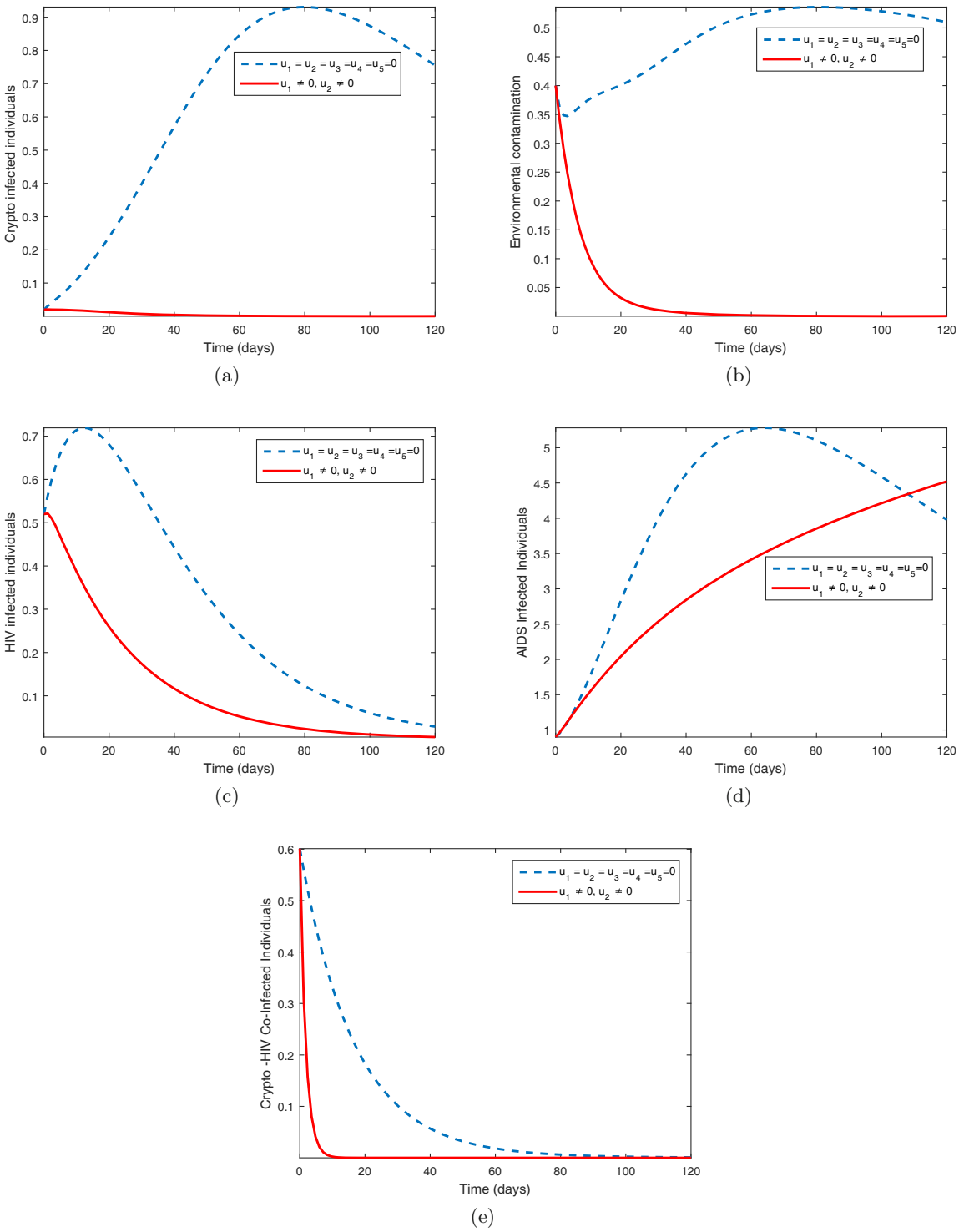

Fig. 5. Simulations of the model showing the effect of cryptosporidiosis-HIV prevention and treatment on transmission.

8 Conclusion

In this paper, we examined a co-infection of cryptosporidiosis-HIV/AIDS deterministic model, by incorporating time-dependent control preventions and treatments. The model basic properties were studied. The sub-models stability analyses were carried out and proved to be locally and globally stable. The centre manifold technique was employed to explore the possibility of the presence of the bifurcation phenomenon in the sub-models as well as the co-infected model

which is found to exhibit backward bifurcation phenomena. Furthermore, we incorporated five controls and explored different strategies and their effects on the co-infection. From the numerical results, the application of treatment and prevention of cryptosporidiosis only has no significant impact on reducing HIV-AIDS related problem as shown in fig. 1. The prevention and treatment of HIV-AIDS only strategy, only drastically reduced the number of HIV infected humans and however had no effect on cryptosporidiosis infected humans. But, it has relatively positively impacted on the co-infected humans as shown in fig. 2. The prevention of the two disease same time strategy, resulted in reduction in all cases, see fig. 3, however, in the case of treatment of both diseases the positive impact was seen in cryptosporidiosis humans infected and environmental contamination effect with no difference in the co-infected humans, see fig. 4. When all the controls were optimized, the controlled cases are significantly different from the cases without control. These strategies in all cases have a positive impact in controlling both diseases in a community, see fig. 5.

This work is part of the activities OKO carried out at the Kansas State University during a research visit. Therefore, OKO wishes to appreciate the support of IMU-CDC Simons Foundation African Visiting Scholars Grants towards the visit to Kansas.

Conflict of interests

The authors declare that no competing interests exist.

References

1. F.D. Chierico, M. Onori, S.D. Bella, E. Bordi, N. Petrosillo, D. Menichella, S.M. Caccio, F. Callea, L. Putignani, Ann. Trop. Med. Parasitol. **105**, 339 (2011).
2. S.T. Ogunlade, K.O. Okosun, R.S. Lebelo, M. Mukamuri, Glob. J. Pure Appl. Math. **12**, 4959 (2016).
3. Niklaus Egloff, Thomas Oehler, Marco Rossi, Xuan M. Nguyen, Hansjakob Furrer, J. Travel Med. **8**, 143 (2001).
4. Siobhan M. Mor, Saul Tzipori, Clin. Infect. Dis. **2008**, 915 (2008).
5. Vitaliano Cama, Robert H. Gilman, Aldo Vivar, Eduardo Ticona, Ynes Ortega, Caryn Bern, Lihua Xiao, Emerg. Infect. Dis. **12**, 6 (2006).
6. Gabriela Certad, Alejandro Arenas-Pinto, Leonor Pocaterra, Giuseppe Ferrara, Julio Castro, Andreina Bello, Luz Núñez, Am. J. Trop. Med. Hyg. **73**, 54 (2005).
7. A.S. Kumurya, M.Y. Gwarzo, J. AIDS HIV Res. **5**, 301 (2013).
8. C.N. Nkenfou, C.T. Nana, V.K. Payne, PLoS ONE **8**, e57914 (2013).
9. Li-Guang Tian, Jia-Xu Chen, Tian-Ping Wang, Guo-Jin Cheng, Peter Steinmann, Feng-Feng Wang, Yu-Chun Cai, Xiao-Mei Yin, Jian Guo, Li Zhou, Xiao-Nong Zhou, Parasites Vectors **5**, 36 (2012).
10. P. Paboriboune, N. Phoumindr, E. Borel, K. Sourinphoumy, S. Phaxayaseng *et al.*, PLoS ONE **9**, e91452 (2014).
11. Li-Guang Tian, Tian-Ping Wang, Jia-Xu Chen, Yu-Chun Cai, Xiao-Mei Yin, Guo-Jin Cheng, Wei-Duo Wu, Peter Steinmann, Jian Guo, Xiao-Mei Tong, Lan-Hua Li, Qin Liu, Li Zhou, Feng-Feng Wang, Zhen-Li Wang, Xiao-Nong Zhou, Front. Med. China **4**, 192 (2010).
12. Z. Bentwich, Z. Weisman, C. Moroz, S. Bar-Yehuda, A. Kalinkovich, Clin. Exp. Immunol. **103**, 239 (1996).
13. R. Gopinath, M. Ostrowski, S.J. Justement, A.S. Fauci, Nutman T.B. Filarial, J. Infect. Dis. **182**, 1804 (2000).
14. Arvind Chandora, P.K. Khatri, Saroj Meena, Archana Bora, Laxmi Rathore, Vinod Maurya, KanhaiyaLal Sirvi, Sch. J. Appl. Med. Sci. **3**, 1975 (2015).
15. Li-Guang Tian, Tian-Ping Wang, Shan Lv, Feng-Feng Wang, Jian Guo, Xiao-Mei Yin, Yu-Chun Cai, Mary Kathryn Dickey, Peter Steinmann, Jia-Xu Chen, Infect. Dis. Poverty **2**, 18 (2013).
16. E.E. Tyzzer, Proc. Soc. Exp. Biol. Med. **5**, 12 (1907).
17. S.T. Goldstein, D.D. Juranek, O. Ravenholt, A.W. Hightower, D.G. Martin, J.L. Mesnik *et al.*, Ann. Intern. Med. **124**, 45 (1996).
18. W.L. Current, New Engl. J. Med. **309**, 1325 (1983).
19. P.C. Okhuysen, C.L. Chappell, J.H. Crabb, C.R. Sterling, H.L. DuPont, J. Infect. Dis. **180**, 1275 (1999).
20. M.M. Peng, L. Xiao, A.R. Freeman, M.J. Arrowood, A.A. Escalante, A.C. Weltman, C.S.L. Ong, W.R. MacKenzie, A.A. Lal, C.B. Beard, Emerg. Infect. Dis. **3**, 567 (1997).
21. K.A. Adal, C.R. Sterling, R.L. Guerrant, *Cryptosporidium and related species*, in *Infections of the Gastrointestinal Tract*, edited by M.J. Blaser, P.D. Smith, J.I. Ravdin, H.B. Greenberg, R.L. Guerrant (Raven Press, 1995) pp. 1107–1128.
22. F.M. Awad-El-Kariem, H.A. Robinson, F. Petry, V. McDonald, D. Evans, D. Casemore, Parasitol. Res. **84**, 297 (1998).
23. T.R. Navin, D.D. Juranek, Rev. Infect. Dis. **6**, 313 (1984).
24. N.B. Vakil, S.M. Schwartz, B.P. Buggy, C.F. Brummitt, M. Kherellah, D.M. Letzer *et al.*, New Engl. J. Med. **334**, 19 (1996).
25. J.A. Gbenga, M. Nizar, P.J. Witbooi, K.O. Okosun, Int. J. Biomath. **6**, 1350006 (2013).
26. UN, UNAIDS, World Health Organization, 2011 AIDS epidemic update available, `http://news.yahoo.com/s/afp/20110603/hlafp/healthaidsanniversary-unaids20110603181329` (November 2011).

27. K.O. Okosun, O.D. Makinde, Math. Biosci. **258**, 19 (2014).
28. H. Joshi, S. Lenhart, K. Albright, K. Gipson, Math. Biosci. Eng. **5**, 757 (2008).
29. F. Nyabadza, J. Biol. Sys. **14**, 357 (2006).
30. D.L. Higgins, C. Galavotti, K.R. OReilly, JAMA **266**, 2419 (1991).
31. S. Mushayabasa, C.P. Bhunu, Comput. Math. Methods Med. **2011**, 15 (2011).
32. S. Mushayabasa, C.P. Bhunu, N.A. Mhlanga, Appl. Appl. Math. **9**, 121 (2014).
33. C.P. Bhunu, S. Mushayabasa, H. Kojouharov, J.M. Tchuenche, J. Math. Model. Algorithms **10**, 31 (2011).
34. J.R. Andrews, N. Sarita Shah, D. Weissman, A.P. Moll, G. Friedland, N.R. Gandh, PLoS ONE **5**, e15735 (2010).
35. D. Kirschner, Theor. Popul. Biol. **55**, 94 (1999).
36. S. Ramkissoon, H.G. Mwambi, A.P. Matthews, PLoS ONE **7**, e49492 (2012).
37. W.L. Roeger, Z. Feng, C. Castillo-Chavez, Math. Biosci. Eng. **6**, 815 (2009).
38. O. Sharomi, C. Podder, A.B. Gumel, Math. Biosci. Eng. **5**, 145 (2008).
39. S. Shenoi, S. Heysell, A. Moll, G. Friedland, Curr. Opin. Infect. Dis. **22**, 11 (2009).
40. P.V.D. Driessche, J. Watmough, Math. Biosci. **180**, 29 (2002).
41. C. Castillo-Chavez, B. Song, Math. Biosci. Eng. **1**, 361 (2004).
42. L.J.S. Allen, *An Introduction to Mathematical Biology* (Pearson Education Ltd., USA, 2007).
43. Zindoga Mukandavire, Abba B. Gumel, Winston Garira, Jean Michel Tchuenche, Math. Biosci. Eng. **6**, 333 (2009).
44. S. Lenhart, J.T. Workman, *Optimal Control Applied to Biological Models* (Chapman and Hall, London, 2007).
45. F.B. Agusto, World J. Model. Simul. **5**, 163 (2009).
46. K.O. Okosun, Mirirai Mukamuri, Oluwole Daniel Makinde, Appl. Math. Inf. Sci. **10**, 2137 (2016).
47. C. Bowman, A.B. Gumel, P. van den Driessche, J. Wu, H. Zhu, Bull. Math. Biol. **67**, 1107 (2005).
48. Z. Shuai, J.H. Tien, P. van den Driessche, Bull. Math. Biol. **74**, 2423 (2012).
49. F. Nyabadza, C. Chiyaka, Z. Mukandavire, S.D. Hove-Musekwa, J. Biol. Syst. **18**, 357 (2010).
50. Z. Mukandavire, W. Garira, J. Math. Biol. **54**, 669 (2007).