Mathematical Model for Zika Virus Dynamics with Sexual Transmission Route

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Abstract

Zika virus is a flavivirus transmitted to humans primarily through the bite of infected *Aedes* mosquitoes. In addition to vector-borne spread, however, the virus can also be transmitted through sexual contact. In this paper, we formulate and analyze a new system of ordinary differential equations which incorporates both vector and sexual transmission routes. Theoretical analysis of this model when there is no disease induced mortality shows that the disease-free equilibrium is locally and globally asymptotically stable whenever the associated reproduction number is less than unity and unstable otherwise. However, when we extend this same model to include Zika induced mortality, which have been documented in Latin America, we find that the model exhibits a backward bifurcation. Specifically, a stable disease-free equilibrium co-exists with a stable endemic equilibrium when the associated reproduction number is less than unity. To further explore model predictions, we use numerical simulations to assess the importance of sexual transmission to disease dynamics. This analysis shows that risky behavior involving multiple sexual partners, particularly among male populations, substantially increases the number of infected individuals in the population, contributing significantly to the disease burden in the community.

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1 Introduction

Historically confined to Africa and Southeast Asia [49, 18, 29], the recent introduction of Zika virus (ZIKV) into Latin America [68] has resulted in alarming progression [59] of this disease across much of the New World. Indeed, as of May 26, 2016, only two countries in South America - Chile and Uruguay - had not yet reported autochthonous spread of Zika [14]. Unfortunately, the emergence of Zika under these new conditions has brought with it new discoveries of troubling viral outcomes, including Guillan Barre syndrome [47, 10] and microcephaly [43, 48] in adults and newborns respectively. With the novel realization that Zika can cause severe complications, a disease once described as a ‘mild form of dengue’ has come to the forefront of public health discussions worldwide [54].

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Like all other arboviruses, Zika is predominantly transmitted by mosquitoes - in this case *Aedes* species [30, 41] such as the yellow fever mosquito, *Aedes aegypti* [40]. However, unlike other arboviruses, ZIKV also exhibits a second mode of transmission through sexual contact [27, 21, 42, 64]. This has not been previously documented for other arboviruses. Interestingly, the potential for sexual transmission of ZIKV was first discovered, largely by accident, by a microbiologist returning from studying mosquito-borne diseases in Senegal in 2008 [27]. Unfortunately, however, due to funding constraints, and the relatively minor importance of Zika at the time, little effort was invested into further examining this unusual mechanism for arboviral transmission.

With the ongoing Zika outbreak in the Americas, however, new emphasis has been placed on the study of ZIKV biology, including its various modes of transmission. Interestingly, recent epidemiological studies have demonstrated that, rather than an anomaly, Foy et al.'s early observations of sexual transmission of Zika [27, 21, 42, 64] represent a relatively common mode of spread of this disease [21, 42, 64]. Simultaneously, several additional avenues of investigation have provided further support for the role of sexual transmission. First, ongoing surveillance indicates that the Zika virus can remain in male semen for at least 62 days [39, 5]. Second, an analysis of differences in ZIKV incidence rate among men and women in Rio de Janeiro, Brazil suggests a high rate of male-to-female transmission of this disease [16].

With ever increasing evidence that sexual transmission of ZIKV may be important, novel questions are raised regarding the roles and significance of sexual versus vector transmission and how these different modes of spread jointly contribute to disease epidemiology. Historically, one method for addressing disease dynamics of novel outbreaks has been through mathematical modeling. Although modeling of both arboviruses and sexually transmitted diseases have long histories in epidemiological literature, the combination - namely an arbovirus that is also transmitted through sexual contact - is novel. In this paper, we take a first step towards exploring the dynamics of Zika as it depends on both vector and sexual transmission. Specifically, in Section 2 we formulate the ZIKV model with the two different modes of transmission. Then, in Section 3 we investigate the theoretical properties of the model. Finally, in Section 4 we carry out numerical exploration of the model, with discussion and conclusions stated in Section 5.

2 Model Formulation

We use a compartmental modeling framework to explore Zika virus transmission dynamics when, in addition to vector-borne spread, there is an additional sexual transmission route. Specifically, we divide the human population into female and male sub-populations. We then further divide these subgroups into susceptible (S_i), exposed (E_i), infected (I_i) and recovered (R_i) classes, where $i = F, M$ for females and males respectively. Hence, the equation for the total number of females is: $N_F = S_F + E_F + I_F + R_F$, while the equation for the total number of males is: $N_M = S_M + E_M + I_M + R_M$. The total human population is then given by $N_H = N_F + N_M$.

The total mosquito population, denoted (N_V), is likewise sub-divided into susceptible mosquitoes (S_V), exposed mosquitoes (E_V) and infectious mosquitoes (I_V), hence: $N_V = S_V + E_V + I_V$.

Let Π_H be the recruitment rate of susceptible individuals into the human population and assume that half of these are females. In this case, the rate at which females are born is given by $\Pi_F = \frac{\Pi_H}{2}$. At the same time, the female population is reduced as a result of natural death at a

rate (μ_F). The total number of humans and mosquitoes in the community determines the average number of mosquito bites a human will receive. Here, we assume that the mosquito biting rate, b_V , is constant, and represents the maximal rate allowed by the gonotrophic cycle [67]. Let b_H be the rate at which bites are received by a single human. For the number of bites to be conserved, the total number of bites by mosquitoes must be equal to the total number of bites received by humans. Hence,

$$b_V N_V = b_H(N_H, N_V) N_H$$

so that,

$$N_V = \frac{b_H(N_H, N_V) N_H}{b_V} \quad (2.1)$$

Let $b_H \beta_V$ be the effective contact rate between a susceptible human and infectious mosquitoes, where β_V is the transmission probability per contact from an infectious mosquito to a susceptible human. Also, let $b_V \beta_H$ be the effective contact rate between a susceptible mosquito and infectious human, where β_H is the transmission probability per contact from an infectious human to a susceptible mosquito. In this case, susceptible females acquire infection, following effective contact with an infectious mosquito, at a rate λ_{F1} , given by,

$$\lambda_H(I_V, N_H) = \frac{b_H(N_H, N_V) \beta_H I_V}{N_V}. \quad (2.2)$$

Substituting (2.1) in (2.2) we obtain,

$$\lambda_H(I_V, N_H) = \frac{b_V \beta_H I_V}{N_H}.$$

It can also be shown that the rate at which mosquitoes acquire infection from infectious humans is given by

$$\lambda_V(I_F, I_M, N_H) = \frac{b_V \beta_V (I_F + I_M)}{N_H}.$$

The parameter β_V is the probability that a bite from a susceptible mosquito to a human will lead to infection of the mosquito.

For sexual transmission, we assume that the infection rate of susceptible females by infected males (λ_{FM}) is given as:

$$\lambda_{FM}(I_M, N_M) = \frac{C_F \beta_M I_M}{N_M} \quad (2.3)$$

where the parameter β_M is the probability that a sexual contact with an infectious male will lead to infection of the susceptible female and the parameter C_F is the contact rate between males and females. It is assumed that the contact rate is constant. Thus, for the number of contact to be conserved, the total number of contacts by males (C_{M1}) must be equal to the total number of contacts by females (C_F),

$$C_{M1} N_M = C_F N_F$$

so that,

$$N_M = \frac{C_F N_F}{C_{M1}} \quad (2.4)$$

82 Using equation (2.4) in equation (2.3) we obtain,

$$\lambda_{FM}(I_M, N_F) = \frac{C_{M_1}\beta_M I_M}{N_F}.$$

83 We do not consider sexual transmission between female partners, since this is extremely rare in
84 other sexually transmitted diseases, and thus is not expected to occur for Zika either [51].

85 Hence, susceptible females become infected following effective contact with infected mosquitoes
86 at a rate $\lambda_{F1}(I_V, N_H)$ and from sexual contact with infected males at a rate $\lambda_{FM}(I_M, N_F)$ after
87 which they move to the exposed class. This gives

$$\frac{dS_F}{dt} = \Pi_F - \frac{b_V\beta_H I_V S_F}{N_H} - \frac{C_{M_1}\beta_M I_M S_F}{N_F} - \mu_F S_F.$$

88 Exposed females move to the infectious class due to disease progression at a rate σ_F . The
89 population of exposed females is decreased due to natural death at a rate μ_F . Thus, the equation
90 for the exposed class is represented by

$$\frac{dE_F}{dt} = \frac{b_V\beta_H I_V S_F}{N_H} + \frac{C_{M_1}\beta_M I_M S_F}{N_F} - (\sigma_F + \mu_F)E_F.$$

91 Likewise, the infected class population is decreased as a result of recovery at a rate γ_F and natural
92 death at a rate μ_F . Hence, we have

$$\frac{dI_F}{dt} = \sigma_F E_F - (\gamma_F + \mu_F)I_F.$$

93 Finally, the population of recovered individuals is comprised of individuals that have progressed
94 through the infectious stage and become refractory to further diseases. This population is then
95 decreased due to natural death at a rate μ_F . Thus, the equation for the recovered population
96 becomes:

$$\frac{dR_F}{dt} = \gamma_F I_F - \mu_F R_F.$$

97 The equations for the male sub-population are similarly obtained; additionally, however, we
98 include male-to-male transmission [17]. Although there are no reported cases of female-to-male
99 transmission, this possibility cannot be ruled out and we assume the existence of this transmission
100 route, though possibly with a different transmission probability per encounter.

101 For the vector population, we assume that susceptible mosquitoes are recruited at a rate (Π_V) .
102 This population is then reduced by biting on infectious humans, and as a result of natural death
103 at a rate μ_V . This gives:

$$\frac{dS_V}{dt} = \Pi_V - \frac{b_V\beta_V(I_F + I_M)S_V}{N_H} - \mu_V S_V.$$

When a susceptible mosquito bites an infectious human, then with probability of infection (β_V) ,
the mosquito move to the exposed class (E_V) . The equation for this class is given by:

$$\frac{dE_V}{dt} = \frac{b_V\beta_V(I_F + I_M)S_V}{N_H} - (\sigma_V + \mu_V)E_V$$

where we have again assumed a natural death rate of μ_V . Exposed mosquitoes move to the infected class at the rate σ_V and are again reduced by natural death. Thus, we have:

$$\frac{dI_V}{dt} = \sigma_V E_V - \mu_V I_V.$$

104 Overall, our model for ZIKV, including both sexual and vector-borne transmission, is given as:

$$\begin{aligned} \frac{dS_F}{dt} &= \Pi_F - \frac{b_V \beta_H I_V S_F}{N_H} - \frac{C_{M_1} \beta_M I_M S_F}{N_F} - \mu_F S_F \\ \frac{dE_F}{dt} &= \frac{b_V \beta_H I_V S_F}{N_H} + \frac{C_{M_1} \beta_M I_M S_F}{N_F} - (\sigma_F + \mu_F) E_F \\ \frac{dI_F}{dt} &= \sigma_F E_F - (\gamma_F + \mu_F) I_F \\ \frac{dR_F}{dt} &= \gamma_F I_F - \mu_F R_F \\ \frac{dS_M}{dt} &= \Pi_M - \frac{b_V \beta_H I_V S_M}{N_H} - \frac{C_F \beta_F I_F S_M}{N_M} - \frac{C_{M_2} \beta_M I_M S_M}{N_M} - \mu_M S_M \\ \frac{dE_M}{dt} &= \frac{b_V \beta_H I_V S_M}{N_H} + \frac{C_F \beta_F I_F S_M}{N_M} + \frac{C_{M_2} \beta_M I_M S_M}{N_M} - (\sigma_M + \mu_M) E_M \\ \frac{dI_M}{dt} &= \sigma_M E_M - (\gamma_M + \mu_M) I_M \\ \frac{dR_M}{dt} &= \gamma_M I_M - \mu_M R_M \\ \frac{dS_V}{dt} &= \Pi_V - \frac{b_V \beta_V (I_F + I_M) S_V}{N_H} - \mu_V S_V \\ \frac{dE_V}{dt} &= \frac{b_V \beta_V (I_F + I_M) S_V}{N_H} - (\sigma_V + \mu_V) E_V \\ \frac{dI_V}{dt} &= \sigma_V E_V - \mu_V I_V, \end{aligned} \tag{2.5}$$

105 where $\Pi_F = \frac{\Pi_H}{2}$ and $\Pi_M = \frac{\Pi_H}{2}$.

Females

Males

Mosquitoes

Figure 1: Flow diagram of the Zika virus model (2.5) with sexual transmission route

Variable	Description
$S_F(t), S_M(t)$	Susceptible females and males
$E_F(t), E_M(t)$	Exposed females and males
$I_F(t), I_M(t)$	Infected females and males
$R_F(t), R_M(t)$	Recovered females and males
$S_V(t)$	Susceptible mosquitoes
$E_V(t)$	Exposed mosquitoes
$I_V(t)$	Infected mosquitoes

Parameter	Description
Π_H	Recruitment rate of females and males
C_F, C_{M_1}	Heterosexual contact rate between females and males
C_{M_2}	Homosexual contact rate between males
β_H	Transmission probability <i>per</i> contact of susceptible humans with infected mosquitoes
σ_F, σ_M	Progression rate of exposed females and males
γ_F, γ_M	Recovery rate of females and males
μ_F, μ_M	Natural death rate of females and males
π_V	Recruitment rate of mosquitoes
β_F, β_M	Transmission probability <i>per</i> contact of females and males
b_V	Mosquito biting rate
β_V	Transmission probability <i>per</i> contact of susceptible mosquitoes with infected humans
σ_V	Progression rate of exposed mosquitoes
μ_V	Natural death rate of mosquitoes

Table 1: Description of the state variables and parameters of the Zika virus model (2.5) with sexual transmission route.

2.1 Basic properties

We shall now explore the basic dynamical features of model (2.5). Since model (2.5) describes both human and mosquito populations during the course of a Zika epidemic, it will only be epidemiologically meaningful if all state variables are non-negative for $t \geq 0$. That is, its solution with positive initial data will remain positive for all time ($t > 0$).

Lemma 1. *Let the initial data $F(0) \geq 0$, where $F(t) = (S_F, E_F, I_F, R_F, S_M, E_M, I_M, R_M, S_V, E_V, I_V)$. Then the solutions $F(t)$ of model (2.5) are non-negative for all time $t > 0$. Furthermore*

$$\limsup_{t \rightarrow \infty} N_H(t) = \frac{\Pi_H}{\mu_H}, \quad \limsup_{t \rightarrow \infty} N_V(t) = \frac{\Pi_V}{\mu_V},$$

where $\mu_H = \min\{\mu_F, \mu_M\}$.

with,

$$\begin{aligned} N_F(t) &= S_F(t) + E_F(t) + I_F(t) + R_F(t), \\ N_M(t) &= S_M(t) + E_M(t) + I_M(t) + R_M(t), \\ N_V(t) &= S_V(t) + E_V(t) + I_V(t). \end{aligned}$$

The proof of Lemma 1 is given in Appendix A.

Invariant regions

Model (2.5) will be analyzed in a biologically-feasible region as follows. Consider the feasible region

$$\Gamma = \Gamma_H \times \Gamma_V \subset \mathbb{R}_+^8 \times \mathbb{R}_+^3$$

with,

$$\begin{aligned}\Gamma_H &= \left\{ (S_F(t), E_F(t), I_F(t), R_F(t), S_M(t), E_M(t), I_M(t), R_M(t)) : N_H(t) \leq \frac{\Pi_H}{\mu_H} \right\}, \\ \Gamma_V &= \left\{ (S_V(t), E_V(t), I_V(t)) : N_V(t) \leq \frac{\Pi_V}{\mu_V} \right\}.\end{aligned}$$

Lemma 2. *The region $\Gamma = \Gamma_H \times \Gamma_V \subset \mathbb{R}_+^8 \times \mathbb{R}_+^3$ is positively invariant for the basic model (2.5) with non-negative initial conditions in $\mathbb{R}_+^{11}$.*

The proof of Lemma 2 is given in Appendix B.

3 Analysis of the sub-models

Before analyzing the full Zika virus transmission model (2.5), it is imperative to gain insights into the dynamics of the different transmission routes. Thus, we will separately consider two sub-models: one with the mosquito transmission route only and one with the sexual transmission route only.

3.1 Mosquito transmission route only model

The mosquito transmission route only model is obtained by assuming that Zika virus is not transmitted sexually. Hence, model (2.5) reduces to the following

$$\begin{aligned}
\frac{dS_F}{dt} &= \Pi_F - \frac{b_V \beta_H I_V S_F}{N_H} - \mu_F S_F \\
\frac{dE_F}{dt} &= \frac{b_V \beta_H I_V S_F}{N_H} - (\sigma_F + \mu_F) E_F \\
\frac{dI_F}{dt} &= \sigma_F E_F - (\gamma_F + \mu_F) I_F \\
\frac{dR_F}{dt} &= \gamma_F I_F - \mu_F R_F \\
\frac{dS_M}{dt} &= \Pi_M - \frac{b_V \beta_H I_V S_M}{N_H} - \mu_M S_M \\
\frac{dE_M}{dt} &= \frac{b_V \beta_H I_V S_M}{N_H} - (\sigma_M + \mu_M) E_M \\
\frac{dI_M}{dt} &= \sigma_M E_M - (\gamma_M + \mu_M) I_M \\
\frac{dR_M}{dt} &= \gamma_M I_M - \mu_M R_M \\
\frac{dS_V}{dt} &= \Pi_V - \frac{b_V \beta_V (I_F + I_M) S_V}{N_H} - \mu_V S_V \\
\frac{dE_V}{dt} &= \frac{b_V \beta_V (I_F + I_M) S_V}{N_H} - (\sigma_V + \mu_V) E_V \\
\frac{dI_V}{dt} &= \sigma_V E_V - \mu_V I_V.
\end{aligned} \tag{3.1}$$

Consider the feasible region

$$\Gamma_M = \Gamma_H \times \Gamma_V \subset \mathbb{R}_+^8 \times \mathbb{R}_+^3$$

with,

$$\begin{aligned}
\Gamma_H &= \left\{ (S_F(t), E_F(t), I_F(t), R_F(t), S_M(t), E_M(t), I_M(t), R_M(t)) : N_H(t) \leq \frac{\Pi_H}{\mu_H} \right\}, \\
\Gamma_V &= \left\{ (S_V(t), E_V(t), I_V(t)) : N_V(t) \leq \frac{\Pi_V}{\mu_V} \right\}.
\end{aligned}$$

It can be shown that all solutions of the system (3.1) starting in Γ_M remain in Γ_M for all $t > 0$. Thus, Γ_M is positively-invariant (hence, it is sufficient to consider the dynamics of (3.1) in Γ_M).

3.1.1 Local stability of disease-free equilibrium (DFE)

The disease-free equilibrium (DFE) of the model (3.1) is given as

$$\begin{aligned}
\mathcal{E}_{V_1} &= (S_F^*, E_F^*, I_F^*, R_F^*, S_M^*, E_M^*, I_M^*, R_M^*, S_V^*, E_V^*, I_V^*) \\
&= \left(\frac{\Pi_F}{\mu_F}, 0, 0, 0, \frac{\Pi_M}{\mu_M}, 0, 0, 0, \frac{\Pi_V}{\mu_V}, 0, 0 \right).
\end{aligned}$$

The local asymptotic stability of $\mathcal{E}_{V_1}$ can be established using the next generation matrix method on the system (2.5). Taking the infected compartments $(E_F^*, I_F^*, E_M^*, I_M^*, E_V^*, I_V^*)$ at the DFE and using the notation in [63], the Jacobian matrices F_V and V_V for the new infection terms and the remaining transfer terms are respectively given by,

139

$$F_V =$$

$$\begin{bmatrix} 0 & 0 & 0 & 0 & 0 & \frac{b_V \beta_H S_F^*}{N_H^*} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \frac{b_V \beta_H S_M^*}{N_H^*} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{b_V \beta_V S_V^*}{N_H^*} & 0 & \frac{b_V \beta_V S_V^*}{N_H^*} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

140

$$V_V =$$

$$\begin{bmatrix} k_1 & 0 & 0 & 0 & 0 & 0 \\ -\sigma_F & k_2 & 0 & 0 & 0 & 0 \\ 0 & 0 & k_3 & 0 & 0 & 0 \\ 0 & 0 & -\sigma_M & k_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & k_5 & 0 \\ 0 & 0 & 0 & 0 & -\sigma_V & \mu_V \end{bmatrix}$$

141 where $k_1 = \sigma_F + \mu_F$, $k_2 = \gamma_F + \mu_F$, $k_3 = \sigma_M + \mu_M$, $k_4 = \gamma_M + \mu_M$, $k_5 = \sigma_V + \mu_V$. Hence, the
 142 reproduction number is given by:

$$\mathcal{R}_V = \rho(F_V V_V^{-1}) = \sqrt{\mathcal{R}_{FV} + \mathcal{R}_{MV}},$$

143

$$\text{where } \mathcal{R}_{FV} = \frac{\beta_H \sigma_F S_F^* \beta_V \sigma_V b_V^2 S_V^*}{k_1 k_2 k_5 \mu_V (N_H^*)^2} \text{ and } \mathcal{R}_{MV} = \frac{\beta_H \sigma_M S_M^* \beta_V \sigma_V b_V^2 S_V^*}{k_3 k_4 k_5 \mu_V (N_H^*)^2}.$$

144

Lemma 3. *The disease-free equilibrium (DFE) of the Zika virus model (3.1) with mosquito only
 145 transmission is locally asymptotically stable (LAS) if $\mathcal{R}_V < 1$ and unstable if $\mathcal{R}_V > 1$.*

146

The basic reproduction number $\mathcal{R}_V$ is defined as the average number of new infections that
 147 result from one infectious individual in a population that is fully susceptible [4, 19, 31, 63]. The
 148 epidemiological significance of Lemma 3 is that Zika virus can be eliminated from the community
 149 if the reproduction number ($\mathcal{R}_V$) can be brought to (and maintained at) a value less than unity.
 150 Figures 2 shows convergence of the solutions of the Zika model (3.1) to the DFE ($\mathcal{E}_{V_1}$) for the
 151 case when $\mathcal{R}_V < 1$ (in accordance with Lemma 3).

Figure 2: Simulation of the mosquito transmission route only Zika model (3.1) as a function of time when $\mathcal{R}_V < 1$. (a) Total number of infectious females (b) Total number of infectious males (c) Total number of infectious mosquitoes. Parameter values used are as given in Table 3.

3.1.2 Global Asymptotic Stability of the DFE

Consider the feasible region

$$\Gamma_2 = \{D \in \Gamma_M : S_F \leq S_F^*, S_M \leq S_M^*, S_V \leq S_V^*\}$$

where,

$$D = (S_F, E_F, I_F, R_F, S_M, E_M, I_M, R_M, S_V, E_V, I_V).$$

Lemma 4. *The region Γ_2 is positively-invariant for the Zika virus model (3.1).*

The proof of Lemma 4 is given in Appendix C.

Theorem 1. *The DFE ($\mathcal{E}_{V_1}$) of the Zika virus model (3.1) is globally asymptotically stable (GAS) in Γ_2 , whenever $\mathcal{R}_V \leq 1$.*

The proof of Theorem 1 is given in Appendix D.

3.1.3 Existence of Endemic Equilibrium Point (EEP)

In this section, we will investigate conditions for the existence of endemic equilibria (i.e., equilibria where the infected components of the Zika transmission model (3.1) are non-zero).

Let

$$\mathcal{E}_{V_2} = (S_F^{**}, E_F^{**}, I_F^{**}, R_F^{**}, S_M^{**}, E_M^{**}, I_M^{**}, R_B^{**}, S_V^{**}, E_V^{**}, I_V^{**})$$

be an arbitrary endemic equilibrium of Zika transmission model (3.1), where

$$\begin{aligned} S_F^{**} &= \frac{\Pi_F N_H^{**}}{\beta_H b_V I_V^{**} + N_H^{**} \mu_F}, & E_F^{**} &= \frac{\beta_H b_V I_V^{**} \Pi_F}{k_1 (b_V \beta_H I_V^{**} + N_H^{**} \mu_F)}, \\ I_F^{**} &= \frac{\sigma_F \beta_H b_V I_V^{**} \Pi_F}{k_1 k_2 (b_V \beta_H I_V^{**} + N_H^{**} \mu_F)}, & R_F^{**} &= \frac{\gamma_F \sigma_F b_V \beta_H I_V^{**} \Pi_F}{\mu_F k_1 k_2 (b_V \beta_H I_V^{**} + N_H^{**} \mu_F)}, \\ S_M^{**} &= \frac{\Pi_M N_H^{**}}{b_V \beta_H I_V^{**} + N_H^{**} \mu_M}, & E_M^{**} &= \frac{b_V \beta_H I_V^{**} \Pi_M}{k_3 (b_V \beta_H I_V^{**} + N_H^{**} \mu_M)}, \\ I_M^{**} &= \frac{\sigma_M b_V \beta_H I_V^{**} \Pi_M}{k_3 k_4 (b_V \beta_H I_V^{**} + N_H^{**} \mu_M)}, & R_M^{**} &= \frac{\gamma_M \sigma_M b_V \beta_H I_V^{**} \Pi_M}{\mu_M k_3 k_4 (b_V \beta_H I_V^{**} + N_H^{**} \mu_M)}, \\ S_V^{**} &= \frac{\Pi_V}{\lambda_V^{**} + \mu_V}, & E_V^{**} &= \frac{\lambda_V^{**} \Pi_V}{k_5 (\lambda_V^{**} + \mu_V)}, \\ I_V^{**} &= \frac{\sigma_V \lambda_V^{**} \Pi_V}{k_5 \mu_V (\lambda_V^{**} + \mu_V)}, \end{aligned}$$

are components of the steady-state solution of the equations of the Zika transmission model (3.1).

Also, let

$$\lambda_H^{**} = \frac{b_V \beta_H I_V^{**}}{N_H^{**}}, \quad \lambda_V^{**} = \frac{b_V \beta_V (I_F^{**} + I_M^{**})}{N_H^{**}}, \quad (3.2)$$

be the forces of infection of susceptible humans and mosquitoes at steady-state, respectively.

Substituting the expressions for I_F^{**} and I_M^{**} , into the equation (3.2) for λ_V^{**} and simplifying gives

$$\lambda_V^{**} = \frac{b_V^2 \beta_H \beta_V I_V^{**} \mu_H^2 [a_2 (I_V^{**}) + a_1]}{k_1 k_2 k_3 k_4 \Pi_H (b_V \beta_H I_V^{**} \mu_H + \Pi_H \mu_F) (b_V \beta_H I_V^{**} \mu_H + \Pi_H \mu_M)} \quad (3.3)$$

where

$$a_2 = b_V \beta_H \sigma_M \Pi_M \mu_H k_1 k_2 + b_V \beta_H \sigma_F \Pi_F \mu_H k_3 k_4, \quad a_1 = \sigma_M \Pi_M \Pi_H \mu_F k_1 k_2 + \sigma_F \Pi_F \Pi_H \mu_M k_3 k_4.$$

Substituting expression for I_V^{**} into the force of infection λ_H^{**} in equation (3.2) gives

$$\lambda_H^{**} = \frac{\beta_H b_V \sigma_V \lambda_V^{**} \Pi_V \mu_H}{k_5 \mu_V \Pi_H (\lambda_V^{**} + \mu_V)}$$

and then solving for λ_V^{**} , gives

$$\lambda_V^{**} = -\frac{\lambda_H^{**} k_5 \mu_V^2 \Pi_H}{(\lambda_H^{**} k_5 \mu_V \Pi_H - \beta_H b_V \sigma_V \Pi_V \mu_H)}.$$

Substituting this result into (3.3), and simplifying, leads to the following quadratic equation

$$b_2(\lambda_H^{**})^2 + b_1\lambda_H^{**} + b_0(1 - \mathcal{R}_V^2) = 0, \quad (3.4)$$

where

$$\begin{aligned} b_2 &= \beta_V \mu_V \Pi_H^2 k_5 a_2 + \beta_H \mu_V^2 \Pi_H^3 k_1 k_2 k_3 k_4 k_5, \\ b_1 &= b_V \beta_V \beta_H \Pi_H \mu_H (\mu_V k_5 a_1 - \sigma_V \Pi_V a_2) + \beta_H \Pi_H^3 \mu_V^2 k_1 k_2 k_3 k_4 k_5 (\mu_F + \mu_M), \\ b_0 &= \Pi_H^3 \beta_H \mu_F \mu_M \mu_V^2 k_1 k_2 k_3 k_4 k_5. \end{aligned}$$

From (3.4), it can easily be seen that $b_2 > 0$. Further, $b_0(1 - \mathcal{R}_V^2) < 0$ whenever $\mathcal{R}_V^2 > 1$. Thus, the number of possible positive real roots the polynomial (3.4) can have depends on the signs of b_1 . This can be analyzed using the Descartes Rule of Signs on the quadratic polynomial $g(x) = c_2 x^2 + c_1 x + c_0$, given in (3.4) (with $x = \lambda_H^{**}$, $c_2 = b_2$, $c_1 = b_1$, $c_0 = b_0(1 - \mathcal{R}_V^2)$). The various possibilities for the roots of $g(x)$ are tabulated in Table 2.

Cases	c_2	c_1	c_0	$\mathcal{R}_V$	Number of sign changes	No of possible positive real roots (disease-free/endemic equilibrium)
1	+	+	-	$\mathcal{R}_V > 1$	1	1
2	+	-	-	$\mathcal{R}_V > 1$	1	1

Table 2: Number of Possible Positive Real Roots of $g(x)$ for $\mathcal{R}_V > 1$.

The following results (Theorem 2) follow from the various possible combinations for the roots of $g(x)$, in Table 2.

Theorem 2. *The Zika transmission model (3.1) has a unique endemic equilibrium if $\mathcal{R}_V > 1$.*

Numerical simulations of the Zika transmission model (3.1), depicted in Figure 3, show convergence to an endemic equilibrium when $\mathcal{R}_V > 1$ (suggesting that the unique EEP of the Zika transmission model (3.1) is asymptotically stable when it exists).

3.1.4 Local stability of the endemic equilibrium (EE)

In this Section we will consider the stability of the endemic equilibrium of model (3.1). Let

$$\mathcal{E}_{V_2} = (S_F^{**}, E_F^{**}, I_F^{**}, R_F^{**}, S_M^{**}, E_M^{**}, I_M^{**}, R_M^{**}, S_V^{**}, E_V^{**}, I_V^{**})$$

be the unique endemic equilibrium of the Zika model (3.1).

Lemma 5. *The unique endemic equilibrium ($\mathcal{E}_{V_2}$) of model (3.1) is locally asymptotically stable.*

The proof of Lemma 5 is given in Appendix E. Numerical simulations of the Zika model (3.1), depicted in Figure 3, show convergence to a unique endemic equilibrium when $\mathcal{R}_V > 1$ (suggesting that the unique EEP of the Zika model (3.1) is asymptotically stable when it exists).

(a)

(b)

(c)

Figure 3: Simulation of the mosquito transmission route only Zika model (3.1) as a function of time when $\mathcal{R}_V > 1$. (a) Total number of infectious females (b) Total number of infectious males (c) Total number of infectious mosquitoes. Parameter values used are as given in Table 3

3.2 Sexual transmission route only model

The sexual transmission route only model is obtained by assuming that Zika virus is only transmitted sexually and not through the bites of infectious mosquitoes. Hence, model (2.5) reduces

191 to the following

$$\begin{aligned}
\frac{dS_F}{dt} &= \Pi_F - \frac{C_{M_1}\beta_M I_M S_F}{N_F} - \mu_F S_F \\
\frac{dE_F}{dt} &= \frac{C_{M_1}\beta_M I_M S_F}{N_F} - (\sigma_F + \mu_F) E_F \\
\frac{dI_F}{dt} &= \sigma_F E_F - (\gamma_F + \mu_F) I_F \\
\frac{dR_F}{dt} &= \gamma_F I_F - \mu_F R_F \\
\frac{dS_M}{dt} &= \Pi_M - \frac{C_F\beta_F I_F S_M}{N_M} - \frac{C_{M_2}\beta_M I_M S_M}{N_M} - \mu_M S_M \\
\frac{dE_M}{dt} &= \frac{C_F\beta_F I_F S_M}{N_M} + \frac{C_{M_2}\beta_M I_M S_M}{N_M} - (\sigma_M + \mu_M) E_M \\
\frac{dI_M}{dt} &= \sigma_M E_M - (\gamma_M + \mu_M) I_M \\
\frac{dR_M}{dt} &= \gamma_M I_M - \mu_M R_M.
\end{aligned} \tag{3.5}$$

For this model (3.5), it can be shown (using the approaches in Section 2.1) that the feasible region,

$$\Gamma_S \subset \mathbb{R}_+^8$$

192 with,

$$\Gamma_S = \left\{ (S_F(t), E_F(t), I_F(t), R_F(t), S_M(t), E_M(t), I_M(t), R_M(t)) : N_H(t) \leq \frac{\Pi_H}{\mu_H} \right\},$$

193 is positively-invariant, hence, it is sufficient to consider the dynamics of (3.5) in Γ_S .

194 3.2.1 Local stability of disease-free equilibrium

195 The disease-free equilibrium (DFE) of the model (3.5) is given as

$$\begin{aligned}
\mathcal{E}_{S_1} &= (S_F^*, E_F^*, I_F^*, R_F^*, S_M^*, E_M^*, I_M^*, R_M^*) \\
&= \left(\frac{\Pi_F}{\mu_F}, 0, 0, 0, \frac{\Pi_M}{\mu_M}, 0, 0, 0 \right).
\end{aligned}$$

196 And the associated next generation matrices F_S and V_S of equation (3.5) are:

$$F_S = \begin{pmatrix} 0 & 0 & 0 & C_{M_1}\beta_M \\ 0 & 0 & 0 & 0 \\ 0 & C_F\beta_F & 0 & C_{M_2}\beta_M \\ 0 & 0 & 0 & 0 \end{pmatrix}, \quad V_S = \begin{pmatrix} k_1 & 0 & 0 & 0 \\ -\sigma_F & k_2 & 0 & 0 \\ 0 & 0 & k_3 & 0 \\ 0 & 0 & -\sigma_M & k_4 \end{pmatrix}.$$

197 Thus, the reproduction number for the model (3.5) is given by

$$\mathcal{R}_S = \rho(F_S V_S^{-1}) = \frac{1}{2} \frac{C_{M_2}\beta_M \sigma_M}{k_3 k_4} + \frac{1}{2} \sqrt{\frac{\beta_M \sigma_M}{k_3 k_4} \left[\frac{4C_F\beta_F \sigma_F C_{M_1}}{k_1 k_2} + \frac{C_{M_2}^2 \beta_M \sigma_M}{k_3 k_4} \right]}.$$

Lemma 6. *The disease-free equilibrium (DFE) of the Zika virus model (3.5) with sexual transmission route is locally asymptotically stable (LAS) if $\mathcal{R}_S < 1$ and unstable if $\mathcal{R}_S > 1$.*

The epidemiological significance of Lemma 6 is that, Zika virus will be eliminated from the community if the reproduction number ($\mathcal{R}_S$) can be brought to (and maintained at) a value less than unity.

Figure 4: Simulation of the sexual transmission route only Zika model (3.5) as a function of time when $\mathcal{R}_S < 1$. (a) Total number of infectious females (b) Total number of infectious males. Parameter values used are as given in Table 3.

3.2.2 Global stability of the DFE

Theorem 3. *The DFE of the sexual transmission route only model (3.5), given by $\mathcal{E}_{S_1}$, is GAS in Γ whenever $\mathcal{R}_S < 1$.*

The proof of Theorem 3 is given in Appendix F.

The above result shows that, with only the sexual transmission route, Zika will be eliminated from the community if the threshold quantity $\mathcal{R}_S$ can be brought to a value less than unity.

3.2.3 Existence of Endemic Equilibrium Point (EEP)

In this section, we will investigate conditions for the existence of endemic equilibria of the Zika transmission model (3.5).

Let

$$\mathcal{E}_{S_2} = (S_F^{**}, E_F^{**}, I_F^{**}, R_F^{**}, S_M^{**}, E_M^{**}, I_M^{**}, R_B^{**})$$

be an arbitrary endemic equilibrium of Zika transmission model (3.5). We will study the existence of this equilibrium ($\mathcal{E}_{S_2}$) under two scenarios: when there are only heterosexual couples present, and when there are only homosexual couples present.

Let $\tilde{\mathcal{E}}_{S_{21}} = (S_F^{**}, E_F^{**}, I_F^{**}, R_F^{**}, S_M^{**}, E_M^{**}, I_M^{**}, R_M^{**})$ be an arbitrary equilibrium of the Zika model (3.5) with heterosexual only couples, where

$$\begin{aligned}
S_F^{**} &= \frac{\Pi_F}{\lambda_{FM}^{**} + \mu_F}, & E_F^{**} &= \frac{\Pi_F \lambda_{FM}^{**}}{k_1(\lambda_{FM}^{**} + \mu_F)}, \\
I_F^{**} &= \frac{\sigma_F \Pi_F \lambda_{FM}^{**}}{k_1 k_2 (\lambda_{FM}^{**} + \mu_F)}, & R_F^{**} &= \frac{\gamma_F \sigma_F \Pi_F \lambda_{FM}^{**}}{k_1 k_2 \mu_F (\lambda_{FM}^{**} + \mu_F)}, \\
S_M^{**} &= \frac{\Pi_M}{\lambda_{MF}^{**} + \mu_M}, & E_M^{**} &= \frac{\Pi_M \lambda_{MF}^{**}}{k_3(\lambda_{MF}^{**} + \mu_M)}, \\
I_M^{**} &= \frac{\sigma_M \Pi_M \lambda_{MF}^{**}}{k_3 k_4 (\lambda_{MF}^{**} + \mu_M)}, & R_M^{**} &= \frac{\gamma_M \sigma_M \Pi_M \lambda_{MF}^{**}}{k_3 k_4 \mu_M (\lambda_{MF}^{**} + \mu_M)},
\end{aligned}$$

are components of the steady-state solution of the equations of the Zika transmission model (3.5) with heterosexual only couples. Also, let

$$\lambda_{FM}^{**} = \frac{C_{M_1} \beta_M I_M^{**}}{N_F^{**}}, \quad \lambda_{MF}^{**} = \frac{C_F \beta_F I_F^{**}}{N_M^{**}}, \quad (3.6)$$

be the forces of infection of susceptible heterosexual females and males at steady-state, respectively. Substituting the expressions for I_F^{**} , into equation (3.6) for λ_{MF}^{**} and simplifying gives

$$\lambda_{MF}^{**} = \frac{C_F \beta_F \sigma_F \Pi_F \mu_M \lambda_{FM}^{**}}{k_1 k_2 \Pi_M (\lambda_{FM}^{**} + \mu_F)} \quad (3.7)$$

Substituting the expression for I_M^{**} into the force of infection λ_{FM}^{**} in equation (3.6) gives

$$\lambda_{FM}^{**} = \frac{C_{M_1} \beta_M \sigma_M \Pi_M \mu_F \lambda_{MF}^{**}}{k_3 k_4 \Pi_F (\lambda_{MF}^{**} + \mu_M)} \quad (3.8)$$

and then solving (3.8) for λ_{MF}^{**} , gives

$$\lambda_{MF}^{**} = -\frac{\lambda_{FM}^{**} k_3 k_4 \Pi_F \mu_M}{\lambda_{FM}^{**} k_3 k_4 \Pi_F - C_{M_1} \beta_M \sigma_M \Pi_M \mu_F}.$$

Substituting this result into (3.7), and simplifying, leads to the following linear equation

$$\Pi_F \mu_M (C_F \beta_F \sigma_F k_4 k_3 \Pi_F + k_4 k_3 k_2 k_1 \Pi_M) \lambda_{FM}^{**} + \Pi_F \mu_M k_4 k_3 k_2 k_1 \Pi_M \mu_F (1 - \tilde{\mathcal{R}}_S^2) = 0, \quad (3.9)$$

$$\lambda_{FM}^{**} = \frac{\Pi_F \mu_M k_4 k_3 k_2 k_1 \Pi_M \mu_F (\tilde{\mathcal{R}}_S^2 - 1)}{\Pi_F \mu_M (C_F \beta_F \sigma_F k_4 k_3 \Pi_F + k_4 k_3 k_2 k_1 \Pi_M)}.$$

The quantity $\tilde{\mathcal{R}}_S^2 = \frac{C_F \beta_F \sigma_F C_{M_1} \beta_M \sigma_M}{k_1 k_2 k_3 k_4}$, is the reproduction number when the community consists purely of heterosexual couples. Thus,

$$\lambda_{FM}^{**} > 0, \text{ provided } \tilde{\mathcal{R}}_S^2 > 1.$$

Hence, the polynomial (3.9) has only one root. This result is summarized in the following Theorem 4 below.

Theorem 4. *The Zika transmission model (3.5) with purely heterosexual couples has a unique endemic equilibrium if $\tilde{\mathcal{R}}_S > 1$.*

Notice, however, that if Zika sexual transmission only occurs from males to females, and not in the other direction, then $\beta_F = 0$ and $\tilde{\mathcal{R}}_S^2 = 0$. Thus, as expected, sexual transmission among purely heterosexual couples must be bidirectional in order to support continued Zika transmission in the absence of other modes of spread.

Let $\tilde{\mathcal{E}}_{S22} = (S_F^{**}, 0, 0, 0, S_M^{**}, E_M^{**}, I_M^{**}, R_M^{**})$ be an arbitrary equilibrium of the model with only sexual transmission (3.5) and only homosexual male couples present. In this case

$$\begin{aligned} S_F^{**} &= \frac{\Pi_F}{\mu_F}, & S_M^{**} &= \frac{\Pi_M}{\lambda_M^{**} + \mu_M}, \\ E_M^{**} &= \frac{\Pi_M \lambda_M^{**}}{k_3(\lambda_M^{**} + \mu_M)}, & I_M^{**} &= \frac{\sigma_M \Pi_M \lambda_M^{**}}{k_3 k_4(\lambda_M^{**} + \mu_M)}, \\ R_M^{**} &= \frac{\gamma_M \sigma_M \Pi_M \lambda_M}{k_3 k_4 \mu_M(\lambda_M^{**} + \mu_M)}, & \lambda_M^{**} &= \frac{C_{M2} \beta_M I_M^{**}}{N_M^{**}}. \end{aligned}$$

Furthermore, the quantity λ_M^{**} is the force of infection at the endemic equilibrium steady states for homosexual male couples. Using the approach in the proof of uniqueness of the equilibrium $\tilde{\mathcal{E}}_{S21}$, we have

$$k_3 k_4 \lambda_M^{**} + k_3 k_4 \mu_M (1 - \mathcal{R}_{MS}) = 0,$$

where $\mathcal{R}_{MS} = \frac{C_{M2} \beta_M \sigma_M}{k_3 k_4}$, is the reproduction number for homosexual male only couples. Thus,

$$\lambda_M^{**} > 0, \quad \text{provided} \quad \mathcal{R}_{MS} > 1.$$

Hence, $\tilde{\mathcal{E}}_{S22}$ is a unique equilibrium for model (3.5) when only homosexual males transmit the virus.

Theorem 5. *The Zika transmission model (3.5) with only homosexual male couples has a unique endemic equilibrium if $\mathcal{R}_{MS} > 1$.*

Notice that, in contrast to our scenario with purely heterosexual transmission, the reproduction number for our scenario with purely homosexual transmission only depends on a single transmission probability, reflecting the higher sexual symmetry of male-to-male pairings. Notably, however, this assumes that homosexual men are predominantly versatile (i.e., engage in both insertive and receptive anal intercourse), which appears to be the case for a large portion of the population, though not the population as a whole [37].

Numerical simulations of the Zika virus transmission model (3.5), depicted in Figure 5, show convergence to an endemic equilibrium when $\mathcal{R}_S > 1$ (suggesting that the unique EEP of the Zika transmission model (3.5) is asymptotically stable when it exists).

Figure 5: Simulation of the sexual transmission route only Zika model (3.5) as a function of time when $\tilde{R}_S > 1$. (a) Total number of infectious females (b) Total number of infectious males. Parameter values used are as given in Table 3

3.2.4 Local Stability of the Endemic Equilibrium

As above, we will study the stability of the endemic equilibrium for the sexual transmission route only model (3.5) under scenarios where only heterosexuals couples are present and under scenarios where only homosexual couples are present.

Let $\tilde{\mathcal{E}}_{S_{21}} = (S_F^{**}, E_F^{**}, I_F^{**}, R_F^{**}, S_M^{**}, E_M^{**}, I_M^{**}, R_M^{**})$ be the unique equilibrium of the Zika model (3.5) with only heterosexual couples.

Lemma 7. *The unique endemic equilibrium ($\mathcal{E}_{S_{21}}$) of the sexual transmission route only Zika model (3.5) with only heterosexual couples is locally asymptotically stable.*

The proof of Lemma 7 is given in Appendix G.

Let $\tilde{\mathcal{E}}_{S_{22}} = (S_F^{**}, 0, 0, 0, S_M^{**}, E_M^{**}, I_M^{**}, R_M^{**})$ be the unique equilibrium of the sexual transmission route only Zika model (3.5) with only homosexual male couples.

Lemma 8. *The unique endemic equilibrium ($\tilde{\mathcal{E}}_{S_{22}}$) of the sexual transmission route Zika model (3.5) with only homosexual male couples is locally asymptotically stable.*

The proof of Lemma 8 is given in Appendix H.

3.3 Analysis of the Full Model

3.3.1 Local stability of disease-free equilibrium

The disease-free equilibrium of the full Zika model (2.5) is given as

$$\begin{aligned} \mathcal{E}_{F_1} &= (S_F^*, E_F^*, I_F^*, R_F^*, S_M^*, E_M^*, I_M^*, R_B^*, S_V^*, E_V^*, I_V^*) \\ &= \left(\frac{\Pi_F}{\mu_F}, 0, 0, 0, \frac{\Pi_M}{\mu_M}, 0, 0, 0, \frac{\Pi_V}{\mu_V}, 0, 0 \right). \end{aligned}$$

The local asymptotic stability of $\mathcal{E}_{F_1}$ can be established using the next generation matrix method on the system (2.5). Taking the infected compartments $(E_F^*, I_F^*, E_M^*, I_M^*, E_V^*, I_V^*)$ at the DFE and using the notation in [63], the Jacobian matrices F_F and V_F for the new infection terms and the remaining transfer terms are respectively given by,

$$F_F = \begin{bmatrix} 0 & 0 & 0 & C_{M_1}\beta_M & 0 & \frac{b_V\beta_H S_F^*}{N_H^*} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & C_F\beta_F & 0 & C_{M_2}\beta_M & 0 & \frac{b_V\beta_H S_M^*}{N_H^*} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{b_V\beta_V S_V^*}{N_H^*} & 0 & \frac{b_V\beta_V S_V^*}{N_H^*} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}, \quad V_F = \begin{bmatrix} k_1 & 0 & 0 & 0 & 0 & 0 \\ -\sigma_F & k_2 & 0 & 0 & 0 & 0 \\ 0 & 0 & k_3 & 0 & 0 & 0 \\ 0 & 0 & -\sigma_M & k_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & k_5 & 0 \\ 0 & 0 & 0 & 0 & -\sigma_V & \mu_V \end{bmatrix}.$$

The reproduction number is determined by the spectral radius of the following matrix

$$\mathcal{R}_F = \rho(F_F V_F^{-1}).$$

Lemma 9. *The disease-free equilibrium (DFE) of the Zika virus model (2.5) is locally asymptotically stable (LAS) if $\mathcal{R}_F < 1$ and unstable if $\mathcal{R}_F > 1$.*

3.4 Backward Bifurcation Analysis: Special Case

Zika associated deaths in infected individuals are rare [15, 23] since symptoms of the disease are generally mild. Despite this, a number of deaths have been associated with infection complications in Puerto Rico [20], Venezuela [35], Colombia [55], and more recently in the US [9]. Specifically, in Colombia, fatally occurred from 48 hours to 12 days after the onset of symptoms; all the patients were presented with anaemia before the occurrence of fatality and they all died within 24 hours of admission into the hospital [55]. The patient in US developed septic shock with multiple organ failure; the patient had viremic level that was approximately 100,000 times higher than the average level reported in persons infected with Zika virus [9]. It should be noted that the reported deaths were not in children with microcephaly neither were these in adults who were known to have Guillan-Barre syndrome [9, 20, 35, 55].

Thus, to explore the effect that disease induced death might have on model predictions, we introduced into the symptomatic human compartments disease-induced mortality parameters (δ_F, δ_M) . Thus, the symptomatic human compartments of the Zika model (2.5) can be written as follows:

$$\begin{aligned} \frac{dI_F}{dt} &= \sigma_F E_F - (\gamma_F + \mu_F + \delta_F) I_F \\ \frac{dI_M}{dt} &= \sigma_M E_M - (\gamma_M + \mu_M + \delta_M) I_M \end{aligned} \quad (3.10)$$

It can be shown that the reproduction number for the Zika model with disease induced mortality is given by

$$\tilde{\mathcal{R}}_F = \mathcal{R}_F|_{\delta_F, \delta_M \neq 0} = \rho(F_F V_F^{-1}),$$

where, $k_1 = \sigma_F + \mu_F$, $k_2 = \gamma_F + \mu_F + \delta_F$, $k_3 = \sigma_M + \mu_M$, $k_4 = \gamma_M + \mu_M + \delta_M$, $k_5 = \sigma_V + \mu_V$.

Figure 6: Backward bifurcation plot of the Zika model (2.5) with the symptomatic human compartments given in (3.10). (a). Symptomatic females; (b). Symptomatic males. (c). Infected mosquitoes. Parameter values used are as given in Table 3.

Models of disease transmission typically undergo a simple transcritical bifurcation (exchange of stability from the DFE to an endemic equilibrium) at $\mathcal{R}_0 = 1$. However, backward bifurcation, where a stable DFE co-exists with a stable endemic equilibrium when the reproduction number, $\tilde{\mathcal{R}}_F$, is less than unity [1, 2, 7, 11, 26], is also possible. The epidemiological implication of backward bifurcation is that the effective control (or elimination) of Zika virus in the system is dependent

on the initial sizes of the sub-populations (i.e., the number of infected, susceptible and recovered individuals). We explored the possibility of a backward bifurcation in the Zika model (2.5) with disease induced mortality using the centre manifold theory [11], as described in [13] (Theorem 4.1).

Theorem 6. *The Zika model (2.5) with disease induced mortality (3.10) undergoes backward bifurcation at $\tilde{\mathcal{R}}_F = 1$ whenever the inequality (I-2), given in Appendix I, holds.*

The proof of Theorem 6 is given in Appendix I. The backward bifurcation property of the Zika model (2.5) with the symptomatic human compartments given in (3.10) is illustrated by simulating the model using a set of parameter values given in Table 3 (see Figure 6). The backward bifurcation phenomenon of the Zika model (2.5) with disease induced mortality (3.10) makes the effective control of Zika in the population difficult, since disease control when $\tilde{\mathcal{R}}_F < 1$ is dependent on the initial sizes of the sub-populations of the Zika model (2.5) with the symptomatic human compartments stated in (3.10).

4 Numerical Simulations

In this section, we explore the impact of sexual contact on disease burden in the community. First, we discuss the derivation of the parameters related to sexual contacts. We suppose $C_{M_1} = C_{M_2} = C_F = 2$ per year, which assumes approximately two sexual partners per year, meaning that individuals are mostly monogamous and prefer only one sexual partner at a time.

Next, we assume that the Zika virus transmission probability *per* coital acts during partnership with an infected individual is $\beta_F = \beta_M = 1 - (1 - \alpha)^n$. Here α is the probability of transmission *per* coital act with an infected partner and n is the average number of coital acts performed during a partnership. For HIV, α ranges between 0.001 and 0.1 [28]. Thus, assuming that people have sex on average 60 times per year (or approximately 1-4 times per week) [33], hence, $\beta_F = \beta_M = 0.06$.

Figure 7: Simulation of the Zika model (2.5) as a function of time with different sexual contact rates. Parameter values used are as given in Table 3. (a). Setting the sexual contact rate $C_F = C_{M_1} = C_{M_2} = 2$. (b). Setting the sexual contact rate $C_F = 0$, $C_{M_1} = C_{M_2} = 2$.

Figure 7 depicts the simulation of the Zika model (2.5) with different sexual contact rates over

the entire simulation period. In Figure 7(a), we have made the assumption that both females and males along with mosquitoes can transmit the virus, and the figure shows that, due to homosexual relations within a subset of the male population, the number of infected males is higher than the number of infected females, resulting in a difference of 0.2% between the two sexes (see Table 4). On the other hand when we assume that men cannot contract the virus from infected females (which is in line with all current observations of ZIKV sexual transmission), we observe in 7(b) that the number infected in both populations are the same (see Table 4).

Figure 8: Simulation of the Zika model (2.5) as a function of time with different sexual contact rates. Parameter values used are as given in Table 3.(a). Setting the sexual contact rate $C_F = 0$, $C_{M_1} = 50$, $C_{M_2} = 2$. (b). Setting the sexual contact rate $C_F = 0$, $C_{M_1} = 2$, $C_{M_2} = 80$.

Parameter	Values	References
Π_H	$\frac{1}{15 \times 365}$	[65]
C_F, C_{M_1}, C_{M_2}	$2/365$	Assumed
β_H	0.33	[24, 25, 38, 52, 62]
σ_F	$\frac{1}{7.5}$	[6]
γ_F	$\frac{1}{8.5}$	[6]
μ_F	$\frac{1}{70 \times 365}$	[38]
β_F, β_M	$1 - (1 - 0.001)^{60}$	[28]
σ_M	$\frac{1}{7.5}$	[6]
γ_M	$\frac{1}{8.5}$	[6]
μ_M	$\frac{1}{18.60 \times 365}$	[66]
δ_M	$\frac{38}{3174 \times 365}$	[65]
Π_V	500	[6]
β_V	0.33	[38, 46, 50]
b_V	0.5	[53, 60, 38]
σ_V	$\frac{1}{3.5}$	[22, 25, 44, 56]
μ_V	$\frac{1}{21}$	[57, 60, 61]

Table 3: Parameter values of model (2.5)

Next, we assume that men cannot contract the virus from infected females, additionally, we also

assume males in the population have multiple female sexual partners while the homosexual males maintain a monogamous relationship, we observed in Figure 8(a) that this risky behavior leads to more infected females than males with 2.37% difference between females and males, see also Table 4. When the men maintain a monogamous relationship with females in the population but have multiple sexual partners as homosexual males, we observed that this risky behavior leads to more infected males compared to females, this resulted in about 3.04% difference between the sexes (see Table 4).

Sexual contact rates	Females	Males
$C_F = C_{M_1} = C_{M_2} = 2$	4.894213×10^6	4.912264×10^6
$C_F = 0, C_{M_1} = C_{M_2} = 2$	4.894010×10^6	4.894010×10^6
$C_F = 0, C_{M_1} = 50, C_{M_2} = 2$	5.134227×10^6	4.895659×10^6
$C_F = 0, C_{M_1} = 2, C_{M_2} = 80$	4.897354×10^6	5.204081×10^6

Table 4: Simulation results of the Zika model (2.5) for the cumulative number of infected cases over the simulation period from 0 to 500 days with different sexual contact rates. Parameter values used are as given in Table 3.

We further explore the scenario with no male-to-female transmission and compare this with the transmission in the absence of mosquitoes. We observed in Table 5 more infection in both female and male populations when there are no male-to-female transmission and compare to the transmission in the absence of mosquitoes. This result points to the importance of the sexual route transmission.

	Females	Males
Sexual-only transmission	4.874287×10^6	4.874287×10^6
Mosquitoes-only transmission	8.253976×10^4	1.137854×10^5

Table 5: Simulation results of the Zika model (2.5) for the total number of infected cases with no sexual contact rate and in the absences of mosquitoes. Parameter values used are as given in Table 3.

5 Discussion and Conclusion

In this paper, we develop a new deterministic model to study the transmission dynamics of Zika virus. Our model incorporates both vector-borne and sexual transmission routes. Additionally, it considers both heterosexual and homosexual transmission. Sexual transmission of Zika is interesting for several reasons. First, Zika is the only known arbovirus to exhibit a sexual mode of spread in the human population. Second, unlike most purely venereal diseases, Zika virus appears to exhibit unidirectional transmission. In particular, Zika appears to transmit from males to females, and from males to males, but not from females to males. Although data is still limited, if the trend continues to hold, then of Zika virus cannot persist in a heterosexual population as a purely venereal disease.

By contrast to a heterosexual population, however, Zika sexual transmission may be self-sustaining in a homosexual population. This is because versatility, which is relatively common [28], allows spread to all partners. Consequently, in the absence of mosquitoes and, assuming no bisexuality, Zika would be restricted to homosexual populations. Bisexual males, however, can enable spillover from the homosexual population to the heterosexual population, although this will primarily be to

females. Likewise, vector transmission can also allow disease spread between the sub-populations, enabling long-term disease incidence, including among heterosexual men. Interestingly, however, even within the context of vector-borne transmission the biased directionality of spread between females and males during sexual contact, creates a situation where different sexual modes can result in higher risks to different sub-populations. If, for example, heterosexual couples are more promiscuous than homosexual couples, then disease incidence rises in the female population, creating a large female:male ratio of Zika infections. By contrast, if homosexual couples are more promiscuous than heterosexual couples, then disease incidence rises in the male population, reducing this imbalance.

Another interesting aspect of our model is the finding of a backward bifurcation when there is disease induced mortality. This is particularly striking because it suggests that, once disease spread has taken hold, it can be very difficult to eradicate. In particular, when backward bifurcation occurs, identical conditions (e.g. same levels of mosquito control, same human sexual behavior) can lead to either disease extinction or endemicity depending on initial conditions. Consequently, once the system has gotten out of control, more aggressive management than would otherwise be necessary, may be required to reduce disease spread and return the system to a state below the bifurcation point. Another concerning aspect of backward bifurcation is that disease risk and/or incidence could increase suddenly with even small changes in management strategies. In particular, if the system lies beyond this bifurcation point, then even a slight decrease in mosquito control efforts, or a slight increase in promiscuity could move the system into a regime where only the endemic state is stable, and disease incidence levels are already quite high.

Although our model has explored a range of aspects associated with the interplay between vector and sexual transmission of ZIKV, including the role of heterosexual versus homosexual spread, and the implications of unidirectional transmission during heterosexual encounters, a number of additional biological aspects remain to be explored. As an example, current evidence suggests that Zika can remain in semen for several months, even though it is cleared from the blood within weeks. This suggests that the different modes of spread may have very different timescales. In particular, the slow timescale associated with clearance from sexual organs could increase the importance of this mode of spread with respect to its role in overall disease dynamics. Likewise, although we have considered both heterosexual and homosexual partnerships, incorporation of additional social structure could be informative. Indeed, in other sexually transmitted diseases, it is known that preferential mixing can dramatically influence disease dynamics. These, and other extensions, though they would make our model far less tractable from a mathematical perspective, could be important to consider from a biological standpoint.

In this paper, we formulated and analyzed a system of ordinary differential equations for transmission dynamics of Zika virus. Some of our theoretical and epidemiological findings are summarized below:

- (i). The model disease free equilibrium is locally and globally asymptotically stable when the associated reproduction ($\mathcal{R}_F$) is less than unity and unstable otherwise;
- (ii). The model exhibits in the presence of disease induced mortality the phenomenon of backward bifurcation, where the stable disease-free co-exists with a stable endemic equilibrium, when the associated reproduction number is less than unity;
- (iii). The model has a unique endemic equilibria for the system with heterosexual only and

- homosexual male only couples; these equilibria are locally asymptotically stable when their respective reproduction numbers are greater than unity;
- (iv). Risky behavior among the male population increases the number of infected individuals in that population;
- (v). The sexual transmission route contributes significantly to the disease burden in the community.

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A Appendix A: Proof of Lemma 1

Proof. Let $t_1 = \sup\{t > 0 : F(t) > 0\}$. Thus, $t_1 > 0$. Then it follows from the first equation of the Zika model (2.5) that

$$\frac{dS_F}{dt} = \frac{\Pi_H}{2} - [\lambda_H(I_V, N_H)S_F(t) + \lambda_{FM}(I_M, N_F)S_F(t) - \mu_F S_F(t)]$$

can be re-written as