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Mathematical Modelling of HIV-HCV Co-infection Dynamics in Presence of HIV Therapy

Edison Mayanja[1,2,*], Livingstone S. Luboobi[3], Juma Kasozi[1], Rebecca N. Nsubuga[4]

[1]Department of Mathematics, Makerere University, Kampala, Uganda
edisonmayanja.phd@gmail.com 0000-0002-8077-3083
kasozi@cns.mak.ac.ug 0000-0002-0941-9604

[2]Department of Economics and Statistics, Kabale University, Kabale, Uganda

[3]Independent Researcher, C/O Department of Mathematics,
Makerere University, Kampala, Uganda
luboobi@gmail.com 0000-0003-0438-9845

[4]Independent Researcher, Kampala, Uganda
nrebeccansubuga@gmail.com 0000-0001-8527-6222

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Abstract: **In this work, we formulated and analysed a deterministic model to study the HIV-HCV co-infection dynamics in presence of HIV therapy. The HCV chronic stage was split into two periods: the period before and the period after onset of cirrhosis. This was done because the HCV chronic stage of infection is long, asymptomatic and infectious. The effective reproduction numbers, one of our outcome measures, were computed using the next generation matrix method. Numerical simulations were performed to support the analytical results from the model. The different parameters in the model were subjected to a sensitivity analysis to determine their relative importance on the HIV-HCV co-infection dynamics. The results indicated that both HIV and HCV infections enhance each other; and in the long run, increasing the rates at which people are put on HIV treatment reduces the prevalence of HCV in the community; however, it increases the prevalence of HIV. Therefore, there should be increased safer sexual behaviour campaigns among individuals on HIV treatment.**

Keywords: **HIV/AIDS, HCV, co-infection, reproduction number, sensitivity analysis, therapy**

I. INTRODUCTION

The human immunodeficiency virus (HIV) and hepatitis C virus (HCV) are a global challenge. These two viruses have a considerable impact on the global morbidity and mortality. HIV is a virus that weakens the immune system by destroying the $CD4^+$ T-cells and hence making it harder for the body to fight off other infections. Hepatitis C infection is a liver disease caused by hepatitis C virus (HCV). Globally, chronic HCV infection is the leading cause of chronic liver disease, and is associated with cirrhosis, hepatocellular carcinoma, and liver failure related mortality [1]. Both HCV and HIV are blood borne viruses caught through exposure to HCV and HIV infected blood, respectively; having common routes of transmission [2, 3], namely by: injection drug use, sexual contact, mother to child transmission during pregnancy or birth, blood and blood products transfusion, organ transplants from infected

*Corresponding author

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donors, and exposure to blood by health care professionals [3].

Several treatment options of HCV exist, however, infection with HCV takes long to manifest unlike infection with HIV. Therefore, most of the individuals infected with HCV may not be aware that they are infected until many years later [4], and thus would not seek for treatment. Screening, diagnosis and treatment of HCV infected individuals remains a global challenge. Globally, in most countries there is: lack of prioritization and hence lack of dedicated budgets or programmes for hepatitis C [5]. According to the Global hepatitis report of 2017 [6], it was revealed that globally, in 2015 of the 71 million people living with HCV: only 20% had been tested for HCV and knew their status (Africa had the lowest proportion diagnosed of 6%); 7% started treatment; and cumulatively, 7.7% had ever received HCV treatment; most of these treatments were older, less effective interferon-based regimens. Unlike in industrialized countries, where it is recommended that all HIV infected patients should be screened for HCV on entry into the healthcare system; in most resource limited countries like Uganda there is no mandatory HCV screening even among HIV infected individuals who are under health care. This is due to the high HCV screening and treatment costs [7, 8]. However, HCV screening is only recommended when investigating whether HCV is the possible cause of liver disease among HIV infected patients [7,9]. This is still the situation in Uganda [9].

HIV and HCV share transmission routes, as such HIV-HCV coinfection is common [10]. In 2015, it was estimated that, globally close to 71 million people were chronically infected with HCV; and of the 36.7 million people that were living with HIV, 2.3 million (6.3%) had been co-infected with HCV [6]. Co-infection with HIV completely changes the dynamics of HCV infection. HIV infection reduces the chance of spontaneous clearance of acute HCV [11], with 80% of the acute HCV infected individuals developing chronic HCV infection [10]. There is rapid progression to cirrhosis and higher rates of liver failure in HIV-HCV co-infected individuals than they are in individuals who are infected with HCV only [11,12]. Cirrhosis has been observed to occur 12 to 16 years earlier in persons co-infected with HCV and HIV [10] compared to the 20 to 30 years in individuals infected with only HCV [7].

In this era of antiretroviral therapy (ART) and in efforts to achieve the 95-95-95 (HIV testing, treatment, and viral suppression) target, numbers of AIDS-related deaths have greatly reduced, hence making HIV infection a chronic illness among individuals infected with only HIV. However, co-infection with HCV complicates the management of HIV by increasing the risk of death among HIV infected individuals. For persons living with HIV and co-infected with HCV, liver-related morbidity and mortality has become the leading cause of non-AIDS-related morbidity and deaths [13]. Furthermore, HIV infected individuals on highly active antiretroviral therapy (HAART) and co-infected with HCV, have slower $CD4^+$ T-cells recovery than those infected with only HIV [14].

Over the years, mathematical models have been applied in the modelling of HIV and its common co-infections such as, Tuberculosis, Malaria, and hepatitis viruses to understand the dynamics of HIV and its co-infections. For example, [2, 3, 11, 12, 15] and [16] developed mathematical models to study the dynamics of HIV-HCV co-infection. Some of these models have considered treatment for both HIV and HCV. These models have either considered HCV infection in stages, namely: acute and chronic or simply HCV infection without considering stages of infection. However, the chronic stage of HCV infection needs to be given a special attention because is very long, asymptomatic and infectious. Recently, Mayanja et al. (2020) [17], formulated and analysed a deterministic model to study the HIV and HCV co-infection dynamics in absence of therapy; but with the HCV chronic stage split into two stages i.e. before and after onset of cirrhosis and its complications. Findings revealed that, in the long run, the number of individuals co-infected with HIV and latent HCV was far greater than that in any other class of individuals. The dynamics of HIV-HCV co-infection in absence of therapy were dominated by HIV. In this work, we extend the work in [17] by introducing HIV treatment and model the dynamics of HIV-HCV co-infection in presence of HIV treatment. Though HIV and HCV may share other transmission routes, in this work we only considered sexual transmission among sexually active individuals as done in [17].

II. MODEL FORMULATION

A. Description of the HIV-HCV co-infection dynamics

We categorized the chronic HCV stage as in [17], that is: latent and advanced HCV, where latent HCV is characterized by a long infectious period during which infection is undiagnosable because there are no or mild symptoms for a long time; and advanced HCV characterized by onset of cirrhosis and its related complications. The total population is divided into eleven distinct compartments, defined as follows: the

susceptible, $S(t)$; infected with HIV without AIDS symptoms and not on HIV treatment, $I_h(t)$; infected with HIV without AIDS symptoms and are on HIV treatment, $I_T(t)$; individuals who have developed AIDS symptoms, $\tilde{A}(t)$; acutely HCV-infected, $I_a(t)$; latent HCV, $I_l(t)$; advanced HCV, $\tilde{B}(t)$; co-infected with HIV and acute HCV, not on HIV treatment, $I_{ha}(t)$; co-infected with HIV and acute HCV, on HIV treatment, $I_{Ta}(t)$; co-infected with HIV and latent HCV, not on HIV treatment, $I_{hl}(t)$; and those co-infected with HIV and latent HCV, on HIV treatment, $I_{Tl}(t)$.

The assumptions regarding the transmission of HIV and HCV are as follows: susceptibles are sexually active individuals at age ***a*** and above (mean age of sexual debut in Uganda is 16 years [18], however, 18 years is the legal age of marriage); HCV or HIV transmission is through sexual acts; for simplicity, we assume that HIV and HCV cannot be transmitted simultaneously; individuals infected with HIV are put on HIV treatment immediately they are diagnosed; individuals in the AIDS class do not revert to earlier classes despite successful treatment; AIDS cases on HIV treatment adhere never to have new sexual partners otherwise practice safe sex if they must, whereas those not on HIV treatment have undergone counselling and do not engage in unprotected sexual activities, similarly, for individuals in the advanced HCV class don't spread diseases.

We suppose that there is a constant recruitment rate Λ into the susceptible class through sexual maturing; and a constant natural mortality at a per capita rate μ in all classes. Susceptible individuals are infected with HCV at per capita rate π_c, which is given by:

$$\pi_c = \frac{\tilde{c}\beta_c[I_a + I_l + \rho(I_{ha} + I_{Ta} + I_{hl} + I_{Tl})]}{N}, \quad (1)$$

where $\tilde{c}$ is the average number of sexual partners acquired per year; β_c is the HCV transmission probability per sexual contact; N is the total active population; and $\rho > 1$ is the enhancement factor for increased risk of being infected with HCV by a dually infected individual. Susceptible individuals are infected with HIV at per capita rate π_h, which is given by:

$$\pi_h = \frac{\tilde{c}\beta_h[I_h + r_3 I_T + \omega(I_{ha} + r_3 I_{Ta} + I_{hl} + r_3 I_{Tl})]}{N}, \quad (2)$$

where β_h is the HIV transmission probability per sexual contact; $r_3 < 1$ is a reduction parameter catering for the reduced risk of being infected with HIV by an HIV infected individual on HIV treatment; and $\omega > 1$ is the enhancement factor for increased risk of being infected with HIV by a dually infected individual. Individuals co-infected with HIV and HCV have higher viral loads of HIV and HCV as compared to those mono infected. This may increase their risk of transmission of each of the viruses [19]. Both ω and ρ model the fact that co-infected individuals are more infectious than their counterparts who are mono infected [12].

When susceptible individuals are infected with HIV, they enter the class of HIV infected not on treatment, $I_h(t)$. Individuals in the class $I_h(t)$, once detected are put on HIV treatment at a rate δ_1 to enter the class $I_T(t)$. Individuals in $I_T(t)$ class, progress to AIDS class ($\tilde{A}$) at a rate $r_2\alpha$, where $r_2 < 1$ is a reduction parameter catering for the reduced risk of progression to AIDS due to HIV treatment. Individuals in class $I_h(t)$, who are not on HIV treatment, progress to AIDS class at a rate α. Apart from natural death, individuals in AIDS class have an additional AIDS-induced death at a per capita rate $\sigma_{\tilde{A}}$. Susceptible individuals once infected with HCV enter the class of acute HCV infected, $I_a(t)$. Some of the Individuals in $I_a(t)$ class, clear acute HCV spontaneously at a rate τ and become susceptible to HCV again. Others who fail to spontaneously clear, progress to latent HCV class, $I_l(t)$, at a rate γ. Then, individuals from $I_l(t)$ progress to advanced HCV class, $\tilde{B}(t)$, at a rate ϕ. Apart from natural death, individuals in class $\tilde{B}(t)$ have an additional advanced HCV-induced death at a per capita rate $\sigma_{\tilde{B}}$.

Since HIV weakens the immune system, this leaves the body more vulnerable to other infections and illnesses. Hence, individuals infected with HIV are at higher risk of contracting HCV than their counterparts without HIV [20]. HIV also increases HCV RNA, thus making sexually active HIV infected individuals at an increased risk of sexual transmission of HCV [21]. Due to HIV and HCV having similar ways of transmission, it means that individuals who are infected with HIV are at a high risk of being infected with HCV and vice versa. Therefore, we included amplification parameters, $k_{i=1,2} > 1$, to cater for the increased risk of getting infected with HCV for those individuals who are already infected with HIV. Amplification parameters, $q_{i=1,2} > 1$, were included to cater for the increased risk of getting infected with HIV for those individuals who are already infected with HCV [12].

A sexual encounter between individuals in classes $I_h(t)$ and $I_a(t)$, is likely to result into a co-infection with HIV and acute HCV, where: individuals who are infected with HIV only and not on HIV treatment, $I_h(t)$, get infected with acute HCV at a rate $k_1\pi_C$ to enter the class of those individuals co-infected with

TABLE I
PARAMETER VALUES USED IN THE NUMERICAL SIMULATIONS OF HIV-HCV CO-INFECTION MODEL.

Parameter	Description	Value	Source
β_h	HIV transmission probability	0.0217 yr^{-1}	Assumed
β_c	HCV transmission probability	0.05 yr^{-1}	[15]
$\tilde{c}$	Average number of sexual partners acquired	4^* yr^{-1}	[17]
θ	Rate of progression from $I_{ha}(t)$ to $I_{hl}(t)$	0.52 yr^{-1}	[17]
α	Rate of progression from HIV to AIDS	0.068^* yr^{-1}	Assumed
ϕ	Rate of progression from I_l to $\tilde{B}$ class	0.095^* yr^{-1}	[17]
μ	Per capita natural mortality rate	0.0158 yr^{-1}	[17]
γ	Rate of progression from I_a to I_l class	2 yr^{-1}	[17]
Λ	Recruitment rate	602095 yr^{-1}	[17]
k_1, k_2	Amplification factor for individuals in I_h and I_T classes, respectively	1.001	[12]
q_1, q_2	Amplification factor for individuals in I_a and I_l classes, respectively	1.0001	[12]
ω	Enhancement factor for increased risk of being infected with HIV by a co-infected individual	1.0002	[15]
ρ	Enhancement factor for increased risk of being infected with HCV by a co-infected individual	1.0002	[12]
τ	Rate of spontaneous clearance of acute HCV	0.27 yr^{-1}	[15]
r_1	Reduction factor for risk of acute HCV spontaneous clearance in presence of co-infection	0.25	[11]
r_2	Reduction factor for progressing from I_T to $\tilde{A}$	0.2	Assumed
r_3	Reduction factor of risk of being infected by an HIV infected individual, on HIV treatment	0.5	Assumed
$\delta_{i=1,2,3}$	Rates at which individuals who are infected with HIV are identified and put on HIV treatment	0.12 yr^{-1}	Assumed
φ	Rate of progression from I_{Ta} to I_{Tl} class	0.52 yr^{-1}	[17]

Parameter values with * have: $\tilde{c} \in [1, 4]$, $\alpha \in [0.066, 0.1]$, $\phi \in [0.095, 0.1]$; yr represents year.

HIV and acute HCV but not on HIV treatment, $I_{ha}(t)$; whereas those who are infected with acute HCV, $I_a(t)$, become co-infected with HIV at a rate $q_1\pi_h$. In addition, some of the individuals who are in class $I_{ha}(t)$ can spontaneously clear acute HCV at a rate $r_1\tau$ and return to the $I_h(t)$ class. These individuals are susceptible to HCV infection again. Due to the fact that the probability of spontaneous clearance of the HCV virus is reduced in case of co-infection [11], a reduction parameter $r_1 < 1$ was introduced to cater for the reduced risk of spontaneous clearance of acute HCV due to the co-infection of acute HCV and HIV.

Some of the individuals in class $I_{ha}(t)$ who fail to spontaneously clear acute HCV, are detected to be co-infected with HIV and are immediately put on HIV treatment at a rate δ_3 to enter the class of dually infected with HIV and acute HCV but on HIV treatment, $I_{Ta}(t)$; whereas those undetected to be co-infected with HIV, progress to dually infected with latent HCV and HIV but not on HIV treatment, $I_{hl}(t)$, at a rate θ. When individuals in classes $I_h(t)$ and $I_l(t)$ sexually interact, individuals who are in the class $I_h(t)$ are likely to become co-infected with acute HCV at a rate $k_1\pi_c$ to enter $I_{ha}(t)$ class whereas individuals in the class $I_l(t)$ are likely to become co-infected with HIV at a rate $q_2\pi_h$ to enter $I_{hl}(t)$ class.

When individuals in classes $I_T(t)$ and $I_a(t)$ sexually interact, individuals who are in the class $I_T(t)$ are likely to become co-infected with acute HCV at a rate $k_2\pi_c$ to enter class $I_{Ta}(t)$; whereas individuals in the class $I_a(t)$ are likely to become co-infected with HIV at a rate $q_1\pi_h$ to enter class $I_{ha}(t)$. When individuals in classes $I_T(t)$ and $I_l(t)$ sexually interact, individuals who are in the class $I_T(t)$ are likely to become co-infected with acute HCV at a rate $k_2\pi_c$ to enter class $I_{Ta}(t)$ whereas individuals in the class $I_l(t)$ are likely to become co-infected with HIV at a rate $q_2\pi_h$ to enter class $I_{hl}(t)$.

Individuals who are dually infected with latent HCV and HIV but not on HIV treatment, $I_{hl}(t)$, are detected and put on HIV treatment at a rate δ_2 to enter the class $I_{Tl}(t)$. Some of the individuals in class $I_{Ta}(t)$ spontaneously clear acute HCV at a rate $r_1\tau$ and return to $I_T(t)$ whereas those who fail to spontaneously clear acute HCV, progress to class $I_{Tl}(t)$ at a rate of φ.

As we summarize the description of the HIV-HCV co-infection dynamics, the parameters presented in the description of HIV-HCV co-infection dynamics in Subsection II-A are summarized in Table I.

B. Compartmental model for the HIV-HCV co-infection dynamics

The HIV-HCV co-infection dynamics are presented in a compartmental diagram (Figure 1).

C. Mathematical model

From the compartmental diagram in Figure 1, the associated mathematical model is shown as a system of differential Equations (3a)–(3k):

$$\frac{dS}{dt} = \Lambda + \tau I_a - \mu S - \pi_c S - \pi_h S, \tag{3a}$$

$$\frac{dI_h}{dt} = \pi_h S + r_1\tau I_{ha} - k_1\pi_c I_h - \delta_1 I_h - \mu I_h - \alpha I_h, \tag{3b}$$

$$\frac{dI_T}{dt} = \delta_1 I_h + r_1\tau I_{Ta} - k_2\pi_c I_T - r_2\alpha I_T - \mu I_T, \tag{3c}$$

$$\frac{dI_a}{dt} = \pi_c S - \tau I_a - q_1\pi_h I_a - \gamma I_a - \mu I_a, \tag{3d}$$

$$\frac{dI_l}{dt} = \gamma I_a - q_2\pi_h I_l - \phi I_l - \mu I_l, \tag{3e}$$

$$\frac{dI_{ha}}{dt} = k_1\pi_c I_h + q_1\pi_h I_a - r_1\tau I_{ha} - \theta I_{ha} - \delta_3 I_{ha} - \mu I_{ha}, \tag{3f}$$

$$\frac{dI_{hl}}{dt} = \theta I_{ha} + q_2\pi_h I_l - \delta_2 I_{hl} - \mu I_{hl}, \tag{3g}$$

$$\frac{dI_{Tl}}{dt} = \delta_2 I_{hl} + \varphi I_{Ta} - \mu I_{Tl}, \tag{3h}$$

$$\frac{dI_{Ta}}{dt} = k_2\pi_c I_T + \delta_3 I_{ha} - \varphi I_{Ta} - \mu I_{Ta} - r_1\tau I_{Ta}, \tag{3i}$$

$$\frac{d\tilde{A}}{dt} = r_2\alpha I_T + \alpha I_h - \sigma_{\tilde{A}}\tilde{A} - \mu\tilde{A}, \tag{3j}$$

$$\frac{d\tilde{B}}{dt} = \phi I_l - \sigma_{\tilde{B}}\tilde{B} - \mu\tilde{B}, \tag{3k}$$

where π_c and π_h are as defined in (1) and (2), respectively. The initial values of the variables of the system (3a)–(3k) are as follows: $S(0) > 0, I_h(0) \geq 0, I_T(0) \geq 0, \tilde{A}(0) \geq 0, I_a(0) \geq 0, I_l(0) \geq 0, \tilde{B}(0) \geq 0, I_{ha}(0) \geq 0, I_{hl}(0) \geq 0$, $I_{Tl}(0) \geq 0$ and $I_{Ta}(0) \geq 0$.

Since we assume that due to diminished immunity, AIDS cases, $\tilde{A}(t)$, and advanced HCV infected cases, $\tilde{B}(t)$, do not engage in sexual activity. As a result, Equations (3a)–(3i) are independent of $\tilde{A}(t)$ and $\tilde{B}(t)$. Therefore, compartments $\tilde{A}$ and $\tilde{B}$ do not feed into any other compartments. Thus, the total active population at time t, N(t), is given by (4):

$$N(t) = S(t) + I_h(t) + I_T(t) + I_a(t) + I_l(t) + I_{ha}(t) + I_{hl}(t) + I_{Tl}(t) + I_{Ta}(t). \tag{4}$$

III. MODEL ANALYSIS AND RESULTS

A. Positivity and boundedness of solutions of HIV-HCV co-infection model

It is important to establish whether system (3a)–(3i) is well posed and biologically meaningful. A study of the non-negativity and boundedness properties of the solutions of the HIV-HCV co-infection model (3a)–(3i) is made in this Subsection.

Lemma 1. *The solutions $S(t)$, $I_h(t)$, $I_T(t)$, $I_a(t)$, $I_l(t)$, $I_{ha}(t)$, $I_{hl}(t)$, $I_{Tl}(t)$, $I_{Ta}(t)$ of the system (3a)–(3i) are non-negative for $t \geq 0$.*

Proof: Let the initial values of the variables of the system (3a)–(3i) be non-negative with $S(0) > 0$. We prove that the solution component of $S(t)$ remains positive. Assume that there exists a first time $t_1 : S(t_1) = 0$, $S'(t_1) < 0$ and $S(t) > 0, I_h(t) > 0, I_T(t) > 0, I_a(t) > 0, I_l(t) > 0, I_{ha}(t) > 0, I_{hl}(t) > 0, I_{Tl}(t) > 0$, $I_{Ta}(t) > 0$ for $0 < t < t_1$.

From (3a) of the system, we have:

$$\frac{dS(t_1)}{dt} = \Lambda + \tau I_a(t_1) > 0,$$

which is a contradiction and consequently $S(t)$ remains positive. The non-negativity of the other variables can similarly be proved. ■

Therefore, the solutions of the system are non-negative for $t \geq 0$.

Lemma 2 (Invariant region)**.** *The region*

$$\Omega = \Big\{(S(t), I_h(t), I_T(t), I_a(t), I_l(t), I_{ha}(t), I_{hl}(t), I_{Tl}(t), I_{Ta}(t)) \in R_+^9 : N(t) \leq \max\Big\{N_0, \frac{\Lambda}{\mu}\Big\}\Big\},$$

is positively invariant and attracting with respect to the model.

Proof: Let

$$(S(t), I_h(t), I_T(t), I_a(t), I_l(t), I_{ha}(t), I_{hl}(t), I_{Tl}(t), I_{Ta}(t)) \in R_+^9$$

be any solution of the system with non-negative initial condition given by

$$(S(0), I_h(0), I_T(0), I_a(0), I_l(0), I_{ha}(0), I_{hl}(0), I_{Tl}(0), I_{Ta}(0)).$$

Adding Equations (3a)–(3i), gives:

$$\frac{dN}{dt} = \Lambda - \mu N - \alpha I_h(t) - r_2\alpha I_T - \phi I_l. \tag{5}$$

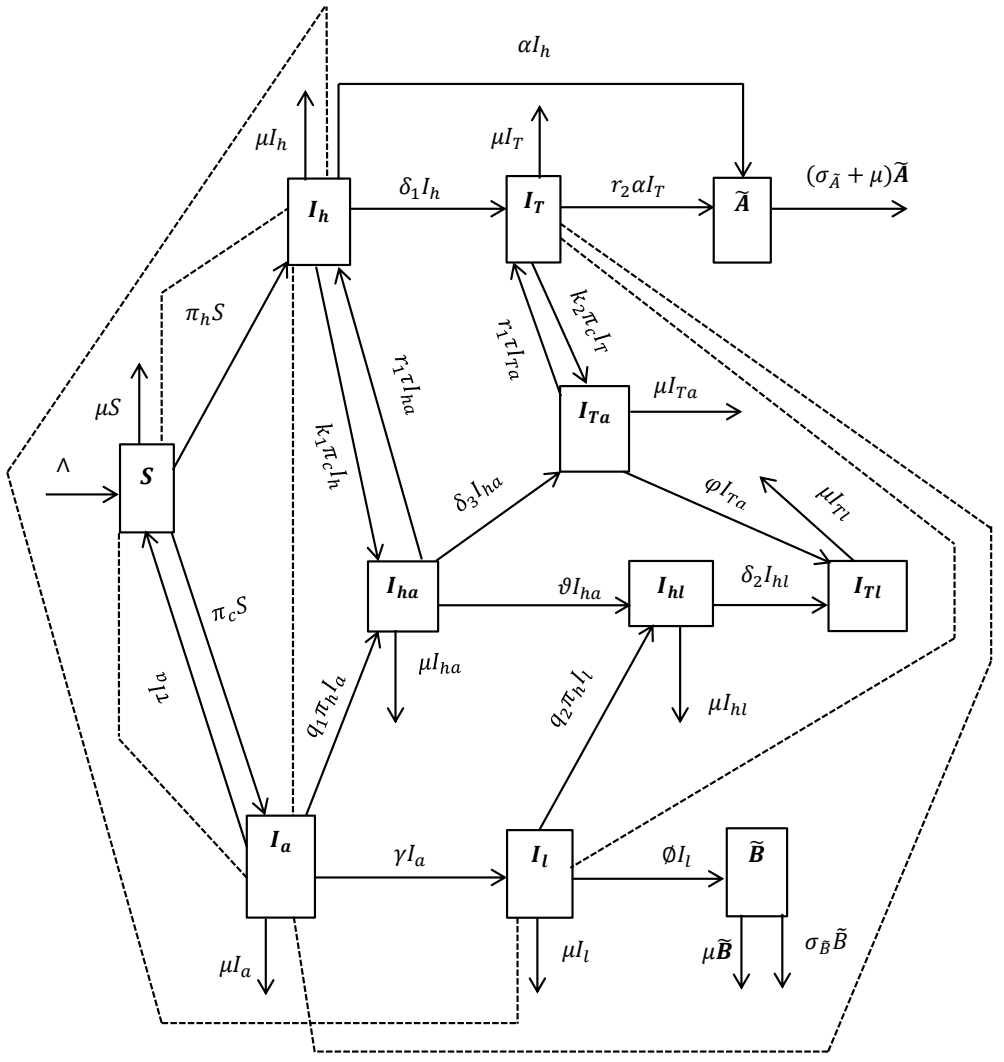


Fig. 1. Compartmental diagram for HIV-HCV co-infection dynamics. Solid arrows indicate movement from one compartment to another whereas dashed connections indicate the interaction between the connected compartments.

For $I_h(t), I_T(t), I_l(t) \geq 0$ for $t \geq 0$, (5) reduces to:

$$\frac{dN(t)}{dt} \leq \Lambda - \mu N, \tag{6}$$

from which

$$N(t) \leq \frac{\Lambda}{\mu} + \left(N_0 - \frac{\Lambda}{\mu}\right) e^{-\mu t} \tag{7}$$

where $N_0 \geq 0$ is the initial total population size.

Two observations are made:

I: If $N_0 > \frac{\Lambda}{\mu}$, then (7) implies $N(t) \leq N_0$ for all values of t.

II: If $N_0 < \frac{\Lambda}{\mu}$, then (7) implies $N(t) \leq \frac{\Lambda}{\mu}$ for all values of t.

Therefore, $N(t) \leq \max\{N_0, \frac{\Lambda}{\mu}\}$ for all values of $t \geq 0$. Hence, every feasible solution of the model system that starts in the region Ω remains in the region for all values of t. Thus, the region Ω is biologically feasible and positively invariant. ■

Therefore, the model is epidemiologically and mathematically well posed.

Before analysing the dynamics of the HIV-HCV co-infection model (3a)–(3i), it is instructive to first analyse the HIV-only and HCV-only submodels. This is done in the Subsections III-B, III-C and III-D.

B. The HIV-only submodel

We set $I_a(t) = I_l(t) = I_{ha}(t) = I_{hl}(t) = I_{Tl}(t) = I_{Ta}(t) = 0$ in system (3a)–(3i), thus the HIV-only submodel is as in (8a)–(8c):

$$\frac{dS_{HIV}}{dt} = \Lambda - \pi_h S_{HIV} - \mu S_{HIV}, \tag{8a}$$

$$\frac{dI_h}{dt} = \pi_h S_{HIV} - \alpha I_h - \delta_1 I_h - \mu I_h, \tag{8b}$$

$$\frac{dI_T}{dt} = \delta_1 I_h - r_2\alpha I_T - \mu I_T, \tag{8c}$$

where

$$\pi_h = \frac{\tilde{c}\beta_h[I_h + r_3 I_T]}{N_{HIV}} \tag{9}$$

and

$$N_{HIV} = S_{HIV} + I_h + I_T. \tag{10}$$

1) The HIV-free equilibrium and effective reproduction number: The HIV-free equilibrium point, ε^0_{HIV}, for system (8a)–(8c) is obtained by setting the right-hand side of system (8a)–(8c) equal to zero, and hence is found to be: $\varepsilon^0_{HIV} = (S^0_{HIV}, I^0_h, I^0_T) = (\frac{\Lambda}{\mu}, 0, 0)$.

The effective reproduction number is defined as the spectral radius of the next generation matrix [23]. As interpreted in [12], it is the "expected number of secondary infections produced by a single infectious individual during his/her entire infectious period in the presence of an intervention strategy".

Using the next generation matrix method [23], we obtain the Jacobian matrices of new HIV infections, F_{HIV}, and for the rate of transfer into and out of compartment i by all other processes, V_{HIV}, evaluated at HIV-free equilibrium as:

$$F_{HIV} = \begin{bmatrix} \tilde{c}\beta_h & \tilde{c}\beta_h r_3 \\ 0 & 0 \end{bmatrix}$$

and

$$V_{HIV} = \begin{bmatrix} (\delta_1 + \alpha + \mu) & 0 \\ -\delta_1 & (r_2\alpha + \mu) \end{bmatrix}.$$

The effective reproduction number of the HIV-only submodel, R_{HIV}, is given by the spectral radius of the next generation matrix, $F_{HIV}V^{-1}_{HIV}$. That is,

$$R_{HIV} = \frac{\tilde{c}\beta_h}{(\delta_1 + \alpha + \mu)}\left(1 + \frac{r_3\delta_1}{(r_2\alpha + \mu)}\right). \tag{11}$$

Expressing (11) as:

$$\begin{aligned} R_{HIV} &= \frac{\tilde{c}\beta_h}{(r_2\alpha + \mu)}\left(\frac{r_2\alpha + \mu + r_3\delta_1}{\delta_1 + \mu + \alpha}\right) \\ &= \frac{\tilde{c}\beta_h}{(r_2\alpha + \mu)} f(\delta_1), \end{aligned} \tag{12}$$

in which

$$f(\delta_1) = \left(\frac{r_2\alpha + \mu + r_3\delta_1}{\delta_1 + \mu + \alpha}\right) = \frac{i + r_3\delta_1}{g + \delta_1}, \tag{13}$$

where $i = r_2\alpha + \mu$ and $g = \alpha + \mu$. Now,

$$\lim_{\delta_1 \to +\infty} f(\delta_1) = r_3 \quad \text{and} \quad \lim_{\delta_1 \to 0} f(\delta_1) = \frac{i}{g}. \tag{14}$$

From (12) and (14), we deduce that, varying δ_1 alone while other parameters are kept fixed, R_{HIV} is bounded, that is:

$$R_{HIV}(\delta_1) \leq \frac{\tilde{c}\beta_h}{(r_2\alpha + \mu)} \max\left\{\frac{i}{g}, r_3\right\}. \tag{15}$$

Using Theorem 2 in [23], the following result follows.

Theorem 1. *The HIV-free equilibrium ε^0_{HIV} is locally asymptotically stable if $R_{HIV} < 1$ and unstable otherwise.*

We can establish the following results using, for instance, the techniques in [17]:

Theorem 2. *The HIV-free equilibrium ε^0_{HIV} is globally-asymptotically stable whenever $R_{HIV} < 1$.*

Theorem 3. *The HIV-only submodel has a unique endemic equilibrium if and only if $R_{HIV} > 1$.*

The global stability property of the endemic equilibrium of the HIV-only submodel can be investigated using the techniques in [17].

C. The HCV-only submodel

To obtain the HCV-only submodel, we set $I_h(t) = I_T(t) = I_{ha}(t) = I_{hl}(t) = I_{Tl}(t) = I_{Ta}(t) = 0$ in (3a)–(3i). Thus, we obtain:

$$\frac{dS_{HCV}}{dt} = \Lambda + \tau I_a - \pi_c S_{HCV} - \mu S_{HCV}, \tag{16a}$$

$$\frac{dI_a}{dt} = \pi_c S_{HCV} - \gamma I_a - \tau I_a - \mu I_a, \tag{16b}$$

$$\frac{dI_l}{dt} = \gamma I_a - \mu I_l - \phi I_l, \tag{16c}$$

where

$$\pi_c = \frac{\tilde{c}\beta_c[I_a + I_l]}{N_{HCV}} \quad \text{and} \quad N_{HCV} = S_{HCV} + I_a + I_l. \tag{17}$$

Basic reproduction number: The HCV-only submodel has a basic reproduction number, R_{HCV}, as derived in [17], is given by:

$$R_{HCV} = \frac{\tilde{c}\beta_c}{(\gamma + \tau + \mu)}\Big(1 + \frac{\gamma}{(\mu + \phi)}\Big). \tag{18}$$

In [17], it is deduced that, keeping other parameters constant and varying γ alone, R_{HCV} is bounded. That is:

$$R_{HCV}(\gamma) \leq \frac{\tilde{c}\beta_c}{(\mu+\phi)}\max\Big\{\frac{d}{e},1\Big\}, \tag{19}$$

where $d=\mu+\phi$ and $e=\mu+\tau$.

Existence and stability of HCV-free and HCV endemic equilibria: The existence of HCV-free and HCV endemic equilibria and their stability is as studied in [17].

D. The disease-free equilibrium and effective reproduction number for the HIV-HCV co-infection model

The disease-free equilibrium of the HIV-HCV co-infection model (3a)–(3i) is given by:

$$\begin{aligned}\varepsilon^0 &= (S^{0f}, I_h^{0f}, I_T^{0f}, I_a^{0f}, I_l^{0f}, I_{ha}^{0f}, I_{hl}^{0f}, I_{Tl}^{0f}, I_{Ta}^{0f})\\ &= \Big(\frac{\Lambda}{\mu},0,0,0,0,0,0,0,0\Big).\end{aligned}$$

Using the next generation matrix method [23] on model Equations (3a)–(3i), we obtain Jacobian of new infections matrix at disease free-equilibrium $\tilde{F}$ as:

$$\begin{bmatrix}\tilde{c}\beta_h & \tilde{c}\beta_h r_3 & 0 & 0 & n_1 & n_1 & n_1 r_3 & n_1 r_3\\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & \tilde{c}\beta_c & \tilde{c}\beta_c & \tilde{c}\beta_c\rho & \tilde{c}\beta_c\rho & \tilde{c}\beta_c\rho & \tilde{c}\beta_c\rho\\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\end{bmatrix}$$

where $n_1 = \tilde{c}\beta_h\omega$; and the Jacobian matrix for the rate of transfer from one compartment to another by all other processes at disease-free equilibrium V as:

$$V = \begin{bmatrix} a_1 & 0 & 0 & 0 & -r_1\tau & 0 & 0 & 0\\ -\delta_1 & a_2 & 0 & 0 & 0 & 0 & 0 & -r_1\tau\\ 0 & 0 & a_3 & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & -\gamma & a_4 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & a_5 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & -\theta & a_6 & 0 & 0\\ 0 & 0 & 0 & 0 & 0 & -\delta_2 & a_7 & -\varphi\\ 0 & 0 & 0 & 0 & -\delta_3 & 0 & 0 & a_8\end{bmatrix}$$

where

$$\begin{aligned} a_1 &= (\delta_1+\alpha+\mu), & a_2 &= (r_2\alpha+\mu),\\ a_3 &= (\gamma+\tau+\mu), & a_4 &= (\phi+\mu),\\ a_5 &= (r_1\tau+\theta+\delta_3+\mu), & a_6 &= (\delta_2+\mu),\\ a_7 &= \mu, & a_8 &= (\varphi+\mu+r_1\tau).\end{aligned}$$

The effective reproduction number, R_0, for the HIV-HCV co-infection model is the maximum of eigenvalues of the next generation matrix $\tilde{F}V^{-1}$:

$$\begin{aligned}\lambda_1 &= \frac{\tilde{c}\beta_h}{(\delta_1+\mu+\alpha)}\Big(1+\frac{r_3\delta_1}{(r_2\alpha+\mu)}\Big),\\ \lambda_2 &= \frac{\tilde{c}\beta_c}{(\gamma+\tau+\mu)}\Big(1+\frac{\gamma}{(\mu+\phi)}\Big),\end{aligned}$$

and $\lambda_3=\lambda_4=\lambda_5=\lambda_6=\lambda_7=\lambda_8=0$.

That is,

$$\begin{aligned}R_0 = \max\Big\{&\frac{\tilde{c}\beta_h}{(\delta_1+\mu+\alpha)}\Big(1+\frac{r_3\delta_1}{(r_2\alpha+\mu)}\Big),\\ &\frac{\tilde{c}\beta_c}{(\gamma+\tau+\mu)}\Big(1+\frac{\gamma}{(\mu+\phi)}\Big),0,0,0,0,0,0\Big\}.\end{aligned} \tag{20}$$

Thus

$$R_0 = \max\{R_{HIV}, R_{HCV}\} \tag{21}$$

where R_{HIV} and R_{HCV} are the reproduction numbers of HIV-only and HCV-only submodels as indicated in Equations (11) and (18), respectively. From (21), it is deduced that the disease with the bigger effective reproduction number will dominate the dynamics of the HIV-HCV co-infection.

Using Theorem 2 in [23], the following result follows.

Theorem 4. *The disease-free equilibrium ε^0 of the HIV-HCV co-infection model is locally asymptotically stable if $R_0<1$ and unstable otherwise.*

1) Global stability of disease-free equilibrium for HIV-HCV co-infection model: To study the global behaviour of system (3a)–(3i), we use the Theorem in [24] as shown in Appendix A. Re-writing model (3a)–(3i) in the form of Equation (A.1) and using the same notation as used in [24], we have:

$$\begin{aligned}X &= (S),\\ Z &= (I_h, I_T, I_a, I_l, I_{ha}, I_{hl}, I_{Tl}, I_{Ta}),\\ F(X,0) &= [\Lambda-\mu S],\end{aligned}$$

and

$$A = \begin{bmatrix} g_1 & h_1 & 0 & 0 & h_2 & \tilde{c}\beta_h\omega & \omega h_1 & \omega h_1\\ \delta_1 & g_2 & 0 & 0 & 0 & 0 & 0 & r_1\tau\\ 0 & 0 & g_3 & \tilde{c}\beta_c & \tilde{c}\beta_c\rho & \tilde{c}\beta_c\rho & \tilde{c}\beta_c\rho & \tilde{c}\beta_c\rho\\ 0 & 0 & \gamma & g_4 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & g_5 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & \theta & g_6 & 0 & 0\\ 0 & 0 & 0 & 0 & 0 & \delta_2 & g_7 & \varphi\\ 0 & 0 & 0 & 0 & \delta_3 & 0 & 0 & g_8\end{bmatrix}$$

where

$$\begin{aligned} g_1 &= \tilde{c}\beta_h - (\delta_1 + \alpha + \mu), & g_2 &= -(r_2\alpha + \mu), \\ g_3 &= \tilde{c}\beta_c - (\gamma + \tau + \mu), & g_4 &= -(\phi + \mu), \\ g_5 &= -(r_1\tau + \theta + \mu + \delta_3), & g_6 &= -(\delta_2 + \mu), \\ g_7 &= -\mu, & g_8 &= -(\varphi + \mu + r_1\tau), \\ h_1 &= \tilde{c}\beta_h r_3, & h_2 &= \tilde{c}\beta_h\omega + r_1\tau. \end{aligned}$$

$\hat{G}$ defined as $\hat{G}(X,Z) = AZ - G(X,Z)$ is given by:

$$\hat{G}(X,Z) = \begin{bmatrix} \hat{G}_1(X,Z) \\ \hat{G}_2(X,Z) \\ \hat{G}_3(X,Z) \\ \hat{G}_4(X,Z) \\ \hat{G}_5(X,Z) \\ \hat{G}_6(X,Z) \\ \hat{G}_7(X,Z) \\ \hat{G}_8(X,Z) \end{bmatrix}$$

$$= \begin{bmatrix} \tilde{c}\beta_h(1 - \frac{S}{N})(I_h + r_3 I_T + \omega I_{ha} + \omega r_3 I_{Ta} \\ +\omega I_{hl} + \omega r_3 I_{Tl}) + k_1\pi_c I_h \\ k_2\pi_c I_T \\ \tilde{c}\beta_c(1 - \frac{S}{N})(I_a + I_l + \rho I_{ha} + \rho I_{Ta} + \rho I_{hl} \\ +\rho I_{Tl}) + q_1\pi_h I_a \\ q_2\pi_h I_l \\ -k_1\pi_c I_h - q_1\pi_h I_a \\ -q_2\pi_h I_l \\ 0 \\ -k_2\pi_c I_T \end{bmatrix}.$$

It can be seen that since $\hat{G}_5(X,Z) < 0$, $\hat{G}_6(X,Z) < 0$, and $\hat{G}_8(X,Z) < 0$, then $\hat{G}(X,Z) < 0$. This implies that the second condition $(H2)$ in Theorem by [24] is not fulfilled. Thus, the disease-free equilibrium of system (3a)–(3i) may not be globally asymptotically stable for $R_0 < 1$.

2) HIV-HCV co-infection endemic equilibrium: Establishment of the expressions for the endemic equilibrium for the HIV-HCV co-infection model (3a)–(3i) analytically is laborious, therefore, its existence and stability could be numerically investigated as, for instance, done in [17], by varying the initial values of the variables to determine whether they would level off to the same non-zero values in the long run, irrespective of the different initial values of the variables.

3) Impact of HIV infection on HCV infection and vice versa: The impact of HCV infection on HIV infection and vice versa is analysed by expressing the reproduction number of one infection in terms of the other. The impact of HIV infection on HCV infection is analysed by expressing the reproduction number of HCV infection in terms of that of HIV infection, that is,

$$R_{HCV} = \frac{R_{HIV}\beta_c(\delta_1 + \alpha + \mu)(r_2\alpha + \mu)(\mu + \phi + \gamma)}{\beta_h(r_2\alpha + \mu + r_3\delta_1)(\gamma + \tau + \mu)(\mu + \phi)}. \tag{22}$$

Now, taking the partial derivative of R_{HCV} in (22) with respect to R_{HIV}, gives:

$$\frac{\partial R_{HCV}}{\partial R_{HIV}} = \frac{\beta_c(\delta_1 + \alpha + \mu)(r_2\alpha + \mu)(\mu + \phi + \gamma)}{\beta_h(r_2\alpha + \mu + r_3\delta_1)(\gamma + \tau + \mu)(\mu + \phi)}. \tag{23}$$

Since, according to (23), $\frac{\partial R_{HCV}}{\partial R_{HIV}} > 0$, epidemiologically this is an implication that an increase in HIV cases would result in an increase in HCV cases in the population. That is, HIV prevalence enhance HCV infections in the population. Thus, HIV control has a positive effect in controlling the HCV transmission dynamics.

Similarly, it can be shown that

$$\frac{\partial R_{HIV}}{\partial R_{HCV}} = \frac{\beta_h(\gamma + \tau + \mu)(\mu + \phi)(r_2\alpha + \mu + r_3\delta_1)}{\beta_c(\mu + \phi + \gamma)(\delta_1 + \alpha + \mu)(r_2\alpha + \mu)}. \tag{24}$$

Since, from (24), $\frac{\partial R_{HIV}}{\partial R_{HCV}} > 0$, this implies that an increase in HCV cases would result in an increase in HIV cases in the population. That is, HCV prevalence enhance HIV infections in the population. Thus, HIV and HCV infections enhance each other. This is in concurrence with the findings in [2] and [12].

E. Sensitivity analysis

1) Derivation of parameter values: In Uganda's efforts to achieve the 90-90-90 targets, in 2018, of the 1.4 million Ugandans that were living with HIV, 84% knew their HIV status, 72% were on treatment and 64% were virally suppressed [22]. In this work, the rate at which HIV infected individuals are identified and put on HIV treatment has been assumed to be 0.12, that is: $\delta_{i=1,2,3} = 0.12$. We make a further assumption that there is no difference in the duration in acute HCV stage between individuals who are dually infected with HIV and on HIV treatment, and those not on HIV treatment. Hence, $\theta = \varphi = 0.52$. Some of the parameter values are cited from the respective studies with literature similar to this work, and others have been assumed only to illustrate numerical results. All the parameter input values are summarised in Table I indicating the sources of parameter values.

2) Computation of R_0: Substituting for the parameter values in Table I in (11) and (18), we obtain $R_{HIV} = 1.295$ and $R_{HCV} = 1.667$. From (21), $R_0 = \max\{1.295, 1.667\} = 1.667$ which is R_{HCV}.

Hence, the dynamics of HIV-HCV co-infection in presence of HIV therapy is dominated by HCV. Introduction of HIV treatment changes the dynamics of HIV-HCV co-infection. For the HIV-HCV co-infection dynamics in absence of treatment, the dynamics were dominated by HIV [17]. Therefore, there is need to investigate the dynamics of HIV-HCV co-infection in presence of therapies for both infections.

3) Computation of sensitivity indices of the effective reproduction numbers with respect to the parameters of the HIV-HCV co-infection model: The sensitivity analysis of the effective reproduction number of the HIV-HCV co-infection model, R_0, to each of the parameter values has been performed using the normalized forward sensitivity index method [25]. This helps to determine the relative contribution of each parameter on R_0 such that appropriate intervention strategies can be taken. The normalized forward sensitivity index of R_e with respect to parameter, x, is defined as the ratio of the relative change in R_e to the relative change in parameter, x, that is:

$$r_x^{R_e} = \frac{\partial R_e}{\partial x} \times \frac{x}{R_e}. \tag{25}$$

Sensitivity analysis of R_0 to each of the parameter values has been computed separately for R_{HIV} and R_{HCV}, since $R_0 = \max\{R_{HIV}, R_{HCV}\}$. Sensitivity indices of R_{HIV} and R_{HCV} have been calculated analytically using formulas

$$r_x^{R_{HIV}} = \frac{\partial R_{HIV}}{\partial x} \times \frac{x}{R_{HIV}} \tag{26}$$

and

$$r_x^{R_{HCV}} = \frac{\partial R_{HCV}}{\partial x} \times \frac{x}{R_{HCV}}, \tag{27}$$

respectively.

Table II presents sensitivity indices of both R_{HIV} and R_{HCV}.

TABLE II
SENSITIVITY INDICES OF R_{HIV} AND R_{HCV} WITH RESPECT TO PARAMETERS.

Parameter	Index of R_{HIV}	Parameter	Index of R_{HCV}
β_h	$+1.0000$	β_c	$+1.0000$
$\tilde{c}$	$+1.0000$	$\tilde{c}$	$+1.0000$
r_2	-0.3105	ϕ	-0.8123
r_3	$+0.6712$	μ	-0.14201
α	-0.6442	τ	-0.1181
μ	-0.4382	γ	$+0.0725$
δ_1	$+0.0823$		

The interpretation of the sensitivity indices presented in Table II is as follows: for a parameter with a negative index, it implies that the corresponding basic reproduction number decreases (increases) with an increase (decrease) in the value of that parameter while keeping the values of other parameters fixed. More still, a positive index implies that the corresponding basic reproduction number increases (decreases) with an increase (decrease) in the value of that parameter. For example, increasing (decreasing) the value of average number of sexual partners acquired per year, $\tilde{c}$, by 10% while other parameter values are kept fixed, increases (decreases) the value of R_{HIV} by 10%. In addition, a 10% increase (decrease) in the value of the rate of progression of individuals infected with HIV to AIDS, α, while other parameter values are kept fixed, decreases (increases) the value of R_{HIV} by 6.4%. Similarly, the sensitivity indices of other parameters can be interpreted.

From Table II, we deduce that endemicity of HIV infection increases when the values of β_h, $\tilde{c}$, δ_1, and r_3 are increased and or those of r_2, α, and μ are decreased. The most sensitive parameters in HIV infection are $\tilde{c}$ and β_h (which are equally sensitive) followed by r_3, α and r_2. Therefore, interventions should target and concentrate on reducing the values of $\tilde{c}$ and β_h. Parameters $\tilde{c}$, β_h, δ_1, r_2, r_3 and α are related in a way that: an increase in the rate at which individuals who are infected with only HIV are identified and put on HIV treatment, δ_1, reduces the value of reduction factor of HIV individuals on treatment progressing to AIDS, r_2, hence increasing the duration in the HIV stage (reduction in α). An increase in δ_1 results into increased r_3 which in the long run leads to increased HIV infections. This is because HIV infected individuals on treatment have a prolonged life span, look healthy and can easily get many sexual partners as they would wish like any HIV negative individual. They have a prolonged time of infecting other individuals with HIV. Therefore, for reduced HIV infections, HIV infected individuals on HIV treatment need to be sensitised on how to live positively (for example, having safe sex using condoms and having few sexual partners).

The sensitivity indices of R_{HCV} in Table II are similar to those in [17], since the HCV-only submodel and the corresponding parameter values in this work are the same as those in [17]. Thus, from Table II, we deduce that endemicity of HCV infection increases when the values of β_c, $\tilde{c}$, and γ are increased and or those of ϕ, τ, and μ are decreased. The most sensitive parameters in HCV infection are $\tilde{c}$ and β_c (which are equally sensitive) followed by ϕ. In Subsection III-E2, it is revealed that the dynamics of HIV-HCV co-infection

in presence of HIV therapy is dominated by HCV. Therefore, R_0 will be more sensitive to β_c, $\tilde{c}$, and ϕ just like R_{HCV}.

From sensitivity analysis, we deduce that, β_h (or β_c) and $\tilde{c}$ are equally likely to increase HIV (or HCV) infections. Increment in the values of these parameters is leading other parameters in increasing the HIV (or HCV) infection. This is in agreement with the findings in [17] in which they investigated the dynamics of HIV-HCV co-infection in absence of treatment for the two infections. Therefore, for reduced HIV (or HCV) infections: individuals need to greatly reduce the rate of sexual partner acquisition, $\tilde{c}$; and transmit-ability probabilities β_h (or β_c); that is, by having safe sex which doesn't expose them to infected blood, like using condoms as recommended in [17].

IV. NUMERICAL SIMULATIONS

We use the ode45 solver in Matlab to perform a numerical simulation of the HIV-HCV co-infection model using parameter values presented in Table I. The initial values for the variables are set as follows: in Uganda, the total population in 2014 was $34,634,650$ of which 49.2% was aged 15-64 years [26]. In this study, the population aged 15-64 years is taken to be sexually active. This implies that sexually active population, $P = \frac{49.2}{100} \times 34,634,650 = 17,040,248$.

In 2015, the HIV prevalence in Uganda was 6.2% [22]. This implies that sexually active population that was living with HIV in 2015 $= \frac{6.2}{100} \times 17,040,248 = 1,056,496$. In Uganda, HCV prevalence is 2.7% [1]. This implies that sexually active population infected with HCV=$\frac{2.7}{100} \times 17,040,248 = 460,087$. Sexually active population co-infected with HIV and HCV=$\frac{2.7}{100} \times 1,056,496 = 28,526$.

In 2018, 72% of HIV infected Ugandans were on HIV treatment [22]. In [3, 4] and [12] it is revealed that approximately 85% of the people infected with acute HCV develop chronic HCV. Basing on these facts, the following initial values for the variables are derived: $I_T(0) = 740,138, I_h(0) = 287,832, I_{Tl}(0) = 17,458, I_{Ta}(0) = 3,081, I_l(0) = 366,827, I_a(0) = 64,734, I_{hl}(0) = 6,789$ and $I_{ha}(0) = 1,198$. Therefore, $S(0) = P - [I_T(0) + I_h(0) + I_l(0) + I_a(0) + I_{Tl}(0) + I_{Ta}(0) + I_{ha}(0) + I_{hl}(0)] = 15,552,191$.

In Figures 2, 3, 4, and 5, values for the rates at which individuals who are infected with only HIV, dually infected with HIV and latent HCV, and dually infected with HIV and acute HCV are identified and put on HIV treatment, δ_1, δ_2, and δ_3, respectively, are varied to investigate the effect of increasing HIV treatment on the number of individuals co-infected with HIV and HCV. Starting with $\delta_1 = \delta_2 = \delta_3 = 0.12$, these values were doubled, tripled, multiplied four times, and lastly multiplied five times.

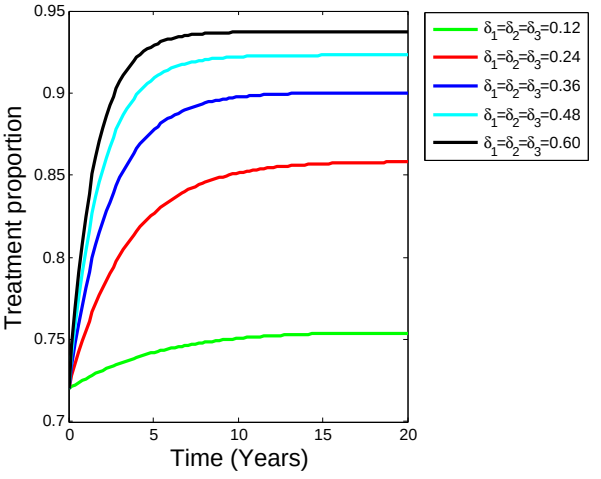


Fig. 2. Proportion on HIV treatment under varying rates of initiation on HIV treatment.

Figure 2 shows that increasing the rate at which individuals are identified and put on HIV treatment, in the long run increases the proportion of individuals on HIV treatment. A country with such increasing treatment proportions, will nearly achieve the second "95" of the 95-95-95 targets.

Figure 3 shows the effect of increasing the values of δ_1, δ_2, and δ_3 on HCV and HIV prevalences. Figure 3(b) is a magnification of Figure 3(a). From Figures 3(a) and 3(b), it is revealed that increasing the values of δ_1, δ_2, and δ_3, eventually, leads to the decrease in the prevalence of HCV. This implies that HIV control has a positive effect in controlling the HCV transmission dynamics as mentioned in subsection III-D3. HIV treatment boosts the immunity of the body to fight off opportunistic infections such as HCV.

Figure 3(c) reveals that increasing the rate at which individuals are identified and put on HIV treatment, in the long run increases the prevalence of HIV. This is due to HIV treatment improving the health of these people and prolonging their life span. They get many sexual partners and infect them with HIV. This is in concurrence with the findings in [27] and [28] in which it is inferred that treatment of HIV/AIDS patients would prolong the patients' lives, and if the treatment does not reduce the infectiousness of such people, they become key agents in the spread of the HIV/AIDS. Therefore, for reduced HIV infections, HIV positively

infected people need continuous sensitisation on how to live positively as mentioned in this work in subsection III-E3.

Figure 4(a) shows that increasing the rate at which people are identified and put on HIV treatment, decreases the number of individuals who are co-infected with HIV and acute HCV not on HIV treatment in the long run. On the other hand, increasing the rate at which people are identified and put on HIV treatment, increases the number of individuals who are co-infected with HIV and acute HCV on treatment in the long run as shown in Figure 4(b).

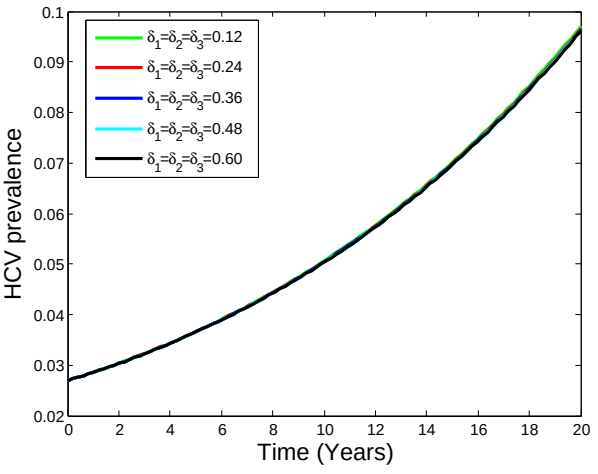
Figure 5(a) reveals that with increasing values of δ_1, δ_2, and δ_3, in the long, there are decreasing numbers of people co-infected with HIV and latent HCV not on HIV treatment, however, the population co-infected with HIV and latent HCV on HIV treatment increases as shown in Figure 5(b).

Figures 6 and 7 show the effect of varying amplification parameters catering for increased risk of getting infected with HCV (or HIV) for those individuals who are already infected with HIV (or HCV), k_1 and k_2 (or q_1 and q_2), on the size of individuals co-infected with HIV and HCV. Figure 6(a) shows that when the value of k_1, is increased, eventually, there will be an increase in the number of individuals infected with HIV but on treatment becoming co-infected with acute HCV. More still, Figure 6(b) shows that when the value of k_2, is increased, in the long run, there will be an increase in the number of individuals infected with HIV but on treatment becoming co-infected with acute HCV.

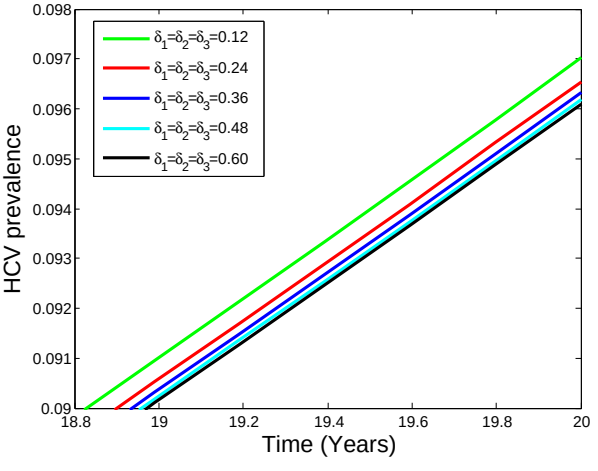
Figure 7(a) reveals that when the value of q_1 is increased, eventually, there will be an increase in the number of individuals acutely infected with HCV getting co-infected with HIV. In addition, Figure 7(b) shows that when the value of q_2 is increased, there will be an increase in the number of individuals latently infected with HCV becoming co-infected with HIV, in the long run. Therefore, Figures 7 and 6 confirm that individuals who are already infected with HIV (or HCV) are at an increased risk of being infected with HCV (or HIV). This is in agreement with the literature in [20] and [12] which reveals that individuals who are already infected with HIV have an increased risk of contracting HCV and vice versa.

V. CONCLUSION

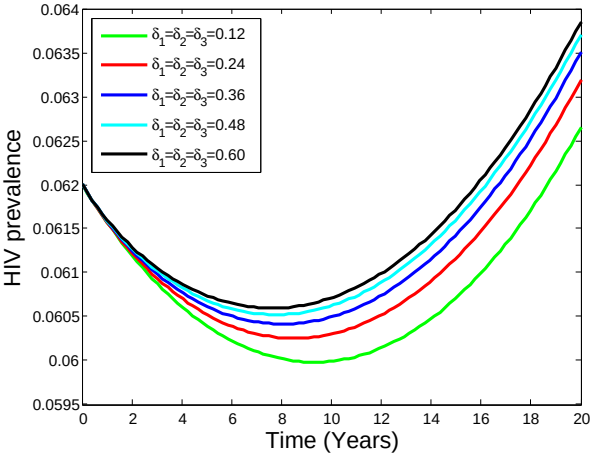
Building on the earlier work in [17], we have added the aspect of HIV treatment. Thus, we formulated and analysed a mathematical model for the HIV-HCV co-infection dynamics in presence of HIV therapy.



(a) HCV prevalence against time

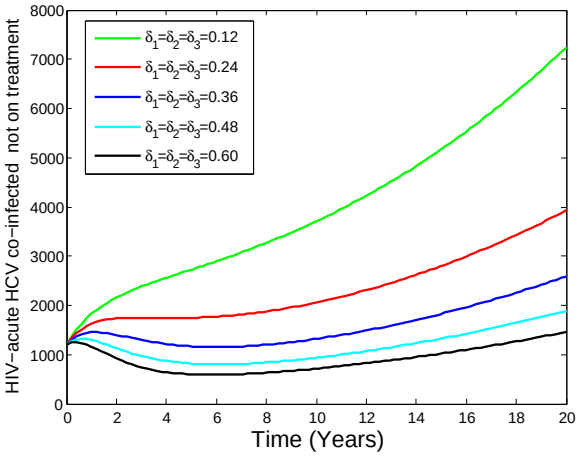


(b) Magnified graph of HCV prevalence against time

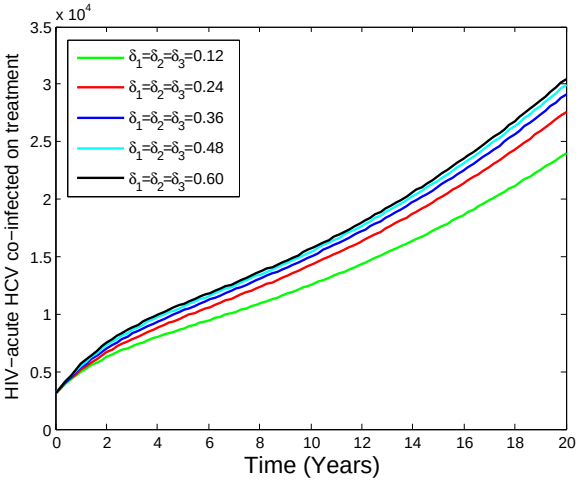


(c) HIV prevalence against time

Fig. 3. Simulation results showing HIV-HCV co-infection dynamics under varying rates of initiation on HIV treatment.

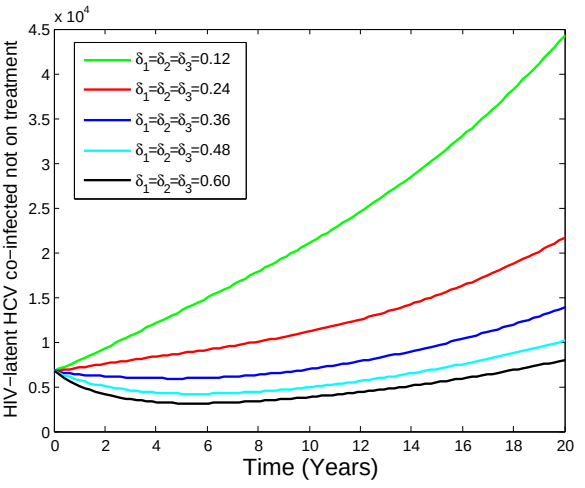


(a) Population co-infected with HIV and acute HCV not on HIV treatment against time

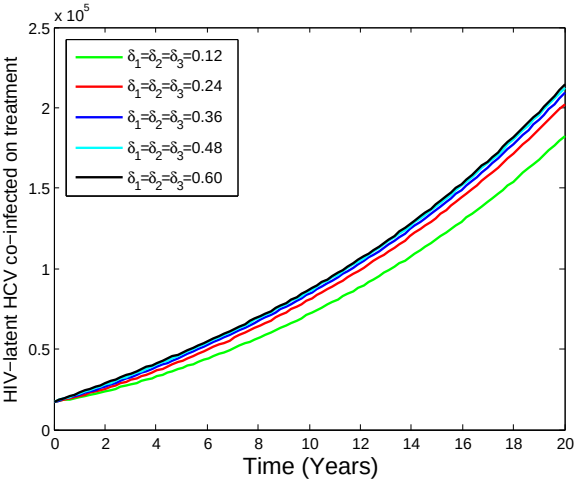


(b) Population co-infected with HIV and acute HCV on HIV treatment against time

Fig. 4. HIV-acute HCV co-infection dynamics under varying rates of initiation on HIV treatment.



(a) Population co-infected with HIV and latent HCV not on HIV treatment against time



(b) Population co-infected with HIV and latent HCV on HIV treatment against time

Fig. 5. HIV-latent HCV co-infection dynamics under varying rates of initiation on HIV treatment.

Analytical analysis revealed that both HIV and HCV infections enhance each other. The different parameters in the HIV-HCV co-infection model were subjected to a sensitivity analysis and it was deduced that HIV (or HCV) transmission probability per sexual contact and average number of sexual partners acquired per year are not only equally likely to result into increased HIV (or HCV) infections, but also increment in the values of these parameters is leading other parameters in increasing the HIV (or HCV) infections, just like the case in the work in [17] when there was no treatment for both infections. Through numerical simulations it was revealed that in the long run, increasing the rates at which people are put on HIV treatment reduces the prevalence of HCV in the community, however, it increases the prevalence of HIV. We recommend that there should be increased safer sexual behaviour campaigns among individuals on HIV treatment. This work can be extended by including treatment for HCV in the model.

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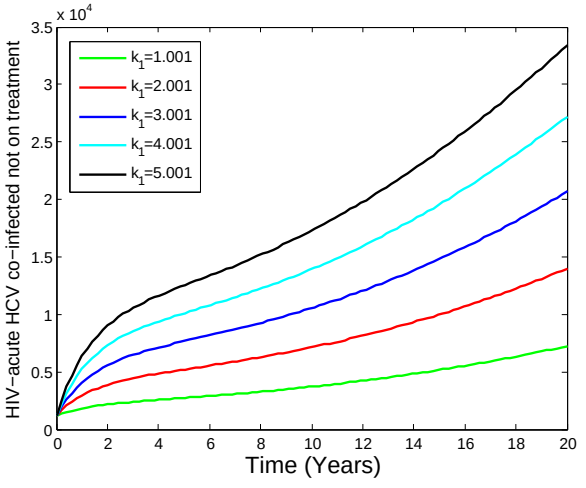
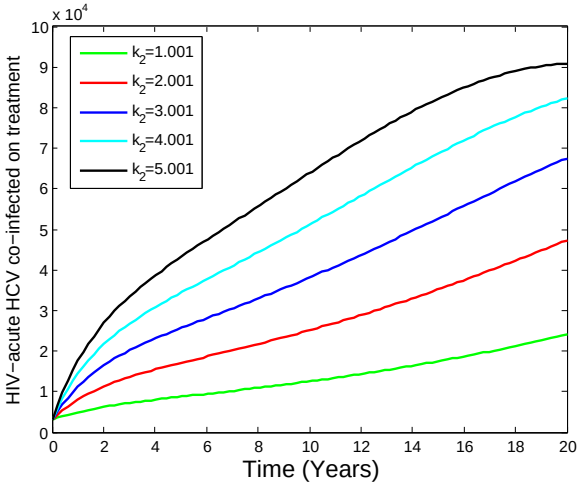
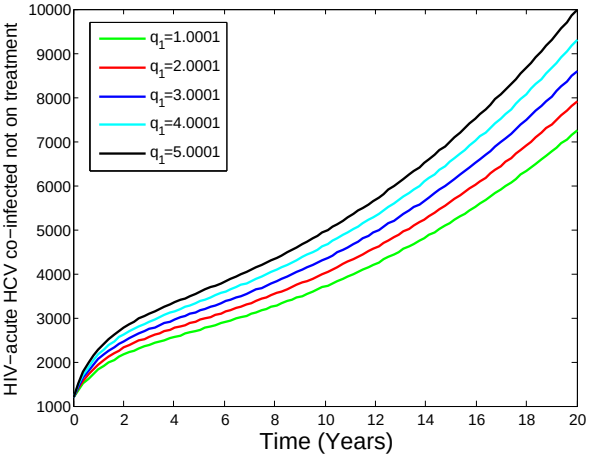


(a) I_{ha} under varying values of k_1

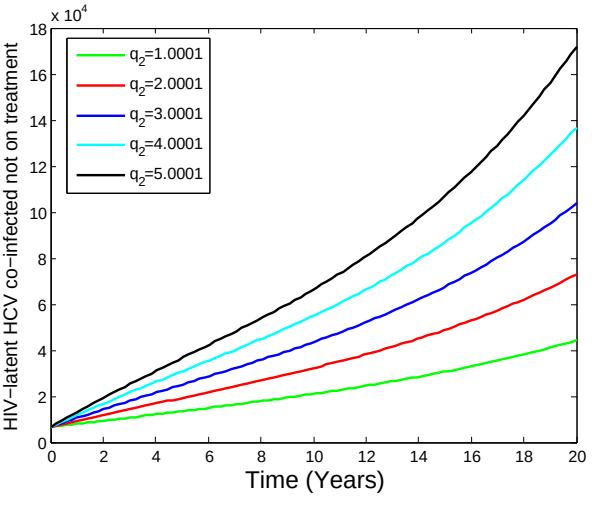


(b) I_{Ta} under varying values of k_2

Fig. 6. HIV-HCV co-infection dynamics under varying values of amplification parameters for the risk of getting co-infected with HCV for HIV infected individuals, k_1 and k_2.



(a) I_{ha} under varying values of q_1



(b) I_{hl} under varying values of q_2

Fig. 7. HIV-HCV co-infection dynamics under varying values of amplification parameters for the risk of getting co-infected with HIV for HCV infected individuals, q_1 and q_2.

APPENDIX A
GLOBAL STABILITY CONDITIONS FOR THE DISEASE-FREE EQUILIBRIUM WHEN $R_0 < 1$

According to Castillo-Chavez et al. [24], for the system written in the form:

$$\begin{cases} \dfrac{dX}{dt} = F(X,Z), \\ \dfrac{dZ}{dt} = G(X,Z), \quad G(X,0) = 0, \end{cases} \tag{A.1}$$

where the components of $X \in R^m$ denotes the number of uninfected individuals and the components of $Z \in R^n$ denotes the number of infected individuals. Let $U_0 = (X^*, 0)$ denote the disease-free equilibrium of this system. The fixed point $U_0 = (X^*, 0)$ is a globally asymptotically stable equilibrium of system (A.1) provided that $R_0 < 1$ and the following conditions $(H1)$ and $(H2)$ are satisfied:

$(H1)$: For $\frac{dX}{dt} = F(X, 0)$, X^* is globally asymptotically stable,

$(H2)$: $G(X,Z) = AZ - \hat{G}(X,Z)$, $\hat{G}(X,Z) \geq 0$ for $(X,Z) \in \Omega$, where $A = D_Z G(X^*, 0)$ is an M–matrix (the off diagonal elements of A are non-negative) and Ω is the region where the model makes biological sense.

If system (A.1) satisfies conditions $(H1)$ and $(H2)$, then the Theorem below holds:

Theorem ([24]). *The fixed point* $U_0 = (X^*, 0)$ *is a globally asymptotic stable equilibrium of system* (A.1) *provided* $R_0 < 1$ *(locally asymptotically stable) and that conditions* $(H1)$ *and* $(H2)$ *are satisfied.*

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