HIV and COVID-19 co-infection: A mathematical model and optimal control

N. Ringa [a,b,1], M.L. Diagne [c,1], H. Rwezaura [d,1], A. Omame [e,f,*,1], S.Y. Tchoumi [g,1], J.M. Tchuenche [h,i,1]

[a] Data and Analytic Services, British Columbia Centre for Disease Control, 655 W 12th Ave, Vancouver, BC, Canada V5Z 4R4
[b] School of Population and Public Health, University of British Columbia, 2329 West Mall Vancouver, BC, Canada V6T 1Z4
[c] Département de Mathématiques, UFR des Sciences et Technologies, Université de Thiès, BP 967 Thiès, Senegal
[d] Mathematics Department, University of Dar es Salaam, P.O. Box 35062, Dar es Salaam, Tanzania
[e] Department of Mathematics, Federal University of Technology, Owerri, Nigeria
[f] Abdus Salam School of Mathematical Sciences, Government College University Lahore, Pakistan
[g] Department of Mathematics and Computer Sciences ENSAI, University of Ngaoundéré, P.O. Box 455 Ngaoundéré, Cameroon
[h] School of Computer Science and Applied Mathematics, University of the Witwatersrand, Private Bag 3, Wits 2050, Johannesburg, South Africa
[i] School of Computational and Communication Sciences and Engineering, Nelson Mandela African Institution of Science and Technology, P.O. Box 447, Arusha, Tanzania

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ABSTRACT

A new mathematical model for COVID-19 and HIV/AIDS is considered to assess the impact of COVID-19 on HIV dynamics and vice-versa. Investigating the epidemiologic synergy between COVID-19 and HIV is important. The dynamics of the full model is driven by that of its sub-models; therefore, basic analysis of the two sub-models; HIV-only and COVID-19 only is carried out. The basic reproduction number is computed and used to prove local and global asymptotic stability of the sub-models' disease-free and endemic equilibria. Using the *fmincon* function in the Optimization Toolbox of MATLAB, the model is fitted to real COVID-19 data set from South Africa. The impact of intervention measures, namely, COVID-19 and HIV prevention interventions and COVID-19 treatment are incorporated into the model using time-dependent controls. It is observed that HIV prevention measures can significantly reduce the burden of co-infections with COVID-19, while effective treatment of COVID-19 could reduce co-infections with opportunistic infections such as HIV/AIDS. In particular, the COVID-19 only prevention strategy averted about 10,500 new co-infection cases, with similar number also averted by the HIV-only prevention control.

1. Introduction

The new coronavirus disease 2019 (COVID-19) is an ongoing highly viral respiratory infectious disease caused by Severe Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) [1–4], which originated in China in 2019 [5,6], and has since spread to over 280 million people and led to over 5.4 million deaths across the globe [7]. The COVID-19 virus has mutated into several variants including B.1.1.7 (Alpha), P.1 (Gamma), B.1.351 (Beta), B.1.617.2 (Delta) and B.1.1.529 (Omicron), which have varying genomic properties leading to differences in transmissibility and severity of symptoms [8,9]. The primary modes of transmission for COVID-19 are inhalation of infectious respiratory droplets and touching of contaminated body parts or surfaces followed by ingestion of the pathogen [4,10,11]. The natural transition compartments of COVID-19 are susceptible; asymptomatic noninfectious and infectious states; symptomatic infectious states; and removed (by recovery or death) [12,

13]. Each infectious stage of COVID-19 is about 1 to 2 weeks, and there has not been enough data to approximate the length of natural immunity to the disease. Symptoms of COVID-19 include fever or chills, cough, shortness of breath, fatigue, muscle or body aches, headache, loss of taste or smell, sore throat, which may result in mild to severe illness, and death [14]. The severity of symptoms and the risk of hospitalization and death from COVID-19 have been associated with crucial epidemiological properties of a host individual including old age and simultaneous presence of underlying compromising health conditions such as cancer, kidney disease, lung diseases, neurological conditions, diabetes, heart conditions, liver diseases and human immunodeficiency virus (HIV) infection, which are known to weaken the body's ability to fight off the COVID-19 virus [15–18]. Conventional control strategies against COVID-19 are based on contact avoidance measures, including isolation of those who are ill, use of personal protective equipment

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such as gloves and face masks, and physical distancing [19,20], but recently a number of vaccines have been developed and administered to further reduce the risk of COVID-19 transmission. Despite these control measures, currently most countries around the world are experiencing the fourth wave of COVID-19, and efforts to curb the spread are ongoing. The effectiveness of vaccination and other COVID-19 control measures has been challenged by factors such as inadequate vaccine supply, vaccine uptake hesitancy, vaccine efficacy, vaccine waning, non-adherence to public health orders and virus mutation [21].

HIV, which was first discovered in 1981, is a (primarily) sexually transmitted virus that attacks the body's immune systems leading to Acquired Immunodeficiency Syndrome (AIDS) [22]. The virus exists in two main strains HIV-1 and HIV-2, and the former is the principal cause of the pandemic. HIV has led to more than 33 million deaths worldwide and 37.7 million people currently live with the virus [23]. The three main stages of HIV infection are acute HIV infection; chronic HIV infection; and AIDS [24,25]. Acute HIV infection is the earliest stage of HIV infection, and it generally develops within 2 to 4 weeks following infection with the virus. Symptoms of HIV infection at this stage include flu-like symptoms, such as fever, headache and rash. In the acute stage of infection, HIV multiplies rapidly and spreads throughout the body, attacks and destroys the body's infection-fighting CD4 cells, and is highly transmissible. The second stage of HIV infection, chronic HIV infection (also called the clinical latency stage), is characterized by a reduced rate of virus multiplication in the body. This stage can last up to 10 years while, without treatment, an infected individual can transmit the virus, although at a relatively lower rate, to HIV-negative partners during sex. The final and most severe stage of HIV infection is AIDS, which results after the immune system has been severely damaged and the body cannot fight off opportunistic infections. Once a person is diagnosed with AIDS, they can have a high viral load and are able to transmit HIV to others at an increased rate. Without treatment, people with AIDS usually survive about 3 years. Preventative measures against HIV infection include abstinence from unprotected sex, correct use of condoms during sex and limitation of the number of sexual partners [22]. There is no cure for HIV/AIDS. HIV treatment involves taking the HIV medicine called antiretroviral therapy (ART), which works by blocking the replication of the virus in the body and slow down the disease progress [26]. The effective control of HIV has been averted by factors such as challenges in the development of HIV vaccine, nondisclosure of status, lack of HIV testing, lack of awareness of infection, constrained access to treatment, socioeconomic inequalities, limited resources and complacency [27–29].

COVID-19 and HIV co-infection have been reported in the literature [30–34]. Because HIV infection results in an immunosuppressed state, people living with HIV appear to have an increased risk of infection, severity of symptoms, reinfection and death from COVID-19 [35,36], although there has not been enough data to support the observation conclusively. For instance, people living with HIV were more likely to receive a positive diagnosis, and were about 32% and 86% more likely to be admitted to hospital and require mechanical ventilation, respectively, due to COVID-19 infection than those who were HIV-negative [37,38]. However, the increased risk of COVID-19 complications in people living with HIV, has mostly been observed among those with low CD4 cell count, advanced disease, those not taking antiretroviral treatment, and those with other underlying health conditions [39–42]. In this study, the dynamics of COVID-19 and HIV co-infection at the population level in the context of South Africa is explored.

Following the first detection of COVID-19 in South Africa in February 2020, the government moved to implement several control measures, at various points in time, including travel ban, school closures, remote working, restriction of social gatherings, lock downs, curfews and vaccination. Although Africa accounts for just 3.5% of all confirmed cases of COVID-19 globally, South Africa carries a striking 35% of the confirmed cases and 42% of total deaths in the continent [43].

The first case of HIV in South Africa was recorded in 1982. Today, about 95% of people living with HIV, live in developing countries; Sub-Saharan Africa accounts for about 70% of the global burden of HIV infection; and about 20% of the global population of people living with HIV, live in South Africa [44–46].

A lot of mathematical models have been formulated to understand the dynamics of COVID-19 [47–51]. Geographical overlap of COVID-19 with other commodities such as HIV, malaria and TB is of global public health concern. The authors in [52] considered a fractional order model for dual variants of COVID-19 and HIV with bilinear incidence. Herein, a co-infection HIV and COVID-19 co-dynamic model, using the standard incidence rate with optimal control strategies for mitigating the spread of the co-infections is formulated, with South Africa as a case study. The choice of South Africa is two-fold: South Africa has the highest HIV and COVID-19 prevalences in Africa. Mathematical studies of co-infection of COVID-19 and dengue [53], COVID-19 and malaria [54], and COVID-19 and tuberculosis [55,56] are beginning to flourish in the literature. Evidence from past pandemics, as well as emerging evidence specific to COVID-19 suggests that co-infection of both diseases could be a double blow, with potential devastating consequences worldwide.

A mathematical model capturing the potential interplay between transmission dynamics of COVID-19 and HIV in the context of South Africa, a country in which both disease are co-circulating is formulated and analyzed using dynamical systems theory. The choice of South Africa is because it is the most HIV-affected country in the world, and also the most affected COVID-19 country on the African continent. Elaiw et al. [57] analyzed a within-host SARS-CoV and HIV co-infection model with latency. Besides the work in [52], this study is seemingly the first of its kind to theoretically investigate the co-dynamics of COVID-19 and HIV, with specific inclusion of the AIDS compartment into the mathematical model. The impact of key prevention and therapeutic measures, namely, COVID-19 and HIV prevention and COVID-19 treatment are also incorporated into the model using time-dependent controls, and three strategies are explored and results depicted graphically.

The rest of the paper is structured as follows. Our proposed HIV and COVID-19 co-infection model is formulated in Section 2. In Section 3, the HIV and COVID-19 sub-models are analyzed. To mitigate the spread of these two diseases, three time variant controls are incorporated into the full model in Section 4. The optimal control problem is then analyzed using the Pontragyn's maximum principle. Numerical simulations are provided in Section 5, while Section 6 concludes the paper.

2. The model

Consider a homogeneously mixing population. At any time t, the total population $N(t)$ is subdivided into several epidemiological states depending on individuals health status: susceptible $S(t)$, individuals vaccinated against COVID-19 $V(t)$, infectious individuals with COVID-19 $A(t)$, individuals who have recovered from COVID-19 $R(t)$, individuals with HIV $E(t)$, individuals with full blown AIDS $H(t)$, individuals co-infected with COVID-19 and HIV $A_E(t)$, and individuals co-infected with COVID-19 and full blown AIDS $A_H(t)$.

The model assumes that there is an increased

(i.) transmissibility of COVID-19 among co-infected individuals due to increased viral load, and this is represented by the parameter η.

(ii.) susceptibility of HIV/AIDS infected individuals to COVID-19 infection as well as an in-creased transmissibility of HIV/AIDS among co-infected individuals and those with full blown AIDS due to increased viral load.

From Fig. 1, the model is given by the following system of non-linear ordinary differential equations (model parameters are explained in Table 1):

$$\frac{dS}{dt} = \Pi_{\scriptscriptstyle H} - \left(\frac{\chi_1[A + \eta(A_{\scriptscriptstyle H} + A_{\scriptscriptstyle E})]}{N} + \alpha_{\scriptscriptstyle H} + \beta \right. \\ \left. + \frac{\chi_2[E + \varpi(H + A_{\scriptscriptstyle E} + A_{\scriptscriptstyle H})]}{N} \right) S,$$

$$\frac{dV}{dt} = \beta S - \left((1 - \vartheta)\frac{\chi_1[A + \eta(A_{\scriptscriptstyle H} + A_{\scriptscriptstyle E})]}{N} + \alpha_{\scriptscriptstyle H} \right. \\ \left. + \frac{\chi_2[E + \varpi(H + A_{\scriptscriptstyle E} + A_{\scriptscriptstyle H})]}{N} \right) V,$$

$$\frac{dA}{dt} = \frac{\chi_1[A + \eta(A_{\scriptscriptstyle H} + A_{\scriptscriptstyle E})]}{N}[S + (1 - \vartheta)V] \\ - \left(\phi_1 + \frac{\chi_2[E + \varpi(H + A_{\scriptscriptstyle E} + A_{\scriptscriptstyle H})]}{N} + \alpha_{\scriptscriptstyle H} + \delta_1 \right) A,$$

$$\frac{dR}{dt} = \phi_1 A - \left(\alpha_{\scriptscriptstyle H} + \frac{\chi_2[E + \varpi(H + A_{\scriptscriptstyle E} + A_{\scriptscriptstyle H})]}{N} \right) R, \qquad (1)$$

$$\frac{dE}{dt} = \frac{\chi_2[E + \varpi(H + A_{\scriptscriptstyle E} + A_{\scriptscriptstyle H})]}{N}(S + V + R) + \phi_2 A_{\scriptscriptstyle E} \\ - \left(\Lambda_1 \frac{\chi_1[A + \eta(A_{\scriptscriptstyle H} + A_{\scriptscriptstyle E})]}{N} + \gamma_1 + \alpha_{\scriptscriptstyle H} \right) E,$$

$$\frac{dH}{dt} = \gamma_1 E + \phi_3 A_{\scriptscriptstyle H} - \left(\alpha_{\scriptscriptstyle H} + \delta_2 + \Lambda_2 \frac{\chi_1[A + \eta(A_{\scriptscriptstyle H} + A_{\scriptscriptstyle E})]}{N} \right) H,$$

$$\frac{dA_{\scriptscriptstyle E}}{dt} = \frac{\chi_2[E + \varpi(H + A_{\scriptscriptstyle E} + A_{\scriptscriptstyle H})]}{N}A + \Lambda_1 \frac{\chi_1[A + \eta(A_{\scriptscriptstyle H} + A_{\scriptscriptstyle E})]}{N}E \\ - (\gamma_2 + \alpha_{\scriptscriptstyle H} + \phi_2 + \delta_1)A_{\scriptscriptstyle E},$$

$$\frac{dA_{\scriptscriptstyle H}}{dt} = \gamma_2 A_{\scriptscriptstyle E} + \Lambda_2 \frac{\chi_1[A + \eta(A_{\scriptscriptstyle H} + A_{\scriptscriptstyle E})]}{N}H - (\alpha_{\scriptscriptstyle H} + \phi_3 + \delta_3)A_{\scriptscriptstyle H}.$$

3. Model analysis

Due to the strong non-linearity of system (1), it is mathematically intractable to carry out some rigorous mathematical analysis of the full co-infection model. The HIV only and COVID-19 only sub-models shall now be qualitatively analyzed in this section.

3.1. COVID-19 only model

By setting $E(t) = H(t) = A_{\scriptscriptstyle E}(t) = A_{\scriptscriptstyle H}(t) = 0$, in the complete system (1), the following COVID-19 only model is obtained:

$$\frac{dS}{dt} = \Pi_{\scriptscriptstyle H} - \chi_1 \frac{A}{N}S - (\alpha_{\scriptscriptstyle H} + \beta)S,$$

$$\frac{dV}{dt} = \beta S - (1 - \vartheta)\chi_1 \frac{A}{N}V - \alpha_{\scriptscriptstyle H}V,$$

$$\frac{dA}{dt} = \chi_1 \frac{A}{N}S + (1 - \vartheta)\chi_1 \frac{A}{N}V - (\phi_1 + \alpha_{\scriptscriptstyle H} + \delta_1)A, \qquad (2)$$

$$\frac{dR}{dt} = \phi_1 A - \alpha_{\scriptscriptstyle H}R,$$

where $N = S(t) + V(t) + A(t) + R(t)$. Adding up all the equations of the system (2) gives

$$\dot{N}_h = \Pi_{\scriptscriptstyle H} - \alpha_{\scriptscriptstyle H}N - \delta_1 A. \qquad (3)$$

The given initial conditions of the system (2) ensure that $N(0) \geq 0$. Thus, the total human population is positive and bounded for all finite time $t > 0$. Solving the differential equation (3) yields

$$N(t) = N(0)e^{-\alpha_{\scriptscriptstyle H}t} + \frac{\Pi_{\scriptscriptstyle H}}{\alpha_{\scriptscriptstyle H}}(1 - e^{-\alpha_{\scriptscriptstyle H}t}). \qquad (4)$$

As $t \to +\infty$, then $0 \leq N(t) \leq \frac{\Pi_{\scriptscriptstyle H}}{\alpha_{\scriptscriptstyle H}}$. From the theory of differential equations [58,59], in the region

$$\Omega_C = \left\{ (S, V, A, R) \in \mathbb{R}_+^4 : N(t) \leq \frac{\Pi_{\scriptscriptstyle H}}{\alpha_{\scriptscriptstyle H}} \right\},$$

all solutions of the COVID-19 only model autonomous system (2) starting in Ω_C remain in Ω_C for all $t \geq 0$. This implies that Ω_C

is positively invariant and attracting [60]. Thus, the model (2) is mathematically and epidemiologically well-posed, and it is sufficient to study its dynamics in Ω_C [61,62].

3.1.1. Stability of the disease-free equilibrium

The disease-free equilibrium (DFE) of the COVID-19 only model system (2) is obtained by setting each of the system of model system (2) to zero. Also, at the DFE, there are no infections and recovery. Thus, the DFE of the COVID-19 only sub-model (2) is given by

$$\mathcal{E}_{C0} = (S^0, V^0, A^0, R^0) = \left(\frac{\Pi_{\scriptscriptstyle H}}{\alpha_{\scriptscriptstyle H} + \beta}, \frac{\beta}{\alpha_{\scriptscriptstyle H}}\frac{\Pi_{\scriptscriptstyle H}}{\alpha_{\scriptscriptstyle H} + \beta}, 0, 0 \right). \qquad (5)$$

The linear stability of $\mathcal{E}_{C0}$ is established using the next generation operator method on system (2). Using the notations of [63], the basic reproduction number given by

$$R_{0_{cov}} = \frac{\chi_1\alpha_{\scriptscriptstyle H} + (1 - \vartheta)\chi_1\beta}{(\alpha_{\scriptscriptstyle H} + \beta)(\phi_1 + \alpha_{\scriptscriptstyle H} + \delta_1)}. \qquad (6)$$

From Theorem 2 of [63], the following result follows.

Lemma 3.1. *The disease-free equilibrium $\mathcal{E}_{C0}$ of the COVID-19 only model system (2) is locally asymptotically stable if $R_{0_{cov}} < 1$ and unstable otherwise.*

Proof. The stability of $\mathcal{E}_{C0}$ is obtained from the roots of the characteristic polynomial, which states that the equilibrium is stable if the roots of the characteristic polynomial are all negative. For $\mathcal{E}_{C0}$, the Jacobian matrix of the system is obtained as

$$J(\mathcal{E}_{C0}) = \begin{pmatrix} -(\alpha_{\scriptscriptstyle H} + \beta) & 0 & -\frac{\chi_1\alpha_{\scriptscriptstyle H}}{(\alpha_{\scriptscriptstyle H} + \beta)} & 0 \\ \beta & -\alpha_{\scriptscriptstyle H} & -\frac{(1 - \vartheta)\chi_1\beta}{(\alpha_{\scriptscriptstyle H} + \beta)} & 0 \\ 0 & 0 & \frac{\chi_1\alpha_{\scriptscriptstyle H}}{(\alpha_{\scriptscriptstyle H} + \beta)} + \frac{(1 - \vartheta)\chi_1\beta}{(\alpha_{\scriptscriptstyle H} + \beta)} - (\phi_1 + \alpha_{\scriptscriptstyle H} + \delta_1) & 0 \\ 0 & 0 & \phi_1 & -\alpha_{\scriptscriptstyle H} \end{pmatrix}.$$

The eigenvalues of the characteristic are $e_1 = -(\alpha_{\scriptscriptstyle H} + \beta)$, $e_2 = -\alpha_{\scriptscriptstyle H}$, $e_3 = -\alpha_{\scriptscriptstyle H}$ and

$$e_4 = \frac{\chi_1\alpha_{\scriptscriptstyle H}}{(\alpha_{\scriptscriptstyle H} + \beta)} + \frac{(1 - \vartheta)\chi_1\beta}{(\alpha_{\scriptscriptstyle H} + \beta)} - (\phi_1 + \alpha_{\scriptscriptstyle H} + \delta_1).$$

All eigenvalues are negative provided the largest eigenvalue e_4 above which represents the COVID-19 basic reproduction number is negative, that is, if $R_{0_{cov}} < 1$. Hence, the DFE $\mathcal{E}_{C0}$ of the COVID-19 only sub-model (2) is locally asymptotically stable when $R_{0_{cov}} < 1$. ∎

Next, the following result on the global stability of the DFE of the COVID-19 only sub-model (5) is proved using a suitably chosen Lyapunov function.

Theorem 3.1. *The DFE of the COVID-19 only sub-model (2) is globally asymptotically stable whenever $R_{0_{cov}} < 1$.*

Proof. Consider the following Lyapunov function

$$W = A.$$

The time derivative of W computed along the solutions of (10) is given by

$$\dot{W} = \chi_1 \frac{A}{N}S + (1 - \vartheta)\chi_1 \frac{A}{N}V - (\phi_1 + \alpha_{\scriptscriptstyle H} + \delta_1)A.$$

From the HIV only sub-model system (10), as $t \to \infty$,

$$N \to N_\infty = S_\infty + V_\infty + A_\infty + R_\infty \geqslant S_\infty + V_\infty = S^0 + V^0.$$

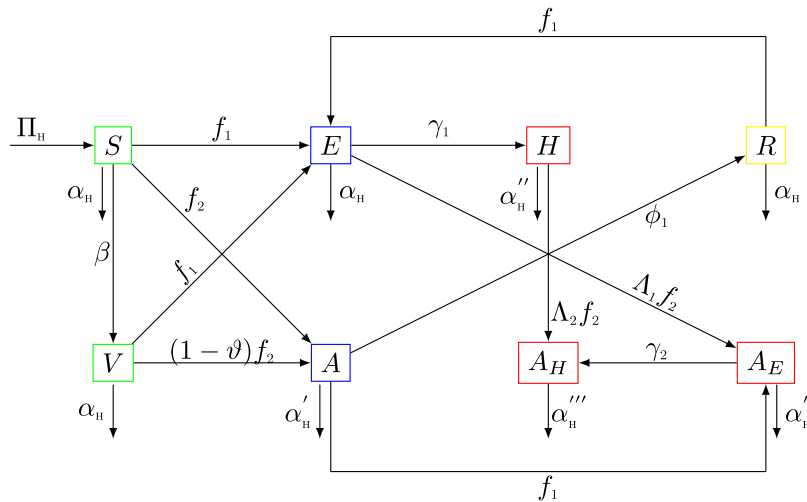Since $S \leqslant S^0$ and $V \leqslant V^0$, the following inequalities which will be used subsequently hold:

Fig. 1. Compartment diagram of the model, where $f_1 = \frac{\chi_2[E + \varpi(H + A_E + A_H)]}{N}$ and $f_2 = \frac{\chi_1[A + \eta(A_H + A_E)]}{N}$ represent respectively the force of infection for COVID-19 and HIV. Also, $\alpha_H' = \alpha_H + \delta_1, \alpha_H'' = \alpha_H + \delta_2, \alpha_H''' = \alpha_H + \delta_3$.

$$\frac{S}{N} \leqslant \frac{S^0}{S^0 + V^0}, \quad \text{and} \quad \frac{V}{N} \leqslant \frac{V^0}{S^0 + V^0}. \text{ Thus,}$$

$$\dot{W} \leqslant \chi_1 A \frac{S^0}{S^0 + V^0} + (1 - \vartheta)\chi_1 A \frac{V^0}{S^0 + V^0} - (\phi_1 + \alpha_H + \delta_1)A,$$

$$\leqslant \frac{\chi_1 \alpha_H}{\alpha_H + \beta} A + \frac{(1 - \vartheta)\chi_1 \beta}{\alpha_H + \beta} A - (\phi_1 + \alpha_H + \delta_1)A,$$

$$\leqslant \left[\frac{\chi_1 \alpha_H}{\alpha_H + \beta} + \frac{(1 - \vartheta)\chi_1 \beta}{\alpha_H + \beta} - (\phi_1 + \alpha_H + \delta_1) \right]A,$$

$$\leqslant \frac{1}{\alpha_H + \beta} \left[\chi_1 \alpha_H + (1 - \vartheta)\chi_1 \beta - (\alpha_H + \beta)(\phi_1 + \alpha_H + \delta_1) \right]A,$$

$$\leqslant \frac{1}{\alpha_H + \beta} \left[R_{0_{cov}}(\alpha_H + \beta)(\phi_1 + \alpha_H + \delta_1) - (\alpha_H + \beta)(\phi_1 + \alpha_H + \delta_1) \right]A,$$

$$\leqslant \frac{(\phi_1 + \alpha_H + \delta_1)}{(\alpha_H + \beta)}(R_{0_{cov}} - 1)A,$$

$$\leqslant 0, \quad \text{for } R_{0_{cov}} \leqslant 1.$$

∎

3.2. Stability of the endemic equilibrium

Solving the COVID-19 only sub-model at an arbitrary equilibrium denoted by $\mathcal{E}_{C1} = (S^\star, V^\star, A^\star, R^\star)$ yields

$$S^\star = \frac{\Pi_H \alpha_H d_2(\theta \lambda_c^\star + \alpha_H)}{\alpha_H d_2(\lambda_c^\star + d_1)(\theta \lambda_c^\star + \alpha_H)},$$

$$V^\star = \frac{\alpha_H \beta d_2 \Pi_H}{\alpha_H d_2(\lambda_c^\star + d_1)(\theta \lambda_c^\star + \alpha_H)},$$

$$A^\star = \frac{\alpha_H \left[\lambda_c^\star \Pi_H(\theta \lambda_c^\star + \alpha_H) + \theta \lambda_c^\star \beta \Pi_H \right]}{\alpha_H d_2(\lambda_c^\star + d_1)(\theta \lambda_c^\star + \alpha_H)}, \qquad (7)$$

$$R^\star = \frac{\phi_1 \left[\lambda_c^\star \Pi_H(\theta \lambda_c^\star + \alpha_H) + \theta \lambda_c^\star \beta \Pi_H \right]}{\alpha_H d_2(\lambda_c^\star + d_1)(\theta \lambda_c^\star + \alpha_H)},$$

where

$$d_1 = \beta + \alpha_H, \quad d_2 = (\phi_1 + \alpha_H + \delta_1), \quad \theta = 1 - \nu,$$

and

$$\lambda_c^\star = \frac{\chi_1 A^\star}{V^\star + V^\star + A^\star + R^\star}. \qquad (8)$$

Substituting (8) into (7), and after some little algebraic manipulations and rearrangements shows that the endemic equilibria of the COVID only sub-model (2) satisfy the following polynomial (in terms of $\lambda_c^\star$)

$$A(\lambda_c^\star)^2 + B\lambda_c^\star + C = 0, \qquad (9)$$

where

$$A = \theta \alpha_H \Pi_H(\phi_1 + \alpha_H),$$
$$B = \theta \Pi_H \beta(\phi_1 + \alpha_H) + \theta \alpha_H \Pi_H d_2 - \chi_1 \theta \alpha_H \Pi_H,$$
$$C = \alpha_H \Pi_H(d_1 d_2 - \chi_1 \theta \beta - \chi_1 \alpha_H) = \alpha_H \Pi_H d_1 d_2(1 - R_{0_{cov}}).$$

For backward bifurcation to occur, multiple non-zero (endemic) equilibria must exist. The quadratic equation (9) can be analyzed for the possibility of multiple equilibria. The coefficient A is always positive, and C is positive (or negative). If $C > 0$, for the model to have two endemic equilibria, B must be negative and $B^2 - 4AC > 0$, however, the coefficient B cannot be negative since the COVID-19 contact rate $\chi_1 < \frac{\beta \phi_1}{\alpha_H} + \beta + d_2$. Hence, the following result is established.

Theorem 3.2. *The COVID-19 only sub-model* (2) *has precisely one unique endemic equilibrium when* $R_{0_{cov}} > 1$.

Note that $R_{0_{cov}} > 1$ implies $C < 0$. The uniqueness of the endemic equilibrium of the COVID-19 only sub-model (2) and the non occurrence of the phenomenon of backward bifurcation imply that this equilibrium is both locally and globally asymptotically stable. Consequently, co-existence of a stable disease-free equilibrium with a stable endemic equilibrium does not hold in the COVID-19 only sub-model, which agrees with similar result in Tchoumi et al. [54].

3.3. HIV only model

By setting $V(t) = A(t) = A_E = A_H(t) = 0$ in the complete system (1), the following HIV only model is obtained:

$$\frac{dS}{dt} = \Pi_H - \chi_2 \frac{E + \varpi H}{N} S - \alpha_H S,$$
$$\frac{dE}{dt} = \chi_2 \frac{E + \varpi H}{N} S - (\gamma_1 + \alpha_H)E, \qquad (10)$$
$$\frac{dH}{dt} = \gamma_1 E - (\alpha_H + \delta_2)H,$$

where $N = S + E + H$.

The feasible region for the model system (10) is

$$\Omega_{HIV} = \left\{ (S, E, H, S_v) \in \mathbb{R}^3_+ : N(t) \leq \frac{\Pi_H}{\alpha_H} \right\},$$

Table 1
Model parameters and variables.

Parameter	Description	Value	Reference
χ_1	COVID-19 contact rate	0.1175	Fitted
χ_2	HIV contact rate	0.3425	[64]
Π_{H}	Recruitment rate	$\frac{39{,}609{,}704}{64.13 \times 365}$	[65]
ϑ	COVID-19 vaccine efficacy	0.95	
β	COVID-19 vaccination rate	0.2	Assumed
η	Modification parameter for increased transmissibility of COVID-19 among co-infected individuals due to increased viral load	1.0	Assumed
γ_1, γ_2	Progression rates to fully developed AIDS by those in compartments E and A_{E}, respectively		
α_{H}	Natural death rate	$\frac{1}{64.13 \times 365}$	[65]
δ_1	COVID-19 induced death rate	0.15	Fitted
δ_2, δ_3	Disease induced death rate for individuals in compartments H and A_{H}, respectively	0.15	Assumed
Λ_1, Λ_2	Modification parameter for susceptibility of HIV/AIDS infected individuals to COVID-19 infection	1.2	[35]
ϖ	modification parameter for increased transmissibility of HIV/AIDS among co-infected individuals and those with full blown AIDS due to increased viral load	1.1	Assumed
ϕ_1	COVID-19 recovery rate for singly-infected	$\frac{1}{15}$	[66]
ϕ_1, ϕ_3	COVID-19 recovery rates for co-infected individuals in compartments A_{E} and A_{H}, respectively	$\frac{1}{15}$	Assumed

which is positively invariant and attracting, that is, solution starting in Ω_m will remain in Ω_{HIV} for all time $t \geq 0$. Thus, it is sufficient to consider the dynamics of the model system (10) in Ω_{HIV}).

3.3.1. Stability of the disease-free equilibrium

The DFE of the HIV only model (10) is given by

$$\mathcal{E}_{HIV_0} = (\bar{S}, \bar{E}, \bar{H}) = \left(\frac{\Pi_{\text{H}}}{\alpha_{\text{H}}}, 0, 0, \right). \tag{11}$$

Using the next generation matrix method in [63], the associated next generation matrix is given by

$$\mathcal{F} = \begin{pmatrix} \chi_2 \frac{E + \varpi H}{N} S \\ 0 \end{pmatrix}, \tag{12}$$

and the rate of transfer of individual to the compartments is given by

$$\mathcal{V} = \begin{pmatrix} (\gamma_1 + \alpha_{\text{H}})E \\ -\gamma_1 E + (\alpha_{\text{H}} + \delta_2)H \end{pmatrix}.$$

Hence, the new infection terms F and the remaining transfer terms V are respectively given by

$$F = \begin{pmatrix} \chi_2 & \chi_2 \varpi \\ 0 & 0 \end{pmatrix},$$

$$V = \begin{pmatrix} (\gamma_1 + \alpha_{\text{H}}) & 0 \\ -\gamma_1 & (\alpha_{\text{H}} + \delta_2) \end{pmatrix},$$

and

$$V^{-1} = \frac{1}{(\gamma_1 + \alpha_{\text{H}})(\alpha_{\text{H}} + \delta_2)} \begin{pmatrix} (\alpha_{\text{H}} + \delta_2) & 0 \\ \gamma_1 & (\gamma_1 + \alpha_{\text{H}}) \end{pmatrix}.$$

The dominant eigenvalue or spectral radius of the next generation matrix FV^{-1} which represents the basic reproductive number is given by

$$R_{0_{HIV}} = \frac{\chi_2(\varpi \gamma_1 + \alpha_{\text{H}} + \delta_2)}{(\gamma_1 + \alpha_{\text{H}})(\alpha_{\text{H}} + \delta_2)}. \tag{13}$$

Next is to prove the global stability of the disease-free equilibrium (11).

Theorem 3.3. *The DFE of the HIV only model (10) is globally asymptotically stable when $R_{0_{HIV}} < 1$.*

Proof. Consider the following Lyapunov function

$$V = (\alpha_{\text{H}} + \delta_2)E + \chi_2 \varpi H.$$

The time derivative of V computed along the solutions of (10) is given by

$$
\begin{aligned}
\dot{V} &= (\alpha_{\text{H}} + \delta_2)\dot{E} + \chi_2 \varpi \dot{H}, \\
&= (\alpha_{\text{H}} + \delta_2)\chi_2 \frac{E + \varpi H}{N} S - (\alpha_{\text{H}} + \delta_2)(\gamma_1 + \alpha_{\text{H}})E, \\
&\quad + \chi_2 \varpi \gamma_1 E - \chi_2 \varpi (\alpha_{\text{H}} + \delta_2)H, \\
&\leqslant (\alpha_{\text{H}} + \delta_2)\chi_2 (E + \varpi H) - (\alpha_{\text{H}} + \delta_2)(\gamma_1 + \alpha_{\text{H}})E, \\
&\quad + \chi_2 \varpi \gamma_1 E - \chi_2 \varpi (\alpha_{\text{H}} + \delta_2)H, \\
&\leqslant (\alpha_{\text{H}} + \delta_2)\chi_2 E - (\alpha_{\text{H}} + \delta_2)(\gamma_1 + \alpha_{\text{H}})E + \chi_2 \varpi \gamma_1 E, \\
&\leqslant \chi_2(\varpi \gamma_1 + \lambda_1 + \alpha_{\text{H}} + \delta_2)E - (\alpha_{\text{H}} + \delta_2)(\gamma_1 + \alpha_{\text{H}})E, \\
&\leqslant R_{0_{HIV}}(\alpha_{\text{H}} + \delta_2)(\gamma_1 + \alpha_{\text{H}})E - (\alpha_{\text{H}} + \delta_2)(\gamma_1 + \alpha_{\text{H}})E, \\
&\leqslant (\alpha_{\text{H}} + \delta_2)(\gamma_1 + \alpha_{\text{H}})E(R_{0_{HIV}} - 1), \\
&\leqslant 0, \quad \text{for } R_{0_{HIV}} \leqslant 1.
\end{aligned}
$$

Because all the model parameters are non-negative, it follows that $\dot{V} \leq 0$ (negative semi-definite) for $R_{0_{HIV}} \leqslant 1$, with $\dot{V} = 0$ if and only if $E = H = 0$. Substituting $(E, H) = (0,0)$ into the HIV only sub-model system (10) shows that $S \to \frac{\Pi_{\text{H}}}{\alpha_{\text{H}}}$ as $t \to \infty$. Hence, V is a Lyapunov function on Ω_{HIV} and the largest compact invariant set in $\{(S, E, H) \in \Omega_{HIV} : \dot{V} = 0\}$ is $\mathcal{E}_{HIV_0}$. Thus, by LaSalle's invariance
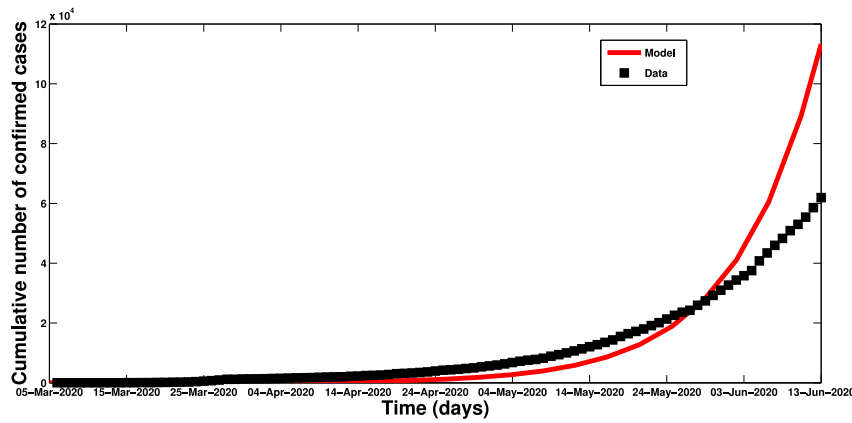
Fig. 2. Fitting of the model to cumulative COVID-19 cases.

principle [67], every solution of (10), with initial conditions in Ω_{HIV} approaches $\mathcal{E}_{HIV_0}$, as $t \to \infty$ whenever $R_{0_{HIV}} \leqslant 1$. ∎

Theorem 3.4. *The HIV only sub-model system (10) has a unique endemic equilibrium if and only if $R_{0_{HIV}} > 1$.*

Proof. Denote the endemic equilibrium by $\mathcal{E}_H = (S^\star, E^\star, H^\star)$, the force of infection at steady state $\lambda_H^\star$ is given by

$$\lambda_H^\star = \chi_2 \frac{E^\star + \varpi H^\star}{S^\star + E^\star + H^\star}. \tag{14}$$

By setting the right hand sides of the sub-model system (10) to zero yields

$$S^\star = \frac{\Pi_{\text{H}} D_1 D_2}{D},$$
$$E^\star = \frac{\Pi_{\text{H}} D_1 \lambda_H^\star}{D}, \tag{15}$$
$$H^\star = \frac{\Pi_{\text{H}} \gamma_1 \lambda_H^\star}{D},$$

where $D_1 = \gamma_1 + \alpha_{\text{H}}$, $D_2 = \lambda_1 + \alpha_{\text{H}} + \delta_2$ and $D = D_1 D_2(\lambda_H^\star + \alpha_{\text{H}})$. Substituting (15) into (14) gives

$$(D_2 + \gamma_1)\lambda_H^\star + D_1 D_2 - \chi_2(\varpi\gamma_1 + \lambda_1 + \alpha_{\text{H}} + \delta_2) = 0. \tag{16}$$

The linear system (16) has a unique positive solution given by

$$\lambda_H^\star = \frac{\chi_2(\varpi\gamma_1 + \lambda_1 + \alpha_{\text{H}} + \delta_2) - D_1 D_2}{(D_2 + \gamma_1)},$$

or after some rearrangement

$$(D_2 + \gamma_1)\lambda_H^\star = D_1 D_2 (R_{0_{HIV}} - 1),$$

which positive or biologically meaningful whenever $R_{0_{HIV}} > 1$. Note that $R_{0_{HIV}} < 1$ implies that $\chi_2(\varpi\gamma_1 + \lambda_1 + \alpha_{\text{H}} + \delta_2) - D_1 D_2 < 0$. In this case the force of infection $\lambda_H^\star$ is negative, which is not feasible. ∎

Now, consider

$$\Omega_{H0} = \{(S, E, H) \in \Omega_{HIV} : E = H = 0\},$$

the following result can be claimed.

Theorem 3.5. *The endemic equilibrium of the HIV only sub-model (10) is globally asymptotically stable (GAS) in $\Omega_{HIV} \setminus \Omega_{H0}$ whenever $R_{0_{HIV}} > 1$.*

Proof. It can be shown, as for the case of Theorem 3.4, that the unique endemic equilibrium for this case exists only if $R_{0_{HIV}} > 1$. Further $N = \frac{\Pi_{\text{H}}}{\alpha_{\text{H}}}$ as $t \to +\infty$.

Using $S = \frac{\Pi_{\text{H}}}{\alpha_{\text{H}}} - E - H$, and substituting into (10) gives the following limiting system

$$\frac{dE}{dt} = \lambda_H \left(\frac{\Pi_{\text{H}}}{\alpha_{\text{H}}} - E - H \right) - (\gamma_1 + \alpha_{\text{H}})E,$$
$$\frac{dH}{dt} = \gamma_1 E - (\alpha_{\text{H}} + \delta_2)H. \tag{17}$$

Using the Dulac's multiplier $\frac{1}{EH}$ (see [62] for further details), it follows that

$$\frac{\partial}{\partial E}\left[\chi_2 \frac{E + \varpi H}{EH \Pi_{\text{H}}/\alpha_{\text{H}}}(\frac{\Pi_{\text{H}}}{\alpha_{\text{H}}} - E - H) - \frac{(\gamma_1 + \alpha_{\text{H}})}{H}\right] + \frac{\partial}{\partial H}\left(\frac{\gamma_1}{H} - \frac{(\alpha_{\text{H}} + \delta_2)}{E}\right)$$
$$= -\left(\frac{\chi_2}{H \Pi_{\text{H}}/\alpha_{\text{H}}} + \frac{\chi_2\beta}{E^2} + \frac{\chi_2\beta H}{E^2 \Pi_{\text{H}}/\alpha_{\text{H}}} + \frac{\gamma_1}{H^2}\right)$$
$$< 0.$$

Thus, by Dulac's criterion, there are no periodic orbits $\in \Omega_{HIV}$. Since Ω_{HIV} is positively invariant, and the endemic equilibrium exists whenever $R_{0_{HIV}} > 1$, then it follows from the Poincare–Bendixson Theorem [58] that all solutions of the limiting system originating in Ω_{HIV} remain in Ω_{HIV} for all t. Further, the absence of periodic orbits in Ω_{HIV} implies that the unique endemic equilibrium of the HIV only sub-model is GAS whenever $R_{0_{HIV}} > 1$. ∎

Because the dynamics of the full model is driven by that of its sub-models, therefore, since both sub-models' equilibria are both locally and globally asymptotically stable, the full HIV–COVID-19 model cannot exhibit the phenomenon of backward bifurcation (where both the disease-free and endemic equilibria co-exist when the basic reproduction number is less than unity) [54,68]. That is, the DFE and endemic equilibria of the full model system (1) exist, are unique, locally and globally asymptotically stable [61,62].

3.4. COVID-19 and HIV model

The feasible region for system (1) is given by $\Omega_{CH} = \Omega_C \times \Omega_{HIV}$, where Ω_C and Ω_{HIV} are already defined in the preceding sections. It can be shown following the approach in [61,62] that all solutions of the complete COVID-19 and HIV model system (1) with non negative initial conditions remain non negative for all time $t \geq 0$. Also, following the theory of permanence in [60], all solutions on the boundary of Ω_{CH} will remain in the interior of Ω_{CH}. Thus, Ω_{CD} is positively-invariant and attracting under the flow induced by the system (1)

3.4.1. Stability of the disease-free equilibrium of the COVID-19 and HIV

The disease-free equilibrium of the HIV–COVID-19 (1) is given by

$$\mathcal{E}_0 = (S, V, I, R, E, H, A_{\text{E}}, A_{\text{H}}) = \left(\frac{\Pi_{\text{H}}}{\alpha_{\text{H}} + \beta}, \frac{\beta}{\alpha_{\text{H}}} \frac{\Pi_{\text{H}}}{\alpha_{\text{H}} + \beta}, 0, 0, 0, 0, 0, 0\right). \tag{18}$$

Since the basic reproduction numbers for the COVID-19 only and HIV only sub-models using the next generation method in [63] have already been derived, the associated reproduction number for the full model system (1) is given by

$$\mathcal{R} = \max \left\{ R_{0_{cov}}, R_{0_{HIV}} \right\}. \tag{19}$$

The following result follows from Theorem 2 in [63].

Theorem 3.6. *The DFE of the COVID-19 and HIV model (1) is locally asymptotically stable if the threshold parameter $\mathcal{R}_0 < 1$, and unstable if $\mathcal{R}_0 > 1$.*

4. Optimal control model

To investigate the impact of intervention measures, time-dependent controls $u_1(t), u_2(t), u_3(t)$ into (1) are incorporated into the model. The controls are defined below:

    i. u_1: COVID-19 prevention control,
    ii. u_2: HIV prevention control,
    iii. u_3: COVID-19 treatment control.

The optimal control system is given by the following system:

$$
\begin{aligned}
\frac{dS}{dt} &= \Pi_{\text{H}} - \left(\frac{(1-u_1)\chi_1[A + \eta(A_{\text{H}} + A_{\text{E}})]}{N} + \alpha_{\text{H}} + \beta \right. \\
&\quad \left. + \frac{(1-u_2)\chi_2[E + \varpi(H + A_{\text{E}} + A_{\text{H}})]}{N} \right) S, \\
\frac{dV}{dt} &= \beta S - \left((1-\vartheta) \frac{(1-u_1)\chi_1[A + \eta(A_{\text{H}} + A_{\text{E}})]}{N} + \alpha_{\text{H}} \right. \\
&\quad \left. + \frac{(1-u_2)\chi_2[E + \varpi(H + A_{\text{E}} + A_{\text{H}})]}{N} \right) V, \\
\frac{dA}{dt} &= \frac{(1-u_1)\chi_1[A + \eta(A_{\text{H}} + A_{\text{E}})]}{N}[S + (1-\vartheta)V] \\
&\quad - \left((1+u_3)\phi_1 + \frac{(1-u_2)\chi_2[E + \varpi(H + A_{\text{E}} + A_{\text{H}})]}{N} + \alpha_{\text{H}} + \delta_1 \right) A, \\
\frac{dR}{dt} &= (1+u_3)\phi_1 A - \left(\alpha_{\text{H}} + \frac{(1-u_2)\chi_2[E + \varpi(H + A_{\text{E}} + A_{\text{H}})]}{N} \right) R, \\
\frac{dE}{dt} &= \frac{(1-u_2)\chi_2[E + \varpi(H + A_{\text{E}} + A_{\text{H}})]}{N}(S + V + R) + (1+u_3)\phi_2 A_{\text{E}} \\
&\quad - \left(\Lambda_1 \frac{(1-u_1)\chi_1[A + \eta(A_{\text{H}} + A_{\text{E}})]}{N} + \gamma_1 + \alpha_{\text{H}} \right) E, \\
\frac{dH}{dt} &= \gamma_1 E + (1+u_3)\phi_3 A_{\text{H}} \\
&\quad - \left(\alpha_{\text{H}} + \delta_2 + \Lambda_2 \frac{(1-u_1)\chi_1[A + \eta(A_{\text{H}} + A_{\text{E}})]}{N} \right) H, \\
\frac{dA_{\text{E}}}{dt} &= \frac{(1-u_2)\chi_2[E + \varpi(H + A_{\text{E}} + A_{\text{H}})]}{N} A \\
&\quad + \Lambda_1 \frac{(1-u_1)\chi_1[A + \eta(A_{\text{H}} + A_{\text{E}})]}{N} E - (\gamma_2 + \alpha_{\text{H}} + (1+u_3)\phi_2 + \delta_1)A_{\text{E}}, \\
\frac{dA_{\text{H}}}{dt} &= \gamma_2 A_{\text{E}} + \Lambda_2 \frac{(1-u_1)\chi_1[A + \eta(A_{\text{H}} + A_{\text{E}})]}{N} H \\
&\quad - (\alpha_{\text{H}} + (1+u_3)\phi_3 + \delta_3)A_{\text{H}}.
\end{aligned}
\tag{20}
$$

subject to the initial conditions $S(0) = S^0, V(0) = V^0, A(0) = A^0, R(0) = R^0, E(0) = E^0, H(0) = H^0, A_{\text{E}}(0) = A_{\text{E}}^0, A_{\text{H}}(0) = A_{\text{H}}^0$.

The following objective function is considered.

$$J[u_1, u_2, u_3] = \int_0^T \left[A(t) + E(t) + H(t) + A_{\text{E}}(t) + A_{\text{H}}(t) + \frac{w_1}{2}u_1^2 + \frac{w_2}{2}u_2^2 + \frac{w_3}{2}u_3^2 \right] dt, \tag{21}$$

where T is the final time.

The goal is to find an optimal control, $u_1^*, u_2^*, u_3^*, u_4^*, u_5^*$, such that

$$J(u_1^*, u_2^*, u_3^*) = min\{J(u_1^*, u_2^*, u_3^*)|u_1, u_2, u_3 \in U\}, \tag{22}$$

where $U = \{(u_1^*, u_2^*, u_3^*)\}$, such that u_1^*, u_2^*, u_3^* are measurable with $0 \leq u_1^* \leq 0.9, 0 \leq u_2^* \leq 0.9, 0 \leq u_3^* \leq 0.9$, for $t \in [0, T]$ is the control set. The Hamiltonian is given by

$$
\begin{aligned}
\mathcal{Z} &= A(t) + E(t) + H(t) + A_{\text{E}}(t) + A_{\text{H}}(t) + \frac{w_1}{2}u_1^2 + \frac{w_2}{2}u_2^2 + \frac{w_3}{2}u_3^2 \\
&\quad + \lambda_1 \left(\Pi_{\text{H}} - \left(\frac{(1-u_1)\chi_1[A + \eta(A_{\text{H}} + A_{\text{E}})]}{N} + \alpha_{\text{H}} + \beta \right. \right. \\
&\quad \left. \left. + \frac{(1-u_2)\chi_2[E + \varpi(H + A_{\text{E}} + A_{\text{H}})]}{N} \right) S \right) \\
&\quad + \lambda_2 \left(\beta S - \left((1-\vartheta) \frac{(1-u_1)\chi_1[A + \eta(A_{\text{H}} + A_{\text{E}})]}{N} + \alpha_{\text{H}} \right. \right. \\
&\quad \left. \left. + \frac{(1-u_2)\chi_2[E + \varpi(H + A_{\text{E}} + A_{\text{H}})]}{N} \right) V \right) \\
&\quad + \lambda_3 \left(\frac{(1-u_1)\chi_1[A + \eta(A_{\text{H}} + A_{\text{E}})]}{N}[S + (1-\vartheta)V] \right. \\
&\quad \left. - \left((1+u_3)\phi_1 + \frac{(1-u_2)\chi_2[E + \varpi(H + A_{\text{E}} + A_{\text{H}})]}{N} + \alpha_{\text{H}} + \delta_1 \right) A \right) \\
&\quad + \lambda_4 \left((1+u_3)\phi_1 A - \left(\alpha_{\text{H}} + \frac{(1-u_2)\chi_2[E + \varpi(H + A_{\text{E}} + A_{\text{H}})]}{N} \right) R \right) \\
&\quad + \lambda_5 \left(\frac{(1-u_2)\chi_2[E + \varpi(H + A_{\text{E}} + A_{\text{H}})]}{N}(S + V + R) + (1+u_3)\phi_2 A_{\text{E}} \right. \\
&\quad \left. - \left(\Lambda_1 \frac{(1-u_1)\chi_1[A + \eta(A_{\text{H}} + A_{\text{E}})]}{N} + \gamma_1 + \alpha_{\text{H}} \right) E \right) \\
&\quad + \lambda_6 \left(\gamma_1 E + (1+u_3)\phi_3 A_{\text{H}} \right. \\
&\quad \left. - \left(\alpha_{\text{H}} + \delta_2 + \Lambda_2 \frac{(1-u_1)\chi_1[A + \eta(A_{\text{H}} + A_{\text{E}})]}{N} \right) H \right) \\
&\quad + \lambda_7 \left(\frac{(1-u_2)\chi_2[E + \varpi(H + A_{\text{E}} + A_{\text{H}})]}{N} A \right. \\
&\quad \left. + \Lambda_1 \frac{(1-u_1)\chi_1[A + \eta(A_{\text{H}} + A_{\text{E}})]}{N} E - (\gamma_2 + \alpha_{\text{H}} + (1+u_3)\phi_2 + \delta_1)A_{\text{E}} \right) \\
&\quad + \lambda_8 \left(\gamma_2 A_{\text{E}} + \Lambda_2 \frac{(1-u_1)\chi_1[A + \eta(A_{\text{H}} + A_{\text{E}})]}{N} H \right. \\
&\quad \left. - (\alpha_{\text{H}} + (1+u_3)\phi_3 + \delta_3)A_{\text{H}} \right).
\end{aligned}
\tag{23}
$$

The full expression of the adjoint functions λ_i' of the optimality system (20) are provided in Appendix.

Theorem 4.1. *Suppose the set $\{u_1, u_2, u_3\}$ minimizes J over U, then the adjoint variables, $\lambda_1, \lambda_2, \ldots, \lambda_8$ satisfy the adjoint equations (where the adjoint functions are given in the Appendix)*

$$-\frac{\partial \lambda_i}{\partial t} = \frac{\partial \mathcal{Z}}{\partial i},$$

with

$$\lambda_i(t_f) = 0, \qquad where, \quad i = S, V, A, R, E, H, A_{\text{E}}, A_{\text{H}}. \tag{24}$$

Furthermore see equations given in Box I.

Proof of Theorem 4.1.

Consider $U^* = (u_1^*, u_2^*, u_3^*)$ and $S^*, V^*, A^*, R^*, E^*, H^*, A_{\text{E}}^*, A_{\text{H}}^*$ being the associated solutions. Pontryagin's maximum principle is applied, such that there exist adjoint variables satisfying:

$$
\begin{aligned}
-\frac{d\lambda_1}{dt} &= \frac{\partial \mathcal{Z}}{\partial S}, \quad \lambda_1(t_f) = 0, \quad -\frac{d\lambda_2}{dt} = \frac{\partial \mathcal{Z}}{\partial V}, \quad \lambda_2(t_f) = 0, \\
-\frac{d\lambda_3}{dt} &= \frac{\partial \mathcal{Z}}{\partial A}, \quad \lambda_3(t_f) = 0, \\
-\frac{d\lambda_4}{dt} &= \frac{\partial \mathcal{Z}}{\partial R}, \quad \lambda_4(t_f) = 0, -\frac{d\lambda_5}{dt} = \frac{\partial \mathcal{Z}}{\partial E}, \quad \lambda_5(t_f) = 0, \\
-\frac{d\lambda_6}{dt} &= \frac{\partial \mathcal{Z}}{\partial H}, \quad \lambda_6(t_f) = 0, \\
-\frac{d\lambda_7}{dt} &= \frac{\partial \mathcal{Z}}{\partial A_{\text{E}}}, \quad \lambda_7(t_f) = 0, \quad -\frac{d\lambda_8}{dt} = \frac{\partial \mathcal{Z}}{\partial A_{\text{H}}}, \quad \lambda_8(t_f) = 0,
\end{aligned}
\tag{26}
$$

$$u_1^* = \min\left\{1, \max\left(0, \frac{\chi_1[A + \eta(A_E + A_H)][S(\lambda_3 - \lambda_1) + (1-\vartheta)V(\lambda_3 - \lambda_2) + E(\lambda_7 - \lambda_5) + H(\lambda_8 - \lambda_2)]}{w_1 N_H}\right)\right\},$$

$$u_2^* = \min\left\{1, \max\left(0, \frac{\chi_2[E + \varpi(A_E + A_H)][S(\lambda_5 - \lambda_1) + V(\lambda_5 - \lambda_2) + R(\lambda_5 - \lambda_4) + A(\lambda_7 - \lambda_3)]}{w_2 N_H}\right)\right\},$$ (25)

$$u_3^* = \min\left\{1, \max\left(0, \frac{A\phi_1(\lambda_3 - \lambda_4) + A_E\phi_2(\lambda_7 - \lambda_5) + A_H\phi_3(\lambda_8 - \lambda_6)}{w_3}\right)\right\}.$$

Box I.

$$u_1^* = \frac{\chi_1[A + \eta(A_E + A_H)][S(\lambda_3 - \lambda_1) + (1-\vartheta)V(\lambda_3 - \lambda_2) + E(\lambda_7 - \lambda_5) + H(\lambda_8 - \lambda_2)]}{w_1 N_H},$$

$$u_2^* = \frac{\chi_2[E + \varpi(A_E + A_H)][S(\lambda_5 - \lambda_1) + V(\lambda_5 - \lambda_2) + R(\lambda_5 - \lambda_4) + A(\lambda_7 - \lambda_3)]}{w_2 N_H},$$

$$u_3^* = \frac{A\phi_1(\lambda_3 - \lambda_4) + A_E\phi_2(\lambda_7 - \lambda_5) + A_H\phi_3(\lambda_8 - \lambda_6)}{w_3},$$ (28)

$$u_1^* = \min\left\{1, \max\left(0, \frac{\chi_1[A + \eta(A_E + A_H)][S(\lambda_3 - \lambda_1) + (1-\vartheta)V(\lambda_3 - \lambda_2) + E(\lambda_7 - \lambda_5) + H(\lambda_8 - \lambda_2)]}{w_1 N_H}\right)\right\},$$

$$u_2^* = \min\left\{1, \max\left(0, \frac{\chi_2[E + \varpi(A_E + A_H)][S(\lambda_5 - \lambda_1) + V(\lambda_5 - \lambda_2) + R(\lambda_5 - \lambda_4) + A(\lambda_7 - \lambda_3)]}{w_2 N_H}\right)\right\},$$ (29)

$$u_3^* = \min\left\{1, \max\left(0, \frac{A\phi_1(\lambda_3 - \lambda_4) + A_E\phi_2(\lambda_7 - \lambda_5) + A_H\phi_3(\lambda_8 - \lambda_6)}{w_3}\right)\right\}.$$

Box II.

with

$\lambda_1(t_f) = \lambda_2(t_f) = \lambda_3(t_f) = \lambda_4(t_f) = \lambda_5(t_f) = \lambda_6(t_f) = \lambda_7(t_f) = \lambda_8(t_f) = 0.$

On the interior of the set, where $0 < u_j < 1$ for all $(j = 1, 2, 3)$,

$$0 = \frac{\partial \mathcal{Z}}{\partial u_1} = w_1 N_H u_1^* - \chi_1[A + \eta(A_E + A_H)][S(\lambda_3 - \lambda_1) + (1-\vartheta)V(\lambda_3 - \lambda_2)$$
$$+ E(\lambda_7 - \lambda_5) + H(\lambda_8 - \lambda_2)],$$

$$0 = \frac{\partial \mathcal{Z}}{\partial u_2} = w_2 N_H u_2^* - \chi_2[E + \varpi(A_E + A_H)][S(\lambda_5 - \lambda_1)$$
$$+ V(\lambda_5 - \lambda_2) + R(\lambda_5 - \lambda_4) + A(\lambda_7 - \lambda_3)],$$

$$0 = \frac{\partial \mathcal{Z}}{\partial u_3} = w_3 N_H u_3^* - [A\phi_1(\lambda_3 - \lambda_4) + A_E\phi_2(\lambda_7 - \lambda_5) + A_H\phi_3(\lambda_8 - \lambda_6)].$$

(27)

Therefore, see equations given in Box II.

5. Numerical simulations

Simulations carried out on the control system (1), adjoint Eqs. (26), and characterizations of the control (29) are run in MATLAB using the forward backward sweep by the Runge Kutta method. The model parameter values used for the simulations are provided in Table 1. Whenever parameter values are not available from the literature or are not estimated/fitted, assumption within realistic ranges are made for a potential scenario in for the purpose of illustration.

The quadratic cost functions $\frac{1}{2}\omega_1 u_1^2$, $\frac{1}{2}\omega_2 u_2^2$ and $\frac{1}{2}\omega_3 u_3^2$ are applied, over time, in order to compute the total cost for each strategy implemented. The weight constants are assumed as follows: $\omega_1 = 1000, \omega_2 = 1200, \omega_3 = 1200$.

The fitting of the model to the cumulative COVID-19 cases for South Africa was done using the *fmincon* function in the Optimization Toolbox of MATLAB [69], and the results are presented in Figs. 2 and 3. The period of the fitting covered 100 days, from March 5, 2020 (when the first case of COVID-19 was confirmed in South Africa) to June 12, 2020. The figures show that our proposed model fits well to the data set.

5.1. Strategy A: Impact of COVID-19 prevention control $(u_1 \neq 0)$

The population of South Africa is estimated to be 60,041,996 [65]. However, the sexually active individuals (aged 15–64) constitute about 66% of the entire population. The initial conditions used for the simulations are set thus: $S(0) = 30,000,000$; $V(0) = 2,000,000$; $A(0) = 300$; $R(0) = 500$; $E(0) = 500$; $H(0) = 1000$; $A_E(0) = 500$, $A_H(0) = 500$.. The simulations of the optimal control system (1) when the strategy that prevents COVID-19 $(u_1 \neq 0)$ is implemented, are respectively depicted in Figs. 4, 5, and 6. On implementation of this intervention strategy, for $\chi_1 = 0.3; \chi_2 = 0.12; \beta = 0, \vartheta = 0, \phi_1 = 1/15; \gamma_1 = 0.15; \delta_1 = 0.15$, so that $\mathcal{R}_0 = \max\{R_{0_{cov}}, R_{0_{HIV}}\} = 1.5993 > 1$, there is a significant decrease in the total number of individuals infected with COVID-19, as expected (shown in Fig. 4). Amazingly, this strategy also has significant impact on co-infected cases. It is observed that, a good number of co-infected cases of COVID-19 and HIV/AIDS are averted by this control strategy (as depicted in Figs. 5 and 6). The control profile for this strategy, shown in Fig. 7, reveals that this control has significant impact throughout the simulation period. The COVID-19 prevention control u_1 in Fig. 7 starts at a nominal value of about 50% and increases gradually to nearly 70% in about 150 days before decreasing. The decrease which corresponds to the end of the first wave of the pandemic, also corresponds to when South Africa returned to alert level 1, with most restrictions either eased or lifted.

5.2. Strategy B: Impact of HIV prevention controls $(u_2 \neq 0)$

The simulations of the optimal control system (1) when the strategy that prevents HIV $(u_2 \neq 0)$ is implemented, are respectively depicted in Figs. 8, 9, 10, and 11. Implementing this intervention strategy, for $\chi_1 = 0.3; \chi_2 = 0.12; \beta = 0, \vartheta = 0, \phi_1 = 1/15; \gamma_1 = 0.15; \delta_1 = 0.15$, so that $\mathcal{R}_0 = \max\{R_{0_{cov}}, R_{0_{HIV}}\} = 1.5993 > 1$, reveals a significant decrease in the total number of individuals infected with HIV, and those infected with full blown AIDS, shown in Figs. 8 and 9. Interestingly, this strategy also has significant impact reducing co-infected cases. It is
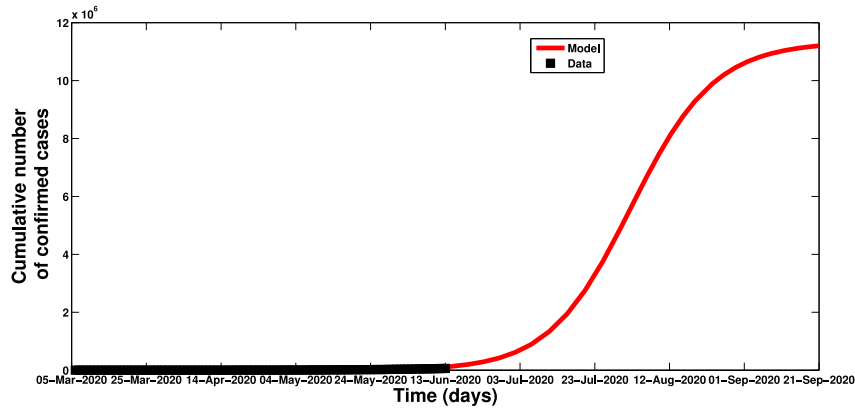
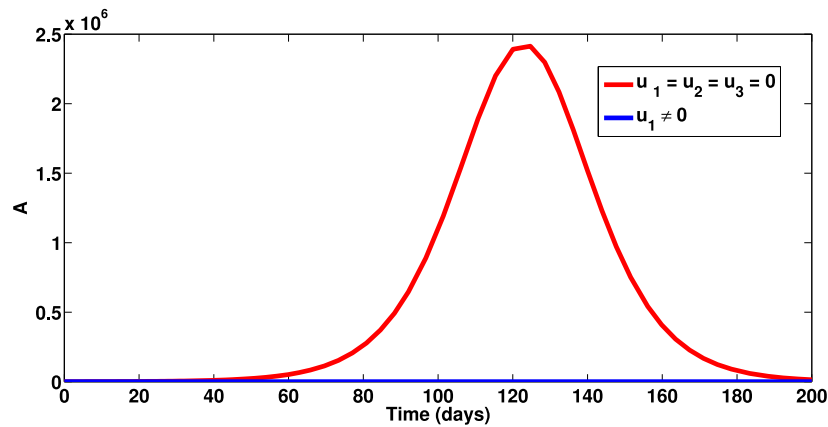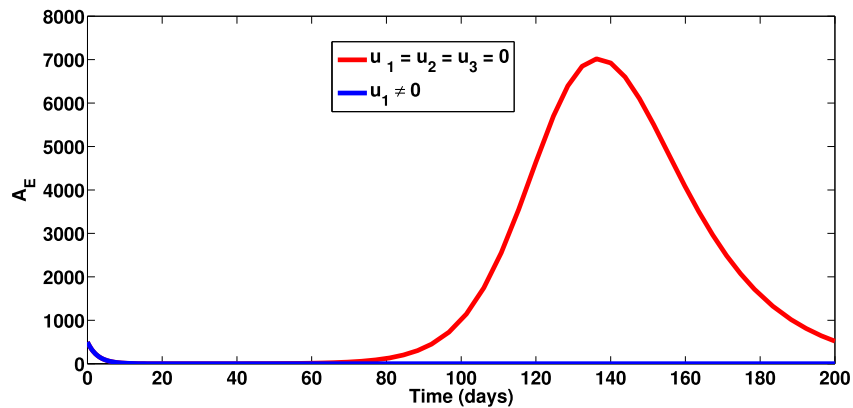**Fig. 3.** Projections for the cumulative COVID-19 cases.

Fig. 4. Impact of COVID-19 prevention on individuals in A epidemiological class. Here, $\chi_1 = 0.3; \chi_2 = 0.12; \beta = 0, \vartheta = 0, \phi_1 = 1/15; \gamma_1 = 0.15; \delta_1 = 0.15$, so that $\mathcal{R}_0 = \max\{R_{0_{cov}}, R_{0_{HIV}}\} = 1.5993 > 1$.

Fig. 5. Impact of COVID-19 prevention on individuals in A_E epidemiological class. Here, $\chi_1 = 0.3; \chi_2 = 0.12; \beta = 0, \vartheta = 0, \phi_1 = 1/15; \gamma_1 = 0.15; \delta_1 = 0.15$, so that $\mathcal{R}_0 = \max\{R_{0_{cov}}, R_{0_{HIV}}\} = 1.5993 > 1$.

observed that, significant co-infected cases of COVID-19 and HIV/AIDS are averted by this control strategy (as depicted in Figs. 10 and 11). The control profile for this strategy, shown in Fig. 12, reveals that this control has significant impact throughout the simulation period. Note that during the first 50 days of the COVID-19 pandemic, HIV prevention measures seems to have suffered greatly as most attention was being diverted to the pandemic with its then several unknown epidemiological characteristics. For HIV prevention to have a positive impact on co-infections, control u_2 should be at its optimum value throughout, see Fig. 12.

5.3. Strategy C: Impact of COVID-19 treatment ($u_3 \neq 0$)

The simulations of the optimal control system (1) when effective COVID-19 treatment strategy ($u_3 \neq 0$) is implemented, are respectively depicted in Figs. 13, 14, and 15. Implementing this intervention strategy, for $\chi_1 = 0.3; \chi_2 = 0.12; \beta = 0, \vartheta = 0, \phi_1 = 1/15; \gamma_1 = 0.15; \delta_1 = 0.15$, so that $\mathcal{R}_0 = \max\{R_{0_{cov}}, R_{0_{HIV}}\} = 1.5993 > 1$, reveals a significant decrease in the total number of individuals infected with COVID-19 (as expected). This is shown in Fig. 13. Furthermore, this strategy also has significant impact reducing co-infected cases. It is observed that, a good number of co-infected cases of COVID-19 and HIV/AIDS
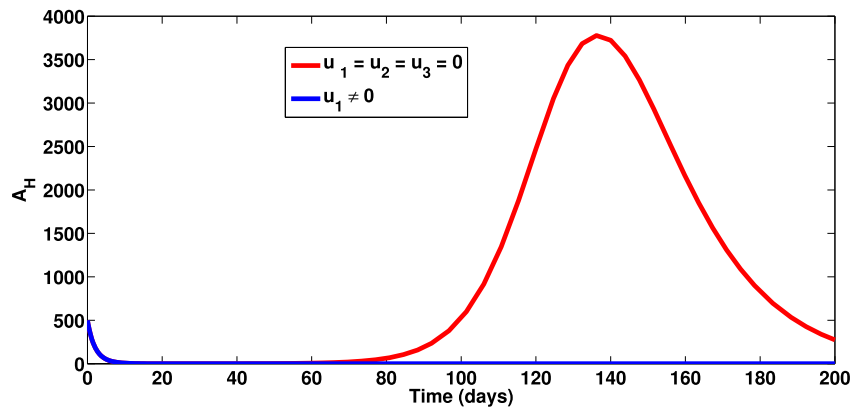
Fig. 6. Impact of COVID-19 prevention on individuals in A_H epidemiological class. Here, $\chi_1 = 0.3; \chi_2 = 0.12; \beta = 0, \vartheta = 0, \phi_1 = 1/15; \gamma_1 = 0.15; \delta_1 = 0.15$, so that $\mathcal{R}_0 = \max\{R_{0_{cov}}, R_{0_{HIV}}\} = 1.5993 > 1$.
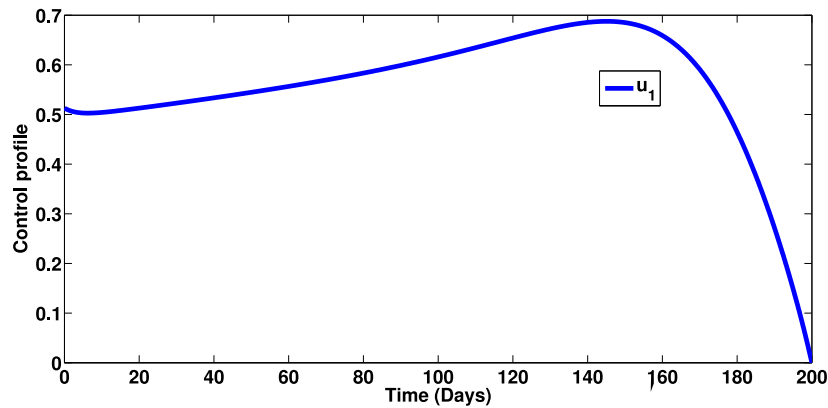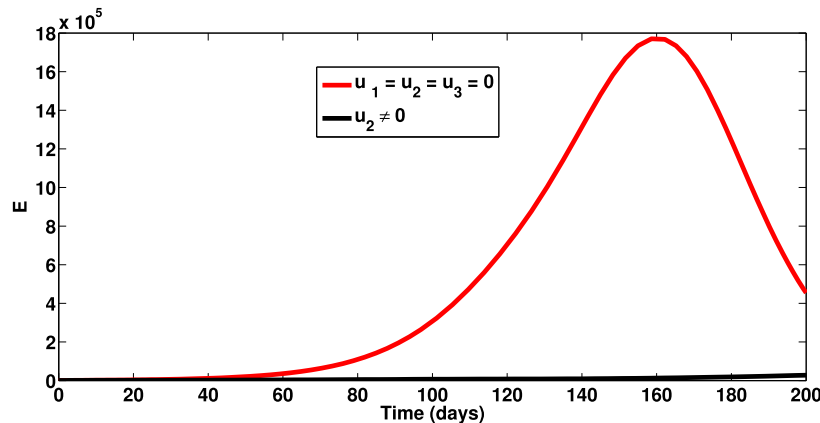

Fig. 7. Control Profile for u_1.

Fig. 8. Impact of HIV prevention on individuals in E epidemiological class. Here, $\chi_1 = 0.3; \chi_2 = 0.12; \beta = 0, \vartheta = 0, \phi_1 = 1/15; \gamma_1 = 0.15; \delta_1 = 0.15$, so that $\mathcal{R}_0 = \max\{R_{0_{cov}}, R_{0_{HIV}}\} = 1.5993 > 1$.

are averted by this control strategy (as depicted in Figs. 14 and 15). Effective treatment for COVID-19 will enhance the immune system of those infected with the disease thereby reducing co-infections with opportunistic infections such as HIV/AIDS. The control profile for this strategy, shown in Fig. 16, reveals that this control has positive impact when properly implemented. Because treatment in the early days of the pandemic was mainly palliative, the profile of u_3 (treatment control) has a somehow strange shape to what one should expect for a treatment profile, but this is not surprising due to the hesitancy as several drugs that were being publicized as potential treatment.

6. Conclusion

COVID-19, a highly viral respiratory infectious disease is an ongoing global public health concern, with several mutated variant strains co-circulating. People living with HIV appear to have an increased risk of infection, severity of symptoms, reinfection and death from COVID-19. COVID-19 wide geographical overlap with HIV/AIDS, and with its high morbidity and mortality, co-infection with both disease could be a double blow (deadly duo), especially due to COVID-19 primary direct and indirect transmission routes (inhalation of infectious droplets, touching of contaminated surfaces, ingestion of the pathogen).
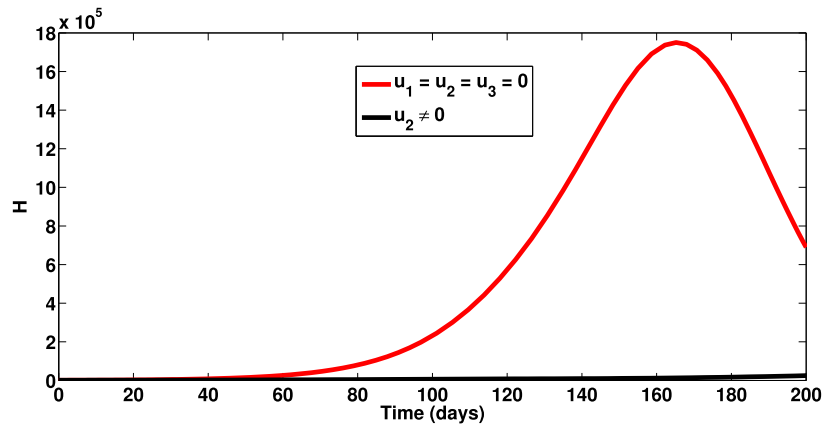
Fig. 9. Impact of HIV prevention on individuals in H epidemiological class. Here, $\chi_1 = 0.3; \chi_2 = 0.12; \beta = 0, \vartheta = 0, \phi_1 = 1/15; \gamma_1 = 0.15; \delta_1 = 0.15$, so that $\mathcal{R}_0 = \max\{R_{0_{cov}}, R_{0_{HIV}}\} = 1.5993 > 1$.

Fig. 10. Impact of COVID-19 prevention on individuals in A_E epidemiological class. Here, $\chi_1 = 0.3; \chi_2 = 0.12; \beta = 0, \vartheta = 0, \phi_1 = 1/15; \gamma_1 = 0.15; \delta_1 = 0.15$, so that $\mathcal{R}_0 = \max\{R_{0_{cov}}, R_{0_{HIV}}\} = 1.5993 > 1$.
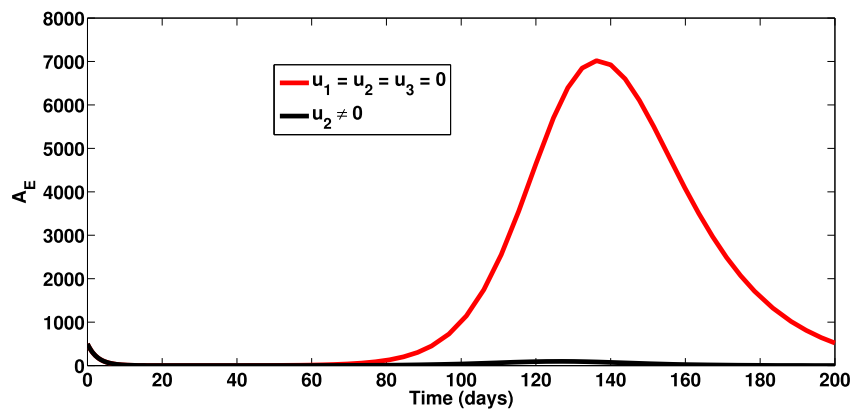

Fig. 11. Impact of COVID-19 prevention on individuals in A_H epidemiological class. Here, $\chi_1 = 0.3; \chi_2 = 0.12; \beta = 0, \vartheta = 0, \phi_1 = 1/15; \gamma_1 = 0.15; \delta_1 = 0.15$, so that $\mathcal{R}_0 = \max\{R_{0_{cov}}, R_{0_{HIV}}\} = 1.5993 > 1$.
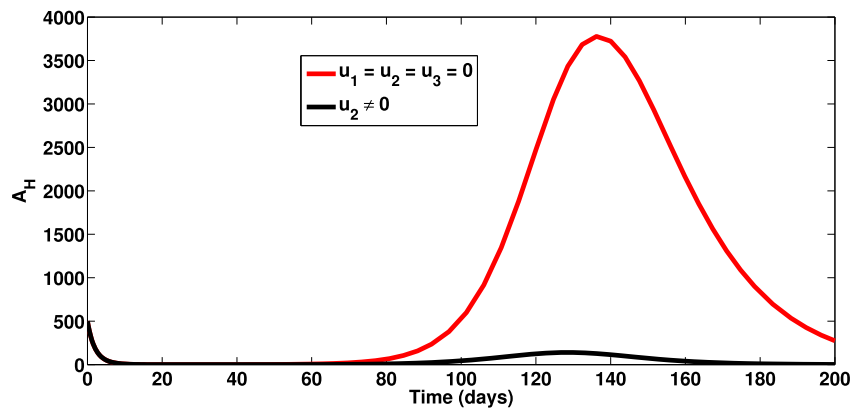
The COVID-19 pandemic has adversely affected the entire world. A seemingly novel mathematical model of the co-infection of COVID-19 and HIV to assess the impact of COVID-19 on HIV dynamics and vice-versa is formulated. The local and global stability analysis of the sub-models are carried out. To control the co-circulation of both diseases adequately under an endemic setting, time dependent controls in the form of COVID-19 prevention and treatment as well as HIV prevention, are incorporated into the model and analyzed via the Pontryagin's maximum principle to establish conditions for the existence of the optimal control problem and the optimality system

for the co-infection model. The model is fitted to real COVID-19 data for South Africa (a country with the co-circulation of both diseases). The simulations shows that COVID-19 prevention could greatly reduce the burden of co-infections with HIV. Also, HIV prevention control can significantly reduce the burden of co-infections with COVID-19, while effective treatment of COVID-19 could enhance the immune system of those infected with the disease, thereby reducing co-infections with opportunistic infections such as HIV/AIDS. These results enable a holistic understanding of the impact of implementing one strategy over the other. Results for each of these strategies are shown graphically.
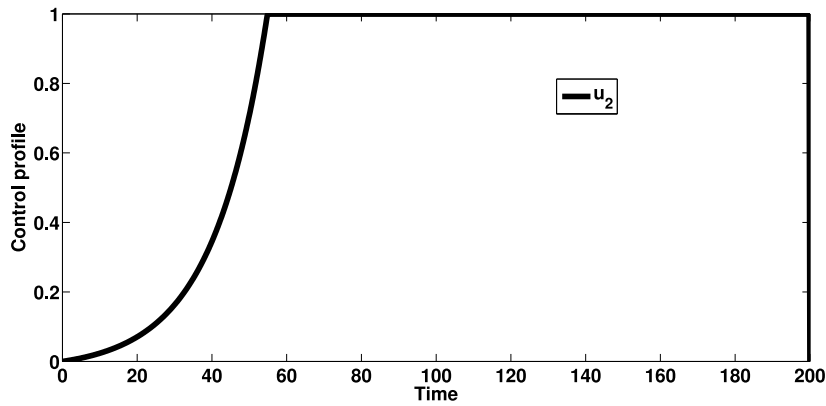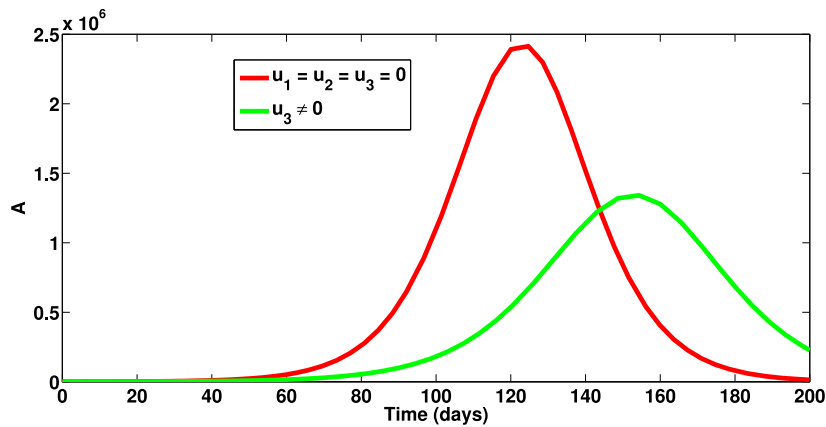
Fig. 12. Control Profile for u_2.

Fig. 13. Impact of COVID-19 treatment on individuals in A epidemiological class. Here, $\chi_1 = 0.3; \chi_2 = 0.12; \beta = 0, \vartheta = 0, \phi_1 = 1/15; \gamma_1 = 0.15; \delta_1 = 0.15$, so that $\mathcal{R}_0 = \max\{R_{0_{cov}}, R_{0_{HIV}}\} = 1.5993 > 1$.

Fig. 14. Impact of COVID-19 treatment on individuals in A_E epidemiological class. Here, $\chi_1 = 0.3; \chi_2 = 0.12; \beta = 0, \vartheta = 0, \phi_1 = 1/15; \gamma_1 = 0.15; \delta_1 = 0.15$, so that $\mathcal{R}_0 = \max\{R_{0_{cov}}, R_{0_{HIV}}\} = 1.5993 > 1$.

The proposed study could be extended to investigate the impact of HIV (palliative) treatment, COVID-19 vaccination as well as cost-effectiveness of the control measures. Also, a study focusing on the in-host dynamics of both diseases is viable.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix. Adjoint functions of the optimality system (20)

$$\lambda_1' = \lambda_5 \left(\frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H\right)\right) \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)} \right.$$
$$- \frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H\right)\right) \left(u_2 - 1\right) \left(S + V + R\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}$$
$$\left. + \frac{E \Lambda_1 \chi_1 \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2} \right)$$
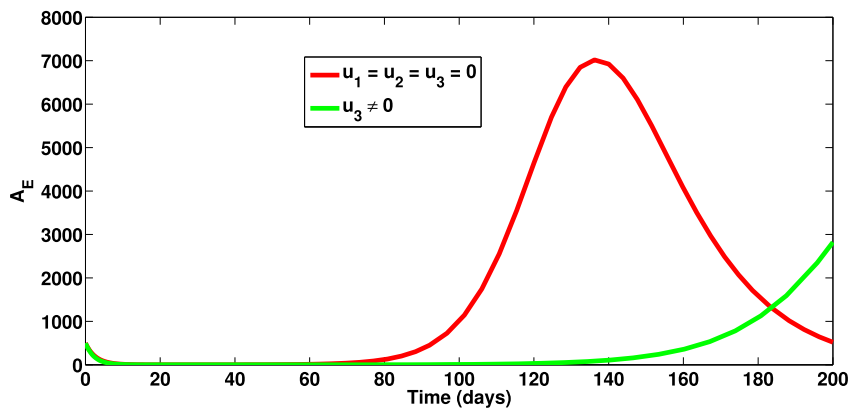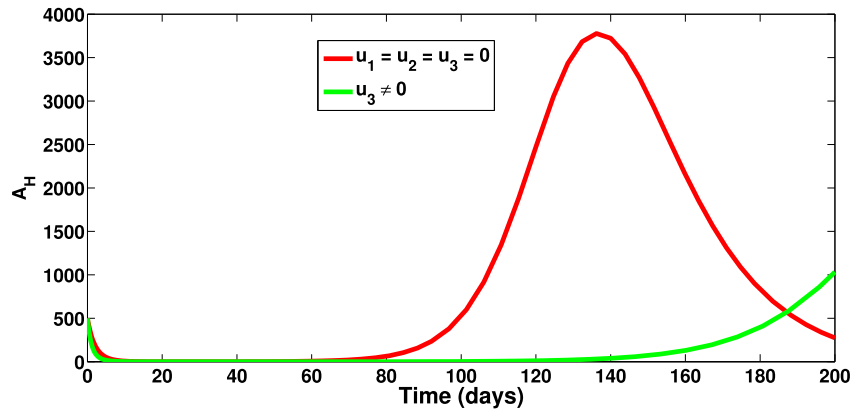
Fig. 15. Impact of COVID-19 treatment on individuals in A_H epidemiological class. Here, $\chi_1 = 0.3; \chi_2 = 0.12; \beta = 0, \vartheta = 0, \phi_1 = 1/15; \gamma_1 = 0.15; \delta_1 = 0.15$, so that $\mathcal{R}_0 = \max\{R_{0_{cov}}, R_{0_{HIV}}\} = 1.5993 > 1$.
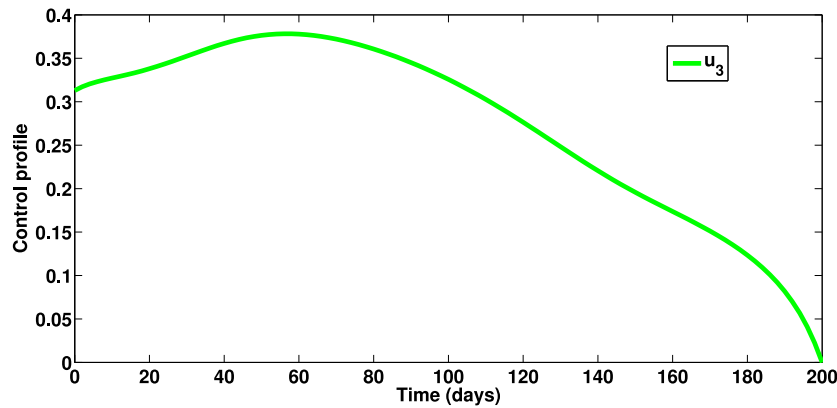

Fig. 16. Control Profile for u_3.

$$
\begin{aligned}
&- \lambda_7 \left(\frac{A\,\chi_2\,(E + \varpi\,(H + A_E + A_H))\,(u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \right. \\
&\quad \left. + \frac{E\,\Lambda_1\,\chi_1\,(A + \eta\,(A_E + A_H))\,(u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \right) \\
&+ \lambda_2 \left(V \left(\frac{\chi_2\,(E + \varpi\,(H + A_E + A_H))\,(u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \right. \right. \\
&\quad \left. \left. - \frac{\chi_1\,(A + \eta\,(A_E + A_H))\,(u_1 - 1)\,(\vartheta - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \right) - \beta \right) \\
&+ \lambda_3 \left(\frac{\chi_1\,(A + \eta\,(A_E + A_H))\,(u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)} \right. \\
&\quad - \frac{\chi_1\,(S - V\,(\vartheta - 1))\,(A + \eta\,(A_E + A_H))\,(u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \\
&\quad \left. + \frac{A\,\chi_2\,(E + \varpi\,(H + A_E + A_H))\,(u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \right) \\
&+ \lambda_1 \left(\alpha_H + S \left(\frac{\chi_2\,(E + \varpi\,(H + A_E + A_H))\,(u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \right. \right. \\
&\quad \left. + \frac{\chi_1\,(A + \eta\,(A_E + A_H))\,(u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \right) \\
&\quad + \beta - \frac{\chi_2\,(E + \varpi\,(H + A_E + A_H))\,(u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)} \\
&\quad \left. - \frac{\chi_1\,(A + \eta\,(A_E + A_H))\,(u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)} \right)
\end{aligned}
$$

$$
\begin{aligned}
&+ \frac{R\,\chi_2\,\lambda_4\,(E + \varpi\,(H + A_E + A_H))\,(u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \\
&+ \frac{H\,\Lambda_2\,\chi_1\,\lambda_6\,(A + \eta\,(A_E + A_H))\,(u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \\
&- \frac{H\,\Lambda_2\,\chi_1\,\lambda_8\,(A + \eta\,(A_E + A_H))\,(u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \\
\lambda_2' = &\; \lambda_5 \left(\frac{\chi_2\,(E + \varpi\,(H + A_E + A_H))\,(u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)} \right. \\
&\quad - \frac{\chi_2\,(E + \varpi\,(H + A_E + A_H))\,(u_2 - 1)\,(S + V + R)}{(S + V + A + R + E + H + A_E + A_H)^2} \\
&\quad \left. + \frac{E\,\Lambda_1\,\chi_1\,(A + \eta\,(A_E + A_H))\,(u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \right) \\
&- \lambda_7 \left(\frac{A\,\chi_2\,(E + \varpi\,(H + A_E + A_H))\,(u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \right. \\
&\quad \left. + \frac{E\,\Lambda_1\,\chi_1\,(A + \eta\,(A_E + A_H))\,(u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \right) \\
&- \lambda_3 \left(\frac{\chi_1\,(S - V\,(\vartheta - 1))\,(A + \eta\,(A_E + A_H))\,(u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \right. \\
&\quad - \frac{A\,\chi_2\,(E + \varpi\,(H + A_E + A_H))\,(u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \\
&\quad \left. + \frac{\chi_1\,(A + \eta\,(A_E + A_H))\,(u_1 - 1)\,(\vartheta - 1)}{(S + V + A + R + E + H + A_E + A_H)} \right)
\end{aligned}
$$

$$+ \lambda_2 \left(\alpha_{\text{H}} + V \left(\frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right. \right.$$

$$\left. - \frac{\chi_1 \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right) \left(\vartheta - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right)$$

$$- \frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)}$$

$$+ \frac{\chi_1 \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right) \left(\vartheta - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)} \right)$$

$$+ S \lambda_1 \left(\frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right.$$

$$\left. + \frac{\chi_1 \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right)$$

$$+ \frac{R \chi_2 \lambda_4 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2}$$

$$+ \frac{H \Lambda_2 \chi_1 \lambda_6 \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2}$$

$$- \frac{H \Lambda_2 \chi_1 \lambda_8 \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2}$$

$$\lambda_3' = \lambda_3 \left(\alpha_{\text{H}} + \delta_1 + \phi_1 \left(u_3 + 1 \right) - \frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)} \right.$$

$$+ \frac{\chi_1 \left(S - V \left(\vartheta - 1 \right) \right) \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)}$$

$$- \frac{\chi_1 \left(S - V \left(\vartheta - 1 \right) \right) \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2}$$

$$+ \frac{A \chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right)$$

$$- \lambda_4 \left(\phi_1 \left(u_3 + 1 \right) - \frac{R \chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right)$$

$$+ \lambda_7 \left(\frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)} \right.$$

$$+ \frac{E \Lambda_1 \chi_1 \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)}$$

$$- \frac{A \chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2}$$

$$- \frac{E \Lambda_1 \chi_1 \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right)$$

$$+ \lambda_8 \left(\frac{H \Lambda_2 \chi_1 \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)} \right.$$

$$- \frac{H \Lambda_2 \chi_1 \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right)$$

$$- \lambda_5 \left(E \left(\frac{\Lambda_1 \chi_1 \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)} \right. \right.$$

$$- \frac{\Lambda_1 \chi_1 \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right)$$

$$+ \frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right) \left(S + V + R \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right)$$

$$+ V \lambda_2 \left(\frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right.$$

$$+ \frac{\chi_1 \left(u_1 - 1 \right) \left(\vartheta - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)}$$

$$- \frac{\chi_1 \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right) \left(\vartheta - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right)$$

$$+ S \lambda_1 \left(\frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right.$$

$$- \frac{\chi_1 \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)}$$

$$+ \frac{\chi_1 \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right)$$

$$- H \lambda_6 \left(\frac{\Lambda_2 \chi_1 \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)} \right.$$

$$\left. - \frac{\Lambda_2 \chi_1 \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right) - 1$$

$$\lambda_4' = \lambda_4 \left(\alpha_{\text{H}} - \frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)} \right.$$

$$\left. + \frac{R \chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right)$$

$$- \lambda_7 \left(\frac{A \chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right.$$

$$\left. + \frac{E \Lambda_1 \chi_1 \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right)$$

$$+ \lambda_5 \left(\frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)} \right.$$

$$- \frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right) \left(S + V + R \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2}$$

$$\left. + \frac{E \Lambda_1 \chi_1 \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right)$$

$$- \lambda_3 \left(\frac{\chi_1 \left(S - V \left(\vartheta - 1 \right) \right) \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right.$$

$$\left. - \frac{A \chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right)$$

$$+ V \lambda_2 \left(\frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right.$$

$$\left. - \frac{\chi_1 \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right) \left(\vartheta - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right)$$

$$+ S \lambda_1 \left(\frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H \right) \right) \left(u_2 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right.$$

$$\left. + \frac{\chi_1 \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2} \right)$$

$$+ \frac{H \Lambda_2 \chi_1 \lambda_6 \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2}$$

$$- \frac{H \Lambda_2 \chi_1 \lambda_8 \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)^2}$$

$$\lambda_5' = \lambda_5 \left(\alpha_{\text{H}} + \gamma_1 + \frac{\chi_2 \left(u_2 - 1 \right) \left(S + V + R \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)} \right.$$

$$- \frac{\Lambda_1 \chi_1 \left(A + \eta \left(A_E + A_H \right) \right) \left(u_1 - 1 \right)}{\left(S + V + A + R + E + H + A_E + A_H \right)}$$

$$- \frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H\right)\right) \left(u_2 - 1\right) \left(S + V + R\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}$$

$$+ \frac{E \Lambda_1 \chi_1 \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}\Bigg)$$

$$- \lambda_3 \Bigg(A \Bigg(\frac{\chi_2 \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)}$$

$$- \frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H\right)\right) \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}\Bigg)$$

$$+ \frac{\chi_1 \left(S - V \left(\vartheta - 1\right)\right) \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}\Bigg)$$

$$- \lambda_6 \Bigg(\gamma_1 - \frac{H \Lambda_2 \chi_1 \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}\Bigg)$$

$$+ \lambda_7 \Bigg(\frac{A \chi_2 \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)}$$

$$+ \frac{\Lambda_1 \chi_1 \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)}$$

$$- \frac{A \chi_2 \left(E + \varpi \left(H + A_E + A_H\right)\right) \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}$$

$$- \frac{E \Lambda_1 \chi_1 \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}\Bigg)$$

$$- V \lambda_2 \Bigg(\frac{\chi_2 \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)}$$

$$- \frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H\right)\right) \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}$$

$$+ \frac{\chi_1 \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right) \left(\vartheta - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}\Bigg)$$

$$+ S \lambda_1 \Bigg(\frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H\right)\right) \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}$$

$$- \frac{\chi_2 \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)}$$

$$+ \frac{\chi_1 \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}\Bigg)$$

$$- R \lambda_4 \Bigg(\frac{\chi_2 \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)}$$

$$- \frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H\right)\right) \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}$$

$$- \frac{H \Lambda_2 \chi_1 \lambda_8 \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2} - 1$$

$$\lambda_6' = \lambda_6 \Bigg(\alpha_H + \delta_2 - \frac{\Lambda_2 \chi_1 \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)}$$

$$+ \frac{H \Lambda_2 \chi_1 \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}\Bigg)$$

$$- \lambda_7 \Bigg(\frac{A \chi_2 \left(E + \varpi \left(H + A_E + A_H\right)\right) \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}$$

$$- \frac{A \chi_2 \varpi \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)}$$

$$+ \frac{E \Lambda_1 \chi_1 \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}\Bigg)$$

$$- \lambda_3 \Bigg(A \Bigg(\frac{\chi_2 \varpi \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)}$$

$$- \frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H\right)\right) \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}\Bigg)$$

$$+ \frac{\chi_1 \left(S - V \left(\vartheta - 1\right)\right) \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}\Bigg)$$

$$+ \lambda_5 \Bigg(\frac{\chi_2 \varpi \left(u_2 - 1\right) \left(S + V + R\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)}$$

$$- \frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H\right)\right) \left(u_2 - 1\right) \left(S + V + R\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}$$

$$+ \frac{E \Lambda_1 \chi_1 \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}\Bigg)$$

$$+ \lambda_8 \Bigg(\frac{\Lambda_2 \chi_1 \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)}$$

$$- \frac{H \Lambda_2 \chi_1 \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}\Bigg)$$

$$- V \lambda_2 \Bigg(\frac{\chi_2 \varpi \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)}$$

$$- \frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H\right)\right) \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}$$

$$+ \frac{\chi_1 \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right) \left(\vartheta - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}\Bigg)$$

$$+ S \lambda_1 \Bigg(\frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H\right)\right) \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}$$

$$- \frac{\chi_2 \varpi \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)}$$

$$+ \frac{\chi_1 \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}\Bigg)$$

$$- R \lambda_4 \Bigg(\frac{\chi_2 \varpi \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)}$$

$$- \frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H\right)\right) \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}\Bigg) - 1$$

$$\lambda_7' = \lambda_5 \Bigg(E \Bigg(\frac{\Lambda_1 \chi_1 \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}$$

$$- \frac{\Lambda_1 \chi_1 \eta \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)}\Bigg)$$

$$- \phi_2 \left(u_3 + 1\right) + \frac{\chi_2 \varpi \left(u_2 - 1\right) \left(S + V + R\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)}$$

$$- \frac{\chi_2 \left(E + \varpi \left(H + A_E + A_H\right)\right) \left(u_2 - 1\right) \left(S + V + R\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}\Bigg)$$

$$- \lambda_8 \Bigg(\gamma_2 + \frac{H \Lambda_2 \chi_1 \left(A + \eta \left(A_E + A_H\right)\right) \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}$$

$$- \frac{H \Lambda_2 \chi_1 \eta \left(u_1 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)}\Bigg)$$

$$+ \lambda_7 \left(\alpha_H + \delta_1 + \gamma_2 + \phi_2 \left(u_3 + 1\right)\right)$$

$$+ \frac{A \chi_2 \varpi \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)}$$

$$- \frac{A \chi_2 \left(E + \varpi \left(H + A_E + A_H\right)\right) \left(u_2 - 1\right)}{\left(S + V + A + R + E + H + A_E + A_H\right)^2}$$

$$- \frac{E \, \Lambda_1 \, \chi_1 \, (A + \eta \, (A_E + A_H)) \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2}$$

$$+ \frac{E \, \Lambda_1 \, \chi_1 \, \eta \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)} \Bigg)$$

$$- \lambda_3 \Bigg(A \Bigg(\frac{\chi_2 \, \varpi \, (u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)}$$

$$- \frac{\chi_2 \, (E + \varpi \, (H + A_E + A_H)) \, (u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \Bigg)$$

$$+ \frac{\chi_1 \, (S - V \, (\vartheta - 1)) \, (A + \eta \, (A_E + A_H)) \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2}$$

$$- \frac{\chi_1 \, \eta \, (S - V \, (\vartheta - 1)) \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)} \Bigg)$$

$$- V \, \lambda_2 \Bigg(\frac{\chi_2 \, \varpi \, (u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)}$$

$$- \frac{\chi_2 \, (E + \varpi \, (H + A_E + A_H)) \, (u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2}$$

$$+ \frac{\chi_1 \, (A + \eta \, (A_E + A_H)) \, (u_1 - 1) \, (\vartheta - 1)}{(S + V + A + R + E + H + A_E + A_H)^2}$$

$$- \frac{\chi_1 \, \eta \, (u_1 - 1) \, (\vartheta - 1)}{(S + V + A + R + E + H + A_E + A_H)} \Bigg)$$

$$- S \, \lambda_1 \Bigg(\frac{\chi_1 \, \eta \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)}$$

$$+ \frac{\chi_2 \, \varpi \, (u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)}$$

$$- \frac{\chi_2 \, (E + \varpi \, (H + A_E + A_H)) \, (u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2}$$

$$- \frac{\chi_1 \, (A + \eta \, (A_E + A_H)) \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \Bigg)$$

$$- R \, \lambda_4 \Bigg(\frac{\chi_2 \, \varpi \, (u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)}$$

$$- \frac{\chi_2 \, (E + \varpi \, (H + A_E + A_H)) \, (u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \Bigg)$$

$$+ H \, \lambda_6 \Bigg(\frac{\Lambda_2 \, \chi_1 \, (A + \eta \, (A_E + A_H)) \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2}$$

$$- \frac{\Lambda_2 \, \chi_1 \, \eta \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)} \Bigg) - 1$$

$$\lambda_8' = \lambda_7 \Bigg(\frac{A \, \chi_2 \, \varpi \, (u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)}$$

$$- \frac{A \, \chi_2 \, (E + \varpi \, (H + A_E + A_H)) \, (u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2}$$

$$- \frac{E \, \Lambda_1 \, \chi_1 \, (A + \eta \, (A_E + A_H)) \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2}$$

$$+ \frac{E \, \Lambda_1 \, \chi_1 \, \eta \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)} \Bigg)$$

$$+ \lambda_6 \Bigg(H \Bigg(\frac{\Lambda_2 \, \chi_1 \, (A + \eta \, (A_E + A_H)) \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2}$$

$$- \frac{\Lambda_2 \, \chi_1 \, \eta \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)} \Bigg) - \phi_3 \, (u_3 + 1) \Bigg)$$

$$+ \lambda_8 \, (\alpha_H + \delta_3 + \phi_3 \, (u_3 + 1))$$

$$- \frac{H \, \Lambda_2 \, \chi_1 \, (A + \eta \, (A_E + A_H)) \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2}$$

$$+ \frac{H \, \Lambda_2 \, \chi_1 \, \eta \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)} \Bigg)$$

$$+ \lambda_5 \Bigg(E \Bigg(\frac{\Lambda_1 \, \chi_1 \, (A + \eta \, (A_E + A_H)) \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2}$$

$$- \frac{\Lambda_1 \, \chi_1 \, \eta \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)} \Bigg) \Bigg).$$

$$+ \frac{\chi_2 \, \varpi \, (u_2 - 1) \, (S + V + R)}{(S + V + A + R + E + H + A_E + A_H)}$$

$$- \frac{\chi_2 \, (E + \varpi \, (H + A_E + A_H)) \, (u_2 - 1) \, (S + V + R)}{(S + V + A + R + E + H + A_E + A_H)^2} \Bigg)$$

$$- \lambda_3 \Bigg(A \Bigg(\frac{\chi_2 \, \varpi \, (u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)}$$

$$- \frac{\chi_2 \, (E + \varpi \, (H + A_E + A_H)) \, (u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \Bigg)$$

$$+ \frac{\chi_1 \, (S - V \, (\vartheta - 1)) \, (A + \eta \, (A_E + A_H)) \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2}$$

$$- \frac{\chi_1 \, \eta \, (S - V \, (\vartheta - 1)) \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)} \Bigg)$$

$$- V \, \lambda_2 \Bigg(\frac{\chi_2 \, \varpi \, (u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)}$$

$$- \frac{\chi_2 \, (E + \varpi \, (H + A_E + A_H)) \, (u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2}$$

$$+ \frac{\chi_1 \, (A + \eta \, (A_E + A_H)) \, (u_1 - 1) \, (\vartheta - 1)}{(S + V + A + R + E + H + A_E + A_H)^2}$$

$$- \frac{\chi_1 \, \eta \, (u_1 - 1) \, (\vartheta - 1)}{(S + V + A + R + E + H + A_E + A_H)} \Bigg)$$

$$- S \, \lambda_1 \Bigg(\frac{\chi_1 \, \eta \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)}$$

$$+ \frac{\chi_2 \, \varpi \, (u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)}$$

$$- \frac{\chi_2 \, (E + \varpi \, (H + A_E + A_H)) \, (u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2}$$

$$- \frac{\chi_1 \, (A + \eta \, (A_E + A_H)) \, (u_1 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \Bigg)$$

$$- R \, \lambda_4 \Bigg(\frac{\chi_2 \, \varpi \, (u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)}$$

$$- \frac{\chi_2 \, (E + \varpi \, (H + A_E + A_H)) \, (u_2 - 1)}{(S + V + A + R + E + H + A_E + A_H)^2} \Bigg) - 1$$

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