Transworld Research Network
37/661 (2), Fort P.O.
Trivandrum-695 023
Kerala, India

Understanding the Dynamics of Emerging and Re-Emerging Infectious Diseases Using Mathematical Models, 2012: 49-89 ISBN: 978-81-7895-549-0 Editors: Steady Mushayabasa and Claver P. Bhunu

3. On the role of alcohol drinking on the dynamics transmission of Hepatitis B

S. Bowong[1,*], D. P. Moualeu[2,*], J. J. Tewa[3,*] and M. A. Aziz-Alaoui[4]

[1]Laboratory of Applied Mathematics, Department of Mathematics and Computer Science, Faculty of Science, University of Douala, PO Box 24157, Douala, Cameroon; [2]Department of Mathematics, Faculty of Science, University of Yaounde I, PO Box 812, Yaounde Cameroon; [3]National High School Polytechnic, Department of Mathematics and Physics, University of Yaounde I, PO Box 8329 Yaounde, Cameroon [4]Laboratoire de Mathématiques Appliquées, Université Le Havre 25 Rue Ph. Lebon, BP540, Le Havre Cedex, France

Abstract. Drinking alcohol cause the liver to become even more damaged in people infected with the hepatitis B virus (HBV). We present a deterministic model for HBV in a community in order to determine the effects of alcohol in the spread of the disease. The important mathematical features of the HBV model are thoroughly investigated. The epidemic threshold known as the basic reproduction number and equilibria for the model are determined and stabilities analyzed. The model is numerically analyzed to assess the effects of alcohol drinking on the transmission dynamics of HBV.

*Presene address: UMI209IRD/UPMC UMMISCO, Bondy ,Projet MASAIE INRIA Grand Est, France and Projet GRIMCAPE, LIRIMA, Cameroon.

Correspondence/Reprint request: Dr. S. Bowong, Laboratory of Applied Mathematics, Department of Mathematics and Computer Science, Faculty of Science, University of Douala, PO Box 24157, Douala Cameroon. E-mail: sbowong@gmail.com

Numerical simulations suggest that drinking alcohol enhances HBV transmission and progression to chronic carriers in a community. So, for patients with hepatitis B, one of the best things to do is to stop drinking or cut down as much as one can. The results suggest that intervention strategies such as vaccination, counseling and educational campaigns should be addressed in communities of alcoholics affected by HBV in order to reduce the burden of the disease.

1. Introduction

Hepatitis B is a disease caused by the hepatitis B virus (HBV) which infects the liver of hominoidea, including humans, and causes an inflammation called hepatitis. Originally knownas "serum hepatitis", the disease has caused epidemics in parts of Asia and Africa (WHO 2008; Lavanchy 2004). The hepatitis B virus is present in body fluids such as blood, saliva, semen and vaginal fluid. It can be passed from person to person through unprotected sex (without using a condom) or by sharing needles to inject drugs, for example. You can also become infected with hepatitis B if you are not immune (resistant) to the virus and have been exposed to the blood or body fluids of an infected person. A vaccine is available to protect against hepatitis B. Infected mothers can also pass the virus to their baby during child birth, often without knowing that they are infected. The incubation period (the time it takes from coming in to contact with the virus to developing infection) is between one and six months. Many people do not even realize that they have been infected with the virus, because the typical flu-like symptoms may not develop immediately, or even at all. Hepatitis B is 100 times more infectious than HIV. About a third of the world's population, more than 2 billion people, have been infected with the hepatitis B virus (WHO 2008). This includes 350 million chronic carriers of the virus. In developing countries, it is estimated that 5 to 15 % of persons are chronic carriers, where as only about 1 % of the population is chronically infected in North America and Western Europe (WHO 2008; Lavanchy 2004).

The risk of developing hepatitis B is primarily related to sexual, household or perinatal exposure to infected individuals. Prevention of perinatal HBV transmission is an important step in controlling hepatitis B in endemic countries. As infection by hepatitis B in the perinatal period leads to almost 90 % development of chronic hepatitis, screening for HBsAg (hepatitis B surface antigen) positive mothers to determine new borns at risk and to target them for immunoprophylaxis has been one strategy used to break the cycle of transmission. Almost 90% of infants born to HBsAg-positive/HBeAg-positive women and 10% of infants born to HBsAg-

positive/HBeAg-negative women become infected (Shepard *et al*., 2006; Goldstein *et al*., 2005). Also, infants infected perinatally have the highest probability of chronic infection (around 90%) and adults have the lowest (less than 5%) (Hyams, 1995).

There is no widely available effective treatment for chronic HBV carriers. Immunization with hepatitis B vaccine (HepB) is the most important prevention measure (Shepard *et al*., 2006). Several vaccines have been developed for the prevention of HBV infection, which rely on the use of one of the viral envelope proteins (HBsAg). Vaccine can be received by infants to adults and provides protection for 85-90% of individuals (Shepard *et al*., 2006; Maynard *et al*., 1989). The main vaccinations include the 3-dose HepB vaccination and the timely HepB birth-dose (i.e., within 24h of birth). In 1991, WHO recommended that hepatitis B vaccination should be included in national immunization system in all countries with an HbsAg carrier prevalence 8% by 1995 and all countries by 1997. By 2002, 154 countries had routine infant immunization with Hep B(Lavanchy, 2004; Hou *et al*., 2005).

Alcohol has been identified as a major risk factor for chronic disease and injury (Rehm *et al*. 2006). However, no infectious disease has been included in the list of alcohol-attributable disease categories, even though several such diseases have consistent associations with alcohol. Although, there are various factors which play a significant role on the spread of HBV in the community such as HIV/AIDS, tobacco, HCV, etc., it has long been known that there is an association between hepatitis and alcohol. Mortality due to alcohol over-consumption is high, in particular among young men (Mokdad 2000). Alcohol abuse not only increases the risk for liver disease but is also responsible for malignancies, accidents, violence, and social problems (Bellentani 1997; Vaillant 1995). Alcohol consumption in excess of 20-30 g for women and 40-60 g for men per day markedly increases the risk for liver disease (Becker 1996; Lucey 2008). However, liver cirrhosis is seen only in a minority of subjects with high alcohol consumption; less than 10% of subjects who drink more than 120 g of alcohol daily have cirrhosis (Bellentani 1997). In addition to the level of alcohol consumption, various other factors, such as sex, other genetic characteristics, and co-morbidities contribute to the risk for liver disease (Nishigushi 1991; Becker 1996; Bellentani 1997; McCollough 1998; de Alwis 2007; Lucey 2009).

Alcohol abuse most often causes fat accumulation of hepatocytes, called hepatic steatosis. Alcohol-induced steatosis is in general reversible after alcohol abstinence. Continued alcohol abuse in the presence of steatosis markedly increases the risk for development of hepatitis, fibrosis and

cirrhosis (Teli 1995; Cubero 2009). Patients with alcohol-induced cirrhosis have a significantly increased risk for hepato cellular carcinoma (McCollough 1998). Patients with only fatty liver in the absence of inflammation and fibrosis have a much lower risk for development of cirrhosis than those with fatty liver plus presence of inflammation and fibrosis. The latter group of patients with alcoholic fatty liver, inflammation and fibrosis is defined as alcoholic steato-hepatitis (ASH). The liver histology of patients with ASH is similar when compared to patients with non-alcoholic steato-hepatitis (NASH) that is often associated with obesity and diabetes (Ludwig 1980; Brunt 1999).

A number of theoretical studies has been carried out on the mathematical modeling of HBV transmission dynamics (Anderson and May, 1991; Anderson *et al*. 1992; Williams *et al*. 1996; Edmunds *et al*. 1993; Medley *et al*. 2001; McLean and Blumberg 1994; Thornley *et al*. 2008). Some mathematical models have been used frequently to study the transmission dynamics of HBV in various regions. Anderson and May (1991) used a simple deterministic, compartmental mathematical model to illustrate the effects of carriers on the transmission of HBV. Anderson *et al*. (1992) and Williams *et al*. (1996) described models of the sexual transmission of HBV, which include heterogeneous mixing with respect to age and sexual activity. Edmunds *et al*. (1993) illustrated the relation between the age at infection with HBV and the development of the carrier state. Medley *et al*. (2001) gave a model to show that the prevalence of infection is largely determined by a feedback mechanism that relates the rate of transmission, average age at infection and age-related probability of developing carriage following infection. Thornley *et al*. (2008) applied the model of Medley *et al*. (2001) to predict chronic hepatitis B infection in New Zealand. The prevalence of HBV in developing countries is different from that in developed countries, since it appears that the rate of transmission in childhood is the major determinant of the level of HBV endemicity (Edmunds *et al*., 1996c), and little is known on the rates and patterns of sexual contact in developing countries. McLean and Blumberg (1994) and Edmunds *et al*. (1996a) studied models of HBV transmission on developing countries and Williams *et al*. (1996) described a model of HBV in the UK.

However, none of these studies has considered the effects of drinking alcohol on the transmission dynamics of HBV. Since mathematical models on the effect of drinking alcohol in the spread of HBV are lacking, it is therefore the intention of this study to investigate the impact of drinking alcohol on the transmission dynamics of HBV in the community. The model incorporates some key epidemiological features of HBV such as vaccination

and immunity. The main objective in this study is to forecast future trends in the incidence of HBV and also to quantify the association between drinking alcohol and HBV in the community.

The paper is structured as follows. In the next section, our HBV transmission model is formulated and results on the long-term dynamics are presented in Section 3. Simulation results are presented in Section 4. Concluding remarks and discussions round up the paper.

2. Model

As a first step, we assume random mixing of the population, even though non-heavy and heavy alcohol drinkers may well have different mixing patterns. The potential effect of non-random mixing patterns will be addressed in the near future. The model sub-divides the total population at time t denoted by N, into various mutually-exclusive compartments depending on their disease status and their habit: susceptible who are non-heavy alcohol drinkers $(S_1(t))$, susceptible who are heavy alcohol drinkers $(S_2(t))$, vaccinated who are non-heavy alcohol drinkers $(V_1(t))$, vaccinated who are heavy alcohol drinkers $(V_2(t))$, acute infected who are non-heavy alcohol drinkers $(I_1(t))$, acute infected who are heavy alcohol drinkers $(I_2(t))$, chronic carriers who are non-heavy alcohol drinkers $(C_1(t))$, chronic carriers who are heavy alcohol drinkers $(C_2(t))$, recovered with protective immunity who are non-heavy alcohol drinkers $(R_1(t))$ and recovered with protective immunity who are heavy alcohol drinkers $(R_2(t))$. The total population is

$$N(t)=S_1(t)+V_1(t)+I_1(t)+C_1(t)+R_1(t)+S_2(t)+V_2(t)+I_2(t)+C_2(t)+R_2(t). \quad (1)$$

Susceptible who never been successfully vaccinated, or who have been vaccinated but the protective effect of vaccination worn off acquire HBV infection following effective contact with individuals in the acute and chronic carriers stage of HBV infection at rate λ_B given by

$$\lambda_B = \beta_B \frac{I_1 + \varepsilon I_2 + \eta(C_1 + \eta_1 C_2)}{N}. \quad (2)$$

In Eq. (2), β_B is the effective contact rate for HBV transmission, ε accounts for the relative infectiousness of acute infected who are heavy alcohol drinkers (I_2) in comparison to acute infected who are non-heavy alcohol drinkers (I_1). The parameter η models the reduced transmission rate of

individuals in the chronic stage of HBV infection with respect to the infectiousness of individuals in the acute stage of HBV infection. Finally, η_1 is the modification parameter accounting the fact that chronic carriers who are heavy alcohol drinkers (C_2), are more infectious than chronic carriers who are heavy alcohol drinkers (C_1).

It is assumed that all potential non-heavy alcohol drinkers (those in the S_1, V_1, I_1, C_1 and R_1 classes) can acquire alcohol drinking habits via *effective contact* with heavy alcohol drinkers (those in the S_2, V_2, I_2, C_2 and R_2 classes) at the rate λ_A defined by

$$\lambda_A = \beta_A \phi_A \frac{S_2 + V_2 + I_2 + C_2 + R_2}{N}, \tag{3}$$

where β_A is the average number of contacts per unit time and ϕ_A is the probability that non-heavy alcohol drinkers become heavy alcohol drinkers. We point out that the expression of effective contacts is taken here not in its etymological sense, but in the sense of being attracted by or drawn by stimulating interest, or by exciting admiration or by invitation. This includes factors such as advertising and mass consumption of alcohol in the community. It is assumed that the acquisition of alcohol drinking habitis analogous to acquiring disease infection.

We also suppose that acute infected, chronic carriers and recovered with protective immunity who are heavy alcohol drinkers (those in the I_2, C_2 and R_2 classes) can abandon alcohol drinking via *effective contact* with non-heavy alcohol drinkers (those in the S_1, V_1, I_1, C_1 and R_1 classes) at the rate λ_C defined by

$$\lambda_C = \beta_C \phi_C \frac{S_1 + V_1 + I_1 + C_1 + R_1}{N}, \tag{4}$$

where β_C is the effective contact rate fornon-heavy alcohol drinkers (contacts sufficient that result to the abandon of alcohol drinking habit) and ϕ_C is the probability that heavy alcohol drinkers become non-heavy alcohol drinkers. This can occur when the patients who are heavy alcohol drinkers take an antibiotic treatment, are interned in the hospital or have follow advertising and education on the damage caused by alcohol (because most patients who are sick often abandon alcohol when the sickness is severe).

The model is based on the following assumptions. The mixing between individuals is homogeneous. We neglect the vertical transmission of HBV.

The vaccine-induced immunity acquired by vaccinated individuals is supposed to wane and the way to vaccinated individuals to acquire HBV infection is through the waning of vaccine-induced protection, and individuals there fore enter the HBV acute infection class. It is assumed that death from natural causes is not influenced by individuals's status (non-drinking or drinking alcohol). Every susceptible vaccinated neonate enters the vaccinated classes representing the assumption that vaccination prevents perinatal transmission from infectious women.

Potential heavy alcohol drinkers are recruited through birth at rate Λ. Susceptible individuals who are potential heavy alcohol drinkers and who HBV vaccination was successful enter the class V_1 of vaccinated who are non-heavy drinkers at rate φ_1. Susceptible individuals who are potential heavy alcohol drinkers are infected with HBV at rate λ_B and move to the class I_1 of HBV acute infected who are non-heavy alcohol drinkers. The vaccine-induced immunity acquired by HBV vaccinated who are non-heavy alcohol drinkers is supposed to wane at rate π_1 and the way that HBV vaccinated who are non-heavy alcohol drinkers acquire HBV infection is through the wanning of vaccine-induced protection, and individuals therefore enter the class I_1 of HBV acute infected who are non-heavy alcohol drinkers. Thus, HBV vaccinated who are non-heavy alcohol drinkers can experience break-through infection (due to incomplete protection provided by vaccine) and they are moved in the class I_1 of HBV acute infected who are non-heavy alcohol drinkers at rate $\pi_1\ \lambda_B$. We define by q_1 the average probability that a potential HBV acute infected who is a non-heavy alcohol drinker fails to clear an acute infection and develops a chronic state (C_1). Then, individuals in the class I_1 progress to the class C_1 at rate $q_1\ \gamma_1$, while the remain der enters the class R_1 at rate $\gamma_1(1- q_1)$. Further, potential chronic carriers who are non-heavy alcohol drinkers (those in the class C_1) progress to the class $R_1$of recovered with protective immunity who are non-heavy alcohol drinkers at rate δ_1.

Susceptible who are heavy alcohol drinkers who HBV vaccination was successful enter the vaccinated class V_2 at rate φ_2. Also, susceptible who are heavy alcohol drinkers are infected with HBV at rate $\theta\lambda_B$ with $\theta >1$, since alcohol drinking acts as a carrier of HBV (Teli 1995; Bellentani 1997; Cubero 2009) and enter the class I_2 of HBV acute infected who are heavy alcohol drinkers. The vaccine-induced immunity acquired by HBV vaccinated who are heavy alcohol drinkers is supposed to wane at rate π_2. Thus, HBV vaccinated who are heavy alcohol drinkers and who the vaccine-induced immunity acquired is waned are infected with HBV at rate $\theta\pi_2\lambda_B$ and

enter the HBV acute infection class I_2 of HBV acute infected who are heavy alcohol drinkers. Individuals in the HBV acute class I_2 progress to the chronic carriers class C_2 at rate $q_2\gamma_2$, while the remainder enters the class R_2 of recovered with protective immunity who are heavy alcohol drinkers at rate $\gamma_2(1-q_2)$ where q_2 is the average probability that a HBV acute infected who is a heavy alcohol drinker fails to clear an acute infection and develops a chronic state (C_2). Further, individuals in the class C_2 progress to the class R_2 of recovered with protective immunity who are heavy alcohol drinkers at rate δ_2. Individuals who are heavy alcohol drinkers may abandon alcohol drinking (possibly due to counseling, health reasons, pressure at work, poverty or any other reason) at rate α.

Individuals in all sub-classes experience natural death at rate μ. Chronic carriers are prone to the background death rate that applies to the whole community but have additional death rates d_1 and d_2 for chronic carriers who are non-heavy and heavy alcohol drinkers because of their hepatitis B carrier status. It is important to note here that $d_2 > d_1$ as drinking alcohol experience greater disease induced deaths than their corresponding non-drinking alcohol counterparts (Mokdad 2000).

The structure of the model is shown in Fig.1.

Putting the formulations and the assumptions together gives the following system of

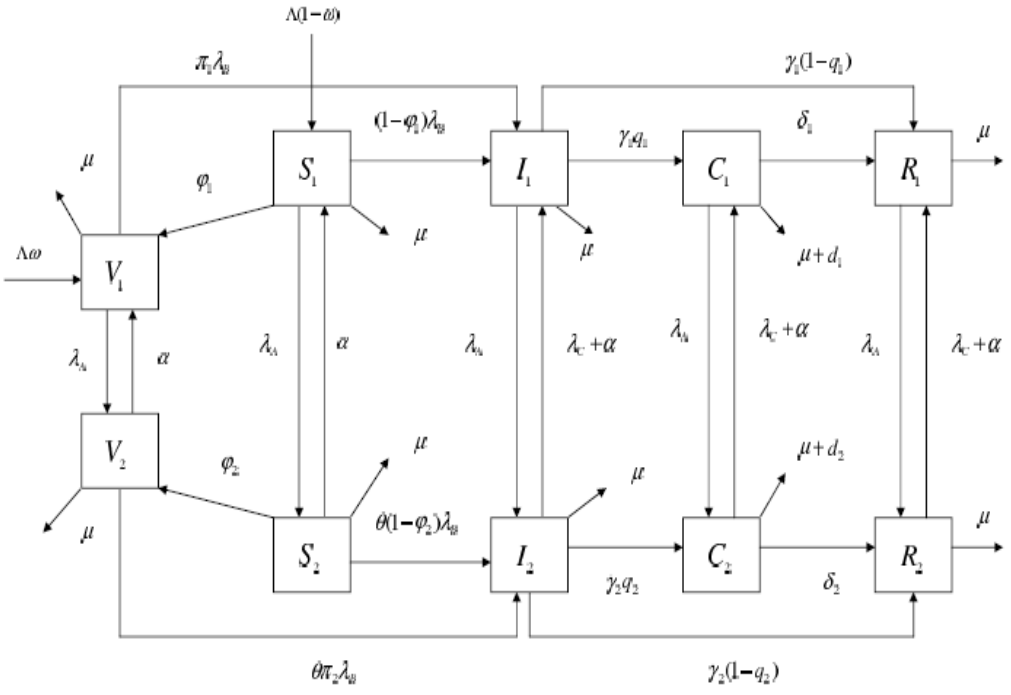

Figure 1. Structure of the model.

differential equations:

$$\begin{cases} S_1' &= \Lambda(1-\omega)+\alpha S_2-[\mu+\varphi_1+\lambda_A+(1-\varphi_1)\lambda_B]S_1,\\ V_1' &= \Lambda\omega+\varphi_1 S_1+\alpha V_2-(\mu+\lambda_A+\pi_1\lambda_B)V_1,\\ I_1' &= [(1-\varphi_1)S_1+\pi_1 V_1]\lambda_B+(\lambda_C+\alpha)I_2-(\mu+\gamma_1+\lambda_A)I_1,\\ C_1' &= q_1\gamma_1 I_1+(\lambda_C+\alpha)C_2-(\mu+d_1+\delta_1+\lambda_A)C_1,\\ R_1' &= \gamma_1(1-q_1)I_1+\delta_1 C_1+(\lambda_C+\alpha)R_2-(\mu+\lambda_A)R_1,\\ S_2' &= \lambda_A S_1-[\mu+\alpha+\varphi_2+\theta(1-\varphi_2)\lambda_B]S_2,\\ V_2' &= \lambda_A V_1+\varphi_2 S_2-[\mu+\alpha+\theta\pi_2\lambda_B]V_2,\\ I_2' &= \theta[(1-\varphi_2)S_2+\pi_2 V_2]\lambda_B+\lambda_A I_1-(\mu+\alpha+\gamma_2+\lambda_C)I_2,\\ C_2' &= q_2\gamma_2 I_2+\lambda_A C_1-(\mu+d_2+\alpha+\delta_2+\lambda_C)C_2,\\ R_2' &= \gamma_2(1-q_2)I_2+\delta_2 C_2+\lambda_A R_1-(\mu+\alpha+\lambda_C)R_2. \end{cases} \tag{5}$$

System (5) can be written in the following compact form:

$$\begin{cases} x' &= \Gamma+A_x x-\lambda_B\sum_{i=1}^{4}B_i\langle e_i\mid x\rangle+\lambda_A\sum_{i=1}^{2}\mathcal{D}_i\langle e_i\mid x\rangle,\\ y' &= \lambda_B[\sum_{i=1}^{2}\mathcal{K}_i\langle \varrho_i\mid x\rangle+\lambda_A\sum_{i=1}^{3}\mathcal{G}_i\langle\omega_i\mid y\rangle+\lambda_C\sum_{i=1}^{3}\mathcal{H}_i\langle\sigma_i\mid y\rangle+A_y y, \end{cases} \tag{6}$$

where $x=(x_1,x_2,x_3,x_4)^T=(S_1,V_1,S_2,V_2)^T\in\mathbb{R}^4_{\geq 0}$ is the vector representing the compartments of non transmitting individuals (susceptible and vaccinated individuals), $y=(y_1,y_2,y_3,y_4,y_5,y_6)^T=(I_1,C_1,R_1,I_2,C_2,R_2)^T\in\mathbb{R}^6_{\geq 0}$ is the vector representing the state compartment of different infected individuals and immune (acute infected, chronic carriers and recovered with protective immunity), $\Gamma=(\Lambda(1-\omega),\Lambda\omega,0,0)^T$, $\lambda_B=\langle B\mid y\rangle/N$, $N=\sum_{i=1}^{4}x_i+\sum_{i=1}^{6}y_i$, $B=(\beta_B,\beta_B\eta,0,\beta_B\varepsilon,\beta_B\eta\eta_1,0)$, $B_1=(1-\varphi_1,0,0,0)^T$, $B_2=(0,\pi_1,0,0)^T$, $B_3=(0,0,\theta(1-\varphi_2),0)^T$, $B_4=(0,0,0,\pi_2)^T$, $e_1=(1,0,0,0)$, $e_2=(0,1,0,0)$, $e_3=(0,0,1,0)$, $e_4=(0,0,0,1)$, $\mathcal{K}_1=(1,0,0,0,0,0)^T$, $\mathcal{K}_2=(0,0,0,1,0,0)^T$, $\varrho_1=(1-\varphi_1,\pi_1,0,0)$, $\varrho_2=(0,0,\theta(1-\varphi_2),\theta\pi_2)$, $\mathcal{G}_1=(-1,0,0,1,0,0)^T$, $\mathcal{G}_2=(0,-1,0,0,1,0)^T$, $\mathcal{G}_3=(0,0,-1,0,0,1)^T$, $\mathcal{D}_1=(-1,0,1,0)^T$, $\mathcal{D}_2=(0,-1,0,1)^T$, $\mathcal{H}_1=(1,0,0,-1,0,0)^T$, $\mathcal{H}_2=(0,1,0,0,-1,0)^T$, $\mathcal{H}_3=(0,0,1,0,0,-1)^T$, $\omega_1=(1,0,0,0,0,0)$, $\omega_2=(0,1,0,0,0,0)$, $\omega_3=(0,0,1,0,0,0)$, $\sigma_1=(0,0,0,1,0,0)$, $\sigma_2=(0,0,0,0,0,1,0)$, $\sigma_3=(0,0,0,0,0,1)$, $\lambda_A=[\langle\psi_1\mid x\rangle+\langle\tau_1\mid y\rangle]/N$, $\psi_1=(0,0,\beta_A\phi_A,\beta_A\phi_A)$, $\tau_1=(0,0,0,\beta_A\phi_A,\beta_A\phi_A,\beta_A\phi_A)$, $\lambda_C=[\langle\psi_2\mid x\rangle+\langle\tau_2\mid y\rangle]/N$, $\psi_2=(\beta_C\phi_C,\beta_C\phi_C,0,0)$, $r_2=(\beta_C\phi_C,\beta_C\phi_C,\beta_C\phi_C,0,0,0)$,

$$A_x = \begin{bmatrix} -(\mu+\varphi_1) & 0 & \alpha & 0 \\ \varphi_1 & -\mu & 0 & \alpha \\ 0 & 0 & -(\mu+\alpha+\varphi_2) & 0 \\ 0 & 0 & \varphi_2 & -(\mu+\alpha) \end{bmatrix},$$

and

$$A_y = \begin{bmatrix} -(\mu+\gamma_1) & 0 & 0 & \alpha & 0 & 0 \\ q_1\gamma_1 & -(\mu+d_1+\delta_1) & 0 & 0 & \alpha & 0 \\ \gamma_1(1-q_1) & \delta_1 & -\mu & 0 & 0 & \alpha \\ 0 & 0 & 0 & -(\mu+\alpha+\gamma_2) & 0 & 0 \\ 0 & 0 & 0 & q_2\gamma_2 & -(\mu+d_2+\alpha+\delta_2) & 0 \\ 0 & 0 & 0 & \gamma_2(1-q_2) & \delta_2 & -(\mu+\alpha) \end{bmatrix}.$$

In Eq. (6), $\langle a \mid b \rangle = a^T b$ is the usual inner scalar product.

The parameter values used for numerical simulation are given Table 1.

In Table 1, NIS means National Institute of Statistics (Cameroon), *a** denotes a parameter value from Edmunds et al. (1996) and *b** from (Hahnea *et al*. 2004).

Due to lack of data, the parameters that are not estimated are assumed within realistic ranges (for the purpose of illustration) based on current understanding of the qualitative and the essential biological and epidemiological features of HBV.

3. Analysis of the model

3.1. Basic properties

3.1.1. Positivity and boundedness of solutions

For model system (5) to be epidemiologically meaningful, it is important to prove that all its state variables are non-negative for all time. In other words, solutions of model system (5) with positive initial data remain positive for all time $t > 0$.

Theorem 1 : *Let the initial data be* $S_1(0) > 0$, $V_1(0) > 0$, $I_1(0) > 0$, $C_1(0) > 0$, $R_1(0) > 0$, $S_2(0) > 0$, $V_2(0) > 0$, $I_2(0) > 0$, $C_2(0) > 0$ *and* $R_2(0) > 0$. *Then, the solutions* $(S_1, V_1, I_1, C_1, R_1, S_2, V_2, I_2, C_2, R_2) \in \mathbb{R}^{10}_{\geq 0}$ *of model system (5) are positive for all* $t > 0$. *Furthermore,*

$$\limsup_{t\to\infty} N(t) \leq \frac{\Lambda}{\mu}. \tag{7}$$

Table 1. Numerical values for the parameters of model system (5).

Parameters	Symbol	Value	Source
Birth rate	Λ	500/yr	Assumed
Natural mortality rate	μ	1/51.5/yr	NIS
Proportion of births without successful vaccination	ω	0.35/yr	Assumed
HBV transmission coefficient	β_B	Variable	
Rate of waning vaccine-induced immunity of vaccinated who are non-heavy alcohol drinkers	π_1	0.1/yr	a^*
Vaccination rate of susceptible who are non-heavy alcohol drinkers	φ_1	0.7/yr	Assumed
Probability that an individual who is a non-heavy alcohol drinker fails to clear an acute infection and develops to carriers state	q_1	0.0885/yr	b^*
Rate moving from acute infected who are non-heavy alcohol drinkers to chronic carriers who are non-heavy alcohol drinkers	γ_1	4/yr	
Rate moving from chronic carriers who are non-heavy alcohol drinkers to immune who are non-heavy alcohol drinkers	δ_1	0.025/yr	a^*
HBV induced death rate of chronic carriers who are non-heavy alcohol drinkers	d_1	0.002/yr	Assumed
Effective contact rate to become heavy alcohol drinkers	β_A	2	Assumed
Probability of being heavy alcohol drinkers	ϕ_A	0.85	Assumed
Rate of waning vaccine-induced immunity of vaccinated who are heavy alcohol drinkers	π_2	0.2/yr	Assumed
Vaccination rate of susceptible who are heavy alcohol drinkers	φ_2	0.6/yr	Assumed
Probability that a heavy alcohol drinker fail to clear an acute infection and develops to carrier state	q_2	0.09/yr	Assumed
Rate moving from acute infected who are heavy alcohol drinkers to chronic carrier who are heavy alcohol drinkers	γ_2	3/yr	Assumed
Rate moving from chronic carrier who are heavy alcohol drinkers to immune who are heavy alcohol drinkers	δ_2	0.03/yr	Assumed
HBV induced death rate of carriers who are heavy alcohol drinkers	d_2	0.005/yr	Assumed
Rate of quitting alcohol drinking	α	0.10/yr	Assumed
Modification parameter	ε	1.2	Assumed
Modification parameter	η	0.16	a^*
Modification parameter	η_1	0.2	Assumed
Effective contact rate to become infected individuals who are non-heavy alcohol drinkers	β_C	1.5	Assumed
Probability of being infected individuals who are non-heavy alcohol drinkers	ϕ_C	0.65	Assumed
Alcohol drinking enhancement factor for HBV transmission of individuals in the S_2, V_2, I_2, C_2 and R_2 classes	θ	1.2	Assumed

Proof: Suppose, for example, the variable S_1 becomes zero for some time $\bar{t} > 0$, i.e., $S_1(\bar{t}) = 0$, while all other variables are positive. Then, from the S_1 equation, we have $dS_1(\bar{t})/dt > 0$. Thus, $S_1(t) \geq 0$ for all $t > 0$. Similarly, it can be shown that all variables remain non negative for all $t > 0$.

Now, adding all the equations in the differential system (5) gives

$$N'(t) = \Lambda - \mu N - d_1 C_1 - d_2 C_2. \tag{8}$$

From Eq.(8), it follows that

$$\Lambda - (\mu + d_1 + d_2)N(t) \leq N'(t) \leq \Lambda - \mu N(t).$$

Thus,

$$\frac{\Lambda}{\mu + d_1 + d_2} \leq \liminf_{t\to\infty} N(t) \leq \limsup_{t\to\infty} N(t) \leq \frac{\Lambda}{\mu},$$

so that

$$\limsup_{t\to\infty} N(t) \leq \frac{\Lambda}{\mu}.$$

This completes the proof.

3.1.2. Invariant region

Model system (5) will be analyzed in a suitable region as follows. We first show that model system (5) is dissipative. That is, all solutions are uniformly bounded in a proper subset $\Omega \subset \mathbb{R}^{10}_{\geq 0}$. Let $(S_1, V_1, I_1, C_1, R_1, S_2, V_2, I_2, C_2, R_2) \in \mathbb{R}^{10}_{\geq 0}$ be any solution with non-negative initial conditions.

Model system (5) has a varying population size ($N \neq 0$) and therefore a trivial equilibrium is not feasible. Let $\xi = \min(d_1, d_2)$, then, from Eq. (5), it follows that

$$\begin{aligned} N'(t) &= \Lambda + \mu N(t) - d_1 C_1(t) - d_2 C_2(t), \\ &\leq \Lambda + -\mu N(t) - \xi(C_1(t) + C_2(t)), \\ &\leq \Lambda - \mu N(t). \end{aligned} \tag{9}$$

So that (cf. Birkhoff and Rota 1982)

$$0 \leq N(t) \leq \frac{\Lambda}{(\mu)} + \left(N(0) - \frac{\Lambda}{\mu}\right) e^{-\mu t}, \tag{10}$$

where N (0) represents the value of N (t) evaluated at the initial values of the respective variables. The lower limit comes naturally from the fact that the model variables and parameters are non-negative (for all $t \geq 0$), since they monitor human populations. Thus, as $t \to \infty$, $0 \leq N(t) \leq \Lambda/\mu$.Therefore, all feasible solutions of model system (5) enter the region

$$\Omega = \left\{(S_1, V_1, I_1, C_1, R_1, S_2, V_2, I_2, C_2, R_2) \in \mathbb{R}^{10}_{\geq 0}, \;\; N(t) \leq \frac{\Lambda}{\mu}\right\}. \tag{11}$$

Thus, Ω is positively invariant (it can also be shown that Ω is attracting) and it is sufficient to consider solutions of model system (5) in Ω. Existence, uniqueness and continuation results for model system (5) hold in this region. It can be shown that all solutions of model system (5) starting in Ω remain in Ω for all $t \geq 0$.

3.2. Stability of the disease-free equilibrium (DFE)

3.2.1. The disease-free equilibrium (DFE)

The disease-free equilibrium of model system (5) is given by $Q_0 = (S_1^0, V_1^0, S_2^0, V_2^0)$ where S_1^0, V_1^0, S_2^0 and V_2^0 satisfy

$$\begin{cases} \Lambda(1-\omega) + \alpha S_2^0 - (\mu + \varphi_1 + \lambda_A^0) S_1^0 = 0, \\ \Lambda\omega + \varphi_1 S_1^0 + \alpha V_2^0 - (\mu + \lambda_A^0) V_1^0 = 0, \\ \lambda_A^0 S_1^0 - (\mu + \alpha + \varphi_2) S_2^0 = 0, \\ \lambda_A^0 V_1^0 + \varphi_2 S_2^0 - (\mu + \alpha) V_2^0 = 0, \end{cases} \tag{12}$$

where $\lambda_A^0 = \beta_A \phi_A \dfrac{(S_1^0 + V_1^0)}{N_0}$ and $N_0 = S_1^0 + V_1^0 + S_2^0 + V_2^0$ Expression S_1^0, V_1^0, S_2^0 and V_2^0 in terms of λ_A^0 gives

$$
\begin{aligned}
S_1^0 &= \frac{\Lambda(1-\omega)(\mu+\alpha+\varphi_2)}{\lambda_A^0(\mu+\varphi_2)+(\mu+\varphi_1)(\mu+\alpha+\varphi_2)},\\
V_1^0 &= \frac{\Lambda[\lambda_A^0[(\mu+\alpha)(\mu+\varphi_2)(1-\alpha)+(1-\omega)\alpha\varphi_2]+(\mu+\alpha+\varphi_2)(\mu+\alpha)(\varphi_1+\mu\omega)]}{\mu(\mu+\alpha+\lambda_A^0)[\lambda_A^0(\mu+\varphi_2)+(\mu+\varphi_1)(\mu+\alpha+\varphi_2)]},\\
S_2^0 &= \frac{\Lambda(1-\omega)\lambda_A^0}{\lambda_A^0(\mu+\varphi_2)+(\mu+\varphi_1)(\mu+\alpha+\varphi_2)},\\
V_2^0 &= \frac{\Lambda\lambda_A^0[\mu(1-\omega)\varphi_2+\omega(\mu+\varphi_1)(\mu+\alpha+\varphi_2)+(1-\omega)\varphi_1(\mu+\alpha+\varphi_2)+\lambda_A^0V_0]}{\mu(\mu+\alpha+\lambda_A^0)[\lambda_A^0(\mu+\varphi_2)+(\mu+\varphi_1)(\mu+\alpha+\varphi_2)]}.
\end{aligned}
\tag{13}
$$

where $V_0 = \omega\varphi_2 + (1-\omega)(\mu+\varphi_2)$ and λ_A^0 satisfies the following quadratic equation:

$$\lambda_A^0[a_2(\lambda_A^0)^2 + a_1\lambda_A^0 + a_0] = 0, \tag{14}$$

with

$$
\begin{aligned}
a_2 &= -(\mu+\varphi_2),\\
a_1 &= \beta_A\phi_A(\mu+\varphi_2) - (\mu+\varphi_2)(2\mu+\varphi_2+\alpha) - \alpha(\mu+\varphi_1),\\
a_0 &= (\mu+\varphi_1)(\mu+\alpha+\varphi_2)(\beta_A\phi_A - \mu - \alpha).
\end{aligned}
$$

From Eq. (14), $\lambda_A^0 = 0$ gives

$$S_1^0 = \frac{\Lambda(1-\omega)}{\mu+\varphi_1} \qquad V_1^0 = \frac{\Lambda(\varphi_1+\mu\omega)}{\mu(\mu+\varphi_1)} \qquad \text{and} \qquad S_2^0 = V_2^0 = 0. \tag{15}$$

This equilibrium is free of heavy alcohol drinkers and is an unrealistic equilibrium point because we deal with a population with heavy alcohol drinkers. However, the quadratic equation (14) has exactly one non-zero positive real root:

$$\lambda_A^0 = \frac{a_1 + \sqrt{a_1^2 + 4(\mu+\varphi_2)a_0}}{\mu+\varphi_2} \tag{16}$$

whenever $\beta_A\phi_A \geq \mu+\alpha$. Thus, the disease-free equilibrium exists whenever $\beta_A\phi_A \geq \mu+\alpha$. Note that the condition $\beta_A\phi_A \geq \mu+\alpha$ holds when the effective contacts rate of non-heavy drinkers that is sufficient to transmit the alcohol drinking habit to heavy alcohol drinkers is great than the rate of

abandon alcohol drinking by heavy alcohol drinkers. In the sequel, we only consider the disease-free equilibrium where both non-heavy and heavy alcohol drinkers coexist.

3.2.2. The basic reproduction number and its analysis

The linear stability of Q_0 is governed by the basic reproductive number $\mathcal{R}_0$ (Diekmann *et al*, 1990; van den Driessche and Watmough, 2002). The stability of this equilibrium will be investigated using the next generation operator (van den Driessche and Watmough, 2002). Using the notations in (van den Driessche and Watmough, 2002) for model system (6), the matrices F and V for the new infection terms and there maining transfer terms are, respectively, given by

$$F = \frac{1}{N_0}\sum_{i=1}^{2} \mathcal{K}_i B \langle \varrho_i \mid x_i^0 \rangle,$$

and

$$V = \begin{bmatrix} \mu+\gamma_1+\tilde{\beta}_A & 0 & 0 & -\alpha-\tilde{\beta}_C & 0 & 0 \\ -q_1\gamma_1 & \tilde{A}_1 & 0 & 0 & -\alpha-\tilde{\beta}_C & 0 \\ -\gamma_1(1-q_1) & -\delta_1 & \mu+\tilde{\beta}_A & 0 & 0 & -\alpha-\tilde{\beta}_C \\ -\tilde{\beta}_A & 0 & 0 & \tilde{A}_2 & 0 & 0 \\ 0 & -\tilde{\beta}_A & 0 & -q_2\gamma_2 & \tilde{A}_3 & 0 \\ 0 & 0 & -\tilde{\beta}_A & -\gamma_2(1-q_2) & -\delta_2 & \mu+\alpha+\tilde{\beta}_C \end{bmatrix},$$

where

$$\tilde{\beta}_A = \beta_A\phi_A\frac{S_2^0+V_2^0}{N_0}, \qquad \tilde{\beta}_C = \beta_C\phi_C\frac{S_1^0+V_1^0}{N_0}, \qquad \tilde{A}_1 = \mu+d_1+\delta_1+\tilde{\beta}_A,$$

$$\tilde{A}_2 = \mu+\alpha+\gamma_2+\tilde{\beta}_C \qquad \text{and} \qquad \tilde{A}_3 = \mu+d_2+\alpha+\delta_2+\tilde{\beta}_C.$$

Then, the basic reproduction number is defined as

$$\mathcal{R}_0 = \rho(FV^{-1}) = \frac{1}{N_0}\sum_{i=1}^{2}\langle B \mid V^{-1}\mathcal{K}_i\rangle \langle \varrho_i \mid x_i^0\rangle, \tag{17}$$

where ρ represents the spectral radius.

Thus, using Theorem 2 of (van den Driessche and Watmough, 2002) yields the following result.

Lemma 1: The disease-free equilibrium Q_0 of model system (5) is locally a symptotically stable if $\mathcal{R}_0 < 1$, and unstable if $\mathcal{R}_0 > 1$.

The basic reproductive number measures the average number of new infections generated by a single infected individual in a completely susceptible population. Thus, Theorem 1 implies that HBV can be eliminated from the community (when $\mathcal{R}_0 < 1$) if the initial sizes of the sub-populations of the model are in the basin of attraction of the disease-free equilibrium.

Now, suppose that there are no heavy alcohol drinkers in the community. In this case $\phi_B = \phi_C = \pi_2 = \alpha = 0$ and $S_2 = V_2 = I_2 = C_2 = R_2 = 0$. Following van den Driessche and Watmough (2002), the basic reproduction number is given by

$$\mathcal{R}_0^1 = \frac{\beta_B(\mu + d_1 + \delta_1 + \eta q_1 \gamma_1)[\mu(1-\varphi_1)(1-\omega) + \pi_1(\varphi_1 + \mu\omega)]}{(\mu + d_1 + \delta_1)(\mu + \gamma_1)(\mu + \varphi_1)}. \tag{18}$$

Note that the parameter φ_1 is important for the prevalence of HBV infection. The parameter influences the dynamics of HBV, in particular the equilibrium states, including the states of susceptible, acute infective, and carriers who are non-heavy alcohol drinkers. It is evident from Eq. (18) that

$$\lim_{\varphi_1 \to 1} \mathcal{R}_0^1 = \frac{\beta_B \pi_1(\mu + d_1 + \delta_1 + \eta q_1 \gamma_1)(1 + \mu\omega)}{(\mu + d_1 + \delta_1)(\mu + 1)(\mu + \gamma_1)} > 0 \tag{19}$$

Thus, a sufficiently effective HBV vaccination program can lead to effective disease control if it results in making the right-hand side of (19) less than unity, that is,

$$\pi_1 < \frac{(\mu + d_1 + \delta_1)(\mu + 1)(\mu + \gamma_1)}{\beta_B(\mu + d_1 + \delta_1 + \eta q_1 \gamma_1)(1 + \mu\omega)}.$$

Further sensitivity analysis on the vaccination parameter of susceptible individuals who are non-heavy alcohol drinkers is carried out by computing the partial derivative of $\mathcal{R}_0^1$ with respect to φ_1 yielding

$$\frac{\partial \mathcal{R}_0^1}{\partial \varphi_1} = -\frac{\beta_B \mu(1-\omega)(\mu + d_1 + \delta_1 + \eta q_1 \gamma_1)(\mu + 1 - \pi_1)}{(\mu + d_1 + \delta_1)(\mu + \gamma_1)(\mu + \varphi_1)^2}. \tag{20}$$

Thus, increasing the vaccination parameter φ_1 will have a positive impact in reducing the propagation of HBV in the community.

Now, let us analyze the basic reproduction number. The following numerical results demonstrate the role of θ,β_A and α on the basic reproduction number $\mathcal{R}_0$.

We begin by investigating how $\mathcal{R}_0$ depends on β_A and θ using parameter values in Table 1. We point out that one may become a heavy alcohol drinker due to peer pressure or by choice. This figure illustrates that for the chosen parameter values, if the susceptibility to HBV due to alcohol drinking does not exceed 2.6 (θ <2.6), then HBV can be controlled irrespective of the value of β_A. The infection will equally persist for θ > 2.6.

We now investigate how $\mathcal{R}_0$ depends on the change in alcohol drinking habit (that is, one may change from being heavy alcohol drinkers through counseling, poverty, health reasons, tax hike on alcohol beverages) and the susceptibility to HBV due to alcohol drinking. This figure is reflecting a large state number of HBV cases for high θ and low α, suggesting that a change in drinking habit for an individual which results in becoming an alcohol addict may increase the spread of HBV. While for low θ and high α, a change in alcohol drinking habit resulting in one becoming a non-heavy alcohol drinker may reduce the spread of HBV in the community. The result is in agreement with various studies which suggested that heavy alcohol drinking is related to high

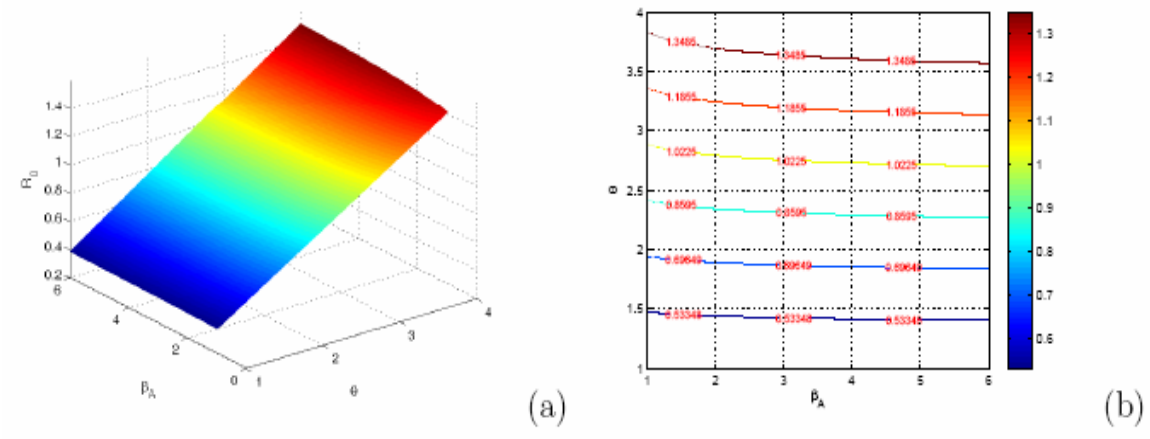

Figure 2. (a) 3-D and (b) contour plot showing effects of varying the parameters β_A and θ on the basic reproduction ratio $\mathcal{R}_0$. All other parameters are as in Table 1.

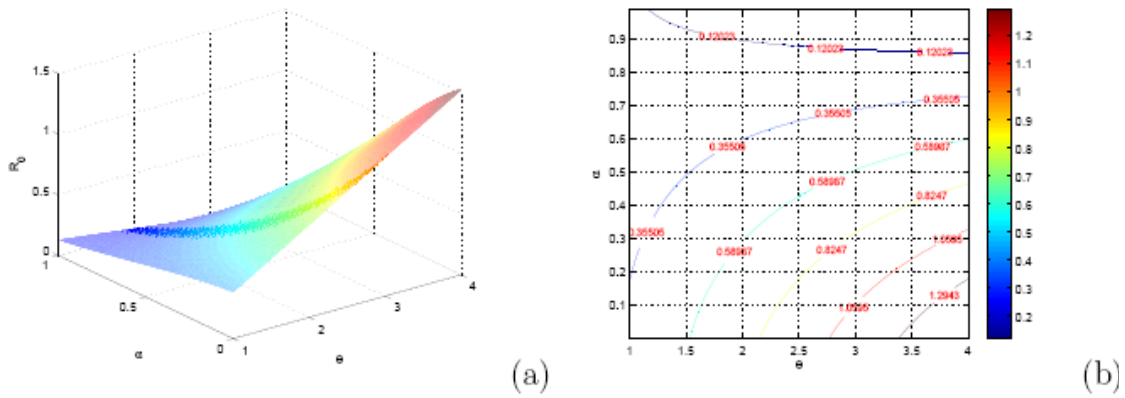

Figure 3. (a) 3-D and (b) contour plot showing effects of varying the parameters α and θ on the basic reproduction ratio $\mathcal{R}_0$. All other parameters are as in Table 1.

risk sexual behavior or sharing needles to inject drugs which, in return, might result in wide spread of HBV.

3.2.3. Sensitivity analysis

Sensitivity analysis is used to determine the relative importance of model parameters to HBV transmission and its prevalence. We perform the analysis by calculating the sensitivity indices of the basic reproduction number, $\mathcal{R}_0$. According to Chitnis et al. (2008), sensitivity analysis is commonly used to determine the robustness of model predictions to parameter values, since there are usually uncertainties in data collection and estimated values. We are thus interested in parameters that significantly affect the basic reproduction number, since these are the parameters that should be taken in to consideration when considering intervention strategies. Sensitivity analysis also permits us to measure the relative change in a state variable when a parameter changes. The normalized forward sensitivity index of a variable to a parameter is the number of the relative change in the variable to the relative change in the parameter. Since the basic reproduction number is a differentiable function of the parameters, the sensitivity index may alternatively be defined using partial derivatives. For instance, the computation of the sensitivity index of $\mathcal{R}_0$ with respect to β_B using the parameter values in Table 2 is given by

$$\prod_{\beta_B}^{\mathcal{R}_0} = \left(\frac{\partial \mathcal{R}_0}{\partial \beta_B}\right)\left(\frac{\beta_B}{\mathcal{R}_0}\right) = 1 > 0 \tag{21}$$

Table 2. Sensitivity indices for the basic reproduction number $\mathcal{R}_0$.

Parameter	Index	Parameter	Index	Parameter	Index
β_B	1	φ_1	-0.0198	γ_2	-0.7754
Λ	0	φ_2	-0.0226	δ_1	-0.0090
ω	-0.0105	π_1	0.0306	δ_2	-0.0821
π_2	0.4764	q_1	0.0271	γ_1	-0.0466
θ	0.9633	μ	-0.0660	d_1	-7.2341×10^{-4}
d_2	-0.0137	β_A	-0.0166	ϕ_A	-0.0166
β_C	0.0162	ϕ_c	0.0162	α	-0.0067
η	0.2713	ε	-2.4886	η_1	0.2352
q_2	0.1521				

This shows that $\mathcal{R}_0$ is an increasing function of β_B and the parameter β_B has a strong influence on the spread of HBV. We tabulate the indices of the remaining parameters in Table 2.

From Table 2, parameters whose sensitivity indices have negative signs decrease the value of the basic reproduction number as their values increase, while those with positive signs increase the value of $\mathcal{R}_0$ as they increase. Those with no signs have no effect on the value of the basic reproduction number. The system is most sensitive to ε, followed by γ_2. It is important to note that increasing (decreasing) ε by 10% decreases (increases) $\mathcal{R}_0$by 24.886%. However, increasing (decreasing) the parameter β_B by 10% increases (decreases) $\mathcal{R}_0$ by 10%.

3.2.4. Local stability of the disease-free equilibrium (DFE)

Using a theorem from Castillo-Chavez et al. (2002), we now show that the disease-free equilibrium may not be globally a symptotically stable in the case that the basic reproduction number is less than the unity ($\mathcal{R}_0 < 1$).

Following Castillo-Chavez et al. (2002), were write model system (5) as

$$\begin{cases} X'(t) &= FX,Y), \\ Y'(t) &= G(X,Y), \qquad G(X,0)=0, \end{cases} \tag{22}$$

where $X \in \mathbb{R}^4_{\geq 0}$ is the number of susceptible and vaccinated who are non-heavy and heavy alcohol drinkers and $Y \in \mathbb{R}^6_{\geq 0}$ denoting (its components) the number of acute infected, chronic carriers and recovered with protective

immunity who are non-heavy and heavy alcohol drinkers. The DFE is now denoted by $Q_0 = (X_0, 0)$ where (S_1^0 ,V_1^0 , S_2^0 , V_2^0) with S_1^0 , V_1^0 , S_2^0 and V_2^0 are defined as in Eqs. (13) and (16).

The conditions (H_1) and (H_2) below must be met to guarantee the global a symptotic stability of Q_0.

$$\begin{aligned} H_1: &\quad \text{For} \quad X'(t) = F(X,0), \quad X_0 \text{ is globally asymptotically stable (GAS)}, \\ H_2: &\quad G(X,Y) = BY - \hat{G}(X,Y), \quad \hat{G}(X,Y) \geq 0 \quad \text{for} \quad (X,Y) \in \Omega, \end{aligned} \tag{23}$$

where $B = D_Y G(X_0, 0)$ is an M-matrix (the off diagonal elements of *B* are non negative) and Ω is the region where the model makes biological sense. We refer the reader to Refs. (Berman and Plemmons, 1994; Lakshmikantham et al. 1989; Jacquez and Simon, 1993) for more details about the properties of a M-matrix. If model system (5) satisfies the conditions in Eq. (23), then the following result holds.

Theorem 2: *Th fixed point* $Q_0 = (X_0, 0)$ *is a globally asymptotically stabl eequilibrium of model system (5) provided that R0 < 1 and the assumptions in Eq. (23) are satisfied.*

Proof in Lemma 1, Q_0 is locally asymptotically stable for $\mathcal{R}_0 < 1$. Consider

$$F(X,0) = \begin{bmatrix} \Lambda(1-\omega) + \alpha S_2 - \beta_A \phi_A \dfrac{S_2+V_2}{N} S_1 - (\mu+\varphi_1) S_1 \\ \Lambda\omega + \varphi_1 S_1 + \alpha V_2 - \beta_A \phi_A \dfrac{S_2+V_2}{N} V_1 - \mu V_1 \\ \alpha R_2 - \beta_A \phi_A \dfrac{S_2+V_2}{N} R_1 - \mu R_1 \\ -\alpha S_2 + \beta_A \phi_A \dfrac{S_2+V_2}{N} S_1 - (\mu+\varphi_2) S_2 \\ \varphi_2 S_2 - \alpha V_2 + \beta_A \phi_A \dfrac{S_2+V_2}{N} V_1 - \mu V_2 \\ -\alpha R_2 + \beta_A \phi_A \dfrac{S_2+V_2}{N} R_1 - \mu R_1 \end{bmatrix},$$

$$B = \begin{bmatrix} \widetilde{\beta}_B^1 - (\mu+\gamma_1+\tilde{\beta}_A) & \eta\widetilde{\beta}_B^1 & \varepsilon\widetilde{\beta}_B^1 & \eta\eta_1\widetilde{\beta}_B^1 \\ q_1\gamma_1 & -\tilde{A}_1 & \alpha+\tilde{\beta}_C & 0 \\ \theta\widetilde{\beta}_B^2 + \tilde{\beta}_A & \theta\eta\widetilde{\beta}_B^2 & \eta\theta\widetilde{\beta}_B^2 - \tilde{A}_3 & \theta\eta\eta_1\widetilde{\beta}_B^2 \\ 0 & \tilde{\beta}_A & \delta_2 & -(\mu+\alpha+\tilde{\beta}_C) \end{bmatrix},$$

where

$$\tilde{\beta}_A = \beta_A \phi_A \frac{S_2^0 + V_2^0}{N_0}, \qquad \tilde{\beta}_C = \beta_C \phi_C \frac{S_1^0 + V_1^0}{N_0}, \qquad \tilde{A}_1 = \mu + d_1 + \delta_1 + \tilde{\beta}_A,$$

$$\tilde{A}_2 = \mu + \alpha + \gamma_2 + \tilde{\beta}_C, \qquad \tilde{A}_3 = \mu + d_2 + \alpha + \delta_2 + \tilde{\beta}_C,$$

$$\widetilde{\beta}_B^1 = \beta_B \frac{(1-\varphi_1)S_1^0 + \pi_1 V_1^0}{N_0} \qquad \text{and} \qquad \widetilde{\beta}_B^2 = \beta_B \frac{(1-\varphi_1)S_1^0 + \pi_2 V_2^0}{N_0}.$$

Thus,

$$\widehat{G}(X,Y) = \begin{pmatrix} \widehat{G}_1(X,Y) \\ \widehat{G}_2(X,Y) \\ \widehat{G}_3(X,Y) \\ \widehat{G}_4(X,Y) \end{pmatrix}$$

where

$$\begin{aligned}
\widehat{G}_1(X,Y) &= N\lambda_B \left(\frac{(1-\varphi_1)S_1^0 + \pi_1 V_1^0}{N_0} - \frac{(1-\varphi_1)S_1 + \pi_1 V_1}{N} \right) + \left(\widetilde{\beta}_C - \lambda_C \right) I_2 \\
&+ \left(\lambda_A - \widetilde{\beta}_A \right) I_1, \\
\widehat{G}_2(X,Y) &= \left(\widetilde{\beta}_C - \lambda_C \right) C_2 + \left(\lambda_A - \widetilde{\beta}_A \right) C_1, \\
\widehat{G}_3(X,Y) &= \theta N\lambda_B \left(\frac{(1-\varphi_1)S_1^0 + \pi_1 V_1^0}{N_0} - \frac{(1-\varphi_1)S_1 + \pi_1 V_1}{N} \right) \\
&+ \left(\lambda_C - \widetilde{\beta}_C \right) I_2 + \left(\widetilde{\beta}_A - \lambda_A \right) I_1, \\
\widehat{G}_4(X,Y) &= \left(\lambda_C - \widetilde{\beta}_C \right) C_2 + \left(\widetilde{\beta}_A - \lambda_A \right) C_1.
\end{aligned}$$

The sign of $\widehat{G}_i(X,Y)$, i=1,...,4 is not obvious, but based on the model parameters, $G(X,Y)$ is neither positive nor equal to zero. Condition (H_2) in (23) is therefore violated and as such, Q_0 may not be a globally asymptotically stable. This achieves the proof.

3.3. Endemic equilibria and stability analysis

Model system (5) has basically two possible endemic equilibria, that is non alcohol drinking only endemic equilibrium when the reare non-heavy alcohol drinkers in the community and the equilibrium point where both non-heavy and heavy alcohol drinkers coexist, herein referred to as the interior equilibrium point. It is worth mentioning that the endemic equilibrium where heavy alcohol drinkers only exist is an unrealistic equilibrium point and for that reason it is not discussed in this paper.

3.3.1. Non alcohol-drinking only endemic equilibrium

This equilibrium is $Q^* = (S_1^*, V_1^*, I_1^*, C_1^*, 0, 0, 0, 0)$. Expressing S_1^*, V_1^*, I_1^* and C_1^* in terms of the force of infection at the steady state λ_B^* gives

$$S_1^* = \frac{\Lambda(1-\omega)}{\mu+\varphi_1+(1-\varphi_1)\lambda_B^*}, \quad V_1^* = \frac{\Lambda[\varphi_1+\mu\omega+\omega(1-\varphi_1)\lambda_B^*]}{(\mu+\pi_1\lambda_B^*)[\mu+\varphi_1+(1-\varphi_1)\lambda_B^*]}, \tag{24}$$

$$I_1^* = \frac{\Lambda[\mu(1-\varphi_1)(1-\omega)+\pi_1(\varphi_1+\mu\omega)+\pi_1(1-\varphi_1)\lambda_B^*]\lambda_B^*}{(\mu+\delta_1)(\mu+\pi_1\lambda_B^*)[\mu+\varphi_1+(1-\varphi_1)\lambda_B^*]}$$

$$C_1^* = \frac{\Lambda q_1\gamma_1[\mu(1-\varphi_1)(1-\omega)+\pi_1(\varphi_1+\mu\omega)+\pi_1(1-\varphi_1)\lambda_B^*]\lambda_B^*}{(\mu+\delta_1)(\mu+\pi_1\lambda_B^*)[\mu+\varphi_1+(1-\varphi_1)\lambda_B^*]} \quad \text{and}$$

$$R_1^* = \frac{\gamma_1(1-q_1)I_1^*+\delta_1 C_1^*}{\mu}.$$

In Eq. (24), λ_B^* satisfies the following quadratic equation:

$$b_2(\lambda_B^*)^2 + b_1\lambda_B^* + b_0 = 0, \tag{25}$$

where

$$\begin{aligned}
b_2 &= \Lambda(1-\varphi_1)[(\mu+d_1+\delta_1)(\mu+\gamma_1)-d_1q_1\gamma_1],\\
b_1 &= (\mu+d_1+\delta_1)(\mu+\gamma_1)[\mu(1-\varphi_1)+\pi_1(\mu+\varphi_1)]\\
&\quad - d_1q_1\gamma_1[\mu(1-\varphi_1)(1-\omega)+\pi_1(\varphi_1+\mu\omega)]-\beta_B\mu\pi_1(1-\varphi_1)(\mu+d_1+\delta_1+\eta q_1\gamma_1),\\
b_0 &= \mu(\mu+\gamma_1)(\mu+\varphi_1)(\mu+d_1+\delta_1)(1-\mathcal{R}_0^1),
\end{aligned}$$

with $\mathcal{R}_0^1$ defined as in Eq. (18). The quadratic equation (25) can be analyzed for the possibility of multiple endemic equilibria. It is worth noting that the coefficient b_0 is positive (negative) if $\mathcal{R}_0^1$ is less than (greater than) the unity. Solving the quadratic equation (25) yields

$$\lambda_B^* = \frac{-b_1 + \sqrt{b_1^2 - 4b_0b_2}}{2b_2}, \tag{26}$$

and the remaining one root is a complex root which is discarded because we are dealing with a population of individuals and is always positive. We only consider conditions for b_2, b_1 and b_0 which gives us $b_1^2 - 4b_0b_2 \geq 0$ and a positive λ_B^* since a negative force of infection is epidemiologically irrelevant We claim the following result.

Lemma 2: *Model system (5) with non-heavy alcohol drinkers could have a unique endemic equilibrium whenever* $\mathcal{R}_0^1 > 1$.

In order to analyze the stability of the endemic equilibrium point, we make use of the Centre Manifold theory (Carr 1981) as described by Theorem 4.1 of Castillo-Chavez and Song (2004), stated below (Theorem 3) for convenience, to establish the local asymptotic stability of the only-alcohol drinking endemic equilibrium. To apply this theory, the following simplification and change of variables are made first of all. Let $z_1 = S_1$, $z_2 = V_1$, $z_3 = I_1$, $z_4 = C_1$ and $z_5 = R_1$ so that $N = z_1 + z_2 + z_3 + z_4 + z_5$. Further, by using the vector notation $z = (z_1, z_2, z_3, z_4)^T$, the HBV model (5) with non-heavy alcohol drinkers can be written in the form $\dot{z} = f(z)$, with $f = (f_1, f_2, f_3, f_4, f_5)^T$, as follows:

$$\begin{cases} z_1' &= f_1 = \Lambda(1-\omega) - [\mu + \varphi_1 + (1-\varphi_1)\lambda_B]z_1, \\ z_2' &= f_2 = \Lambda\omega + \varphi_1 z_1 - (\mu + \pi_1\lambda_B)z_2, \\ z_3' &= f_3 = [(1-\varphi_1)z_1 + \pi_1 z_2]\lambda_B - (\mu + \gamma_1)z_3, \\ z_4' &= f_4 = q_1\gamma_1 z_3 - A_1 z_4, \\ z_5' &= f_5 = \gamma_1(1-q_1)z_3 + \delta_1 z_4 - \mu z_5, \end{cases} \tag{27}$$

where $A_1 = \mu + d_1 + \delta_1$ and $\lambda_B = \dfrac{\beta_B(z_3 + \eta z_4)}{z_1 + z_2 + z_3 + z_4 + z_5}$.

System (27) has a DFE given by $Q_0^1 = (z_1^0, z_2^0, 0, 0, 0)$ where

$$z_1^0 = \frac{\Lambda(1-\omega)}{\mu + \varphi_1} \qquad \text{and} \qquad z_2^0 = \frac{\Lambda(\varphi_1 + \mu\omega)}{\mu(\mu + \varphi_1)}.$$

The Jacobian of system (27), at the DFE Q_0^1, is given by

$$J(Q_0^1) = \begin{pmatrix} -J_1 & 0 & -J_2 & -J_3 & 0 \\ \varphi_1 & -\mu & -J_4 & -J_5 & 0 \\ 0 & 0 & J_6 & J_7 & 0 \\ 0 & 0 & q_1\gamma_1 & -A_1 & 0 \\ 0 & 0 & \gamma_1(1-q_1) & \delta_1 & -\mu \end{pmatrix},$$

where

$$J_1 = \mu + \varphi_1, \qquad J_2 = \beta_B \frac{z_1^0}{N_0}, \qquad J_3 = \nu\nu_1\omega + \beta_B\eta\frac{z_1^0}{N_0}, \qquad J_4 = \beta_B\pi_1\frac{z_2^0}{N_0},$$

$$J_5 = \beta_B\eta\pi_1\frac{z_2^0}{N_0}, \qquad J_6 = \frac{\beta_B[(1-\varphi_1)z_1^0 + \pi_1 z_2^0]}{N_0} - \mu - \varphi_1,$$

$$J_7 = \frac{\beta_B\eta[(1-\varphi_1)z_1^0 + \pi_1 z_2^0]}{N_0} \qquad \text{and} \qquad N_0 = \Lambda/\mu.$$

Consider, next, the case when $\mathcal{R}_0^1 = 1$

Suppose, further, that $\beta_B = \beta_B^*$ is chosen as a bifurcation parameter. Solving for β_B from $\mathcal{R}_0^1 = 1$ gives

$$\beta_B = \frac{(\mu + d_1 + \delta_1)(\mu + \gamma_1)(\mu + \varphi_1)}{(\mu + d_1 + \delta_1 + \eta q_1\gamma_1)[\mu(1-\varphi_1)(1-\omega) + \pi_1(\varphi_1 + \mu\omega)]}$$

It follows that the Jacobian $(J(Q_0^1))$ of system (27) at the DFE Q_0^1, with $\beta_B = \beta_B^*$ denoted by J_{β^*} has a simple zero eigenvalue (with all other eigenvalues having negative real parts). Hence, the Centre Manifold theory (Carr 1981) can be used to analyze the dynamics of system (27). In particular, the theorem in (Castillo and Song 2004), reproduced below for

convenience, will be used to show that when $\mathcal{R}_0^1 > 1$ there exists a unique endemic equilibrium of system (27) (as shown in Lemma 2) which is locally asymptotically stable for $\mathcal{R}_0^1$ near 1 under certain condition.

Theorem 3: (*Castillo-Chavez & Song 2004): Consider the following general system of ordinary differential equations with a parameter* ϕ*:*

$$\frac{dz}{dt} = f(z, \phi), \qquad f : \mathbb{R}^n \times \mathbb{R} \to \mathbb{R} \qquad and \qquad f \in C^2(\mathbb{R}^n, \mathbb{R}). \quad (28)$$

where 0 is an equilibrium point of the system (that is, $f(0, \phi) \equiv 0$ *for all* ϕ*) and assume*

1. $A = D_z f(0,0) = \left(\frac{\partial f_i}{\partial z_j}(0,0)\right)$ *is the linearization matrix of system (28) around the equilibrium 0 with* ϕ *evaluated at 0. Zero is a simple eigenvalue of A and other eigen values of A have negative real parts;*
2. Matrix A has a right eigenvector u and a left eigen vector v (each corresponding to the zero eigenvalue).

Let f_k be the k^{th} component of *f* and

$$a = \sum_{k,i,j=1}^{n} v_k u_i u_j \frac{\partial^2 f_k}{\partial z_i \partial z_j}(0,0),$$

$$b = \sum_{k,i=1}^{n} v_k u_i \frac{\partial^2 f_k}{\partial z_i \partial \phi}(0,0),$$

then, the local dynamics of the system around the equilibrium point 0 is totally determined by the signs of *a* and *b*.

1. $a > 0,\ b > 0$. When $\phi < 0$ with $|\phi| \ll 1,\ 0$ is locally asymptotically stable and there exists a positive unstable equilibrium; when $0 < \phi \ll 0,\ 0$ is unstable and there exists a negative, locally asymptotically stable equilibrium;

2. $a < 0, b < 0$. When $\phi < 0$ with $|\phi| \ll 1$, 0 is unstable; when $0 < \phi \ll 1$, 0is locally asymptotically stable equilibrium, and there exists a positive unstable equilibrium;
3. $a > 0, b < 0$. When $\phi < 0$ with $|\phi| \ll 1$, 0 is unstable, and there exists a locally asymptotically stable negative equilibrium; when $0 < \phi \ll 1$, 0 is stable, and a positive unstable equilibrium appears;
4. $a < 0, b > 0$. When ϕchanges from negative to positive, 0 changes its stability from stable to unstable. Correspondingly a negative unstable equilibrium becomes positive and locally asymptotically stable.

Particularly, $if\ a > 0\ and\ b > 0$, then a backward bifurcation occurs at $\phi = 0$

In order to apply the above theorem, the following computations are necessary (it should be noted that we use β_B^* as the bifurcation parameter, in place of ϕ in Theorem (Castillo-Chavez & Song 2004)).

Eigenvectors of $J_{\beta_B^*}$: For the case when $\mathcal{R}_0^1 = 1$, it can be shown that the Jacobian of system (27) at $\beta_B = \beta_B^*$ (denoted by $J_{\beta_B^*}$) has a right eigenvector (corresponding to the zero eigenvalue), given by $U = (u_1, u_2, u_3, u_4, u_5)^T$, where,

$$\begin{cases} u_1 = -\dfrac{(A_1J_2 + q_1\gamma_1J_3)u_3}{J_1A_1}, \\ u_2 = -\dfrac{[\varphi_1(A_1J_2 + q_1\gamma_1J_3) + J_1J_4A_1 + q_1\gamma_1J_1J_5]u_3}{\mu A_1J_3}, \\ u_3 = u_3 > 0, \\ u_4 = \dfrac{q_1\gamma_1u_3}{A_1}, \\ u_5 = \dfrac{[\gamma_1(1-q_1)A_1 + q_1\gamma_1\delta_1]u_3}{\mu A_1}. \end{cases} \tag{29}$$

Similarly, the components of the left eigenvectors of $J_{\beta_B^*}$ (corresponding to the zero eigen value), denoted by $V = (v_1, v_2, v_3, v_4, v_5)^T$, are given by,

$$\begin{cases} v_1 = 0, \\ v_2 = 0, \\ v_3 = v_3 > 0, \\ v_4 = \dfrac{J_7 v_3}{A_1}, \\ v_5 = 0. \end{cases} \tag{30}$$

Computation of b: For the sign of b, it can be shown that the associated non-vanishing partial derivatives of *f* are

$$\frac{\partial^2 f_3}{\partial z_3 \partial \beta_B^*}(0,0) = \frac{(1-\varphi_1)z_1^0 + \pi_1 z_2^0}{N_0} \quad \text{and} \quad \frac{\partial^2 f_3}{\partial z_4 \partial \beta_B^*}(0,0) = \frac{\eta[(1-\varphi_1)z_1^0 + \pi_1 z_2^0]}{N_0}.$$

Substituting the respective partial derivatives in to the expression

$$b = v_3 \sum_{i=1}^{5} v_i \frac{\partial^2 f_3}{\partial z_i \beta_B^*},$$

gives

$$b = \frac{v_3(u_3 + \eta u_4)}{N_0}[(1-\varphi_1)z_1^0 + \pi_1 z_2^0] > 0. \tag{31}$$

Computation of α: For system (27), the associated non-zero partial derivatives of *f* (at the DFE Q_0^1) are given by

$$\frac{\partial^2 f_3}{\partial z_3^2} = -\frac{2\beta_B^*[(1-\varphi_1)z_1^0 + \pi_1 z_2^0]}{N_0^2}, \qquad \frac{\partial^2 f_3}{\partial z_3 \partial z_4} = \frac{\partial^2 f_3}{\partial z_4 \partial z_3} = -\frac{\beta_B^*(1+\eta)[(1-\varphi_1)z_1^0 + \pi_1 z_2^0]}{N_0^2},$$

$$\frac{\partial^2 f_3}{\partial z_1 \partial z_3} = \frac{\partial^2 f_3}{\partial z_3 \partial z_1} = -\frac{\beta_B^*(\pi_1 + \varphi_1 - 1)z_2^0}{N_0^2}, \qquad \frac{\partial^2 f_3}{\partial z_2 \partial z_3} = \frac{\partial^2 f_3}{\partial z_3 \partial z_2} = \frac{\beta_B^*(\pi_1 + \varphi_1 - 1)z_1^0}{N_0^2},$$

$$\frac{\partial^2 f_3}{\partial z_1 \partial z_4} = \frac{\partial^2 f_3}{\partial z_4 \partial z_1} = -\frac{\beta_B^*\eta(\pi_1 + \varphi_1 - 1)z_2^0}{N_0^2}, \qquad \frac{\partial^2 f_3}{\partial z_2 \partial z_4} = \frac{\partial^2 f_3}{\partial z_4 \partial z_2} = \frac{\beta_B^*\eta(\pi_1 + \varphi_1 - 1)z_1^0}{N_0^2}$$

$$\frac{\partial^2 f_3}{\partial z_4^2} = -\frac{2\beta_B^*\eta[(1-\varphi_1)z_1^0 + \pi_1 z_2^0]}{N_0^2}, \qquad \frac{\partial^2 f_3}{\partial z_3 \partial z_5}(0,0) = \frac{\partial^2 f_3}{\partial z_5 \partial z_3}(0,0) = -\frac{\beta_B^*[(1-\varphi_1)z_1^0 + \pi_1 z_2^0]]}{N_0^2}$$

and $\dfrac{\partial^2 f_3}{\partial z_4 \partial z_5}(0,0) = \dfrac{\partial^2 f_3}{\partial z_5 \partial z_4}(0,0) = -\dfrac{\beta_B^*\eta[(1-\varphi_1)z_1^0 + \pi_1 z_2^0]]}{N_0^2}.$

Then, it follows that

$$\begin{aligned} a &= v_3 \sum_{i,j=1}^{5} u_i u_j \frac{\partial^2 f_3}{\partial z_i \partial z_j}, \\ &= \frac{2\beta_B^* v_3 u_3 (u_3 + \eta u_4)}{N_0^2}[\pi_1[u_2 z_1^0 - z_2^0(u_1 + u_3 + u_4 + u_5)] \\ &+ (1-\varphi_1)[z_1^0(u_2 + u_3 + u_4 + u_5) - u_1 z_2^0]], \end{aligned}$$

so that the bifurcation coefficient $a > 0$ if and only if

$$\pi_1 = \frac{(1-\varphi_1)[z_1^0(u_2 + u_3 + u_4 + u_5) - u_1 z_2^0}{u_2 z_1^0 - z_2^0(u_1 + u_3 + u_4 + u_5)} > 1, \tag{32}$$

where u_1, u_2, u_3, u_4 and u_5 are defined as in Eq. (29).

Thus, $b > 0$ and $a > 0$ or $a < 0$ depending on whether in equality (32) is satisfied. This sign of *b* may be expected in general for epidemic models because, in essence, using β_B as a bifurcation parameter of ten ensures $b > 0$. Using Theorem 3 items (i) and (iv), we established the following result.

Theorem 4: *If condition (32) is satisfied, a > 0, then, system (27) with non-heavy alcohol drinkers undergoes a backward bifurcation at* $\mathcal{R}_0^1 = 1$, *otherwise a < 0 and unique non-alcohol drinking endemic equilibrium* Q_1^*

guaranteed by Lemma 2 is locally asymptotically stable for $\mathcal{R}_0^1 > 1$, *but close to 1.*

The phenomenon of backward bifurcation in disease models, where as table endemic equilibrium coexists with a stable disease-free equilibrium when the associated reproduction number is less than the unity, has important implications for disease control (Sharomi and Gumel 2008). In such a scenario, the classical requirement of there production number being less than the unity becomes only a necessary, but not sufficient condition for disease elimination. For $a < 0$, the model exhibits a forward bifurcation. The bifurcations which occur for different signs of α are shown in Fig.4.

3.3.2. Co-existence of non-heavy and heavy alcohol drinkers endemic equilibrium

This equilibrium point in terms of the force of infection λ_B^{**}, λ_A^* and λ_C^* is given by

$$Q_2^* = (S_1^{**}, V_1^{**}, I_1^{**}, C_1^{**}, R_1^{**}, S_2^{**}, V_2^{**}, I_2^{**}, C_2^{**}, R_2^{**}), \tag{33}$$

with the explicit expression for S_1^{**}, V_1^{**}, I_1^{**}, C_1^{**}, R_1^{**}, S_2^{**}, V_2^{**}, I_2^{**}, C_2^{**}, and R_2^{**} being cumbersome to be written explicitly. The permanence of the disease destabilizes the disease-free equilibrium Q^0 since $\mathcal{R}_0 > 1$, the co-existence of non-heavy and heavy alcohol drinkers endemic equilibrium Q_2^* exists. We claim the following result.

Conjecture 1 : *System (5) is uniformly persistent on Ω.*

Uniform persistence of model system (5) implies that there exists a constant $\zeta > 0$ such that any solution of model system (5) which starts in the interior of Ω remains in Ω. Also,

$$\begin{aligned}
&\zeta \leq \liminf_{t\to\infty} S_1(t), \quad \zeta \leq \liminf_{t\to\infty} V_1(t), \quad \zeta \leq \liminf_{t\to\infty} I_1(t), \quad \zeta \leq \liminf_{t\to\infty} C_1(t),\\
&\zeta \leq \liminf_{t\to\infty} R_1(t), \quad \zeta \leq \liminf_{t\to\infty} S_2(t), \quad \zeta \leq \liminf_{t\to\infty} V_2(t),\\
&\zeta \leq \liminf_{t\to\infty} I_2(t), \quad \zeta \leq \liminf_{t\to\infty} C_2(t) \quad \text{and} \quad \zeta \leq \liminf_{t\to\infty} R_2(t).
\end{aligned} \tag{34}$$

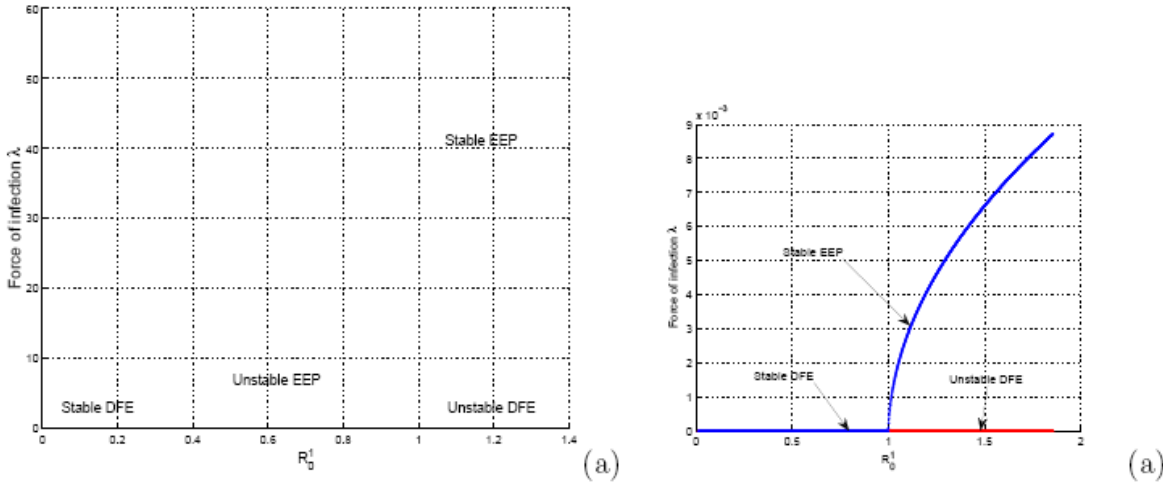

Figure 4. Bifurcation diagram for system (27). The notation EEP stands for endemic equilibrium point. All other parameters are as in Table1.

3.3.3. Co-existence region of non-heavy and heavy alcohol drinkers endemic equilibrium

Here in, we calculate a coexistence threshold which separates the region where only non-heavy alcohol drinkers are at the equilibrium from the region where heavy and non-heavy alcohol drinkers are at the equilibrium in a population where HBV is endemic.

In order to derive the expression for the region of the stability of the boundary equilibrium Q_1^*, we measure the capacity of heavy alcohol drinking to invade and persist in a population where there are non-heavy alcohol drinkers and HBV is endemic. In this context, $Q_1^* = (S_1^*, V_1^*, I_1^*, C_1^*, R_1^*, 0, 0, 0, 0, 0)$ corresponds to an equilibrium free of individuals who are heavy alcohol drinkers. We consider heavy alcohol drinking as a disease. Then, the infected compartments are S_2, V_2, I_2, C_2 and R_2. Following (van den Driessche and Watmough, 2002), the matrices F and V, for the new infection terms and the remaining transfer terms, are, respectively, given by

$$F = \frac{\beta_A \phi_A}{N^*} P^* \varpi \quad \text{and} \quad V = \begin{bmatrix} A_1' & 0 & 0 & 0 & 0 \\ -\varphi_2 & A_2' & 0 & 0 & 0 \\ -\theta(1-\varphi_2)\lambda_B^* & -\pi_2\lambda_B^* & A_3' & 0 & 0 \\ 0 & 0 & -q_2\gamma_2 & A_4' & 0 \\ 0 & 0 & -\gamma_2(1-q_2) & -\delta_2 & A_5' \end{bmatrix},$$

where

$$\varpi = (1,1,1,1,1), \qquad P^* = (S_1^*, V_1^*, I_1^*, C_1^*, R_1^*)^T, \qquad \lambda_B^* = \beta_B \frac{I_1^* + \eta C_1^*}{N^*},$$

$$N^* = S_1^* + V_1^* + I_1^* + C_1^* + R_1^*, \qquad A_1' = \mu + \varphi_2 + \alpha + \theta(1-\varphi_2)\lambda_B^*,$$

$$A_2' = \mu + \alpha + \theta\pi_2\lambda_B^*, \qquad A_3' = \mu + \alpha + \gamma_2 + \beta_C\phi_C,$$

$$A_4' = \mu + d_2 + \alpha + \delta_2 + \beta_C\phi_C \qquad \text{and} \qquad A_5' = \mu + \alpha + \beta_C\phi_C,$$

with I_1^*, C_1^*, V_1^* and R_1^* defined as in Eqs. (24) and (26).

The basic reproduction ratio of alcohol drinking invasion in a population with only non-heavy alcohol drinkers is the spectral radius of the next generation matrix, FV^{-1}:

$$\mathcal{R}_0^1(Q_1^*) = \frac{\beta_A \phi_A}{N^*} \langle \varpi \mid V^{-1} P^* \rangle. \tag{35}$$

The expression of $\mathcal{R}_0^1(Q_1^*)$ is similar to that for $\mathcal{R}_0^1$ in Eq (18) with additional terms containing β_A and ϕ_A which correspond to the effective contact rate to become heavy alcohol drinkers and the probability of being heavy alcohol drinkers.

This formalism permits the derivation of a threshold condition for coexistence, now equivalent to a threshold condition for alcohol drinking invasion in a population where non-heavy alcohol drinkers are at equilibrium, $\mathcal{R}_0^1(Q_1^*) = 1$: only alcohol drinking do not persist in the host population for $\mathcal{R}_0^1(Q_1^*) < 1$, while for $\mathcal{R}_0^1(Q_1^*) > 1$ alcohol drinking can invade a population with non-heavy alcohol drinkers where HBV is endemic, that is, to say coexistence is possible. Lemma 3 below expresses this result in terms of stability for the equilibrium Q_1^*.

Lemma 3: *If* $\mathcal{R}_0^1 > 1$, the alcohol-free equilibrium Q_1^* is stable for $\mathcal{R}_0^1(Q_1^*) < 1$ and unstable for $\mathcal{R}_0^1(Q_1^*) > 1$.

Relation (35) reveals that the coexistence of non-drinking and drinking alcohol in a population depends on the effective contact rate to become heavy alcohol drinkers and the probability of being heavy alcohol drinkers.

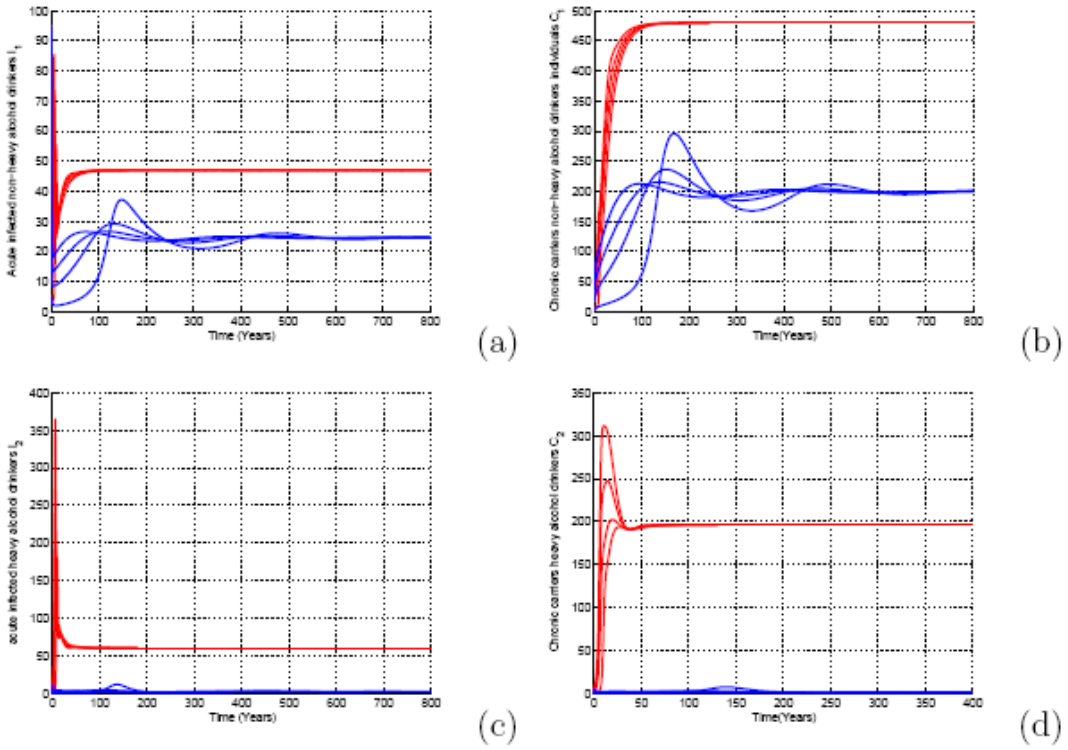

Figure 5. Simulations of model system (5) using various initial conditions when $\beta_A = 0.2$ and $\beta_A = 0.2$ (blue line) (so that $\mathcal{R}_0^1(Q_1^*) = 0.6556$ and $\mathcal{R}_0^T = 1.1435$), and when $\beta_A = 1$ (red line) (so that $\mathcal{R}_0^1(Q_1^*) = 3.2780$ and $\mathcal{R}_0^T = 1.1435$). All other parameters are as in Table 1.

Figure 5 presents the solution profiles of HBV acute infected and chronic carriers who are non-heavy and heavy alcohol drinkers using various initial conditions when $\beta_B = 1$ and $\beta_A = 0.2$ (blue line) (so that $\mathcal{R}_0^1(Q_1^*) = 0.6556$ and $\mathcal{R}_0^1 = 1.1435$, $\beta_A = 1$ and when $\beta_A = 1$ (red line) (so that $\mathcal{R}_0^1(Q_1^* = 3.2780$) and $\mathcal{R}_0^1 = 1.1435$). All other parameters are as in Table 1.

Further, these figures illustrate that when $\mathcal{R}_0^1 > 1$ and $\mathcal{R}_0^1(Q_1^*) < 1$, alcohol drinking cannot persist in the host population with non-heavy alcohol drinkers when HBV is at the equilibrium, while, when $\mathcal{R}_0^1 > 1$ and $\mathcal{R}_0^1(Q_1^*) > 1$, alcohol drinking invade the host population.

4. Numerical studies

Numerical simulations using a set of reasonable parameter values in Table 1 are carried out for illustrative purpose and to support the analytical results. In all simulations, the model was simulated with the following initial conditions: $S_1(0) = 3\times10^3$, $V_1(0) = 6\times10^4$ $I_1(0) = 10^3$, $C_1(0) = 500$, $R_1(0) = 100$

$S_2(0) = 2 \times 10^3$, $V_2(0) = 6 \times 10^3$, $I_2(0) = 100$, $C_2(0) = 50$ and $R_2(0) = 10$. We point out that these initial conditions have been chosen arbitrarily. Also, in all simulations, the HBV transmission rate β_B has been chosen such that $\mathcal{R}_0 > 1$ and $\mathcal{R}_0^1(Q_1^*) > 1$

4.1. General dynamics

Numerical simulations of model system (5) showing the time series plots of the HBV acute infected and chronic carriers who are non-heavy and heavy alcohol drinkers when $\beta_B = 12$ (so that $\mathcal{R}_0 = 1.2988$) are shownin Fig.6. The results obtained using parameter values in Table 1 indicate that more individuals who are heavy drinkers (I_2, C_2) are infected than individuals who are non-heavy alcohol drinkers (I_1, C_1).

4.2. Effect of increased the susceptibility to HBV due to alcohol drinking

Effects of increased susceptibility to HBV as a result of alcohol drinking are explored in Fig.7 by varying the parameter θ. The numerical results in Figs.7 illustrate that an increase in susceptibility to HBV due to alcohol drinking will generally result in an increase in the number of HBV acute infected and chronic carriers who are non-heavy and heavy alcohol drinkers with a significant effect on HBV acute infected and chronic carriers who are

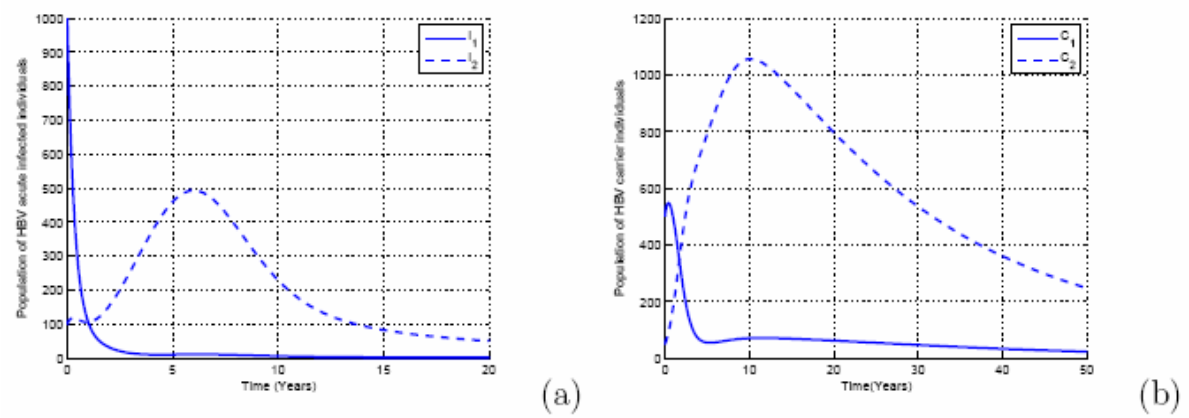

Figure 6. Simulation results showing the general trends for HBV acute infected and chronic carriers who are non-heavy drinkers (I_1; C_1) and who are heavy alcohol drinkers (I_2; C_2) when $\beta_B = 12$ (so that $\mathcal{R}_0 = 1.2988$). All other parameters are as in Table 1.

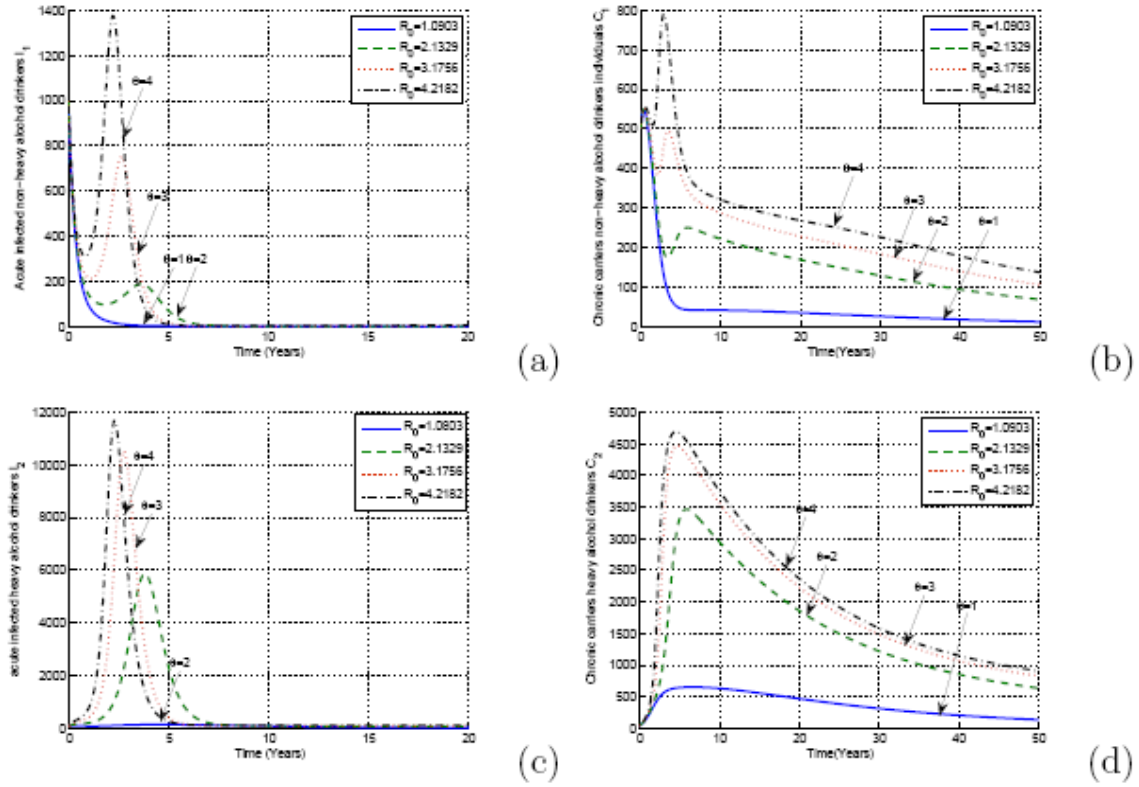

Figure 7. Simulation results showing the effect of increasing susceptibility to HBV due to alcohol drinking θ when $\beta_B = 12$ (so that $\mathcal{R}_0 > 1$). All other parameters are as in Table 1.

heavy alcohol drinkers (as shown in Figs.7 (c) and (d)). The figure shows that changes in θ significantly affect the long term progression of the disease, and significant changes are observed in the initial phases of the epidemic, with more changes being observed in a cute infected and chronic carriers who are heavy alcohol drinkers. Thus, patients with chronic hepatitis B should avoid alcohol because it can cause additional liver damage. The results suggest that intervention strategies such as vaccination, counseling and educational campaigns should be addressed incommunities of heavy alcohol drinkers affected by HBV in order to reduce the burden of the disease.

4.3. Effects of varying the probability of being heavy alcohol drinkers

Simulation results in Fig. 8 illustrate the variation of the probability of being heavy alcohol drinkers ϕ_A on the dynamics of model system (5). Figure 8 suggests that an increase in recruitment of heavy alcohol drinkers in the community will increase the prevalence of HBV cases. This suggests that

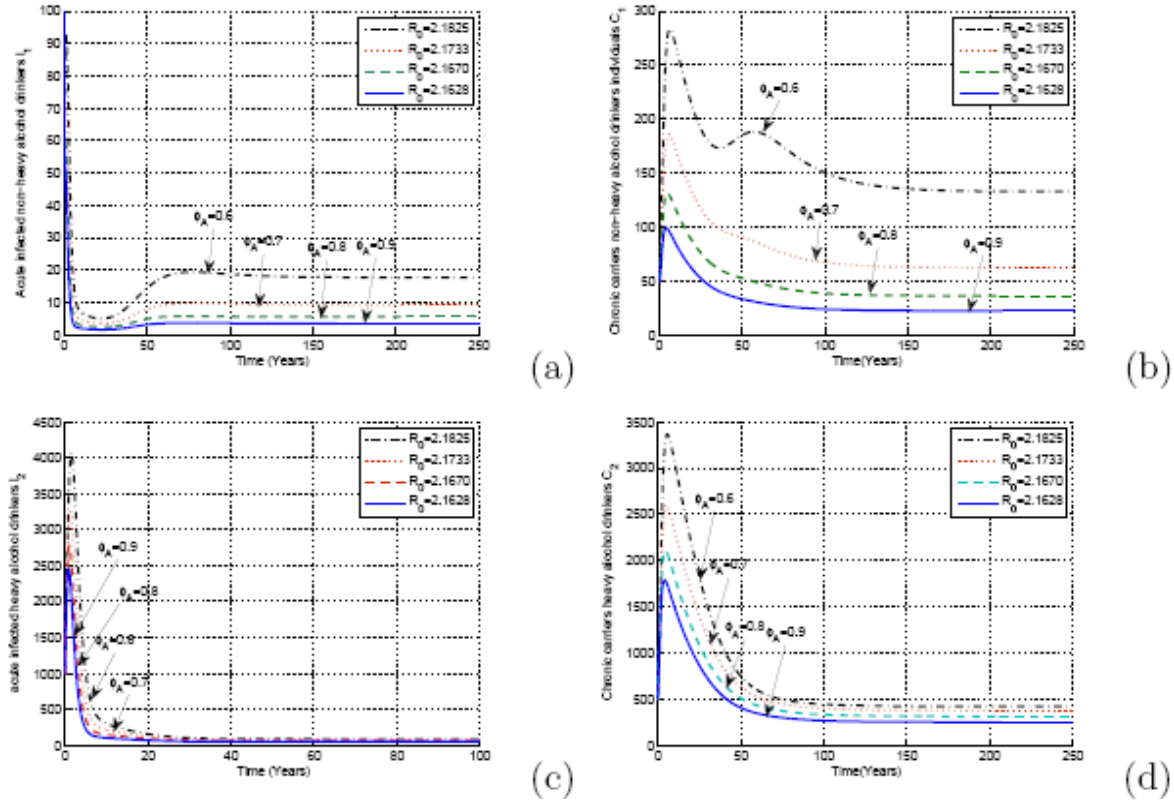

Figure 8. Simulation results showing the effect of increasing parameter ϕ_A when $\beta_B = 15$ (so that $\mathcal{R}_0 > 1$). All other parameters are as in Table 1.

whenever more individuals in the community change their alcohol drinking habit to become heavy alcohol drinkers, this may influence the spread of HBV in the community, but if the reverse is true, with the basic reproduction number greater than the unity, then a number of factors may play a crucial role on the spread of HBV.

4.4. Effects of increase the abandon of alcohol drinking

Numerical results in Fig. 9 demonstrate the role of α on the dynamics of HBV. From this figure, it clearly evident that an increase in the rate of abandon alcohol drinking α will have a positive impact on controlling HBV in the community (especially for high values of α, as demonstrated in Figs. 9 (c) and (d)). This result suggests that alcohol can cause serious problems for someone with hepatitis B. If possible, it is best to stop drinking. If some one can't stop drinking, it is best to try to cut down.

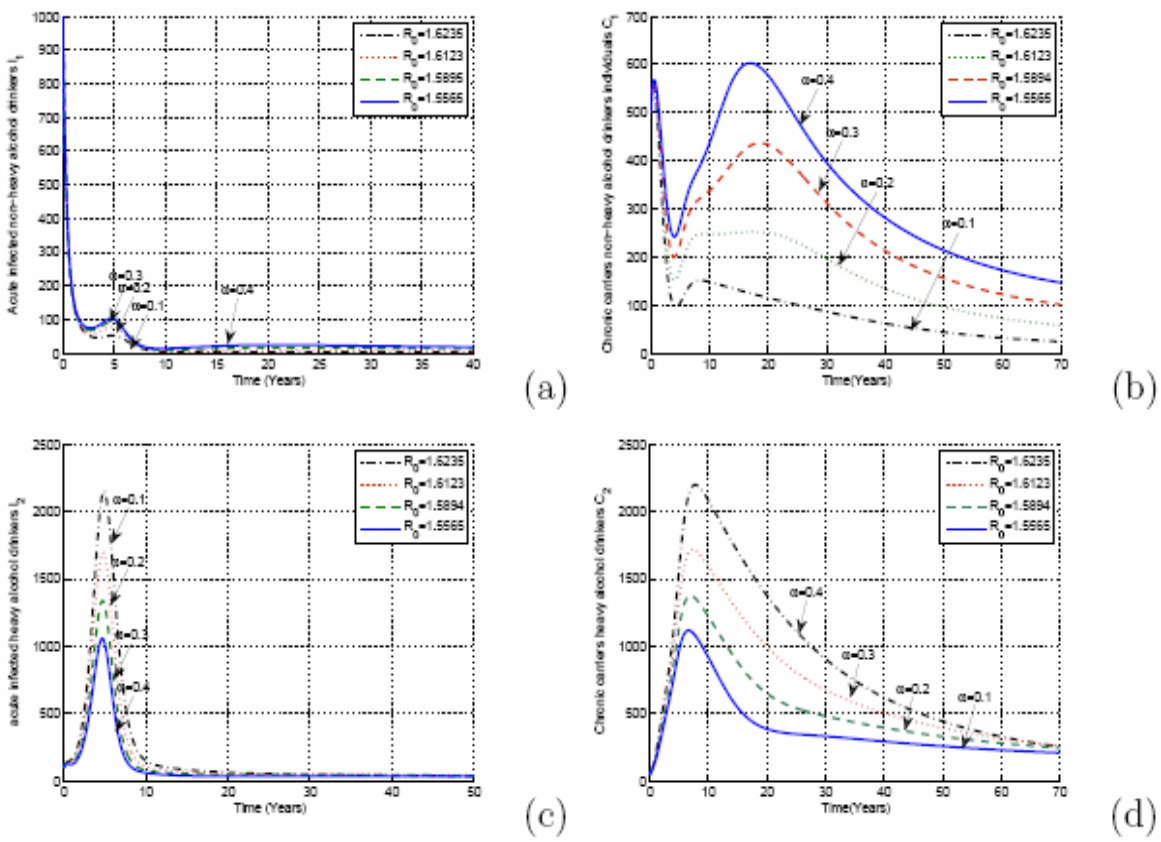

Figure 9. Simulation results showing the effect of increasing the rate of abandon alcohol drinking α when β_B = 15 (so that $\mathcal{R}_0 > 1$). All other parameter values as given in Table 1.

4.5. Effects of varying the percentage of heavy alcohol drinkers in the population

Herein, we now demonstrate the effect of increase the percentage of heavy alcohol drinkers in the population. Figure 10 is a graphical representation of the total number of HBV infected individuals who are non-heavy and heavy alcohol drinkers showing the effects of alcohol drinking on HBV cases when β_E =15 (so that $\mathcal{R}_0 > 1$).

Figures 10 (a) and (b) show what happens in a population with no vaccination inter-ventions (that is, $\varphi_1 = \varphi_2 = 0$ so that $\mathcal{R}_0 = 7.9023$), while Figs. 10 (c) and (d) show what happens in a population with vaccination interventions (that is, $\varphi_1 = 0.7$ and $\varphi_2 = 0.6$ so that $\mathcal{R}_0 = 2.1647$) as the percentage of heavy alcohol drinkers is varied, respectively.

In the absence vaccination interventions, the total number of HBV infected individuals who are non-heavy and heavy alcohol drinkers converge

to their distinct endemic equilibrium states depending on the level of alcohol drinking in the population as shown in Figs. 10 (a) and (b), respectively. The higher the percentage of heavy alcohol drinkers, the larger are the total number of HBV infected individuals who are heavy alcohol drinkers at the endemic equilibrium point. In the presence of vaccination interventions, we observe from Figs. 10 (c) and (d) that in the absence of alcohol drinking, both forms of HBV converge to zero. Thus, HBV vaccination is able to effectively control the epidemic. However, the same cannot be said when the entire population is composed of heavy alcohol drinkers, even when HBV vaccination is available as both forms of HBV converge to their respective equilibria which are not zero. However, it is worth noting that the rate of decrease is higher among HBV patients who are non-heavy alcohol drinkers than among the patients who are heavy alcohol drinkers. This tends to suggest that alcohol drinking negatively affects HBV. A mere look at Fig.10 shows that decreasing the percentage of individuals who are heavy alcohol drinkers to less than in a country where there is effective HBV vaccination

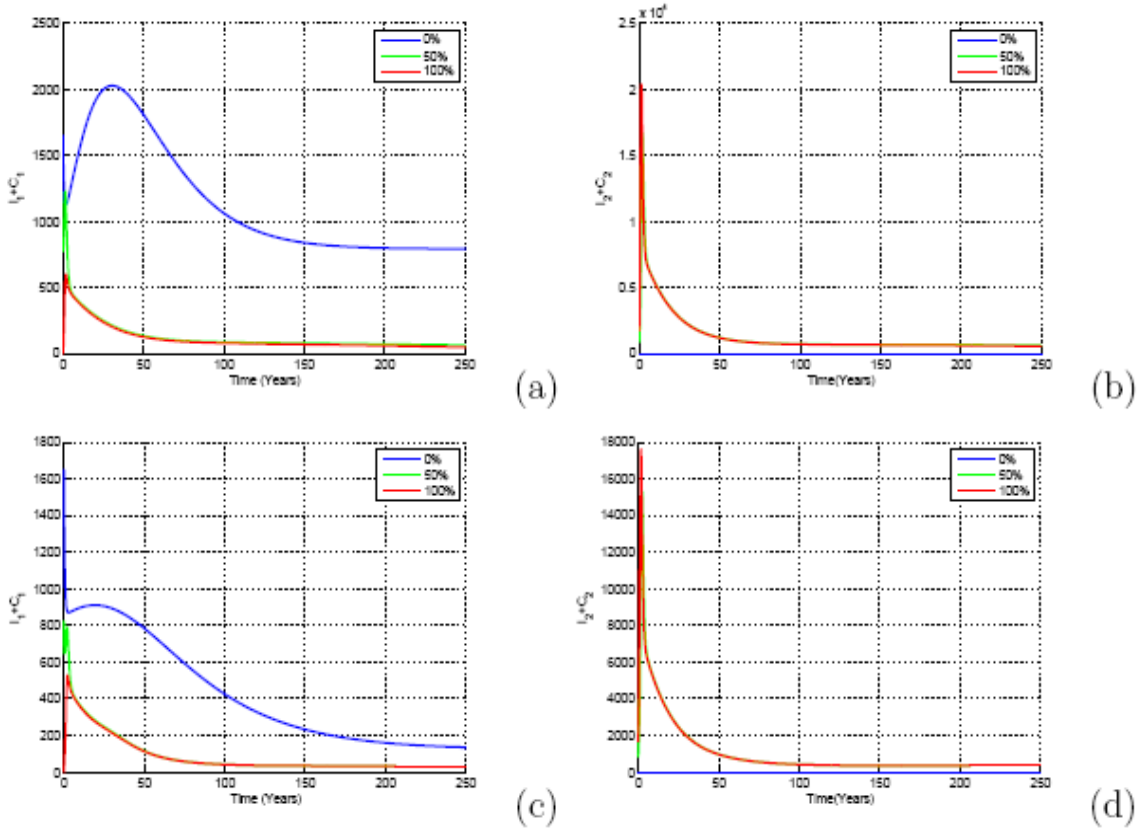

Figure 10. Simulations of model system (5) showing the effects of varying the percentage of heavy alcohol drinkers on the population on HBV infected cases in the absence and presence of vaccination. Parameter values used are in Table 1.

will have a positive impact on HBV control as noted by a rapid depletion of HBV infected. When the percentage is 100% (the whole population is made of heavy alcohol drinkers) as noted in Fig.10, even if effective vaccination is available HBV cannot be managed. This suggests that alcohol drinking positively enhances HBV infection and disease progression while negatively affecting vaccination, implying it should be or has to be discouraged at all levels within the population if HBV is to be eradicated.

5. Discussions and concluding remarks

Drinking alcohol can cause a lot of liver damage in people infected with the hepatitis B virus (HBV). There are many things that happen to our body when we drink alcohol, such as: it stresses out our liver, which is already fighting HBV; our body's natural defenses will not be able to fight HBV as well; we can end up with more hepatitis B viruses; Hepatitis B drugs may not work as well and doctors may not prescribe medication for hepatitis B if we drink.

In this paper, a deterministic compartmental model for investigating the effects of alcohol drinking on the transmission dynamics of hepatitis B in the community is for mulated and analyzed. The effect of alcohol drinking on the actual hepatitis B dynamics is two fold: it increases the transmissibility of HBV in a population of heavy alcohol drinkers, and it also increases the progression from acute infected to chronic carriers in a population of heavy alcohol drinkers. The epidemic threshold parameter which determines the out come of the disease is computed and used to assess the dynamics of the disease in the community. Results show that increasing effective contact rate to become a heavy alcohol drinker and susceptibility to HBV due to alcohol drinking increase the basic reproduction number $\mathcal{R}_0$, while increasing the rate of abandon alcohol drinking decreases the basic reproduction number. This suggests that drinking alcoholic beverages enhances HBV, which agrees with experimental results that alcohol is associated with specific negative health out comes (Bellentani 1997; Vaillant 1995) and promotes the development of HBV (Nishigushi 1991; Becker 1996; Bellentani 1997; McCollough 1998; deAlwis 2007; Lucey 2009).

As customary in epidemiological models, the disease-free and endemic equilibria are found and their stability is investigated depending on the system parameters. Due to the presence of backward bifurcation, in some parameter regimes the system exhibits a bistability between a disease-free and endemic steady states. The Centre Manifold theory was used to determine the local asymptotic stability of the endemic equilibrium.

Numerical results are performed to illustrate various dynamical regimes. Graphical representations clearly show that an increase in susceptibility to HBV due to alcohol drinking will generally result in an increase in the number of HBV infected and chronic carriers with more effecton HBV infected and chronic carriers who are heavy alcohol drinkers. Thus, heavy alcohol drinking increases disease transmission, and the prevalence of disease increases with increased rate of becoming a heavy alcohol drinker. Furthermore, in the presence of HBV vaccination, HBV control is more effective in communities with non-heavy alcohol drinkers than in the communities with heavy alcohol drinkers. Thus, drinking alcohol beverages may reduce the effectiveness of HBV vaccination and enhances HBV transmission and disease progression. Hence, drinking alcohol negatively affect HBV control and as long as this control is taken as a biomedical intervention only, HBV vaccinational one may not be successful in populations where drinking alcohol is common. In the event, when we have more individuals becoming heavy alcohol drinkers, there is urgent need for intervention strategies such as counseling and educational campaigns in order to curtail the HBV spread.

Like in any model development, our model is not without limitations. The proposed model is not exhaustive and has some limitations. For instance, the vertical transmission is not included, which may limit its applicability. One limitation to the model simulations is with regard to the sensitivity analysis of the model parameters. Also, the model that we proposed does not include many features of the greatly complex system involving the HBV epidemiology. Nonetheless, the study highlights an important aspect of the dynamics of HBV in the human population. Most models have focused on how some habits influence the epidemiology of HBV. Host factors such as alcohol drinking are clearly of great importance in the dynamics of the disease. This indicates, to a large extent, that the alcoholic status of individuals affects their susceptibility to infection. The result on HBV infection cases presented in this model are useful for public health planning and performing cost-effectiveness analysis.

References

1. Anderson, R.M., May, R.M., 1991. Infectious Disease of Humans: Dynamics and Control. Oxford University Press, Oxford.

2. Anderson, R.M., May, R.M., Nokes, D.J., 1992. Preliminary analyses of the predicted impacts of various vaccination strategies on the transmission of hepatitis B virus. In: Bennet(Ed.), The Control of Hepatitis B: The Role of Prevention in Adolescence. Gower Medical Publishing, London, pp.95-130.
3. Berman, A., R.J., Plemmons, R.J., 1994. Nonnegative matrices in the mathematical sciences, SIAM.
4. Bellentani, S., Pozzato, G., Saccoccio, G. et al. 1997.
5. Birkhoff, G., Rota, G.C., 1982. Ordinary differential equations. Needham Heights: Ginn. Carr, J., 1981. Applications Centre Manifold Theory. Springer-Verlag, New York.
6. Castillo-Chavez, C., Song, B. 2004. Dynamical models of tuberculosis and their applications. Math. Bios. Eng. 1(2), 361-404.
7. Chitnis, N., Hyman, J.M., Cushing, J.M., 2008. Determining important parameters in the spread of malaria through the sensitivity analysis of a mathematical model. Bull. Math. Biol. 70, 1272-1296.
8. Edmunds, W.J., Medley, G.F., Nokes, D.J., 1996. The transmission dynamics and control of hepatitis B virus in the Gambia Stat. Med. 15, 2215-2233.
9. Edmunds, W.J., Medley, G.F., Nokes, D.J., 1996. Vaccination against hepatitis B virus in highly endemic area: waning vaccine-induced immunity and the need for booster doses. Trans. R. Soc. Trop. Med. Hyg. 90, 436-440.
10. Edmunds, W.J., Medley, G.F., Nokes, D.J., Hall, A.J., Whittle, H.C., 1993. The influence of ageon the development of the hepatitis B carrier state. Proc. R. Soc. Lond. B 253, 197-201.
11. Edmunds, W.J., Medley, G.F., Nokes, D.J., Hall, A.J., Whittle, H.C., 1996. Epidemiological patterns of hepatitis B virus (HBV) in highly endemic areas. Epidemiol. Infect. 117, 313-325.
12. Edmunds WJ, Medley GF, Nokes DJ (1996) The transmission dynamics and control of hepatitis B virus in the Gambia Stat. Med. 15:2215-2233.
13. Ellis, E., and Adler, D. G. 2006, Alcoholic hepatitis, Hospital Physician, pp. 55-60, 2006. www.turner-white.com.
14. Ribes, J., Clèries R., Esteban, R., Moreno, L., and Bosch FX, V. 2008, J Hepatol. 49, 233.
15. Goldstein, S.T., Zhou, F.J., Hadler, S.C., Bell, B.P., Mast, E.E., Margolis, H.S., 2005. A mathematical model to estimate global hepatitis B disease burden and vaccination impact. Int. J. Epidemiol. 34, 1329-1339.
16. Hou, J., Liu, Z., Gu, F., 2005. Epidemiology and prevention of hepatitis B virus infection. Int. J. Med. Sci.2(1), 50-57.
17. Highleyman, L. 2010, Alcohol and Diabetes Increase Risk of Liver Disease Progression in Hepatitis B Patients, 61st Annual Meeting of the American Association for the Study of Liver Diseases (AASLD 2010), October 29-November 2, Boston, MA.
18. Hyams, K.C., 1995. Risks of chronicity following acute hepatitis B virus infection: a review. Clin. Infect. Dis.20, 992-1000.

19. Jacquez, J.A., Simon, C.P., 1993. Qualitative theory of compartmental systems. SIAM Rev. 35, 43-79.
20. Jee, S. H., Ohrr, H., Sull, J. W., and Samet, J. M. 2004, J. Natl. Cancer. Inst. 96, 1851.
21. Mushayabasa, S., and Bhunu, C. P. 2011, Nonlinear Dynamics, DOI: 10.1007/s11071-011-9942-4.
22. Lakshmikantham, V., Leela, S., Martynyuk, A.A., 1989. Stability analysis of nonlinear systems. Marcel Dekker inc., New York and Basel.
23. Lavanchy, D., 2004. Hepatitis B virus epidemiology, diseaseburden, treatment and current and emerging prevention and control measures. J. Viral. Hepat. 11, 97-107.
24. Medley, G.F., Lindop, N.A., Edmunds, W.J., Nokes, D.J., 2001. Hepatitis-B virus endemicity: heterogeneity, catastrophic dynamics and control. Nat. Med.7 (5), 619-624.
25. McLean, A.R., Blumberg, B.S., 1994. Modelling the impact of mass vaccination against hepatitis B. Model formulation and parameter estimation. Proc. R. Soc. Lond. B256, 7-15.
26. Maynard, J.E., Kane, M.A., Hadler, S.C., 1989. Global control of hepatitis B through vaccination:role of hepatitis B vaccine in the expanded programme on immunization. Rev. Infect. Dis. 2 (suppl.3), S574-S578.
27. Roseberry, W., Seale, A., Mphuka, S., 2005. Assessing the application of the three ones principle in Zambia, DFID Health Resources System Centre, London.
28. Sharomi, O., Gumel, A.B., 2008. Curtailing smoking dynamics: a mathematical modeling approach. Appl. Math. Comput. 195(2), 475-499.
29. Shepard, C.W., Simard, E.P., Finelli, L., Fiore, A.E., Bell, B.P., 2006. Hepatitis B virus infection: epidemiology and vaccination. Epidemiol. Rev. 28,112125.
30. Thornley, S., Bullen, C.,Roberts, M., 2008. Hepatitis B in a high prevalence New Zealand population:a mathematical model applied to infection control policy. J. Theor. Biol. 254,599603.
31. van den Driessche P, Watmough, J., 2002. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Math. Bios. 180, 29-28.
32. Williams, J.R., Nokes, D.J., Medley, G.F., Anderson, R.M., 1996. The transmissiondynamics of hepatitis B in the UK: a mathematical model for evaluating costs and effectiveness of immunization programmes. Epidemiol. Infect. 116, 71-89.
33. World Health Organization. 2008, Hepatitis B. /http://www.who.int/mediacentre/ factsheets/fs204/en/ index.htmlS (revised August 2008).
34. World Health Organization, 2002, Meeting on Hepatitis B control through immunization, Tokyo, Japan, 26-28 June 2002.