



A Mathematical Model of the Dynamics of Hepatitis B Virus (HBV) Infection with Controls

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ABSTRACT

In this model we study the dynamics and control of hepatitis B virus (HBV) infection which is a major health problem worldwide by considering condom, vaccination and treatment as control measures. Initially we determined the basic reproduction number R_0 for the model and observe that once $R_0 < 1$, the disease free equilibrium will be stable and HBV infection can be controlled using the three control measures and we also study the solution of the endemic equilibrium point of the model. Next we take the sensitivity analysis of the basic reproduction number of HBV infection and obtain that the endemicity of the infection will reduce with the controls. Finally, the numerical simulation result shows that combination of condom, vaccination and treatment is the most effective way to control hepatitis B infection.

Keywords: *Mathematical model, HBV Infection, HBV Control, Condom, Vaccination, Treatment.*

I. INTRODUCTION

Hepatitis B was called serum hepatitis in the past (Southern Nevada Health District (SNHD), 2015). This virus has a number of serological types and the infection occurs at any age but mostly in adults. The incubation period is 50 to 180 days. The virus enters the blood and is spread by blood and blood products. Antibodies are formed and immunity persists after recovery. Infection usually leads to severe illness lasting 2 to 3 weeks, often followed by a protracted convalescence. Carriers may or may not have had clinical disease. Type B virus (serum hepatitis) may cause massive liver necrosis and death and in less severe cases recovery may be complete (Corazon,

2015). In chronic hepatitis which may develop, live virus continue to circulate in the blood and other body fluids, that is, saliva, semen, vaginal secretions. The condition may predispose to liver cancer. Hepatitis is the inflammation of the liver caused by virus, toxic substances or immunological abnormalities. Infectious hepatitis is caused by viruses, several types of which have been isolated as specific causes of the disease and can be detected by tests.

Associated with acute viral hepatitis is acute infection with hepatitis B virus and it starts with general ill – health such as mild fever, dark urine, nausea, loss of appetite, vomiting, body aches, and then progress to development of jaundice. The illness lasts for few weeks before gradually improves in most effected people. Few patients may die as a result of fulminant hepatic failure and in some individuals, the infection may go unrecognized (asymptomatic) (Pan and Zeng, 2005). Chronic HBV may be either asymptomatic or associated with a chronic inflammation of the liver, leading to cirrhosis over a period of several years. Incidence of hepatocellular carcinoma (liver cancer) increases in chronic HBV patients. Avoidance of alcohol consumption is recommended to chronic carriers of HBV infection because it increases their risk for cirrhosis and liver cancer. Hepatitis B virus has been linked to the development of membranous glomerulonephritis (MGN) (Chang, 2007).

II. Related Literature

Hepatitis B virus infection can be controlled either through prevention or treatment. The most effective way of preventing HBV infection is by immunization with hepatitis B vaccine. Prevention of HBV

transmission during early childhood is important because of the high likelihood of chronic infection and chronic liver diseases that occur when children less than five years of age become infected. In HBV infection, the development of anti – HBs as HBsAg disappears suggests that anti – HBs are the protective antibody. Therefore, immunoprophylaxis of HBV requires the administration of anti – HBs antibodies by vaccination with HBsAg. The vaccine schedule most often used for adult and children has been three dose intra muscular injections in which the second and third doses are administered 1 and 6 months after the first. Recombivax HB has been approved for aged 11 – 15 years. In 2007, Twinrix was approved as a four dose accelerated schedule by Food and Drug Administration (FDA) and the schedule of doses are 0, 7, and 21 – 31 days and a booster dose at 12 months after the initial doses. If the interval between doses is longer than the recommended interval, it is not necessary to restart the series or add doses (Center for Disease Control and Prevention (CDC), 2012). This vaccine is for persons at the age of 18 years and above. Also, there is vaccine for infants born to HBsAg negative mothers (coffin et al, 2011). The first dose can be administered before the newborn is discharged from the hospital. The second dose can be given after 1 to 2 months and the third dose can be given 6 to 18 months later. One cannot be infected with hepatitis B from these vaccines (Chu and Liaw, 2007). Following vaccination, hepatitis B surface antigen may be detected in serum for several days; this is known as vaccine antigenaemia (Arauz-Ruiz et al, 2002). Protection has been observed to last 12 years in individuals who show adequate initial response to the primary course of vaccinations, and that immunity is predicted to last at least 25 years (Glebe and Urban, 2007).

HBV infection can also be prevented through the use of condom or another type of latex barrier while having sex because it has been shown that consistent and correct use of condom is 98 – 99% effective in preventing HBV transmission. Since HBV infection is transmitted through body fluids; prevention is thus the avoidance of such transmission like unprotected sexual contact (use of condom), blood transfusion, reuse of contaminated needles and syringes, and vertical transmission during birth. Acute hepatitis B infection does not usually require treatment because about 95% of most adults clear the infection spontaneously (Shapiro, 1993, Lok et al, 2015). Early antiviral treatment may only be required in fewer than

one percent of patients, whose infection are of great severity (fulminant hepatitis) or who are immunocompromised. In patients with fulminant infection, intravenous (IV) feeding may be needed, if the patient has persistent vomiting and can't take oral foods. Ninety percent of patients with acute HBV infection have a favorable course and recover completely (Jayapal, 2007). On the other hand, treatment of chronic HBV infection may be necessary to reduce the risk of cirrhosis and liver cancer. Chronically infected individuals with persistently elevated serum alanine aminotransferase, a marker of liver damage and HBV DNA level are candidates for therapy (Shi et al, 2011). Thirty to forty percent of patients with chronic hepatitis B respond to *IFN α* treatment.

Immune defense is partially active in chronic hepatitis B patients, since the viral load and HBsAg level are lower (Kosinska et al 2013). Undertaken in various experimental systems is antigen expressing DNA in combination with antiviral therapy or immunotherapy with various HBV derived antigens and example is the work of Michael Roggendorf in infected woodchuck with partial success (Kosinska et al 2013). Hepadnaviral cccNDA silencing or destruction would be the best therapy for control of HBV infection but it is still a science fiction (Gerlich, 2013). The current therapy (GS – 9620) for HBV infection suppresses viral replication and delay progression of liver damage. This GS – 9620 which works by targeting the virus represents the first conceptually new treatment for hepatitis B virus in more than a decade (Texas Biomedical Research Institute, 2013). Other antiviral medicine includes, Lamivudine (Epivir) and the newer nucleotide analogues famciclovir, lobucavir and adefovir (Hepsera), dipivoxil, tenofovir (viread), tesbivudine (Tyzeka), entecavir (Baraclute) (Lok et al, 2015) and they directly block or suppress or destroy the HBV by interfering with its replication (Gerlich, 2013; WHO, 2015). These agents are highly effective and well tolerated. *IFN α* and lamivudine have been approved by FDA for the treating chronic hepatitis B. For decompensated liver disease, liver transplant may be required, i.e., surgery may be required to treat hepatocellular carcinoma (Bonino, 1987 and Jayapal, 2007). However some individuals are much more likely to respond than others and this might be because of the genotype of the infection virus or the patient's heredity. The treatment reduces viral replication in the liver, thereby reducing the viral load (the amount of virus particles as measured in the

blood)(Lok and McMahon, 2007). Response to treatment differs between genotypes. Interferon treatment may produce an e antigen seroconversion rate of 37% in genotype A but only a 6% seroconversion rate in type D. Genotype B has similar seroconversion rates to type A (Zoulim, 2004).

Garib – Zahidi (2012), used the model presented by Nowak et al (1996) to study the kinetics of HBV infection (cellular automation). They showed that cellular automation is sophisticated enough to reproduce the basic dynamical features of the infection. They acknowledged that the basic dynamical features of the infection are the biphasic behavior of viral load and age of various patients. Kamyad et al, (2014) constructed a model with two controls (vaccination and treatment) based on the characteristics of HBV transmission. They observed from the numerical results that mixed control measures responds better than any other independent control.

Abdulrahman et al, (2013) in a model of HBV transmission dynamics in a population with viral dynamics, incorporating vertical transmission and sexual maturity showed that all the parameters in their model are sensitive to the transmission and prevalence of HBV either positively or negatively and that the most influential of the parameters are the natural death rate (μ), birth rate (b), HBV – sexual transmission probability contact rate (p), and the total sexual contact rate (c), with the last two parameters having +1 sensitivity index. In the analysis of the transmission dynamics and control of hepatitis B virus (HBV) infection in Nigeria using six different control strategies with a 25years waning rate of vaccine, it was observed that the present strategie of HBV infection control can never bring about disease control in Nigeria (Abdulrahman et al, 2013). They also stated that effort should be made so that 20% to 30% of sexually active susceptible Nigerians will be vaccinated yearly, to be added to the 66% who are vaccinated yearly at birth.

Momoh et al (2012) confirmed that much progress have been made in understanding the transmission dynamics of HBV infection but maintained that more effort is needed if we want to conquer the infection. Obaid and Elaiw (2014) proposed and analyzed two virus infection models with antibody immune response and chronically infected cells. It is not reachable in practice to vaccinate newborns by a rate

greater than 96%. Therefore, treatment or additional vaccination strategies are needed to control the spread of HBV infection in population (Moneim and Khalil, 2015). Certainly, controlling HBV infection simply indicates reducing the susceptible by vaccination or reducing the latent and infected by treatment scheme Kimbir et al (2014), extended the model of Zou et al (2009) and used it to study the transmission dynamics of HBV infection considering vaccination and treatment as control measure in the host population. They showed from the numerical simulation of their model that effective vaccination and treatment is a good control strategy for HBV infection. But a combination of vaccination and treatment is a better control strategy for the disease. In the recovery of HBV infection, each component of innate and adaptive immune response contributes, but in the absence of one component of innate immunity, the remaining two defense mechanisms are sufficient for viral clearance (Dontwi et al, 2010).

III. MODEL FORMULATION

3.1: THE ASSUMPTIONS OF THE MODEL:

1. We assume that both Susceptible, Exposed (infected), infectious and Recovered individuals die at the same natural rate μ .
2. The treated individuals recover, unless the individual dies naturally (Ahmed et al, 1987 and Oleary et al, 2008).
3. Also, we assume that vaccinated individuals do not acquire permanent immunity because the efficacy of the vaccine wanes (Keeling and Rohani 2008).
4. Exposed (infected) individual can spontaneously recover from the infection
5. Infectious but not treated individuals can recover by the effect of the natural immune response (noncytotoxic responses) (Zou et al, 2010; Kar and Jana 2013).
6. Once an individual progresses to infectious class, he is classified as infectious but treated or infectious but not treated.

3.2: MODEL VARIABLES FOR CONTROL OF HEPATITIS B VIRUS INFECTION

The equations are partitioned into twelve compartments of:

- | | |
|-------------|--|
| $S(t)$ | Susceptible individual; |
| $S_v(t)$ | Susceptible but vaccinated; |
| $S_u(t)$ | Susceptible but not vaccinated; |
| $S_{vc}(t)$ | Susceptible, vaccinated and uses condom; |

$S_{uc}(t)$	Susceptible, not vaccinated but uses condom;	α_1	The rate of exposed (infected) individuals who obtain treatment;
$S_{vnc}(t)$	Susceptible, vaccinated but does not use condom;	α_2	The rate of exposed (infected) individuals who had spontaneous recovery;
$S_{unc}(t)$	Susceptible, not vaccinated and does not use condom;	$1 - \alpha_1$	The rate at which exposed individuals do not obtain treatment and moves to infectious class;
$E(t)$	Exposed (infected);	d	The rate at which infectious individuals are treated;
$E_T(t)$	Exposed (infected) and treated;	$k_4(1 - d)$	The rate at which infectious individuals are not treated;
$I_T(t)$	Infectious and treated;	ξ_1	The rate at which treated infectious individuals move to recovered class;
$I_{nT}(t)$	Infectious and not treated;	γ	Rate at which non treated infectious individuals move to recovered class;
$R(t)$	Recovered.	m	Death rate of non treated infectious individuals due to the infection;

3.3: MODEL FORMULATION FOR HBV CONTROL

The model for control of HBV in human population were formulated using ψ as the recruitment level of the population at time t . This model incorporated vaccination given to susceptible individuals, condom use by vaccinated and non vaccinated individuals and treatment given to exposed (infected) and infectious individuals. In the model, we made use of the following variables and parameters.

3.4: MODEL PARAMETER FOR HBV CONTROL

ψ_1	Recruitment level of susceptible individuals;	μ_1	The natural death rate of both the susceptible class, exposed (infected) class, infectious class and Recovered class.
ρ_1	Rate at which susceptible individuals are vaccinated;		
$a(1 - \rho_1)$	Rate at which susceptible individuals are not vaccinated;		
β_1	Rate at which vaccinated susceptible individuals use condom;		
$a_5(1 - \beta_1)$	Rate at which vaccinated susceptible individuals does not use condom;		
σ	Denote the rate of condom usage by non-vaccinated individuals;		
$b(1 - \sigma)$	Denote the rate at which susceptible individuals who are not vaccinated do not use condom;		
$\phi_1 \tau_1$	The rate at which susceptible individuals who are vaccinated but does not use condom are being exposed to the infection due to waning of the vaccine;		
$\delta(1 - c)$	The rate at which non-vaccinated susceptible individuals who use condom are being exposed to the infection due to error in condom/condom usage;		
v	Denote the rate constant at which susceptible individuals who are not vaccinated and does not use condom move to exposed class		

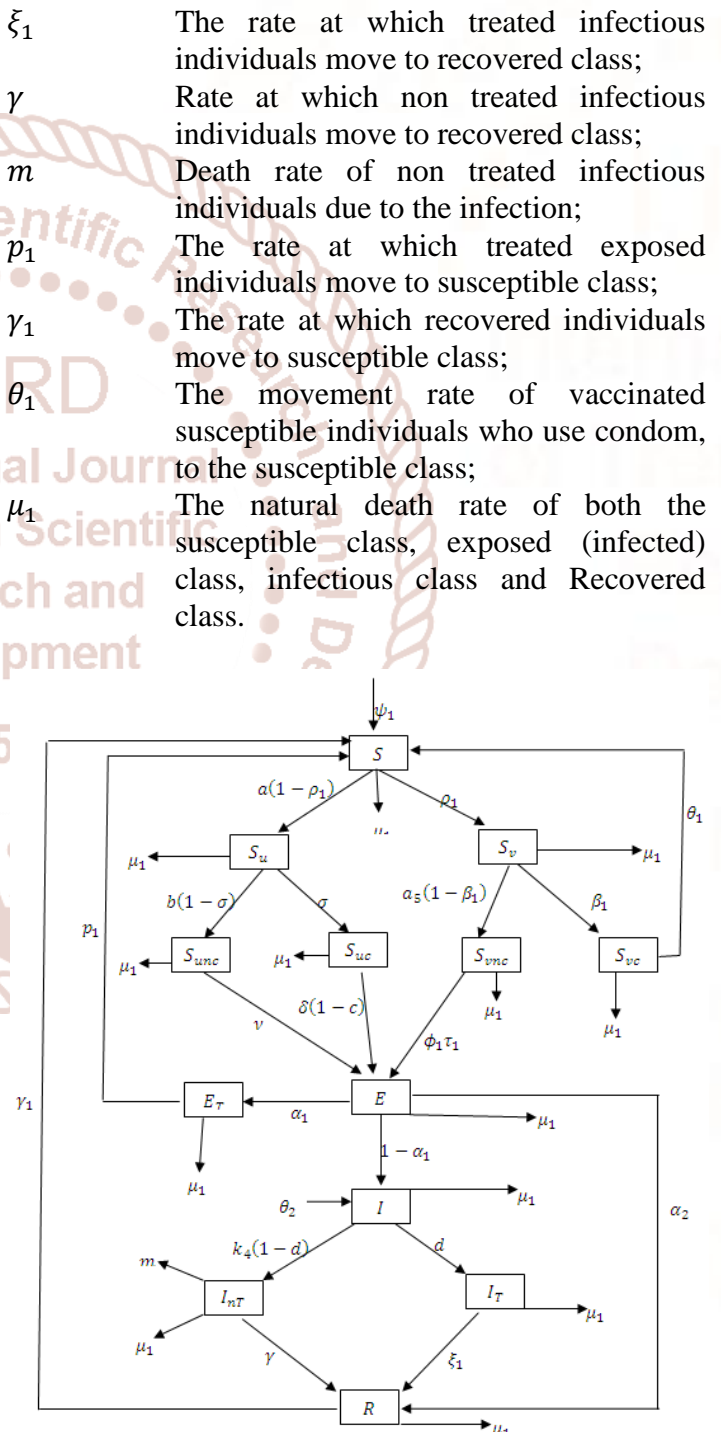


Fig 1: Flow diagram of Hepatitis B Virus Control Model

From the diagram above we obtain the following equations;

$$\begin{aligned}
 \frac{dS}{dt} &= \psi_1 - \rho_1 S - a(1 - \rho_1)S - \mu_1 S + \theta_1 S_{vc} + p_1 E_T + \gamma_1 R \\
 \frac{dS_v}{dt} &= \rho_1 S - \mu_1 S_v - \beta_1 S_v - a_5(1 - \beta_1)S_v \\
 \frac{dS_u}{dt} &= a(1 - \rho_1)S - \mu_1 S_u - \sigma S_u - b(1 - \sigma)S_u \\
 \frac{dS_{vc}}{dt} &= \beta_1 S_v - \mu_1 S_{vc} - \theta_1 S_{vc} \\
 \frac{dS_{uc}}{dt} &= \sigma S_u - \mu_1 S_{uc} - \delta(1 - c)S_{uc} \\
 \frac{dS_{vnc}}{dt} &= a_5(1 - \beta_1)S_v - \mu_1 S_{vnc} - \phi_1 \tau_1 S_{vnc} \\
 \frac{dS_{unc}}{dt} &= b(1 - \sigma)S_u - \mu_1 S_{unc} - v S_{unc} \\
 \frac{dE}{dt} &= \phi_1 \tau_1 S_{vnc} + \delta(1 - c)S_{uc} + v S_{unc} - (1 - \alpha_1)E - \alpha_1 E - \alpha_2 E - \mu_1 E \\
 \frac{dE_T}{dt} &= \alpha_1 E - \mu_1 E_T - p_1 E_T \\
 \frac{dI_T}{dt} &= d(1 - \alpha_1)I_T - \mu_1 I_T - \xi_1 I_T \\
 \frac{dI_{nT}}{dt} &= k_4(1 - d)(1 - \alpha_1)I_{nT} - m I_{nT} - \mu_1 I_{nT} - \gamma I_{nT} \\
 \frac{dR}{dt} &= \xi_1 I_T + \gamma I_{nT} + \alpha_2 E - \mu_1 R - \gamma_1 R
 \end{aligned} \tag{3.1}$$

3.5: ANALYSIS OF THE SYSTEM FOR free equilibrium point and the endemic equilibrium CONTROL

If we assume that the control parameters $\rho_1(t), \beta_1(t), \sigma(t), \alpha_1(t),$ and $d(t)$ are constant functions, we analyze the equilibrium point and the basic reproduction number of the system.

3.6: EQUILIBRIUM POINT AND BASIC REPRODUCTION NUMBER

We shall discuss the two possible non negative equilibrium of system (3.1) and these are the disease

Thus

$$\frac{dS}{dt} = \frac{dS_v}{dt} = \frac{dS_u}{dt} = \frac{dS_{vc}}{dt} = \frac{dS_{uc}}{dt} = \frac{dS_{vnc}}{dt} = \frac{dS_{unc}}{dt} = \frac{dE}{dt} = \frac{dE_T}{dt} = \frac{dI_T}{dt} = \frac{dI_{nT}}{dt} = \frac{dR}{dt} = 0 \tag{3.2}$$

Also let, $(S, S_v, S_u, S_{vc}, S_{uc}, S_{vnc}, S_{unc}, E, E_T, I_T, I_{nT}, R) = (S^*, S_v^*, S_u^*, S_{vc}^*, S_{uc}^*, S_{vnc}^*, S_{unc}^*, E^*, E_T^*, I_T^*, I_{nT}^*, R^*)$ at equilibrium state.

3.7: DISEASE FREE EQUILIBRIUM

The disease free equilibrium state denotes absence of infection, vaccination, use of condom and treatment. Therefore, all the infected class will be zero and the entire population will comprise of Susceptible, Vaccinated, Non vaccinated, Condom compliance and Non condom compliance individuals. At equilibrium state, we set the rate of change of each variable to be equal to zero.

Therefore,

$$\left. \begin{aligned}
 0 &= \psi_1 - \rho_1 S - a(1 - \rho_1)S - \mu_1 S + \theta_1 S_{vc} + p_1 E_T + \gamma_1 R \\
 0 &= \rho_1 S - \mu_1 S_v - \beta_1 S_v - a_5(1 - \beta_1)S_v \\
 0 &= a(1 - \rho_1)S - \mu_1 S_u - \sigma S_u - b(1 - \sigma)S_u \\
 0 &= \beta_1 S_v - \mu_1 S_{vc} - \theta_1 S_{vc} \\
 0 &= \sigma S_u - \mu_1 S_{uc} - \delta(1 - c)S_{uc} \\
 0 &= a_5(1 - \beta_1)S_v - \mu_1 S_{vnc} - \phi_1 \tau_1 S_{vnc} \\
 0 &= b(1 - \sigma)S_u - \mu_1 S_{unc} - v S_{unc} \\
 0 &= \phi_1 \tau_1 S_{vnc} + \delta(1 - c)S_{uc} + v S_{unc} - (1 - \alpha_1)E - \alpha_1 E - \alpha_2 E - \mu_1 E \\
 0 &= \alpha_1 E - \mu_1 E_T - p_1 E_T \\
 0 &= d(1 - \alpha_1)I_T - \mu_1 I_T - \xi_1 I_T \\
 0 &= k_4(1 - d)(1 - \alpha_1)I_{nT} - m I_{nT} - \mu_1 I_{nT} - \gamma I_{nT} \\
 0 &= \xi_1 I_T + \gamma I_{nT} + \alpha_2 E - \mu_1 R - \gamma_1 R
 \end{aligned} \right\} (3.3)$$

Let $k_5 = a(1 - \rho_1)$, $k_6 = a_5(1 - \beta_1)$, $k_7 = \delta(1 - c)$, $k_8 = b(1 - \sigma)$, $k_9 = d(1 - \alpha_1)$, $k_{10} = k_4(1 - d)$. If we label the equations in (3.3) as (i) to (xii) and substitute $E^* = E_T^* = I_T^* = I_{nT}^* = 0$ into (3.3), we have from (3.3xii) that

$$\begin{aligned}
 \xi_1 I_T + \gamma I_{nT} - \mu_1 R - \gamma_1 R &= 0 \\
 (\mu_1 + \gamma_1)R &= 0 \\
 \therefore R &= 0
 \end{aligned} \quad (3.4)$$

From (3.3iv), we have

$$\begin{aligned}
 \beta_1 S_v - \mu_1 S_{vc} - \theta_1 S_{vc} &= 0 \\
 \therefore S_{vc} &= \frac{\beta_1 S_v}{\mu_1 + \theta_1}
 \end{aligned} \quad (3.5)$$

From (3.3ii) we obtain

$$S_v = \frac{\rho_1 S}{\mu_1 + \beta_1 + k_6} \quad (3.6)$$

Substituting (3.4), (3.5) and (3.6) into (3.3i) we get

$$\begin{aligned}
 \psi_1 - \rho_1 S - a(1 - \rho_1)S - \mu_1 S + \theta_1 \left(\frac{\beta_1}{\mu_1 + \theta_1} \right) \left(\frac{\rho_1 S}{\mu_1 + \beta_1 + k_6} \right) + 0 + 0 &= 0 \\
 \therefore S &= \frac{\psi_1(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6)}{(\rho_1 + \mu_1 + k_5)(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6) - \theta_1 \beta_1 \rho_1}
 \end{aligned} \quad (3.7)$$

From (3.6) we have that

$$S_v = \frac{\rho_1 S}{\mu_1 + \beta_1 + k_6}$$

If we substitute (3.7) into (3.6) we obtain

$$S_v = \frac{\rho_1 \psi_1 (\mu_1 + \theta_1)}{(\rho_1 + \mu_1 + k_5)(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6) - \theta_1 \beta_1 \rho_1} \quad (3.8)$$

From (3.3iii) we have that

$$\begin{aligned}
 a(1 - \rho_1)S - \mu_1 S_u - \sigma S_u - b(1 - \sigma)S_u &= 0 \\
 (\mu_1 + \sigma + k_8)S_u &= k_5 S \\
 S_u &= \frac{k_5 S}{\mu_1 + \sigma + k_8}
 \end{aligned} \quad (3.9)$$

Substituting (3.7) into (3.9) gives us

$$S_u = \frac{k_5}{\mu_1 + \sigma + k_8} \left(\frac{\psi_1(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6)}{(\rho_1 + \mu_1 + k_5)(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6) - \theta_1\beta_1\rho_1} \right) \quad (3.10)$$

Remember that (3.5) is

$$S_{vc} = \frac{\beta_1 S_v}{\mu_1 + \theta_1}$$

Therefore, if we substitute (3.8) in (3.5) we obtain

$$S_{vc} = \left(\frac{\beta_1 \rho_1}{(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6)} \right) \left(\frac{\psi(\mu + \theta_1)(\mu + \beta_1 + k_3)}{(\rho_1 + \mu_1 + k_5)(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6) - \theta_1\beta_1\rho_1} \right)$$

$$S_{vc} = \frac{\rho_1 \psi_1 \rho_1}{(\rho_1 + \mu_1 + k_5)(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6) - \theta_1\beta_1\rho_1} \quad (3.11)$$

From (3.3v) we have that

$$\sigma S_u - \mu_1 S_{uc} - \delta(1-c)S_{uc} = 0$$

$$S_{uc} = \frac{\sigma S_u}{\mu_1 + k_7} \quad (3.12)$$

Then, substituting (3.10) into (3.12) we get

$$S_{uc} = \left(\frac{\sigma k_5}{(\mu_1 + k_7)(\mu_1 + \sigma + k_8)} \right) \left(\frac{\psi_1(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6)}{(\rho_1 + \mu_1 + k_5)(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6) - \theta_1\beta_1\rho_1} \right) \quad (3.13)$$

Notice that (3.3vi) is

$$a_5(1 - \beta_1)S_v - \mu_1 S_{vnc} - \phi_1 \tau_1 S_{vnc} = 0$$

$$(\mu_1 + \phi_1 \tau_1) S_{vnc} = k_6 S_v$$

$$S_{vnc} = \frac{k_6 S_v}{\mu_1 + \phi_1 \tau_1} \quad (3.14)$$

We then substitute (3.8) into (3.14) to obtain

$$S_{vnc} = \left(\frac{k_6}{\mu_1 + \phi_1 \tau_1} \right) \left(\frac{\rho_1}{\mu_1 + \beta_1 + k_6} \right) \left(\frac{\psi_1(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6)}{(\rho_1 + \mu_1 + k_5)(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6) - \theta_1\beta_1\rho_1} \right)$$

$$S_{vnc} = \left(\frac{k_6 \rho_1}{\mu_1 + \phi_1 \tau_1} \right) \left(\frac{\psi_1(\mu_1 + \theta_1)}{(\rho_1 + \mu_1 + k_5)(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6) - \theta_1\beta_1\rho_1} \right) \quad (3.15)$$

Also, we have that (3.3vii) is

$$b(1 - \sigma)S_u - \mu_1 S_{unc} - v S_{unc} = 0$$

$$(\mu_1 + v) S_{unc} = k_8 S_u$$

$$S_{unc} = \frac{k_8 S_u}{\mu_1 + v} \quad (3.16)$$

If (3.10) is substituted into (3.16), we obtain

$$S_{unc} = \frac{k_8}{\mu_1 + v} \left(\frac{k_5}{\mu_1 + \sigma + k_8} \right) \left(\frac{\psi_1(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6)}{(\rho_1 + \mu_1 + k_5)(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6) - \theta_1\beta_1\rho_1} \right) \quad (3.17)$$

Let E_0^* be the disease free equilibrium point, then,

$$E_0^* = [S, S_v, S_u, S_{vc}, S_{uc}, S_{vnc}, S_{unc}, 0, 0, 0, 0]$$

Using (4.60) and substituting the value of k_6 and k_5 we have

$$\begin{aligned}
 S_0 &= \frac{\psi_1(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6)}{(\rho_1 + \mu_1 + k_5)(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6) - \theta_1\beta_1\rho_1} \\
 &= \frac{\psi_1(\mu_1 + \theta_1)(\mu_1 + a_5)}{(\mu_1 + a)(\mu_1 + \theta_1)(\mu_1 + a_5) - 0} = \frac{\psi_1}{\mu_1 + a} \\
 S_{v0} &= \frac{\rho_1\psi_1(\mu_1 + \theta_1)}{(\rho_1 + \mu_1 + k_5)(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6) - \theta_1\beta_1\rho_1} \\
 &= \frac{(0)\psi_1(\mu_1 + \theta_1)}{(\mu_1 + a)(\mu_1 + \theta_1)(\mu_1 + a_5) - 0} = 0 \\
 S_{u0} &= \frac{k_5}{\mu_1 + \sigma + k_8} \left(\frac{\psi_1(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6)}{(\rho_1 + \mu_1 + k_5)(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6) - \theta_1\beta_1\rho_1} \right) \\
 &= \frac{a}{\mu_1 + b} \left(\frac{\psi_1(\mu_1 + \theta_1)(\mu_1 + a_5)}{(\mu_1 + a)(\mu_1 + \theta_1)(\mu_1 + a_5) - 0} \right) = \frac{a\psi_1}{(\mu_1 + a)(\mu_1 + b)} \\
 S_{vc0} &= \frac{\psi_1\beta_1\rho_1}{(\rho_1 + \mu_1 + k_5)(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6) - \theta_1\beta_1\rho_1} \\
 &= \frac{\psi_1(0)(0)}{(\mu_1 + a)(\mu_1 + \theta_1)(\mu_1 + a_2) - 0} = 0 \\
 S_{uc0} &= \left(\frac{\sigma k_5}{(\mu_1 + k_7)(\mu_1 + \sigma + k_8)} \right) \left(\frac{\psi_1(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6)}{(\rho_1 + \mu_1 + k_5)(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6) - \theta_1\beta_1\rho_1} \right) \\
 &= \left(\frac{(0)a}{(\mu_1 + k_4)(\mu_1 + b)} \right) \left(\frac{\psi_1(\mu_1 + \theta_1)(\mu_1 + a_5)}{(\mu_1 + a)(\mu_1 + \theta_1)(\mu_1 + a_5) - 0} \right) = 0 \\
 S_{vnc0} &= \left(\frac{k_3\rho_1}{\mu_1 + \phi_1\tau_1} \right) \left(\frac{\psi_1(\mu_1 + \theta_1)}{(\rho_1 + \mu_1 + k_2)(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_3) - \theta_1\beta_1\rho_1} \right) \\
 &= \left(\frac{a_5(0)}{\mu_1 + \phi_1\tau_1} \right) \left(\frac{\psi(\mu_1 + \theta_1)}{(\mu_1 + a)(\mu_1 + \theta_1)(\mu_1 + a_5) - 0} \right) = 0 \\
 S_{unc0} &= \frac{k_8}{\mu_1 + v} \left(\frac{k_5}{\mu_1 + \sigma + k_8} \right) \left(\frac{\psi_1(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6)}{(\rho_1 + \mu_1 + k_5)(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6) - \theta_1\beta_1\rho_1} \right) \\
 &= \frac{b}{\mu_1} \left(\frac{a}{\mu_1 + b} \right) \left(\frac{(\mu_1 + \theta_1)(\mu_1 + a_5)}{(\mu_1 + a)(\mu_1 + \theta_1)(\mu_1 + a_5) - 0} \right) = \frac{ab\psi_1}{\mu_1(\mu_1 + a)(\mu_1 + b)}
 \end{aligned}$$

The disease free equilibrium point of the model $E_0^* = [S, S_v, S_u, S_{vc}, S_{uc}, S_{vnc}, S_{unc}, 0, 0, 0, 0]$ is $\left[\frac{\psi_1}{\mu_1 + a}, 0, \frac{a\psi_1}{(\mu_1 + a)(\mu_1 + a)}, 0, 0, 0, \frac{ab\psi_1}{\mu_1(\mu_1 + a)(\mu_1 + a)}, 0, 0, 0, 0 \right]$.

3.8: STABILITY OF THE DISEASE FREE EQUILIBRIUM (DFE)

In equation (3.1), all the parameters are non negative and we assume stable population with per capita recruitment of susceptible individuals and death rate (both natural and disease induced). For simplicity, the population size is normalized to one, that is $S, S_v, S_u, S_{vc}, S_{uc}$,

$S_{vnc}, S_{unc}, E, E_T, I_T, I_{nT}, R$ are respectively the fraction of the susceptible, susceptible with vaccination, susceptible without vaccination, susceptible with vaccination and uses condom, susceptible with vaccination but does not use condom, susceptible without vaccination but uses condom, susceptible without vaccination and does not use condom, exposed, exposed but treated, infectious but treated, infectious but not treated and recovered. This can be represented thus;

$$S + S_v + S_u + S_{vc} + S_{uc} + S_{vnc} + S_{unc} + E + E_T + I_T + I_{nT} + R = 1 \quad (3.18)$$

According to Pang, (2010) and Kamyard, (2014) equation (3.2) holds and we can omit the equation for R in our analysis so that (3.1) becomes

$$\left. \begin{aligned}
 \frac{dS}{dt} &= \psi_1 - \rho_1 S - a(1 - \rho_1)S - \mu_1 S + \theta_1 S_{vc} + p_1 E_T \\
 &+ \gamma_1 [1 - (S + S_v + S_u + S_{vc} + S_{uc} + S_{vnc} + S_{unc} + E + E_T + I_T + I_{nT})] \\
 \frac{dS_v}{dt} &= \rho_1 S - \mu_1 S_v - \beta_1 S_v - a_5(1 - \beta_1)S_v \\
 \frac{dS_u}{dt} &= a(1 - \rho_1)S - \mu_1 S_u - \sigma S_u - b(1 - \sigma)S_u \\
 \frac{dS_{vc}}{dt} &= \beta_1 S_v - \mu_1 S_{vc} - \theta_1 S_{vc} \\
 \frac{dS_{uc}}{dt} &= \sigma S_u - \mu_1 S_{uc} - \delta(1 - c)S_{uc} \\
 \frac{dS_{vnc}}{dt} &= a_5(1 - \beta_1)S_v - \mu_1 S_{vnc} - \phi_1 \tau_1 S_{vnc} \\
 \frac{dS_{unc}}{dt} &= b(1 - \sigma)S_u - \mu_1 S_{unc} - v S_{unc} \\
 \frac{dE}{dt} &= \phi_1 \tau_1 S_{vnc} + \delta(1 - c)S_{uc} + v S_{unc} - (1 - \alpha_1)E - \alpha_1 E - \alpha_2 E - \mu_1 E \\
 \frac{dE_T}{dt} &= \alpha_1 E - \mu_1 E_T - p_1 E_T \\
 \frac{dI_T}{dt} &= d(1 - \alpha_1)I_T - \mu_1 I_T - \xi_1 I_T \\
 \frac{dI_{nT}}{dt} &= k_4(1 - d)(1 - \alpha_1)I_{nT} - m I_{nT} - \mu_1 I_{nT} - \gamma I_{nT}
 \end{aligned} \right\} \quad (3.19)$$

Let

$$H_1(t) = S(t) + S_v(t) + S_u(t) + S_{vc}(t) + S_{uc}(t) + S_{vnc}(t) + S_{unc}(t) + E(t) + E_T(t) + I_T(t) + I_{nT}(t) \quad (3.20)$$

Then,

$$\begin{aligned}
 H_1(t) &= \psi_1 - \rho_1 S - a(1 - \rho_1)S - \mu_1 S + \theta_1 S_{vc} + p_1 E_T \\
 &+ \gamma_1 [1 - (S + S_v + S_u + S_{vc} + S_{uc} + S_{vnc} + S_{unc} + E + E_T + I_T + I_{nT})] \\
 &+ \rho_1 S - \mu_1 S_v - \beta_1 S_v - a_5(1 - \beta_1)S_v + a(1 - \rho_1)S - \mu_1 S_u - \sigma S_u - b(1 - \sigma)S_u \\
 &+ \beta_1 S_v - \mu_1 S_{vc} - \theta_1 S_{vc} + \sigma S_u - \mu_1 S_{uc} - \delta(1 - c)S_{uc} + a_5(1 - \beta_1)S_v - \mu_1 S_{vnc} - \phi_1 \tau_1 S_{vnc} \\
 &+ b(1 - \sigma)S_u - \mu_1 S_{unc} - v S_{unc} + \phi_1 \tau_1 S_{vnc} + \delta(1 - c)S_{uc} + v S_{unc} - (1 - \alpha_1)E - \alpha_1 E \\
 &- \alpha_2 E - \mu_1 E + \alpha_1 E - \mu_1 E_T - p_1 E_T + d(1 - \alpha_1)I_T - \mu_1 I_T - \xi_1 I_T \\
 &+ k_4(1 - d)(1 - \alpha_1)I_{nT} - m I_{nT} - \mu_1 I_{nT} - \gamma I_{nT}
 \end{aligned}$$

Here it is important to note that in the absence of the disease,

$\alpha_1 E, (1 - \alpha_1)E, \alpha_2 E, d(1 - \alpha_1)I_T, \xi_1 I_T, \gamma I_{nT}, k_4(1 - d)(1 - \alpha_1)I_{nT}, m I_{nT}$ will be zero.

Therefore, we have

$$\begin{aligned}
 H_1(t) &= \\
 \psi_1 - (\mu_1 S + \mu_1 S_v + \mu_1 S_u + \mu_1 S_{vc} + \mu_1 S_{uc} + \mu_1 S_{vnc} + \mu_1 S_{unc} + \mu_1 E + \mu_1 E_T + \mu_1 I_T + \mu_1 I_{nT}) \\
 &+ \gamma_1(1 - H_1)
 \end{aligned}$$

$$\begin{aligned}
 H_1(t) &= \psi_1 - \mu_1 H_1 + \gamma_1(1 - H_1) \\
 H_1(t) &= \psi_1 + \gamma_1 - (\mu_1 + \gamma_1)H_1 \\
 H_1(t) + (\mu_1 + \gamma_1)H_1 &\leq \psi_1 + \gamma_1 \quad (3.21)
 \end{aligned}$$

Now, we integrate both sides of (3.21) using integrating factor method (Kar and Jana, 2013; Birkhoff and Roffa, 1989).

That is,

$$H_1' + g_3(t)dt = f(t)$$

$$\Rightarrow H_1 \leq e^{-\int g_3(t)dt} \left(\int e^{\int g_3(t)dt} f(t)dt + c_2 \right)$$

Where $g_3(t) = \mu_1 + \gamma_1$ and $f(t) = \psi_1 + \gamma_1$. The integrating factor is

$$r(t) = e^{\int g_3(t)dt} = e^{\int(\mu_1+\gamma_1)dt} = e^{(\mu_1+\gamma_1)t}$$

Integrating (3.21) using the value of the integrating factor $r(t) = e^{(\mu_1+\gamma_1)t}$ we get

$$H_1(t) \leq \frac{1}{r(t)} \left[\int f(t).r(t)dt + c_2 \right]$$

$$H_1(t) \leq \frac{1}{e^{(\mu_1+\gamma_1)t}} \left[\int (\psi_1 + \gamma_1).e^{(\mu_1+\gamma_1)t}dt + c_2 \right]$$

$$\leq \frac{1}{e^{(\mu_1+\gamma_1)t}} \left[\frac{\psi_1 + \gamma_1}{\mu_1 + \gamma_1}.e^{(\mu_1+\gamma_1)t}dt + c_2 \right]$$

$$H_1(t) \leq \left[\frac{\psi_1 + \gamma_1}{\mu_1 + \gamma_1}.e^{(\mu_1+\gamma_1)t}dt + c_2 \right] e^{-(\mu_1+\gamma_1)t}$$

$$\therefore H_1(t) \leq \frac{\psi_1 + \gamma_1}{\mu_1 + \gamma_1} + c_2 e^{-(\mu_1+\gamma_1)t} \tag{3.22}$$

Where c_2 is the constant of integration and if we let $t \rightarrow \infty$, we have

$$H_1(t) = \frac{\psi_1 + \gamma_1}{\mu_1 + \gamma_1} = [S + S_v + S_u + S_{vc} + S_{uc} + S_{vnc} + S_{unc} + E + E_T + I_T + I_{nT}] \tag{3.23}$$

But

$$S = \frac{\psi_1(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6)}{(\rho_1 + \mu_1 + k_5)(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6) - \theta_1\beta_1\rho_1}$$

We observe from the dynamic described by (3.1), (3.7) and (3.23) that the region

$$\Gamma_1 = \left\{ \begin{array}{l} (S, S_v, S_u, S_{vc}, S_{uc}, S_{vnc}, S_{unc}, E, E_T, I_T, I_{nT}) \in \mathbb{R}_+^{11}; \\ S \leq \frac{\psi_1(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6)}{(\rho_1 + \mu_1 + k_5)(\mu_1 + \theta_1)(\mu_1 + \beta_1 + k_6) - \theta_1\beta_1\rho_1} \\ [S + S_v + S_u + S_{vc} + S_{uc} + S_{vnc} + S_{unc} + E + E_T + I_T + I_{nT}] \leq \frac{\psi_1 + \gamma_1}{\mu_1 + \gamma_1} \end{array} \right\}$$

is positively invariant. In other words, the system is well posed mathematically since it has a positive invariant. Therefore, for the initial starting point $H_1 \in \mathbb{R}_+^{11}$, the trajectory lies in Γ_1 . Thus, we focus our attention only on the region Γ_1 .

3.9: BASIC REPRODUCTION NUMBER

Definition 1`: Basic reproduction number of an infectious disease model denoted by R_0 is the average number of secondary infections caused by a single infectious individual during their lifetime (Driessche and Watmough, 2002). When the basic reproduction number is less than one, ($R_0 < 1$), the disease free equilibrium point is locally asymptotically stable. But if the basic reproduction number is greater than one, ($R_0 > 1$), then the disease free equilibrium point is unstable.

We shall calculate R_0 using the next generation matrix by starting with those equations of the model that describe the production of new infections and change in state among infected individuals. We refer to these set of equations as the infected sub system and linearize them about the disease free steady state. From equation (3.24) we derive the infection subsystem as transmission part and transition part respectively.

$$\left. \begin{aligned}
 \frac{dS_v}{dt} &= \rho_1 S - \mu_1 S_v - \beta_1 S_v - a_5(1 - \beta_1)S_v \\
 \frac{dS_u}{dt} &= a(1 - \rho_1)S - \mu_1 S_u - \sigma S_u - b(1 - \sigma)S_u \\
 \frac{dS_{vc}}{dt} &= \beta_1 S_v - \mu_1 S_{vc} - \theta_1 S_{vc} \\
 \frac{dS_{uc}}{dt} &= \sigma S_u - \mu_1 S_{uc} - \delta(1 - c)S_{uc} \\
 \frac{dS_{vnc}}{dt} &= a_5(1 - \beta_1)S_v - \mu_1 S_{vnc} - \phi_1 \tau_1 S_{vnc} \\
 \frac{dS_{unc}}{dt} &= b(1 - \sigma)S_u - \mu_1 S_{unc} - v S_{unc} \\
 \frac{dE}{dt} &= \phi_1 \tau_1 S_{vnc} + \delta(1 - c)S_{uc} + v S_{unc} - (1 - \alpha_1)E - \alpha_1 E - \alpha_2 E - \mu_1 E \\
 \frac{dE_T}{dt} &= \alpha_1 E - \mu_1 E_T - p_1 E_T \\
 \frac{dI_T}{dt} &= d(1 - \alpha_1)I_T - \mu_1 I_T - \xi_1 I_T \\
 \frac{dI_{nT}}{dt} &= k_1(1 - d)(1 - \alpha_1)I_{nT} - m I_{nT} - \mu_1 I_{nT} - \gamma I_{nT}
 \end{aligned} \right\} (3.24)$$

Let $M = [S, S_v, S_u, S_{vc}, S_{uc}, S_{vnc}, S_{unc}, E, E_T, I_T, I_{nT}]^T$ where T denotes transpose then we have the linearized infected sub system as transmission (F) and transition (V).

$$\hat{M} = (F + V)M \tag{3.25}$$

The matrix F corresponds to transmission part and it describes the the number of ways that new infections can arise. The matrix V corresponds to transition part which describes the number of ways that individuals can move between compartments and it includes removal by death or acquisition of immunity. Therefore, from (3.24) we obtain the matrices

$$F := \begin{bmatrix}
 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 0 & (1 - \sigma)b & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 0 & 0 & 0 & (1 - c)\delta & \phi_1 \tau_1 & v & 0 & 0 & 0 & 0 & 0 \\
 0 & 0 & 0 & 0 & 0 & 0 & \alpha_1 & 0 & 0 & 0 & 0 \\
 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & (1 - \alpha_1) & 0 \\
 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & (1 - d)(1 - \alpha_1)k_4
 \end{bmatrix}$$

$$V := \begin{bmatrix} \mu_1 + a_3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \mu_1 + b & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -\beta_1 & 0 & \mu_1 + \theta_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\sigma & 0 & \mu_1 + (1-c)\delta & 0 & 0 & 0 & 0 & 0 & 0 \\ -(1-\beta_1)a_3 & 0 & 0 & 0 & \mu_1 + \phi_1 \tau_1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \mu_1 + v & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \mu_1 + \alpha_2 + 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \mu_1 + p & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \mu_1 + \xi_1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \mu_1 + m + \gamma \end{bmatrix}$$

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$$V^{-1} \rightarrow \begin{bmatrix} \frac{1}{a_3 + \mu_1} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{1}{b + \mu_1} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \frac{\beta_1}{a_3 \mu_1 + a_3 \theta_1 + \mu_1 \theta_1 + (\mu_1)^2} & 0 & \frac{1}{\mu_1 + \theta_1} & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\sigma}{\delta \mu_1 + b \mu_1 + \delta b + (\mu_1)^2 - \delta b c - \delta c \mu_1} & 0 & \frac{1}{\delta - \delta c + \mu_1} & 0 & 0 & 0 & 0 & 0 & 0 \\ \frac{a_3 \beta_1 - a_3}{a_3 \mu_1 + (\mu_1)^2 + a_3 \tau_1 \phi_1 + \mu_1 \tau_1 \phi_1} & 0 & 0 & 0 & \frac{1}{\tau_1 \phi_1 + \mu_1} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \frac{1}{v + \mu_1} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \frac{1}{\mu_1 + \alpha_2 + 1} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{1}{p + \mu_1} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{1}{\xi_1 + \mu_1} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{1}{\gamma + m + \mu_1} \end{bmatrix}$$

If we solve equation (54) simultaneously, having in mind that $E^{**} \neq 0$ we have that;

$$\begin{aligned} d(1 - \alpha_1)I_T^* - \mu_1 I_T^* - \xi_1 I_T^* &= 0 \\ (d(1 - \alpha_1) - (\mu_1 + \xi_1))I_T^* &= 0 \end{aligned} \tag{3.28}$$

$$\begin{aligned} k_4(1 - d)(1 - \alpha_1)I_{nT}^* - mI_{nT}^* - \mu_1 I_{nT}^* - \gamma I_{nT}^* &= 0 \\ (k_4(1 - d)(1 - \alpha_1) - (m + \mu_1 + \gamma))I_{nT}^* &= 0 \end{aligned} \tag{3.29}$$

$$\begin{aligned} \xi_1 I_T^* + \gamma I_{nT}^* + \alpha_2 E^* - \mu_1 R^* - \gamma_1 R^* &= 0 \\ I_T^* = \frac{(\mu_1 + \gamma_1)R^* - \alpha_2 E^* - \gamma I_{nT}^*}{\xi_1} \end{aligned} \tag{3.30}$$

$$I_{nT}^* = \frac{(\mu_1 + \gamma_1)R^* - \alpha_2 E^* - \xi_1 I_T^*}{\gamma} \tag{3.31}$$

If we substitute (3.30) into (3.28) we obtain

$$\begin{aligned} (d(1 - \alpha_1) - (\mu_1 + \xi_1)) \left(\frac{(\mu_1 + \gamma_1)R^* - \alpha_2 E^* - \gamma I_{nT}^*}{\xi_1} \right) &= 0 \\ I_{nT}^* = \frac{(\mu_1 + \gamma_1)R^* - \alpha_2 E^*}{\xi_1} \end{aligned} \tag{3.32}$$

Substituting (3.31) into (3.29) we have

$$\begin{aligned} (k_4(1 - d)(1 - \alpha_1) - (m + \mu_1 + \gamma)) \left(\frac{(\mu_1 + \gamma_1)R^* - \alpha_2 E^* - \xi_1 I_T^*}{\gamma} \right) &= 0 \\ I_T^* = \frac{(\mu_1 + \gamma_1)R^* - \alpha_2 E^*}{\gamma} \end{aligned} \tag{3.33}$$

Observe that

$$(d(1 - \alpha_1) - (\mu_1 + \xi_1))I_T^* = 0$$

And

$$(k_4(1 - d)(1 - \alpha_1) - (m + \mu_1 + \gamma))I_{nT}^* = 0$$

Then, we obtain

$$\begin{aligned} \alpha_2 E^* - \mu_1 R^* - \gamma_1 R^* &= 0 \\ R^* = \frac{\alpha_2 E^*}{\mu_1 + \gamma_1} \end{aligned} \tag{3.34}$$

$$\alpha_1 E^* - \mu_1 E_T^* - p_1 E_T^* = 0$$

$$E_T^* = \frac{\alpha_1 E^*}{(\mu_1 + p_1)} \tag{3.35}$$

$$\begin{aligned} \phi_1 \tau_1 S_{vnc}^* + \delta(1 - c)S_{uc}^* + vS_{unc}^* - (1 - \alpha_1)E^* - \alpha_1 E^* - \alpha_2 E^* - \mu_1 E^* &= 0 \\ E^* = \frac{\phi_1 \tau_1 S_{vnc}^* + \delta(1 - c)S_{uc}^* + vS_{unc}^*}{\mu_1 + \alpha_2 + 1} \end{aligned} \tag{3.36}$$

$$b(1 - \sigma)S_u^* - \mu_1 S_{unc}^* - vS_{unc}^* = 0$$

$$S_{unc}^* = \frac{b(1 - \sigma)S_u^*}{\mu_1 + v} \tag{3.37}$$

$$a_5(1 - \beta_1) S_v^* - \mu_1 S_{vnc}^* - \phi_1 \tau_1 S_{vnc}^* = 0$$

$$S_{vnc}^* = \frac{a_5(1 - \beta_1) S_v^*}{\mu_1 + \phi_1 \tau_1} \quad (3.38)$$

$$\sigma S_u^* - \mu_1 S_{uc}^* - \delta(1 - c) S_{uc}^* = 0$$

$$S_{uc}^* = \frac{\sigma S_u^*}{\mu_1 + \delta(1 - c)} \quad (3.39)$$

$$\beta_1 S_v^* - \mu_1 S_{vc}^* - \theta_1 S_{vc}^* = 0$$

$$S_{vc}^* = \frac{\beta_1 S_v^*}{\mu_1 + \theta_1} \quad (3.40)$$

$$a(1 - \rho_1) S^* - \mu_1 S_u^* - \sigma S_u^* - b(1 - \sigma) S_u^* = 0$$

$$S_u^* = \frac{a(1 - \rho_1) S^*}{\mu_1 + \sigma + b(1 - \sigma)} \quad (3.41)$$

$$\rho_1 S^* - \mu_1 S_v^* - \beta_1 S_v^* - a_5(1 - \beta_1) S_v^* = 0$$

$$S_v^* = \frac{\rho_1 S^*}{\mu_1 + \beta_1 + a_5(1 - \beta_1)} \quad (3.42)$$

$$\psi_1 - \rho_1 S^* - a(1 - \rho_1) S^* - \mu_1 S^* + \theta_1 S_{vc}^* + p_1 E_T^* + \gamma_1 R^* = 0 \quad (3.43)$$

$$\begin{aligned} & \psi_1 - \rho_1 S^* - a(1 - \rho_1) S^* - \mu_1 S^* + \frac{\beta_1}{\mu_1 + \theta_1} \left(\frac{\rho_1 S^*}{\mu_1 + \beta_1 + a_5(1 - \beta_1)} \right) \\ & + \frac{p_1 \alpha_1}{(\mu_1 + p_1)} \left(+\delta(1 - c) \left(\frac{\sigma}{\mu_1 + \delta(1 - c)} \right) \left(\frac{a(1 - \rho_1) S^*}{\mu_1 + \sigma + b(1 - \sigma)} \right) \left(\frac{1}{\mu_1 + \alpha_2 + 1} \right) \right. \\ & \quad \left. + v \left(\frac{b(1 - \sigma) S_u^*}{\mu_1 + v} \right) \left(\frac{a(1 - \rho_1) S^*}{\mu_1 + \sigma + b(1 - \sigma)} \right) \right) \\ & + \frac{\gamma_1 \alpha_2}{\mu_1 + \gamma_1} \left(+\delta(1 - c) \left(\frac{\sigma}{\mu_1 + \delta(1 - c)} \right) \left(\frac{a(1 - \rho_1) S^*}{\mu_1 + \sigma + b(1 - \sigma)} \right) \left(\frac{1}{\mu_1 + \alpha_2 + 1} \right) \right. \\ & \quad \left. + v \left(\frac{b(1 - \sigma) S_u^*}{\mu_1 + v} \right) \left(\frac{a(1 - \rho_1) S^*}{\mu_1 + \sigma + b(1 - \sigma)} \right) \right) = 0 \end{aligned}$$

Let

$$A = (\rho_1 + a(1 - \rho_1) + \mu_1)$$

$$B = -\frac{\beta_1}{\mu_1 + \theta_1} \left(\frac{\rho_1}{\mu_1 + \beta_1 + a_5(1 - \beta_1)} \right)$$

$$C = -\frac{\phi_1 \tau_1}{(\mu_1 + \alpha_2 + 1)} \left(\left(\frac{a_5(1 - \beta_1)}{\mu_1 + \phi_1 \tau_1} \right) \left(\frac{\rho_1}{\mu_1 + \beta_1 + a_5(1 - \beta_1)} \right) \right)$$

$$D = -\frac{\delta(1 - c)}{(\mu_1 + 1)} \left(\left(\frac{\sigma}{\mu_1 + \delta(1 - c)} \right) \left(\frac{a(1 - \rho_1)}{\mu_1 + \sigma + b(1 - \sigma)} \right) \right)$$

$$J = -\frac{v}{(\mu_1 + \alpha_2 + 1)} \left(\left(\frac{b(1 - \sigma) S_u^*}{\mu_1 + v} \right) \left(\frac{a(1 - \rho_1)}{\mu_1 + \sigma + b(1 - \sigma)} \right) \right)$$

$$S^* = \frac{\psi_1}{A + B + \left(\frac{p_1 \alpha_1}{(\mu_1 + p_1)}\right)(C + D + J) + \left(\frac{\gamma_1 \alpha_2}{(\mu_1 + \gamma_1)}\right)(C + D + J)} \tag{3.44}$$

3.11: SENSITIVITY ANALYSIS OF THE BASIC REPRODUCTION NUMBER OF HBV INFECTION

The basic reproduction number R_0 is a function of eight parameters $\mu_1, \alpha_2, v, \alpha_1, d, m, \gamma$ and ξ_1 . To control the disease, these parameter values must control R_{01} such that it will be less than one ($R_0 < 1$). Therefore, as the parameter values are changed, we find the rate of change of R_0 . If we let $g_4 = (\mu_1, \alpha_2, v, \alpha_1, d, m, \gamma, \xi_1)$, then the rate of change of R_{01} for a change in the value of parameter g_4 can be estimated from a normalized sensitivity index

$$Z_{g_4}^{R_0} = \frac{\partial R_0}{\partial g_4} \cdot \frac{R_0}{g_4} \tag{3.45}$$

Table 1: The Parameter values for Hepatitis B virus infection used to calculate R_0 .

Parameters	Description	Value Range	Reference
μ_1	Natural death rate	0.0219	Adu et al, 2014
α_2	Movement rate of non treated exposed (infected) individuals to recovered class	0.88	Abdulrahman et al, 2013
v	Movement rate of susceptible individuals who are neither vaccinated nor use condom	0.002	Assumed
α_1	Treatment rate of exposed (infected) individuals	0.7	Kamyad et al, 2014
ξ_1	Movement rate of treated infectious individuals to recovered class	0.98	Kimber et al, 2014
d	Treatment rate of infectious individuals	0.98	Kimber et al, 2014
m	Rate of disease induced death	0.0007	Abdulrahman et a, 2013
γ	Movement rate of non treated infectious individuals to recovered class	0.508	Abdulrahman et al, 2013

To calculate the value of R_0 , we use the parameters as stated in table 1.

$$R_0 = \frac{v}{v + \mu_1} + \frac{\alpha_1}{\mu_1 + \alpha_2 + 1} + \frac{k_4(1-d)(1-\alpha_1)}{\mu_1 + m + \gamma} + \frac{1 - \alpha_1}{\mu_1 + \xi_1}$$

$$= \frac{0.002}{0.0239} + \frac{0.7}{1.9019} + \frac{0.006}{0.5236} + \frac{0.3}{1.0019} = 0.76262$$

The normalized sensitivity index of the basic reproduction number with respect to $\mu_1, \alpha_2, v, \alpha_1, d, m, \gamma$ and ξ_1 is given by

$$Z_v^{R_0} = \frac{\partial R_0}{\partial v} \cdot \frac{R_0}{v} = \frac{\mu_1}{(v + \mu_1)^2} \left(\frac{R_0}{v}\right) = 14619.311$$

$$Z_{\mu_1}^{R_0} = \frac{\partial R_0}{\partial \mu_1} \cdot \frac{R_0}{\mu_1}$$

$$= -\left(\frac{v}{(v + \mu_1)^2} + \frac{\alpha_1}{(\mu_1 + \alpha_2 + 1)^2} + \frac{k_4(1-d)(1-\alpha_1)}{(\mu_1 + m + \gamma)^2} + \frac{1 - \alpha_1}{(\mu_1 + \xi_1)^2}\right) \left(\frac{R_0}{v}\right) = -38.9114493$$

$$Z_{\alpha_1}^{R_0} = \frac{\partial R_0}{\partial \alpha_1} \cdot \frac{R_0}{\alpha_1} = \left(\frac{1}{\mu_1 + \alpha_2 + 1} - \frac{1}{\mu_1 + \xi_1} - \frac{k_4(1-d)}{\mu_1 + m + \gamma}\right) \left(\frac{R_0}{\alpha_1}\right) = -0.39687895$$

$$Z_{\alpha_2}^{R_0} = \frac{\partial R_0}{\partial \alpha_2} \cdot \frac{R_0}{\alpha_2} = -\frac{\alpha_1}{(\mu_1 + \alpha_2 + 1)^2} \left(\frac{R_0}{\alpha_2}\right) = -0.31895975$$

$$Z_d^{R_0} = \frac{\partial R_0}{\partial d} \cdot \frac{R_0}{d} = -\frac{k_4(1-\alpha_1)}{\mu_1+m+\gamma} \left(\frac{R_0}{d}\right) = -0.44586536$$

$$Z_m^{R_0} = \frac{\partial R_0}{\partial m} \cdot \frac{R_0}{m} = -\frac{k_4(1-d)(1-\alpha_1)}{(\mu_1+m+\gamma)^2} \left(\frac{R_0}{m}\right) = -23.8430637$$

$$Z_\gamma^{R_0} = \frac{\partial R_0}{\partial \gamma} \cdot \frac{R_0}{\gamma} = -\frac{k_4(1-d)(1-\alpha_1)}{(\mu_1+m+\gamma)^2} \left(\frac{R_0}{\gamma}\right) = -0.03285462$$

$$Z_{\xi_1}^{R_0} = \frac{\partial R_0}{\partial \xi_1} \cdot \frac{R_0}{\xi_1} = \frac{(1-\alpha_1)}{(\mu_1+\xi_1)^2} = -0.32712716$$

Table 2: The effect of the parameters on R_0 .

Parameters	Value Range	Effect on R_{01}
μ_1	0.0219	-38.9114493
α_2	0.88	-0.31895975
v	0.002	14619.311
α_1	0.7	-0.39687895
ξ_1	0.98	-0.32712716
d	0.98	-0.445865
m	0.0007	-23.8430637
γ	0.508	-0.03285462

The sensitivity index $Z(v)$ is positive and this shows that the value of R_0 increases as the value of v increases. The remaining indices $Z(\mu_1), Z(\alpha_1), Z(\alpha_2), Z(\xi_1), Z(\gamma), Z(d)$ and $Z(m)$ are negative, indicating that the value R_0 decreases as $\mu_1, \alpha_1, \alpha_2, \xi_1, \gamma, d$ and m increases. Actually, the effectiveness of control may be measured by its effect on R_0 . Once the parameters $\mu_1, \alpha_1, \alpha_2, \xi_1, \gamma, d$ and m will reduce $R_0 < 1$, then it is curative if the reduction can be maintained.

Therefore, the endemicity of the will be reduced if there is increase in the value of the following parameters; the rate at which exposed (infected) individuals obtain treatment (α_1), natural death rate of the exposed and infectious individuals (μ_1), spontaneous recovery rate by exposed individuals (α_2), disease induced death rate of infectious individuals (m), rate at which treated infectious individuals move to recovered class (γ), rate at which infectious individuals receive treatment (d) and the rate at which the received treatment is effective (ξ_1). This implies that these parameters can help in reducing the rate of HBV infection over time and if it is maintained, the transmission of the disease may decrease, causing the cases in the population to go below an endemicity threshold.

IV. Analysis of Result

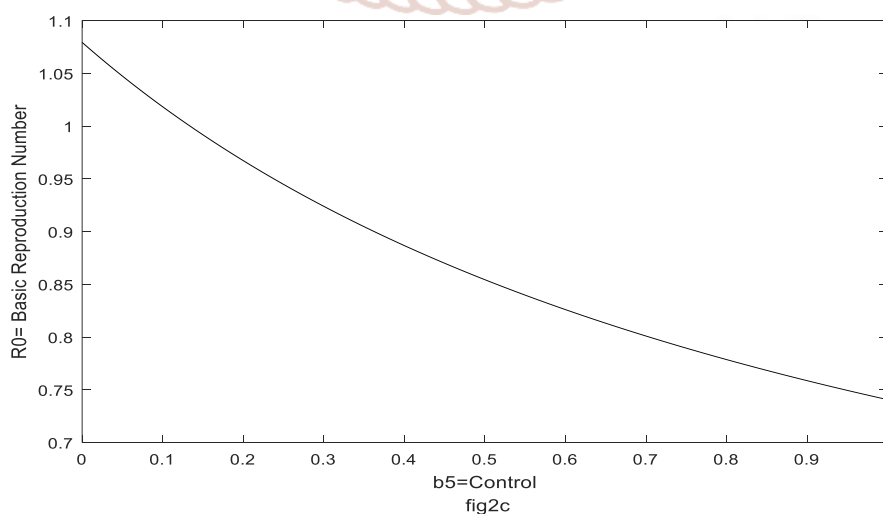
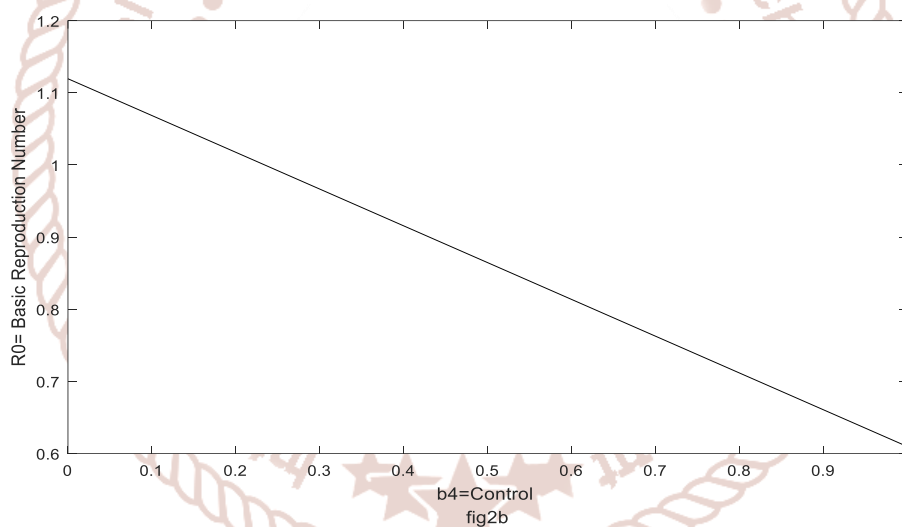
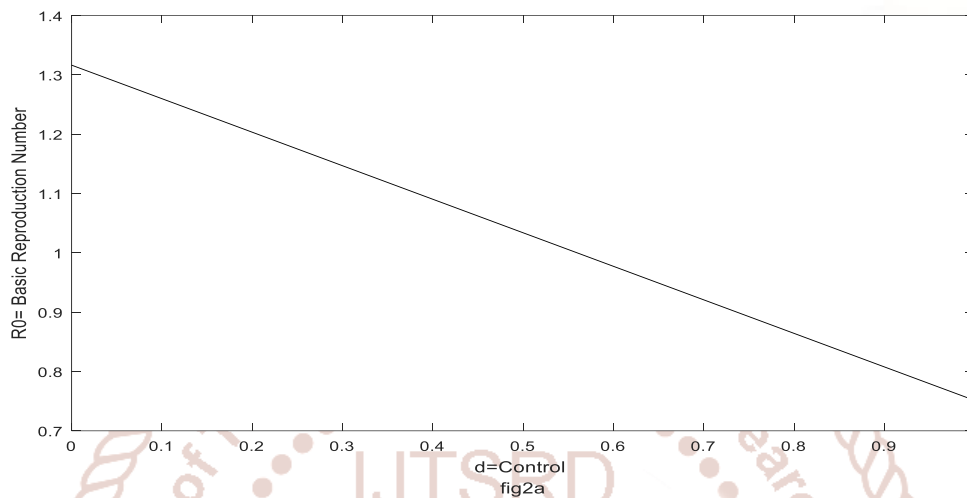
We consider the parameter set $\Delta = \{\psi, a, b, \rho_1, \psi_1, a_5, \sigma, \phi_1\tau_1, \delta(1-c), v, \alpha_1, \alpha_2, d, k_4, \xi_1, \gamma, m, p_1, \gamma_1, \theta_1, \mu_1\}$; some of these parameters are taken from published articles and some are assumed with feasible values. More so, we consider $\nabla = \{S_0, S_{v0}, S_{u0}, S_{vc0}, S_{uc0}, S_{vnc0}, S_{unc0}, E_0, E_{T0}, I_{T0}, I_{nT0}, R_0\}$ as the initial condition for the simulation of the model. We compare the results; having no control and having both vaccine, condom and treatment controls. With the parameter values in table 1, the system asymptotically approaches the endemic equilibrium $E^{**} = (8.62693005, 0.86183812, 0.09575979, 0.95879491, 0.3836662, 1.5315378, 0.52086904, 0.073104, 0.073104, 0, 0, 0.12663685)$.

The basic reproduction number is given as;

$$R_0 = \frac{v}{v+\mu_1} + \frac{\alpha_1}{\mu_1+\alpha_2+1} + \frac{k_4(1-d)(1-\alpha_1)}{\mu_1+m+\gamma} + \frac{1-\alpha_1}{\mu_1+\xi_1}$$

and the value of the basic reproduction number is $R_0 = 0.76262$ which is less than one. Thus, since $R_0 < 1$, then the disease free equilibrium is stable and HBV infection can be controlled in the population using the three

control measure. This confirms the result of the sensitivity analysis of R_0 in table 2, where d (the rate at which the infectious individuals are treated), α_1 (the rate of the exposed individuals who obtain treatment) and α_2 (the rate of exposed individuals who spontaneously recover from the infection) are all negative and it shows that when all these parameters increases, the average number of secondary infections caused by a single infectious individual during their lifetime (I.e, R_0), will decrease. This implies that with effective control measure, the future number of HBV infection cases will decrease as the parameters $\alpha_1, \alpha_2, \mu_1, \xi_1 m, d, \gamma$ increases because even though individuals remain infectious for a longer period and consequently can infect more individuals, the rate of progression to disease decreases.



Figures (2a – 2c): Numerical simulation of the basic reproduction number R_0 using different rate of d, α_1 and α_2 , where α_1 and α_2 are respectively represented with b4 and b5.

The effect of the three control measures on the disease dynamics may be well understood if we consider Figures 2a, 2b and 2c which explains how control reproduction ratio R_0 evolve with different rate of d, α_1 and α_2 where α_1 and α_2 are respectively represented with b4 and b5 in figure 2b and 2c above. It is seen that condom, vaccination and treatment reduces the value of R_0 effectively. But an integrated control works better than either of the control measures.

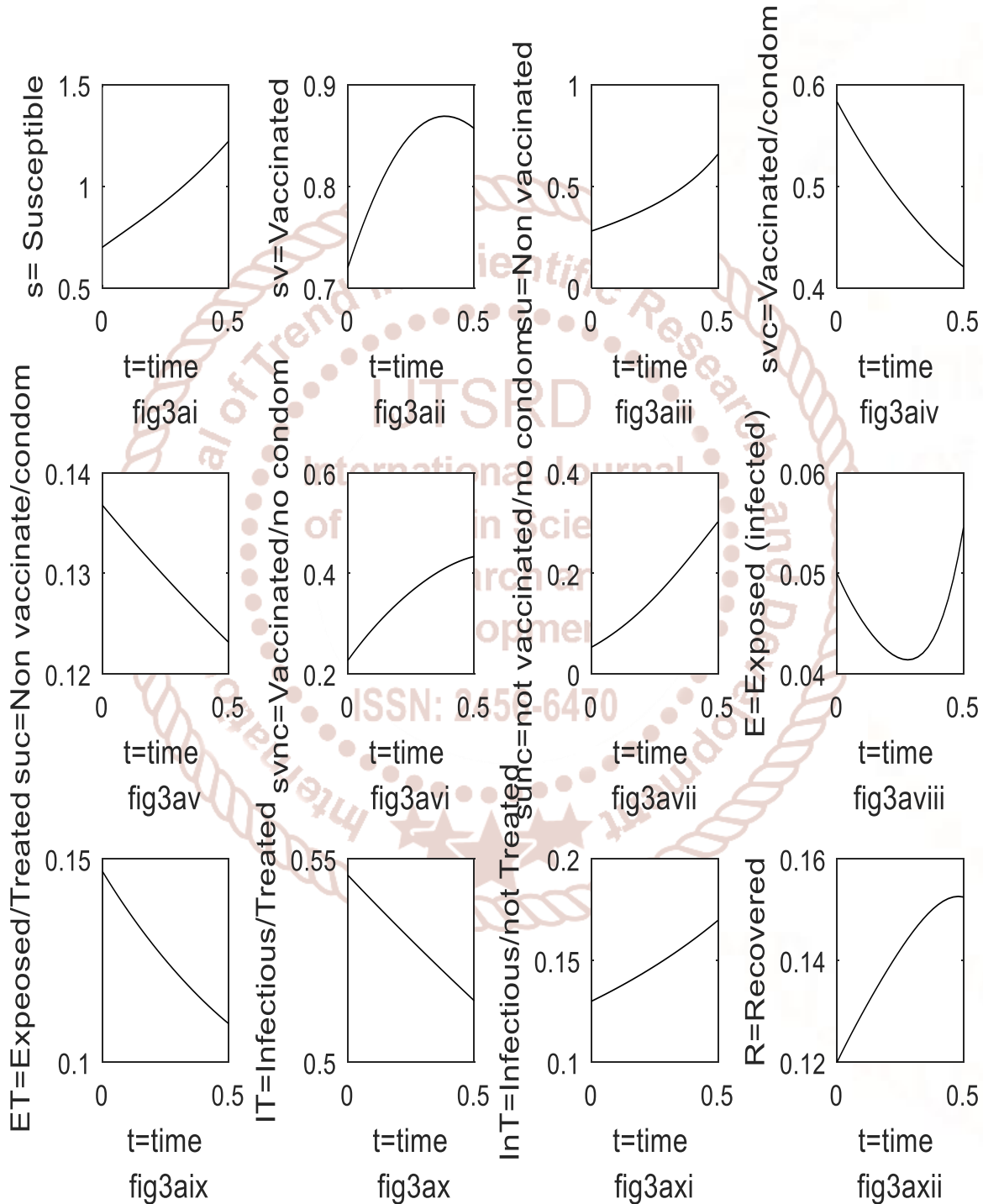


Figure (3ai – 3axii): Numerical simulation of the model system (3.1) when there is no control with time ranging from 0 – 6months.

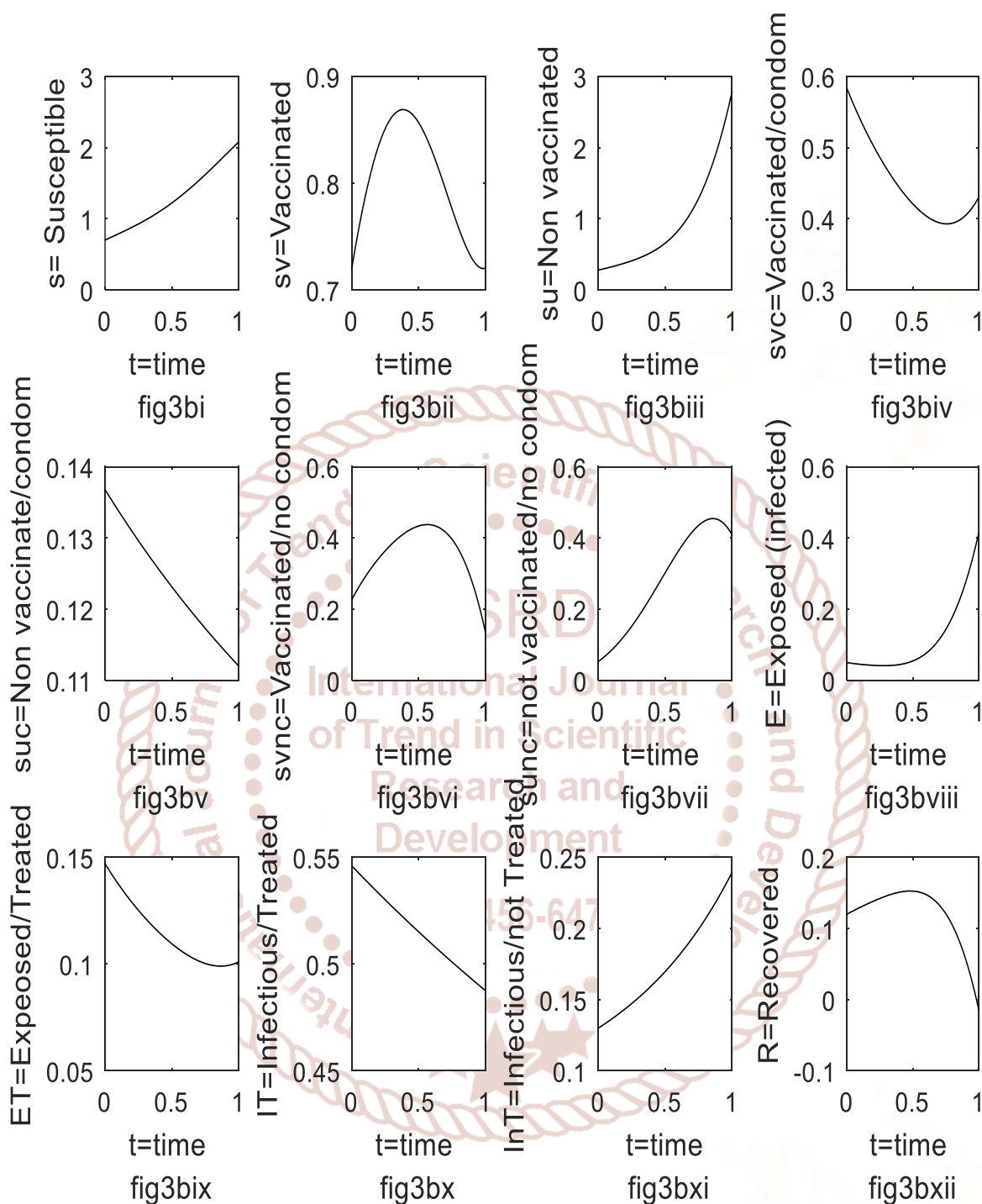


Figure (3bi – 3bxii): Numerical simulation of the model system (3.1) when there is no control with time ranging from 0 – 1year.

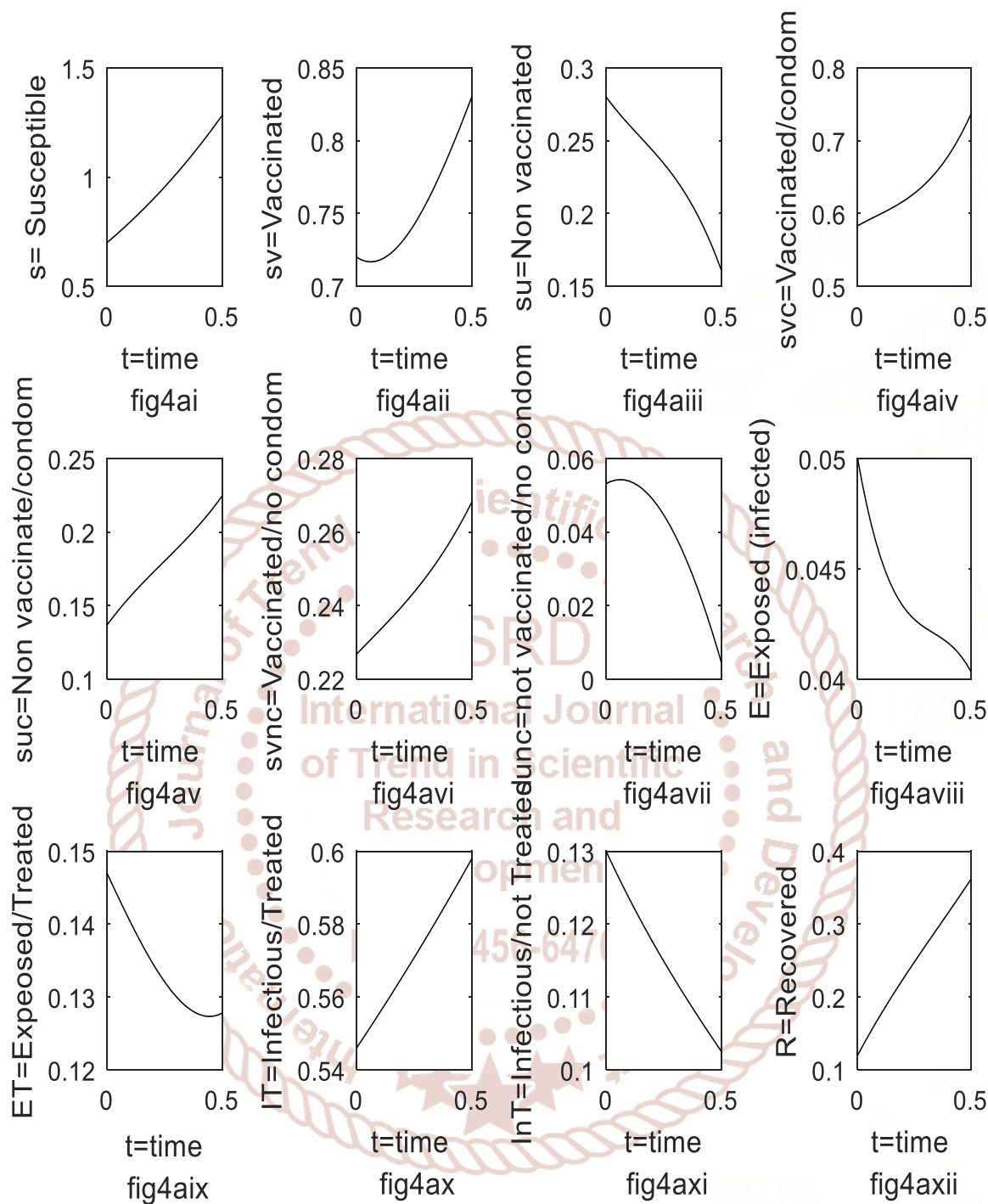


Figure (4ai – 4axii): Numerical simulation of the model system (3.1) when there is control with time ranging from 0 to 6months.

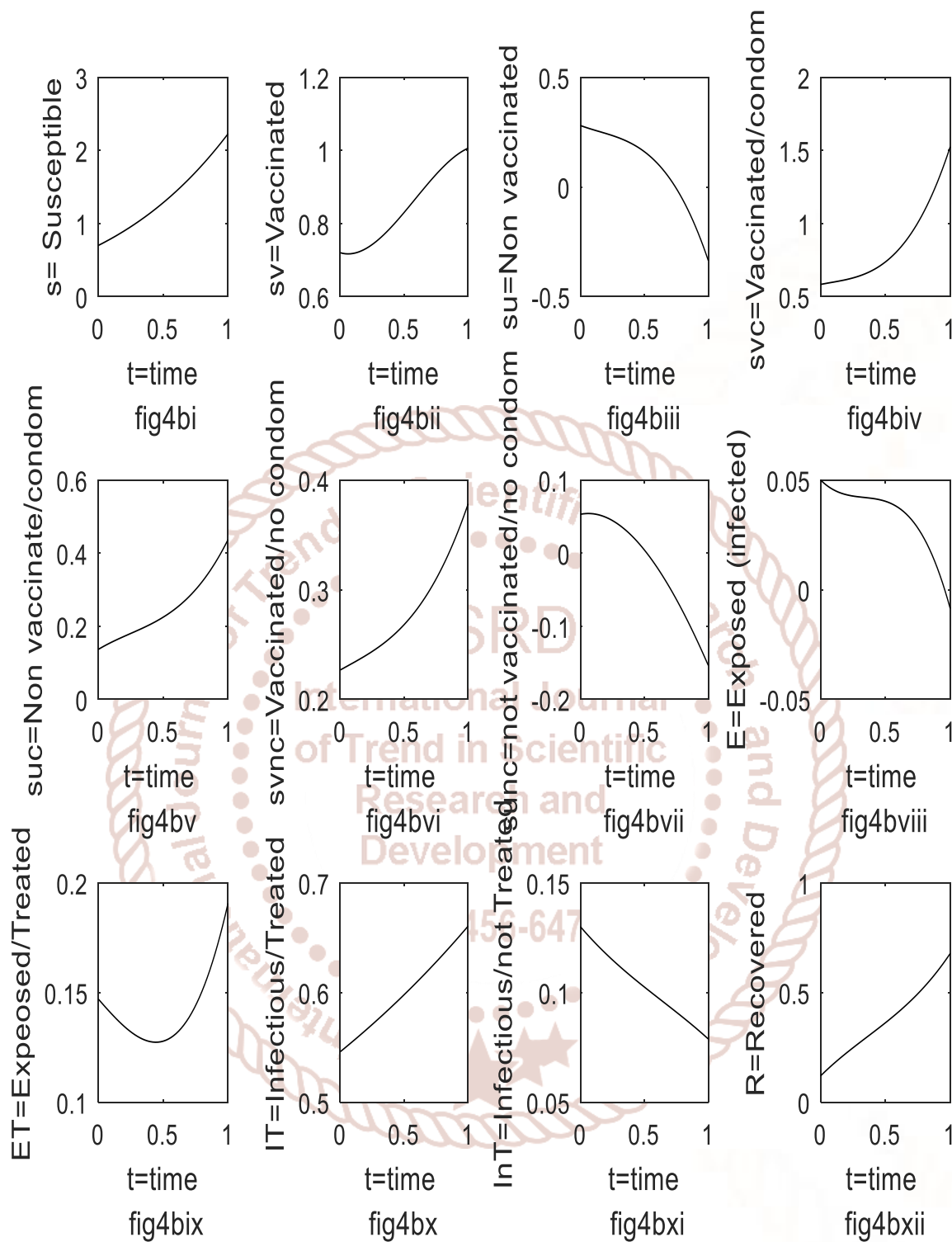


Figure (4bi – 4bxii): Numerical simulation of the model system (3.1) when there is control with time ranging from 0 to 1 year.

Here, we numerically solve the control system (3.1) which consists of twelve differential equations. We have plotted susceptible individuals, vaccinated individuals, non vaccinated individuals, vaccinated individuals who use condom, vaccinated individuals

who does not use condom, non vaccinated individuals who use condom, non vaccinated individuals who does not use condom, Exposed (infected) individuals, Exposed but treated individuals, infectious but treated individuals, infectious but not treated individuals and

recovered individuals, by considering values of the parameters in table 5 and we simulated the system at different level of $\rho_1, \beta_1, \sigma, \alpha_1$ and d.

From figures (3ai – 3axii) and (3bi – 3bxii), we see that the number of both the exposed and the infectious population increases when there is no control. Also from (4ai – 4axii) and (4bi – 4bxii), we observe that the application of control (vaccination, condom and treatment) gives a better result than when there is no control because the population of the exposed and the infectious individuals is reduced. This implies that effective vaccination with appropriate use of condom (condom efficacy) is able to reduce the density of the exposed (infected) individuals, while application of treatment is able to reduce the density of the infectious individuals. Therefore, since our main purpose is to reduce the density of the exposed and infectious individuals and increase the density of the removed with or without permanent immunity, we can conclude that the numerical simulation result shows that combination of vaccination, condom and treatment is the most effective way to control Hepatitis B virus infection.

V. Summary and Conclusion

To control HBV infection at least 96% Or more of newborns should be vaccinated and effort should be made to vaccinate more than 50% of the sexually active susceptible individuals who should also be encouraged to use condom during sex as these combination will go a long way in reducing the density of the exposed (infected) individuals. Also, treatment strategies are needed to control the spread of HBV infection in the population since control of HBV infection implies reducing the susceptible and exposed by vaccination and reducing the infectious by treatment.

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