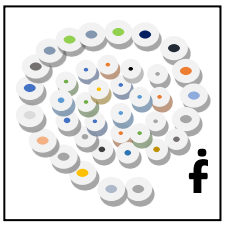

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Population dynamics of a mathematical model for Monkeypox

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Abstract

Monkeypox, a zoonotic disease, is gradually posing a public health challenge to both developed and developing countries of the world. To this end, there is need to come up with prevention and control strategies to help curb the spread of the disease in the population. In this study, a new deterministic mathematical model for monkeypox is developed to critically look at the impact of public awareness campaign, treatment and vaccination on the transmission dynamics, prevention and control of monkeypox. Qualitative analysis of the model shows that it undergoes the phenomenon of backward bifurcation. However, this phenomenon may not occur as a results of the non-availability of monkeypox vaccine in the community. Furthermore, the model is shown to have three endemic equilibria, namely: the human-to-human, animal-to-human and animal-to-animal transmission modes, respectively, when the associated reproduction number is greater than unity. For the special case, where there is only human-to-human transmission of monkeypox (i.e. $\upsilon = \omega = \phi = \beta_a = 0$), the disease-free equilibrium of the model is shown to be globally asymptotically stable (GAS) whenever the associated reproduction number is less than unity. For the same scenario as above, the unique endemic equilibrium of the model is globally asymptotically stable whenever the reproduction number is greater than unity. Both analytical and numerical results show a relationship between the rate of vaccination of the susceptible individuals, the progression rate from the exposed stage of infection to the asymptomatic and symptomatic stages of infection, treatment rate of the symptomatic individuals, public awareness campaign and the reproduction number. Results from the sensitivity analysis of the model, using the human reproduction number number, R_{0h}, show that, the most sensitive parameters are the monkeypox transmission rate from human-to-human (β_h), efficacy of public awareness campaign (ψ), vaccination rate for the susceptible individuals (υ), waning rate of the monkeypox vaccine (ω) and the treatment rate for the symptomatic individuals (τ). The epidemiological implication of these results is that, public awareness campaign in the population should be strengthened by the government and other critical stakeholders in order to educate the populace on the need to be vaccinated against monkeypox infection, get to a health facility immediately when blisters show up on their body and the need to develop vaccines that will not wane within a short period of time. Numerical simulations results show that, increasing the rates of vaccination of the susceptible individuals, efficacy of public awareness campaign and the treatment of symptomatic individuals could help in reducing monkeypox burden in the population.

Keywords:Monkeypox; reproduction number; public awareness campaign; vaccination; bifurcation analysis

1 Introduction

Monkeypox, a zoonotic disease caused by a virus in the orthopoxvirus group which includes smallpox [1, 28], is gradually posing a public health challenge to both developed and developing countries of the

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world. Globally, the disease accounts for over 46,724 confirmed cases and 13 deaths recorded with the highest number of confirmed cases recorded in the United States of America (16,925), followed by Spain (6,284) and then Brazil (3,984)] as at 25th August, 2022, according to [6]. In Africa, monkeypox was first identified in humans in 1970 in the Democratic Republic of the Congo in a 9 months old boy in a region where smallpox had just been eradicated in 1968. As at 8th August, 2022, about 59 confirmed cases and 72 deaths have been recorded in WHO African regions including Cameroon, Central African Republic, Republic of Congo, Democratic Republic of the Congo, Liberia, Nigeria, Sierra Leone and Ghana [29]. In Nigeria, 157 cases have been confirmed and 4 deaths recorded as at 8th August, 2022 [25] . Monkeypox virus (MPV) is transmitted to humans through close contact with an infected animal or with materials contaminated with the virus [7]. Human-to-human transmission of the disease spreads through close contact with body fluids, lesions, respiratory droplets and contaminated materials such as beddings [28]. MPV infection passes through a number of stages. When an individual gets exposed and infected, it can take 5 to 21 days for the first symptoms to appear. The early symptoms of the disease include: fever, headache, muscle aches, back ache, fatigue, chills and swollen lymph nodes as reported in [16]]. After infection, individuals can test positive (Asymptomatic) without symptoms and later develop symptoms (Symptomatic). Thereafter, individuals who have shown blisters are isolated for treatment [1]. These blisters, which usually appears after 1 to 3 days of the early infection, affects the face, palms of the hand, soles of the feet, mouth and genitalia [7, 16, 28]. Persons who have tested positive without symptoms can recover naturally due to strong immunity and for individuals with compromised immune system can progress to the symptomatic stage of infection [1]. Upon completion of treatment at the isolation centre, individuals can recover with permanent immunity and can equally die due to the disease [3]. Monkeypox infection can be controlled and prevented by using the following vaccines to curtail the spread of the disease: vaccinia vaccine (smallpox vaccine) which is 85% effective in preventing an individual from contracting the disease, vaccinia immune globulin (VIG) and antiviral medications (in animals)[16, 29]. At the moment, since there are no known vaccines designed to prevent susceptible individuals from contracting monkeypox infection, antiviral vaccines and drugs developed to protect against smallpox are mostly deployed to prevent and treat monkeypox virus infections [8].

Mathematical models of infectious diseases have over the years provided useful insights into the transmission dynamics, prevention and control of infectious diseases, see for example,[12, 13, 17]. However, for monkeypox, few mathematical models have been developed and used to understand the transmission dynamics, control and prevention of the disease, see for example,[3, 10, 20, 21, 23, 26]. [3], formulated and analyzed a mathematical model on the transmission dynamics of pox-like infections using the basic S-I-R model for both the human and animal population. They assumed that both the human and animal population recover from monkeypox infection after treatment with permanent immunity. Another mathematical model that incorporates treatment and vaccination strategies to curtail the spread of the disease was developed and analyzed by [26]. [10] formulated and analyzed a mathematical model for monkeypox virus transmission dynamics that includes imperfect vaccine compartment for the human sub-population. Another study by [23] developed a mathematical model of monkeypox virus transmission dynamics incorporating the quarantine class and public enlightenment campaign parameters into the human population as a means of curtailing the spread of the disease. Peter et al. [20], designed and analyzed a mathematical model of monkeypox transmission dynamics using the susceptible-exposed-infected-isolated-recovered model for the human sub-population while the susceptible-exposed-infected was used for the rodent sub-population. Recently, [21] fitted a model using the non-linear least square method on cumulative reported cases of monkeypox virus from January to December, 2019. Further, the fractional order mathematical model of monkeypox transmission dynamics was formulated and analyzed with the assumption that the recovered humans confer immunity after treatment. This study presents a new deterministic mathematical model to study the transmission dynamics of monkeypox in a population with public awareness campaign, vaccination and treatment as control strategies. The model is based on the following assumptions:

i. The exposed individuals are broken down into the asymptomatic and symptomatic individuals. This is in line with the information obtained from [6] and [1].

ii. Asymptomatic individuals can recover naturally and equally develop symptoms to progress to the symptomatic class [1].

iii. Individuals recover after treatment with permanent immunity [3, 21].

In all the aforementioned mathematical models of monkeypox, non of them considered the assumptions (i) and (ii) as biologically supported in [1, 9]. In the present study, the exposed class have been split into the asymptomatic and symptomatic classes. Also, public awareness campaign, vaccination and treatment are included as intervention strategies in our model to curtail the spread of the disease in the population. The rest of the paper is organized as follows: The new monkeypox model is formulated in Section 2. The mathematical analysis is carried out in Section 3. Sensitivity analysis is conducted in Sections 4. Results of the numerical simulations are presented in Section 5. The paper is concluded in Section 6.

2 Model Formulation

The total population at time t, denoted by $N_H(t)$, is divided into the human $(N_H(t))$ and animal $(N_A(t))$ populations. The total human population is further sub-divided into the seven mutually-exclusive compartments of the susceptible $(S_H(t))$, vaccinated $(V_H(t))$, exposed $(E_H(t))$, asymptomatic $(A_H(t))$, symptomatic $(I_H(t))$, isolated $(T_H(t))$ and treated individuals who recover from monkeypox infection $(R_H(t))$. Similarly, the total animal population is sub-divided into the susceptible $(S_A(t))$, exposed $(E_A(t))$, infected $(I_A(t))$ and recovered $(R_A(t))$ animal sub-population. Thus,

$$\begin{aligned} N(t) &= N_H(t) + N_A(t), \\ N_H(t) &= S_H(t) + V_H(t) + E_H(t) + A_H(t) + I_H(t) + T_H(t) + R_H(t), \\ N_A(t) &= S_A(t) + E_A(t) + I_A(t) + R_A(t) \end{aligned} \tag{1}$$

The susceptible population (for both human and animals) are increased by the recruitment of new individuals (assumed susceptible) into the population at a rate $\Lambda_h(\Lambda_a)$ for human (animal). Susceptible individuals acquire monkeypox infection, following effective contact with infected animals and humans (i.e. those in the A_H, I_H and I_A classes, at a rate λ_H, given by

$$\lambda_H = (1 - \varepsilon\psi)\Big(\frac{\beta_h(I_H + \eta A_H)}{N_H} + \frac{\beta_a I_A}{N_A}\Big), \tag{2}$$

Similarly, the susceptible animals acquire the infection following effective contact with an infected animal (i.e., those in the I_A class) at a rate

$$\lambda_A = \frac{\beta_r I_A}{N_A}, \tag{3}$$

where the parameters ε and ψ ($0 < \varepsilon < 1$ and $0 < \psi < 1$) represent public awareness campaign and efficacy to public awareness campaign, respectively. The term $\varepsilon\psi$ represent the effectiveness of the public awareness campaign. The terms β_h, β_a and β_r are the probabilities of transmitting monkeypox virus from human-to-human, animal-to-animal and animal-to-animal, respectively. Furthermore, η is the modification parameter associated with the reduced infectiousness of individuals in the asymptomatic class (A_H). Individuals in E_H class progresses to the infected classes (A_H) and (I_H) at rate θ while ρ is the proportion of individuals that progressed to class (A_H). Similarly, the animals in E_A progresses to the infected class I_A at a rate φ. Individuals in the asymptomatic class either recover naturally and move to the recovered class R_H at a rate σ or progress to the the symptomatic class at a rate ϕ. Also, individuals in I_H compartment who show symptoms of monkeypox virus are moved to the isolation centre (T_H) for treatment at a rate τ. The parameter γ_h accounts for the recovery rate of individuals in T_H after treatment, while γ_a is the recovery rate of the animals in I_A class. Furthermore, natural death rate $\mu_h(\mu_a)$ occurs in all the epidemiological classes of human (animal) population while individuals in

I_H and T_H classes suffer an additional monkeypox induced death at rate δ_h.The animal population in I_A equally die due to monkeypox infection at a rate δ_a. Combining all these definitions and assumptions, it follows that the new monkeypox model is given by the system of differential equations in (4). The flow diagram of the model is shown in Figure 1, and the variables of the model are tabulated in Table 1. The variables and parameters of the model are interpreted in Table 1.

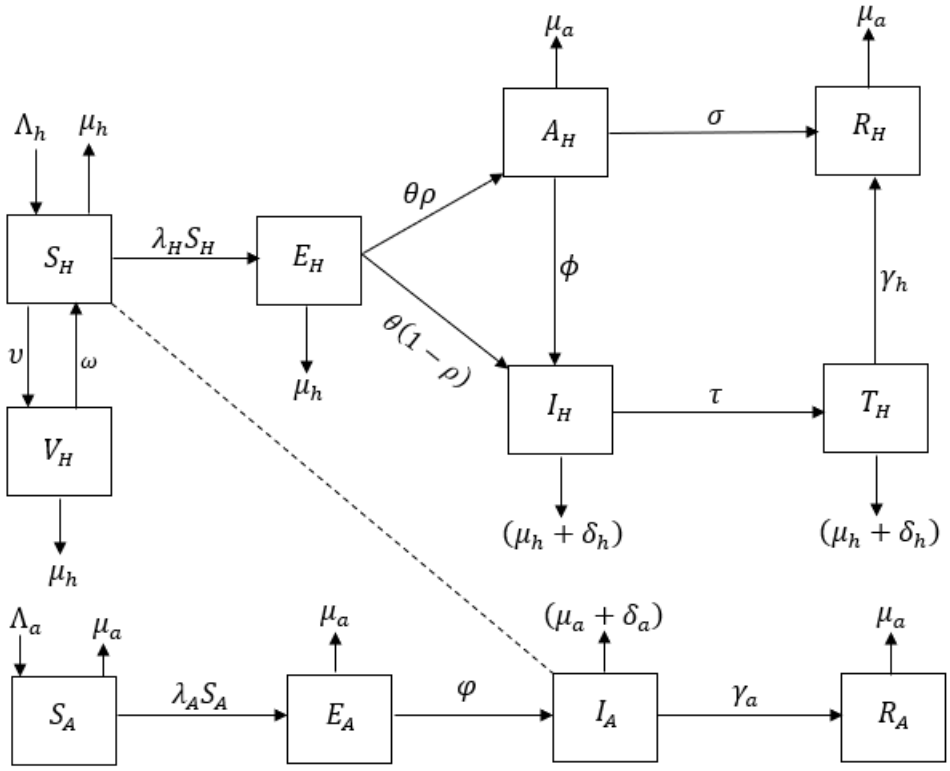

Figure 1: Flow diagram for model (4)

Table 1: Description of parameters in the monkeypox model (4).

Variables/parameters	Interpretation
S_H	Susceptible human population
V_H	Vaccinated human population
E_H	Exposed human population
A_H	Asymptomatic human population
I_H	Symptomatic human population
T_H	Isolated human population
R_H	Recovered human population
S_A	Susceptible animal population
E_A	Exposed animal population
I_A	Infected animal population
R_A	Recovered animal population
Λ_h	Recruitment rate into the susceptible human compartment
υ	Effective vaccination rate of the susceptible humans
μ_h	Natural death rate for the humans
δ_h	Death rate due to monkeypox virus for the humans
θ	Rate of progression from E_H to A_H
ρ	Proportion of the exposed persons moving to class A_H
ϕ	Progression from A_H to I_H due to compromised immunity
σ	Natural recovery rate of the asymptomatic individuals
τ	Treatment rate for the symptomatic individuals
ω	Waning rate of the monkeypox vaccine
η	Modification parameter associated with the reduced rate of MPV transmission for the asymptomatic individuals
ε	Rate of public awareness campaign
ψ	Efficacy rate of public awareness campaign
$\varepsilon\psi$	Effectiveness of public awareness campaign
β_h	Probability of transmitting monkeypox from human-to-human
β_a	Probability of transmitting monkeypox from animal-to-human
β_r	Probability of transmitting monkeypox from animal-to-animal
Λ_a	Recruitment rate into the susceptible animal compartment
μ_a	Natural death rate for the animal population
φ	Progression rate from E_A to I_A
δ_a	Disease induced death rate for the animal population

$$
\begin{aligned}
\frac{dS_H(t)}{dt} &= \Lambda_h - \lambda_H S_H + \omega V_H - (\upsilon + \mu_h) S_H, \\
\frac{dV_H(t)}{dt} &= \upsilon S_H - (\omega + \mu_h) V_H, \\
\frac{dE_H(t)}{dt} &= \lambda_H S_H - (\theta\rho + \theta(1-\rho) + \mu_h) E_H, \\
\frac{dA_H(t)}{dt} &= \theta\rho E_H - (\sigma + \phi + \mu_h) A_H, \\
\frac{dI_H(t)}{dt} &= \phi A_H + \theta(1-\rho) E_H - (\tau + \mu_h + \delta_h) I_H, \\
\frac{dT_H(t)}{dt} &= \tau I_H - (\gamma_h + \mu_h + \delta_h) T_H, \\
\frac{dR_H(t)}{dt} &= \sigma A_H + \gamma_h T_H - \mu_h R_H, \\
\frac{dS_A(t)}{dt} &= \Lambda_a - \lambda_A S_A - \mu_a S_A, \\
\frac{dE_A(t)}{dt} &= \lambda_A S_A - (\varphi + \mu_a) E_A, \\
\frac{dI_A(t)}{dt} &= \varphi E_A - (\gamma_a + \mu_a + \delta_a) I_A, \\
\frac{dR_A(t)}{dt} &= \gamma_a I_A - \mu_a R_A.
\end{aligned}
\tag{4}
$$

where λ_H and λ_A are as given in equations (2) and (3), respectively. The results below holds for the model (4)

Theorem 2.1. *All solutions of the model (4) with positive initial data remain positive for all time $t > 0$. Furthermore, the model is a dynamical system on the region $\Gamma = \Gamma_1 \cup \Gamma_2 \subset \mathbb{R}^7_+ \times \mathbb{R}^4_+$ with,*

$$
\begin{aligned}
\Gamma_1 &= \{(S_H, V_H, E_H, A_H, I_H, T_H, R_H) : S_H + V_H + E_H + A_H + I_H + T_H + R_H = N_H \leq \frac{\Lambda_h}{\mu_h}\}, \\
\Gamma_2 &= \{(S_A, E_A, I_A, R_A) : S_A + E_A + I_A + R_A = N_A \leq \frac{\Lambda_a}{\mu_a}\},
\end{aligned}
\tag{5}
$$

and the region Γ is attracting with respect to the model (4) with initial conditions in $\mathbb{R}^{11}_+$. *Proof.* Following similar approach as in [12], it is easy to see that the equations for human (susceptible and vaccinated individuals) and animal (susceptible animals) in model (4) leads to the following first-order inequality equations:
$\frac{dS_H}{dt} + (\lambda_H + \upsilon + \mu_h) S_H > 0$, $\frac{dV_H}{dt} + (\omega + \mu_h) V_H > 0$ and $\frac{dS_A}{dt} + (\lambda_A + \mu_a) S_A > 0$.

Multiplying these inequalities by the integrating factor

$$
\alpha_{S_H}(t) = exp^{\int [\lambda_H(\tau) + (\upsilon + \mu_h)] d\tau}, \alpha_{V_H}(t) = exp^{\int [(\omega + \mu_h)] d\tau}, \alpha_{S_A}(t) = exp^{\int [\lambda_A(\tau) + \mu_a] d\tau}, \tag{6}
$$

and observing that

$$
\begin{aligned}
\alpha_{S_H}(t)\big[\frac{dS_H}{dt} + (\lambda_H(\tau) + (\upsilon + \mu_h)) S_H\big] &= \frac{dS_H \alpha_{S_H}}{dt}, \\
\alpha_{V_H}(t)\big[\frac{dV_H}{dt} + (\omega + \mu_h) V_H\big] &= \frac{dV_H \alpha_{V_H}}{dt}, \\
\alpha_{S_A}(t)\big[\frac{dS_A}{dt} + (\lambda_A + \mu_a) S_A\big] &= \frac{dS_A \alpha_{S_A}}{dt}
\end{aligned}
$$

,

then integrating with respect to time from 0 to t gives $S_H(t) \geq 0$, $V_H(t) \geq 0$ and $S_A(t) \geq 0$ at all times, respectively. However, this direct approach does not apply to the remaining equations. In any case, having the nonnegativity of S_H, V_H and S_A in mind, it can be shown that the remaining eight equations of the model (4) form a monotone system. Consequently, all its solutions corresponding to positive initial data remain positive at all times $t \geq 0$. By adding the first seven and the last four equations of model (4), the following conservation law is obtained

$$\begin{aligned} \frac{dN_H}{dt} &= \Lambda_h - \mu_h N_H - \delta_h(I_H + T_H), \\ \frac{dN_A}{dt} &= \Lambda_a - \mu_a N_A - \delta_a I_A. \end{aligned} \tag{7}$$

Thus, a standard comparison theorem can be used to show that the general a priori estimates below hold

$$\begin{aligned} 0 \leq N_H(t) &\leq N_H(0)exp^{-\mu_h t} + \frac{\Lambda_h}{\mu_h}\big(1 - exp^{-\mu_h t}\big), \\ 0 \leq N_A(t) &\leq N_A(0)exp^{-\mu_a t} + \frac{\Lambda_a}{\mu_a}\big(1 - exp^{-\mu_a t}\big). \end{aligned} \tag{8}$$

Combining these a priori estimates and the fact that, the right hand side of model (4) is locally Lipschitz, we conclude that there exists a unique global solution in the domain Γ (see Theorem 2.1.5 in [24])). Thus, the model (4) is a dynamical system on Γ. On the other hand, if a solution is outside the region Γ, that is $N_H(t) \geq \frac{\Lambda_h}{\mu_h}$ and $N_A(t) \geq \frac{\Lambda_a}{\mu_a}$, then, it follows from the above conservation law that $\frac{dN_H}{dt} \leq 0$ and $\frac{dN_A}{dt} \leq 0$. Hence, the above general a priori estimates show that $N_H(t)$ tends to $\frac{\Lambda_h}{\mu_h}$ and $N_A(t)$ tends to $\frac{\Lambda_a}{\mu_a}$ as $t \to \infty$. Thus, the region Γ is attracting.

3 Mathematical Analysis

3.1 Asymptotic Stability of Disease-free Equilibrium (DFE)

The DFE of the model (4) is given by $E_0 = (S_H^0, V_H^0, E_H^0, A_H^0, I_H^0, T_H^0, R_H^0, S_A^0, E_A^0, I_A^0, R_A^0)$, where

$$\begin{aligned} &S_H^0 = \frac{\Lambda_h k_2}{k_1 k_2 - \upsilon\omega}, V_H^0 = \frac{\upsilon\Lambda_h}{k_1 k_2 - \upsilon\omega}, E_H^0 = 0, A_H^0 = 0, I_H^0 = 0, T_H^0 \quad = 0, R_H^0 = 0, \\ &S_A^0 = \frac{\Lambda_a}{\mu_a}, E_H^0 = 0, I_A^0 = 0, R_A^0 = 0, \end{aligned}$$

with $k_1 = (\upsilon + \mu_h)$ and $k_2 = (\omega + \mu_h)$.
The local stability of E_0 will be determined using the next generation operator method on model (4) [27]. Using the notation in [27], it follows that matrices F and V, for the new infection terms and the remaining transition terms, respectively, are given by

$$F = \begin{pmatrix} 0 & y_1 & y_2 & 0 & y_3 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \beta_r \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \text{ and } \quad V = \begin{pmatrix} k_3 & 0 & 0 & 0 & 0 \\ -\theta\rho & k_4 & 0 & 0 & 0 \\ -\theta(1-\rho) & -\phi & k_5 & 0 & 0 \\ 0 & 0 & 0 & k_7 & 0 \\ 0 & 0 & 0 & -\varphi & k_8 \end{pmatrix},$$

where

$$\begin{aligned} &y_1 = \frac{(1-\varepsilon\psi)\beta_h\eta k_2}{\upsilon + k_2}, y_2 = \frac{(1-\varepsilon\psi)\beta_h k_2}{\upsilon + k_2}, y_3 = \frac{(1-\varepsilon\psi)\beta_a\mu_a\Lambda_h k_2}{\Lambda_a(k_1 k_2 - \upsilon\omega)}, \\ &k_3 = (\theta\rho + \theta(1-\rho) + \mu_h), k_4 = (\sigma + \phi + \mu_h), k_5 = (\tau + \mu_h + \delta_h), k_7 = (\varphi + \mu_a), \\ &k_8 = (\gamma_a + \mu_a + \delta_a). \end{aligned} \tag{9}$$

It follows that the reproduction numbers of the model (4) are

$$R_0 = \{R_{0h}, R_{0a}\}. \tag{10}$$

with R_{0h} and R_{0a} being the monkeypox induced reproduction numbers for the humans and animals, respectively, which are given by

$$R_{0h} = \frac{(1-\varepsilon\psi)\beta_h k_2\left[\eta k_5\theta\rho + \phi\theta\rho + k_4\theta(1-\rho)\right]}{k_3k_4k_5(\upsilon + k_2)} \tag{11}$$

and

$$R_{0a} = \frac{\beta_r\varphi}{k_7k_8}. \tag{12}$$

The results below follows from Theorem 2 in [27].

Lemma 3.1. *The DFE (E_0) of the model (4) is locally asymptotically stable whenever $R_{0h} < 1$ and $R_{0a} < 1$, and unstable if otherwise.*

The threshold quantity R_0 measures the average number of new monkeypox infections generated by an index case in a completely susceptible population [27]. In particular, $R_{0h}(R_{0a})$ represents the average number of new monkeypox infections in the human (animal) population generated by a single infected human (animal) introduced into a completely susceptible human (animal) population. The epidemiological implication of Lemma 3.1 is that when R_0 is less than unity, monkeypox can be eradicated from the population if the initial sizes of the subpopulation of the model are in the basin of attraction of the DFE (E_0). Hence, a small influx of monkeypox infected humans(animals) into the community will not generate large monkeypox outbreaks, and the disease will die out with time. To ensure that monkeypox eradication is independent of the initial sizes of the sub-population, it is necessary to show that the DFE is globally-asymptotically stable (GAS) if $\widehat{R}_0 < 1$. This is shown for the case where $\upsilon = \omega = \phi = \beta_a = 0$.

3.2 Analysis of the (human) reproduction number, R_{0h}

In this subsection, the threshold parameter, R_{0h} is used to determine the impact of vaccination rate (υ) on the susceptible individuals, the progression rate (θ) from the exposed to the asymptomatic and symptomatic stages of infection and the treatment rate (τ) for the symptomatic individuals on the control of monkeypox infection in the population. It is obvious from (10) that

$$\begin{aligned}
&\lim_{\upsilon\to\infty} R_{0h} = 0,\\
&\lim_{\tau\to\infty} R_{0h} = \frac{(1-\varepsilon\psi)\beta_h(\omega+\mu_h)\theta\eta\rho}{(\upsilon+\omega+\mu_h)(\sigma+\phi+\mu_h)(\theta+\mu_h)} > 0\\
&\lim_{\theta\to\infty} R_{0h} = \frac{(1-\varepsilon\psi)\beta_h(\omega+\mu_h)\left[\eta\rho(\tau+\mu_h+\delta_h) + (\sigma+\phi+\mu_h) - \rho(\sigma+\mu_h)\right]}{(\upsilon+\omega+\mu_h)(\sigma+\phi+\mu_h)(\tau+\mu_h+\delta_h)} > 0
\end{aligned} \tag{13}$$

Therefore, a monkeypox control strategy that results in high vaccination rate ($\upsilon \to \infty$), the progression rate ($\theta \to \infty$) from the exposed stage of infection to the asymptomatic and symptomatic stages of infection and the situation where by individuals in the symptomatic stage of infection are promptly moved to the isolation centre for treatment ($\tau \to \infty$) are high, can lead to the effective control of monkeypox if the results in the respective right hand side of are less than unity. From (13), it is observed that, a near total elimination of monkeypox is achievable. In this case, the strategy is to focus on vaccination programme for individuals in the susceptible class with a high vaccination rate ($\upsilon \to \infty$). This will certainly yield a positive results if the susceptible individuals are vaccinated, their chances of contracting the disease will be low hence reducing the transmission rate in the population.

By computing the partial derivatives of R_{0h} with respect to the parameters υ and τ under investigation reveals further their impacts on the control of monkeypox in the community. Thus, this yields

$$\begin{aligned}
\frac{\partial R_{0h}}{\partial \upsilon} &= -\frac{(1-\varepsilon\psi)\beta_h(\omega+\mu_h)[\theta\rho\eta(\tau+\mu_h+\delta_h)+\phi\theta\rho+\theta(1-\rho)(\sigma+\phi+\mu_h)]}{(\upsilon+\omega+\mu_h)^2(\sigma+\phi+\mu_h)(\theta\rho+\theta(1-\rho)+\mu_h)(\tau+\mu_h+\delta_h)} < 0,\\
\frac{\partial R_{0h}}{\partial \tau} &= -\frac{(1-\varepsilon\psi)\beta_h\theta(\omega+\mu_h)\big[(\sigma+\phi+\mu_h)-\rho(\sigma+\mu_h)\big]}{(\upsilon+\omega+\mu_h)(\sigma+\phi+\mu_h)(\theta+\mu_h)(\tau+\mu_h+\delta_h)^2} < 0,\\
\frac{\partial R_{0h}}{\partial \theta} &= \frac{(1-\varepsilon\psi)\mu_h\beta_h(\omega+\mu_h)\big[\eta\rho(\tau+\mu_h+\delta_h)+(\sigma+\phi+\mu_h)-\rho(\sigma+\mu_h)\big]}{(\upsilon+\omega+\mu_h)(\sigma+\phi+\mu_h)(\theta+\mu_h)^2(\tau+\mu_h+\delta_h)} > 0.
\end{aligned} \tag{14}$$

It is obvious, from (14) that unconditionally, the partial derivatives are less than zero. Hence, effective vaccination rate against monkeypox infection for the susceptible individuals and the rate at which individuals in the symptomatic class are promptly moved to the isolation centre for treatment will have a positive impact in curtailing the spread of the disease in the community, irrespective of the values of the other parameters on the right hand side of (14). Also, exhibiting the progression of the exposed to the infectious stages could be helpful in reducing the spreading chances of the disease.

3.3 Backward Bifurcation Analysis

3.3.1 Existence of backward bifurcation

In this subsection, we wish to determine the number of equilibrium solutions the model (4) can have. Let $E^{**} = \left(S_H^{**}, V_H^{**}, E_H^{**}, A_H^{**}, I_H^{**}, T_H^{**}, R_H^{**}, S_A^{**}, E_A^{**}, I_A^{**}, R_A^{**}\right)$ represent any arbitrary endemic equilibrium of model (4). Then, by setting the right-hand sides of the equations of the model (4) at equilibrium state to zero gives:

$$\begin{aligned}
S_H^{**} &= \frac{\Lambda_h k_2}{[k_2(k_1+\lambda_H^{**})-\upsilon\omega]}, V_H^{**} = \frac{\upsilon\Lambda_h}{[k_2(k_1+\lambda_H^{**})-\upsilon\omega]}, E_H^{**} = \frac{\lambda_H^{**}\Lambda_h k_2}{k_3[k_2(k_1+\lambda_H^{**})-\upsilon\omega]},\\
A_H^{**} &= \frac{\lambda_H^{**}\theta\rho\Lambda_h k_2}{k_3k_4[k_2(k_1+\lambda_H^{**})-\upsilon\omega]}, I_H^{**} = \frac{\lambda_H^{**}k_2(\phi\theta\rho+\theta(1-\rho)k_4)}{k_3k_4k_5[k_2(k_1+\lambda_H^{**})-\upsilon\omega]},\\
T_H^{**} &= \frac{\lambda_H^{**}\tau k_2\Lambda_h(\phi\theta\rho+\theta(1-\rho)k_4)}{k_3k_4k_5k_6[k_2(k_1+\lambda_H^{**})-\upsilon\omega]}, R_H^{**} = \frac{\lambda_H^{**}\Lambda_h k_2[\sigma k_5k_6\theta\rho+\tau\gamma_h(\phi\theta\rho+\theta(1-\rho)k_4)]}{\mu_h k_3k_4k_5k_6[k_2(k_1+\lambda_H^{**})-\upsilon\omega]},\\
S_A^{**} &= \frac{\Lambda_a}{\lambda_A^{**}+\mu_a}, E_A^{**} = \frac{\lambda_A^{**}\Lambda_a}{k_7(\lambda_A^{**}+\mu_a)}, I_A^{**} = \frac{\lambda_A^{**}\varphi\Lambda_a}{k_7k_8(\lambda_A^{**}+\mu_a)}, R_A^{**} = \frac{\lambda_A^{**}\gamma_a\varphi\Lambda_a}{\mu_a k_7k_8(\lambda_A^{**}+\mu_a)}
\end{aligned} \tag{15}$$

where (as before),

$$\begin{aligned}
&k_1 = (\upsilon+\mu_h), k_2 = (\omega+\mu_a), k_3 = [\theta\rho+\theta(1-\rho)+\mu_a], k_4 = (\sigma+\theta(1-\rho)+\mu_h),\\
&k_5 = (\tau+\mu_h+\delta_h), k_6 = (\gamma_h+\mu_h+\delta_h), k_7 = (\varphi+\mu_a), k_8 = (\gamma_a+\mu_a+\delta_a).
\end{aligned} \tag{16}$$

and λ_H^{**}, λ_{AH}^{**} and λ_A^{**} are defined by the following equations

$$\lambda_h^{**} = (1-\varepsilon\psi)\frac{\beta_h(I_H^{**}+\eta A_H^{**})}{N_H^{**}}, \tag{17}$$

$$\lambda_A^{**} = \frac{\beta_r I_A^{**}}{N_A^{**}}, \tag{18}$$

$$\lambda_{AH}^{**} = (1-\varepsilon\psi)\frac{\beta_a I_A^{**}}{N_A^{**}}, \tag{19}$$

to be the associated forces of infection for human-to-human, animal-to-animal and animal-to-human, respectively. We shall consider the cases below for discussion.
Case I: (Human-to-human transmission)

This is the scenario where the transmission of monkeypox is from human-to-human. In this case, $\beta_a = 0$ in equation (2) gives equation (17). Substituting the first seven expressions in (4) into (17) and simplifying gives

$$1 + \frac{\lambda_H^{**} M_2}{(\upsilon + k_2)} = \frac{(1 - \varepsilon\psi)\beta_h k_2 \left[\phi\theta\rho + \theta(1-\rho)k_4 + \eta k_5 \theta\rho\right]}{k_3 k_4 k_5 (\upsilon + k_2)} \tag{20}$$

from (20), we obtain

$$\lambda_H^{**} = \frac{1}{M_3}(R_{0h} - 1) > 1 \tag{21}$$

where $M_2 = \left(\frac{k_2}{k_3} + \frac{\theta\rho k_2}{k_3 k_4} + \frac{(\phi\theta\rho + \theta(1-\rho)k_4)k_2}{k_3 k_4 k_5} + \frac{\tau k_2(\phi\theta\rho + \theta(1-\rho)k_4)}{k_3 k_4 k_5 k_6} + \frac{\sigma k_5 k_6 \theta\rho + \tau\gamma_h(\phi\theta\rho + \theta(1-\rho)k_4)}{\mu_h k_3 k_4 k_5 k_6}\right)$
and $M_3 = \dfrac{M_2}{(\upsilon + k_2)}$.
Thus, a unique endemic equilibrium exists for human-to-human transmission whenever $\lambda_H^{**} > 0$ for $R_{0h} > 1$.

Case II: (Animal-to-animal transmission)
This is the situation where the transmission of monkeypox is from animal to animal. The force of infection at steady state for animal to animal transmission is given by (18). Substituting the last four expressions in (4) into (18) gives

$$1 + M_1 \lambda_A^{**} = \frac{\lambda_r \theta_3}{k_7 k_8} \tag{22}$$

which results in

$$\lambda_A^{**} = \frac{1}{M_1}(R_{0a} - 1) > 1 \tag{23}$$

where $M_1 = \dfrac{1}{k_7} + \dfrac{\theta_3}{k_7 k_8} + \dfrac{\theta_3 \gamma_a}{\mu_a k_7 k_8}$
Hence, a unique endemic equilibrium exists for animal to animal transmission when $R_{0a} > 1$.

Case III: (Animal-to-human transmission)
This is the case where the transmission of monkeypox infection is from animal to human. Here, we set $\beta_h = 0$ in (2), to get equation (19). From (18), we obtain

$$\frac{\lambda_A^{**}}{\beta_r} = \frac{I_A^{**}}{N_A^{**}} \tag{24}$$

Substituting (24) into (19), gives

$$\lambda_{AH}^{**} = \frac{(1 - \varepsilon\psi)\beta_a}{\beta_r} \lambda_A^{**}. \tag{25}$$

Using (23) in (25), yields

$$\lambda_{AH}^{**} = M_4(R_{0a} - 1) > 1, \tag{26}$$

where $M_4 = \dfrac{(1 - \varepsilon\psi)\beta_a}{\beta_r M_1}$.
Here too, a unique endemic equilibrium exists for animal-to-human transmission when $R_{0a} > 1$.

3.4 Backward bifurcation analysis

The phenomenon of backward bifurcation, which is characterized by the existence of a stable DFE and a stable endemic equilibrium when the associated reproduction number of the model is less than unity, can be traced as done over the years in numerous disease transmission models, (see, for example, [4, 14]).

Suppose $E^{**} = (S_H^{**}, V_H^{**}, E_H^{**}, A_H^{**}, I_H^{**}, T_H^{**}, R_H^{**}, S_A^{**}, E_A^{**}, I_A^{**}, R_A^{**})$ represents any arbitrary endemic equilibrium of model (4), that is an equilibrium where at least one of the infected classes is non-zero. We will investigate the existence of backward bifurcation using the centre manifold theory [7, 8]. To apply this theory, it is convenient to define the following change of variables $S_H = x_1$, $V_H = x_2$, $E_H = x_3$, $A_H = x_4$, $I_H = x_5$, $T_H = x_6$, $R_H = x_7$, $S_A = x_8$, $E_A = x_9$, $I_A = x_{10}$ and $R_A = x_{11}$, so that $N_H = x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7$ and $N_A = x_8 + x_9 + x_{10} + x_{11}$. Further, by adopting the vector notation $X = (x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8, x_9, x_{10}, x_{11})^T$, the model (4) can be written in the form $\frac{dX}{dt} = F = (f_1, f_2, f_3, f_4, f_5, f_6, f_7, f_8, f_9, f_{10}, f_{11})^T$, as follows:

$$\begin{aligned}
\frac{dx_1}{dt} &= f_1 = \Lambda_h - \lambda_H x_1 + \omega x_2 - k_1 x_1,\\
\frac{dx_2}{dt} &= f_2 = \upsilon x_1 - k_2 x_2,\\
\frac{dx_3}{dt} &= f_3 = \lambda_H x_1 - k_3 x_3,\\
\frac{dx_4}{dt} &= f_4 = \theta\rho x_3 - k_4 x_4,\\
\frac{dx_5}{dt} &= f_5 = \phi x_4 + \theta(1-\rho)x_3 - k_5 x_5,\\
\frac{dx_6}{dt} &= f_6 = \tau x_5 - k_6 x_6,\\
\frac{dx_7}{dt} &= f_7 = \sigma x_4 + \gamma_h x_6 - \mu_h x_7,\\
\frac{dx_8}{dt} &= f_8 = \Lambda_a - \lambda_A x_8 - \mu_a x_8,\\
\frac{dx_9}{dt} &= f_9 = \lambda_A x_8 - k_7 x_9,\\
\frac{dx_{10}}{dt} &= f_{10} = \varphi x_9 - k_8 x_{10},\\
\frac{dx_{11}}{dt} &= f_{11} = \gamma_a x_{10} - \mu_a x_{11}.
\end{aligned} \tag{27}$$

where

$$\begin{aligned}
&k_1 = (\upsilon + \mu_h), k_2 = (\omega + \mu_h), k_3 = [\theta\rho + \theta(1-\rho) + \mu_h], k_4 = (\sigma + \phi + \mu_h),\\
&k_5 = (\tau + \mu_h + \delta_h), k_6 = (\gamma_h + \mu_h + \delta_h), k_7 = (\varphi + \mu_a), k_8 = (\gamma_a + \mu_a + \delta_a).
\end{aligned} \tag{28}$$

and, the forces of infection are given by

$$\lambda_H = (1 - \varepsilon\psi)[\frac{\beta_h(x_5 + \eta x_4)}{N_H} + \frac{\beta_a x_{10}}{N_A}] \tag{29}$$

and

$$\lambda_A = \frac{\beta_r x_{10}}{N_A}. \tag{30}$$

Consider the case when $\beta_h = \beta_h^*$ and $\beta_r = \beta_r^*$ are chosen as the bifurcation parameters. Solving for $\beta_h = \beta_h^*$ and $\beta_r = \beta_r^*$ from $R_0 = 1$, respectively yields

$$\beta_h = \beta_h^* = \frac{k_3 k_4 k_5 (\upsilon + k_2)}{(1 - \varepsilon\psi)k_2\big[k_4\theta(1-\rho) + \theta\rho(\phi + \eta k_5)\big]} \tag{31}$$

and

$$\beta_r = \beta_r^* = \frac{k_7 k_8}{\varphi}. \tag{32}$$

The Jacobian matrix of the transformed system (28), evaluated at the DFE (E^0) with $\beta_h = \beta_h^*$ and $\beta_r = \beta_r^*$, is given by

$$J(E_0) = \begin{pmatrix} A_{6\times 6} & B_{6\times 5} \\ C_{5\times 6} & D_{5\times 5} \end{pmatrix},$$

where

$$A = \begin{pmatrix} -k_1 & \omega & 0 & -q_1 & -q_2 & 0 \\ \upsilon & -k_2 & 0 & 0 & 0 & 0 \\ 0 & 0 & -k_3 & q_1 & q_2 & 0 \\ 0 & 0 & \theta\rho & -k_4 & 0 & 0 \\ 0 & 0 & \theta_2 & \phi & -k_5 & 0 \\ 0 & 0 & 0 & 0 & \tau & -k_6 \end{pmatrix}, B = \begin{pmatrix} 0 & 0 & 0 & -q_3 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & q_3 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$C = \begin{pmatrix} 0 & 0 & 0 & \sigma & 0 & \gamma_h \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \text{ and } D = \begin{pmatrix} -\mu_h & 0 & 0 & 0 & 0 \\ 0 & -\mu_a & 0 & -\beta_r & 0 \\ 0 & 0 & -k_7 & \beta_r & 0 \\ 0 & 0 & \varphi & -k_8 & 0 \\ 0 & 0 & 0 & \gamma_a & -\mu_a \end{pmatrix},$$

with $q_1 = \dfrac{(1-\varepsilon\psi)\eta\beta_h^* k_2}{(\upsilon + k_2)}$, $q_2 = \dfrac{(1-\varepsilon\psi)\beta_h^* k_2}{(\upsilon + k_2)}$, $q_3 = \dfrac{(1-\varepsilon\psi)\Lambda_h k_2 \beta_a^* \mu_a}{\Lambda_a(k_1k_2 - \upsilon\omega)}$.

Matrix $J(E_0)$ has a right eigenvector (associated with the zero eigenvalue) given by $w = [w_1, w_2, w_3, w_4, w_5, w_6, w_7, w_8, w_9, w_{10}, w_{11}]^T$, where

$$\begin{aligned} w_1 &= -\frac{(1-\varepsilon\psi)\beta_h^* k_2[k_4\theta(1-\rho) + \theta\rho(\phi + \eta k_5)]}{k_4k_5(\upsilon + k_2)(k_1k_2 - \upsilon\omega)}, \\ w_2 &= -\frac{(1-\varepsilon\psi)\upsilon\beta_h^* k_2[k_4\theta(1-\rho) + \theta\rho(\phi + \eta k_5)]}{k_4k_5(\upsilon + k_2)(k_1k_2 - \upsilon\omega)}, w_3 = w_3 > 0, w_4 = \frac{\theta\rho}{k_4}w_3 > 0, \\ w_5 &= \frac{(\phi\theta\rho + k_4\theta(1-\rho))}{k_4k_5}w_3 > 0, w_6 = \frac{\tau(\phi\theta\rho + k_4\theta(1-\rho))}{k_4k_5k_6}w_3 > 0, \\ w_7 &= \frac{[\sigma k_5k_6\theta\rho + \tau\gamma_h(\phi\theta\rho + k_4\theta(1-\rho))]}{\mu_h k_4k_5k_6}w_3 > 0, w_8 = w_9 = w_{10} = w_{11} = 0. \end{aligned} \tag{33}$$

Furthermore, $J(E_0)$ has a left eigenvector (associated with the zero eigenvalue), given by $v = (v_1, v_2, v_3, v_4, v_5, v_6, v_7, v_8, v_9, v_{10}, v_{11})$, satisfying $v.w = 1$, with

$$\begin{aligned} v_1 = v_2 = 0, v_3 = v_3 > 0, v_4 &= \frac{\beta_h^* k_2(1-\varepsilon\psi)(\phi + \eta k_5)}{k_4k_5(\upsilon + k_2)} > 0 \\ v_5 &= \frac{\beta_h^* k_2(1-\varepsilon\psi)}{k_5(\upsilon + k_2)} > 0, v_6 = v_7 = v_8 = v_9 = v_{10} = v_{11}. \end{aligned} \tag{34}$$

It follows from Theorem 4.1 in [8] that if we compute the associated non-zero partial derivatives of F at the DFE (E_0) and simplifying, that

$a = \sum_{k,i,j=1}^{11} v_k w_i w_j \dfrac{\partial^2 f_k}{\partial x_i \partial x_j}(E_0) = \dfrac{2v_3\beta_h^*(1-\varepsilon\psi)(k_1k_2 - \upsilon\omega)}{\Lambda(\upsilon + k_2)^2}[A - B]$. Thus, the bifurcation coefficient, a, is greater than zero whenever $A > B$, where

$A = \dfrac{\eta w_4^2}{\Lambda_h} - k_2 w_2(w_5 + \eta w_4) > 0$, since $w_2 < 0$

and

$B = w_5(w_4k_2 - \upsilon w_1 + k_2w_3 + k_2w_6 + k_2w_7 + w_4k_2\eta + k_2w_5) + w_4\eta(-\upsilon w_1 + w_3k_2 + w_6k_2 + w_7k_2) > 0$, since $w_1 < 0$.
It can therefore, be shown that
$b = \sum_{k,i=1}^{11} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \beta_h^*}(E_0) = \frac{(1-\varepsilon\psi)v_3k_2}{(\upsilon + k_2)}(w_5 + w_4\eta) > 0.$
Hence, it follows, from Theorem 4.1 in [15], that the model (4), exhibits a backward bifurcation at $R_0 < 1$ whenever $A > B$.

3.5 Existence of Unique Endemic Equilibrium: Special Case

Theorem 3.2. *The model (4) has a unique endemic (positive) equilibrium when* $\upsilon = \omega = \phi = \beta_a = 0$ *whenever* $\widehat{R}_0 > 1$ *(i.e. when there is only human-to-human transmission of monkeypox).*

Proof: To establish the existence of endemic equilibria of model (4), for the special case $\upsilon = \omega = \phi = \beta_a = 0$, let $E_1^* = \left(S_H^{**}, E_H^{**}, A_H^{**}, I_H^{**}, T_H^{**}, R_H^{**}\right)$ represent any arbitrary endemic equilibrium of model (4). The equations in (4), with $\upsilon = \omega = \phi = \beta_a = 0$, are solved in terms of the force of infection at equilibrium state to get

$$\begin{aligned} S_H^{**} &= \frac{\Lambda_h}{(\mu_h + \lambda_H^{**})}, E_H^{**} = \frac{\lambda_H^{**}\Lambda_h}{k_3(\mu_h + \lambda_H^{**})}, \\ A_H^{**} &= \frac{\lambda_H^{**}\theta\rho\Lambda_h}{k_3\widehat{k_4}(\mu_h + \lambda_H^{**})}, I_H^{**} = \frac{\lambda_H^{**}\Lambda_h\theta(1-\rho)}{k_3k_5(\mu_h + \lambda_H^{**})}, \\ T_H^{**} &= \frac{\lambda_H^{**}\Lambda_h\tau\theta(1-\rho)}{k_3k_5k_6(\mu_h + \lambda_H^{**})}, R_H^{**} = \frac{\lambda_H^{**}\Lambda_h[\sigma k_5k_6\theta\rho + \tau\gamma_h\widehat{k_4}\theta(1-\rho)}{\mu_hk_3\widehat{k_4}k_5k_6(\mu_h + \lambda_H^{**})}, \end{aligned} \tag{35}$$

where

$$\begin{aligned} &k_3 = (\theta\rho + \theta(1-\rho) + \mu_h), \widehat{k_4} = (\sigma + \mu_h), k_5 = (\tau + \mu_h + \delta_h), \\ &k_6 = (\gamma_h + \mu_h + \delta_h). \end{aligned} \tag{36}$$

and λ_h^{**} (for the human-to-human)is the same as given by equation (17): Substituting (35) and (36) into (17) gives

$$(1 + \lambda_h^{**}M_1) = (1-\varepsilon\psi)\beta_h\frac{\widehat{k_4}\theta(1-\rho) + \eta\theta\rho k_5}{k_3\widehat{k_4}k_5}$$

which yields

$$\lambda_h^{**} = \frac{1}{M_1}(\widehat{R_0} - 1) > 0$$

where

$$M_1 = \frac{1}{k_3} + \frac{\theta\rho}{k_3\widehat{k_4}} + \frac{\tau\theta(1-\rho)}{k_3k_4k_5} + \frac{(\sigma k_5k_6\theta\rho + \gamma_h\tau\widehat{k_4}\theta(1-\rho))}{\mu_hk_3\widehat{k_4}k_5k_6}$$

Hence, a unique endemic equilibrium (for the case $\upsilon = \omega = \phi = \beta_a = 0$) exists when $\widehat{R_0} > 1$.

Let,
$\Gamma_3 = (S_H, E_H, A_H, I_H, T_H, R_H) \in \Gamma : E_H = A_H = I_H = T_H = R_H = 0$ be the stable manifold of the DFE (E_0). We claim the following

Theorem 3.3. *The DFE of model (4), with* $\upsilon = \omega = \phi = \beta_a = 0$ *is globally asymptotically stable in* Γ *whenever* $\widehat{R}_0 \leq 1$.

Proof:

$$V_1 = \left[\eta k_5\theta\rho + \theta(1-\rho)\widehat{k_4}\right]E_H + k_3k_5\eta A_H + k_3\widehat{k_4}I_H \tag{37}$$

The Lyapunov derivative of (37) (where a dot denotes differentiation with respect to t) gives

$$\dot{V}_1 = \left[\eta k_5\theta\rho + \theta(1-\rho)\widehat{k_4}\right]\dot{E}_H + k_3k_5\eta\dot{A}_H + k_3\widehat{k_4}\dot{I}_H \tag{38}$$

Substituting the respective right hand side of model (4) into (38) gives

$$\begin{aligned}\dot{V}_1 &= \big[\eta k_5\theta\rho + \theta(1-\rho)\widehat{k_4}\big]\big(\lambda_H S_H - k_3 E_H\big) + k_3k_5\eta\big(\theta\rho E_H - \widehat{k_4}A_H\big)\\ &\quad + k_3\widehat{k_4}\big[\theta(1-\rho)E_H - k_5 I_H\big]\\ &= \frac{(1-\varepsilon\psi)\beta_h(I_H+\eta A_H)S_H}{N_H}\Big[\eta k_5\theta\rho + \theta(1-\rho)\widehat{k_4}\Big] - k_3\widehat{k_4}k_5\eta A_H - k_3\widehat{k_4}k_5 I_H\\ &= \frac{(1-\varepsilon\psi)\beta_h(I_H+\eta A_H)S_H}{N_H}\Big[\eta k_5\theta\rho + \theta(1-\rho)\widehat{k_4}\Big] - k_3\widehat{k_4}k_5(I_H+\eta A_H)\\ &= k_3\widehat{k_4}k_5(I_H+\eta A_H)\Big[\frac{(1-\varepsilon\psi)\beta_h S_H}{N_H}\frac{[\eta k_5\theta\rho + \theta(1-\rho)\widehat{k_4}]}{k_3\widehat{k_4}k_5} - 1\Big]\end{aligned} \tag{39}$$

It follows from (39), noting that $S_H(t) \le N_H(t)$ and $N_H(t) \le \dfrac{\Lambda_h}{\mu_h}$ in Γ for all $t > 0$, that

$$\dot{V}_1 \le k_3\widehat{k_4}k_5(I_H+\eta A_H)\big[\widehat{R_0} - 1\big] \tag{40}$$

Hence, $\dot{V}_1 \le 0$ if $\widehat{R_0} \le 1$ with $\dot{V}_1 = 0$ if and only if $I_H = A_H = 0$. Therefore, $\dot{V}_1$ is a Lyapunov function in Γ, and it follows from LaSalle's invariance principle [18] that every solution to the equation in (4) (with $\upsilon = \omega = \phi = \beta_a = 0$) with the initial conditions in Γ converges to E_0 as $t \to \infty$, that is $(E_H(t), A_H(t), I_H(t), T_H(t), R_H(t)) \to (0,0,0,0,0)$ as $t \to \infty$. Substituting $E_H = A_H = I_H = T_H = R_H = 0$ into the first equation in (4) gives $S_H \to \dfrac{\Lambda_h}{\mu_h}$ as $t \to \infty$. Thus, $(S_H, E_H, A_H, I_H, T_H, R_H) \to (\dfrac{\Lambda_h}{\mu_h}, 0, 0, 0, 0, 0)$ as $t \to \infty$ for $\widehat{R_0} \le 1$. So the DFE, E_0, is globally asymptotically stable in Γ if $\widehat{R_0} \le 1$ for the case $\upsilon = \omega = \phi = \beta_a = 0$. The above proof is numerically illustrated in Figure 2. The epidemiological implication of Theorem 3.3 is that, when there is no vaccination and progression from asymptomatic to symptomatic stages of infection (i.e. if only treatment is the control strategy), monkeypox could still be effectively controlled in the community if the threshold value $\widehat{R_0} < 1$.

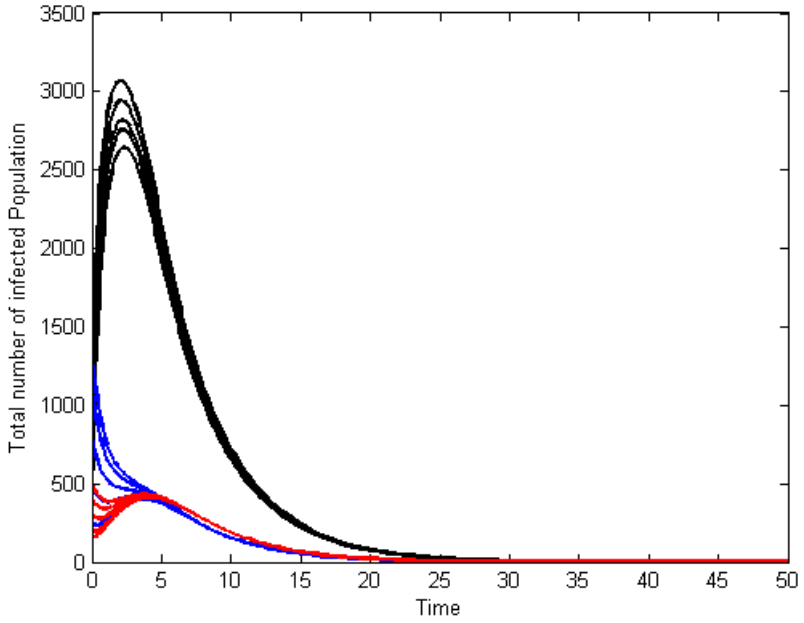

Figure 2: Simulation of model (4), showing the total number of infected population as a function of time, using different initial conditions. Parameter values used are as in Table 2 (so that $\widehat{R_0} = 0.000041$)

Theorem 3.4. *The unique endemic equilibrium of model (4), with* $\upsilon = \omega = \phi = \beta_a = 0$ *is globally asymptotically stable in* $\Gamma \setminus \Gamma_3$ *whenever* $\widehat{R}_0 > 1$.

Proof: We consider model (4) where $\upsilon = \omega = \phi = \beta_a = 0$ and $\widehat{R}_0 > 1$, then the associated unique endemic equilibrium of the model exists. The following non-linear Lyapunov function of the Goh-Volterra type is considered.

$$\begin{aligned} V_2 &= S_H - S_H^{**} - S_H^{**} ln\Big(\frac{S_H}{S_H^{**}}\Big) + E_H - E_H^{**} - E_H^{**} ln\Big(\frac{E_H}{E_H^{**}}\Big) \\ &+ \frac{\eta\widehat{\beta_h} S_H^{**}}{\widehat{k_4}}\Big(A_H - A_H^{**} - A_H^{**} ln\Big(\frac{A_H}{A_H^{**}}\Big)\Big) + \frac{\widehat{\beta_h} S_H^{**}}{k_5}\Big(I_H - I_H^{**} - I_H^{**} ln\Big(\frac{I_H}{I_H^{**}}\Big)\Big) \end{aligned} \tag{41}$$

Taking the time derivative of (40) yields

$$\dot{V}_2 = \dot{S_H} - \frac{S_H^{**}}{S_H}\dot{S_H} + \dot{E_H} - \frac{E_H^{**}}{E_H}\dot{E_H} + \frac{\eta\widehat{\beta_h} S_H^{**}}{\widehat{k_4}}\Big(\dot{A_H} - \frac{A_H^{**}}{A_H}\dot{A_H}\Big) + \frac{\widehat{\beta_h} S_H^{**}}{k_5}\Big(\dot{I_H} - \frac{I_H^{**}}{I_H}\dot{I_H}\Big) \tag{42}$$

Substituting the respective expressions on the right-hand sides of equations (4) into (41) gives

$$\begin{aligned} \dot{V}_2 &= \Lambda_h - \widehat{\beta_h} S_H(I_H + \eta A_H) - \mu_h S_H - \frac{S_H^{**}}{S_H}\Big[\Lambda_h - \widehat{\beta_h} S_H(I_H + \eta A_H) - \mu_h S_H\Big] \\ &+ \widehat{\beta_h} S_H(I_H + \eta A_H) - k_3 E_H - \frac{E_H^{**}}{E_H}\Big[\widehat{\beta_h} S_H(I_H + \eta A_H) - k_3 E_H\Big] \\ &+ \frac{\eta\widehat{\beta_h} S_H^{**}}{\widehat{k_4}}\Big[\theta\rho E_H - \widehat{k_4} A_H - \frac{A_H^{**}}{A_H}(\theta\rho E_H - \widehat{k_4} A_H)\Big] \\ &+ \frac{\widehat{\beta_h} S_H^{**}}{k_5}\Big[\theta(1-\rho) - k_5 I_H - \frac{I_H^{**}}{I_H}(\theta(1-\rho) - k_5 I_H)\Big] \end{aligned} \tag{43}$$

Equation (42) reduces to

$$\begin{aligned} \dot{V}_2 &= \Lambda_h - \widehat{\beta_h} S_H(I_H + \eta A_H) - \mu_h S_H - \frac{S_H^{**}}{S_H}\Lambda_h + \widehat{\beta_h} S_H^{**}(I_H + \eta A_H) + \mu_h S_H^{**} \\ &+ \widehat{\beta_h} S_H(I_H + \eta A_H) - k_3 E_H - \frac{E_H^{**}}{E_H}\widehat{\beta_h} S_H(I_H + \eta A_H) + k_3 E_H^{**} + \frac{\eta\widehat{\beta_h} S_H^{**}\theta\rho E_H}{\widehat{k_4}} \\ &- \widehat{\beta_h} S_H^{**}\eta A_H - \frac{A_H^{**}}{A_H}\frac{\widehat{\beta_h} S_H^{**}}{\widehat{k_4}}\eta\theta\rho E_H + \widehat{\beta_h} S_H^{**}\eta A_H^{**} + \frac{\widehat{\beta_h} S_H^{**}\theta(1-\rho)E_H}{k_5} \\ &- \widehat{\beta_h} S_H^{**} I_H - \frac{\widehat{\beta_h} S_H^{**}}{k_5}\frac{I_H^{**}}{I_H}\theta(1-\rho)E_H + \widehat{\beta_h} S_H^{**} I_H^{**} \end{aligned} \tag{44}$$

$$\begin{aligned} \Lambda_h &= \widehat{\beta_h} S_H^{**}(I_H^{**} + \eta A_H^{**}) + \mu_h S_H^{**} \\ k_3 E_H^{**} &= \widehat{\beta_h} S_H^{**}(I_H^{**} + \eta A_H^{**}) \\ \theta\rho E_H^{**} &= \widehat{k_4} A_H \\ \theta(1-\rho) E_H^{**} &= k_5 I_H^{**} \end{aligned} \tag{45}$$

Substituting (44) into (43) and simplifying yields

$$\begin{aligned} \dot{V}_2 &= \mu_h S_H^{**}\Big(2 - \frac{S_H}{S_H^{**}} - \frac{S_H^{**}}{S_H}\Big) + 3\widehat{\beta_h} S_H^{**}\eta A_H^{**} - \widehat{\beta_h}\frac{S_H^{**2}}{S_H}\eta A_H^{**} - \frac{E_H^{**}}{E_H}\widehat{\beta_h} S_H\eta A_H \\ &- \frac{A_H^{**2}}{A_H}\frac{E_H}{E_H^{**}}\eta\widehat{\beta_h} S_H^{**} + 3\widehat{\beta_h} S_H^{**} I_H^{**} - \widehat{\beta_h}\frac{S_H^{**2}}{S_H} I_H^{**} - \frac{E_H^{**}}{E_H}\widehat{\beta_h} S_H I_H - \widehat{\beta_h} S_H^{**}\frac{I_H^{**2}}{I_H}\frac{E_H}{E_H^{**}} \end{aligned} \tag{46}$$

Equation (45) is further simplified to

$$\begin{aligned}\dot{V}_2 = \mu_h S_H^{**}\Big(2 - \frac{S_H}{S_H^{**}} - \frac{S_H^{**}}{S_H}\Big) + \eta\widehat{\beta_h} S_H^{**} A_H^{**}\Big(3 - \frac{S_H^{**}}{S_H} - \frac{E_H^{**} S_H A_H}{E_H S_H^{**} A_H^{**}} - \frac{A_H^{**} E_H}{A_H E_H^{**}}\Big) \\ + \widehat{\beta_h} S_H^{**} I_H^{**}\Big(3 - \frac{S_H^{**}}{S_H} - \frac{E_H^{**} S_H I_H}{E_H S_H^{**} I_H^{**}} - \frac{I_H^{**} E_H}{I_H E_H^{**}}\Big)\end{aligned} \tag{47}$$

Finally, since the arithmetic mean exceeds the geometric mean, the following inequalities hold

$2 - \frac{S_H}{S_H^{**}} - \frac{S_H^{**}}{S_H} \leq 0$, $3 - \frac{S_H^{**}}{S_H} - \frac{E_H^{**} S_H A_H}{E_H S_H^{**} A_H^{**}} - \frac{A_H^{**} E_H}{A_H E_H^{**}} \leq 0$,

$3 - \frac{S_H^{**}}{S_H} - \frac{E_H^{**} S_H I_H}{E_H S_H^{**} I_H^{**}} - \frac{I_H^{**} E_H}{I_H E_H^{**}} \leq 0.$

Thus,$\dot{V}_2 \leq 0$ for $\widehat{R_0} > 1$. Since the relevant variables in the equations for T_H and R_H are at the endemic equilibrium state, it follows that these can be substituted into the equations for T_H and R_H giving $\Big(T_H(t), R_H(t)\Big) \to \Big(T_H^{**}, R_H^{**}\Big)$ as $t \to \infty$. Hence, V_2 is a Lyapunov function in $\Gamma \setminus \Gamma_3$.

4 Sensitivity Analysis

In order to determine the impact of the model parameters on the transmission dynamics, prevention and control of monkeypox, it is important to conduct sensitivity analysis using the normalized forward sensitivity index [12, 13]. Following [13], the relative importance of the input parameters associated with the output variable R_{oh} is evaluated using the formula:

$$\chi_p^{R_{oh}} = \frac{\partial R_{oh}}{\partial p} \times \frac{p}{R_{oh}}, \tag{48}$$

where p denotes model parameters contained in R_{oh}. Using the parameters values in Table 2 on equations (48), we obtained the sensitivity indices presented in Table 3. Results in Table 3 shows that, the most sensitive parameters are the monkeypox transmission rate from human-to-human (β_h), efficacy of public awareness campaign (ψ), vaccination rate for the susceptible individuals (υ), waning rate of the monkeypox vaccine (ω) and the treatment rate for the symptomatic individuals (τ). The epidemiological implication of these results as in Table 3 is that, public awareness campaign in the population should be strengthened by the government and other critical stakeholders in order to educate the populace on the need to be vaccinated against monkeypox infection, get to a health facility immediately when blisters show up on their body and the need to develop vaccines that will not wane within a short period of time.

5 Numerical Simulations

In this section, numerical simulations are carried out on model (4) using the parameter values in Table 2, and initial data relevant to monkeypox transmission dynamics in Nigeria. Particularly, for the human population, $N = 217,485,651$ was found in [22] while $V_H(0) = 5,000$ was gotten from the works of [26]. Further, we obtained $E_H(0) = 413$, $A_H(0) = 256$ and $I_H(0) = 157$ from [15]. $S_H(0) = 217,479,522$ was estimated based on the above data information. $T_H(0) = 153$ and $R_H(0) = 150$ where assumed since no information was found regarding their initial conditions. For the animal population, information regarding their initial conditions was found in the works of [26]. Hence, we set, $S_A(0) = 250$, $E_A(0) = 125$, $I_A(0) = 75$ and $R_A(0) = 50$. The model (4) is solved numerically using MATLAB ODE45 solver. In Figure 3, an increase in the vaccination rate of the susceptible individuals experienced an increase in the population of the vaccinated individuals (i.e. individuals vaccinated against monkeypox infection). This increase in the vaccination rate of the susceptibles led to the reduction in the population of the susceptibles, asymptomatic and symptomatic individuals. In Figure 4,we observed that, increasing the efficacy rate of public awareness campaign(i.e.

Table 2: The parameters values of model (4)

Parameter	Nominal value	Reference
Λ_h	$0.029\ year^{-1}$	[2]
υ	$0.85\ year^{-1}$	[28]
ω	$0.60\ year^{-1}$	Assumed
μ_h	$0.02\ year^{-1}$	[2]
δ_h	$0.1\ year^{-1}$	[11]
θ	$0.20\ year^{-1}$	[20]
ρ	$0.6\ year^{-1}$	Assumed
ϕ	$0.3\ year^{-1}$	Assumed
σ	$0.4\ year^{-1}$	Assumed
τ	$0.6\ year^{-1}$	Assumed
η	$0.75\ year^{-1}$	Assumed
ε	$0.80\ year^{-1}$	Assumed
ψ	$0.70\ year^{-1}$	Assumed
β_h	$0.000063\ year^{-1}$	[3]
(β_a, β_r)	$(0.000252, 0.0027)$	[3]
Λ_a	$2\ year^{-1}$	[3]
μ_a	$1.5\ year^{-1}$	[3]
φ	$0.3\ year^{-1}$	[26]
γ_a	$0.6\ year^{-1}$	[3]
δ_a	$0.4\ year^{-1}$	[3]

Table 3: Sensitivity indices of some the parameters values

Parameter	Sensitivity indices
β_h	$+1.000000$
ε	-1.272727
ψ	-1.272727
σ	-0.353535
τ	-0.492424
υ	-0.578231
θ	$+0.090909$
ρ	$+0.090909$
μ_h	-0.106347
ω	$+0.559579$
η	$+0.409091$
ϕ	-0.037879
δ_h	-0.082071

sensitizing the public on the need to be vaccinated against monkeypox infection and other safety measures) led to an increase in the number of vaccinated individuals while the population of the susceptibles, asymptomatic and symptomatic reduced greatly. Figure 5 demonstrates the effect of the progression rate from the exposed population to the asymptomatic and symptomatic population on the number of infected population on some stages of monkeypox infection. Here, an increase in the progression rate (θ) led to the reduction in the population of the exposed individuals while a population increase of the asymptomatic, symptomatic and isolated individuals are recorded. From Figure 6, increasing public awareness campaign (ε) and its efficacy (ψ) experienced a reduction in the effective reproduction number (human) below unity.

We demonstrate numerically in Figures 7, 8 and 9 the relationship between the effective reproduction number for the human population and the progression rate (θ), the effective vaccination rate (υ) and the rate at which the symptomatic individuals are moved to the isolation centre for treatment (τ). In Figure 7, we observed that, the effective reproduction number increases with an increase in the progression rate from the exposed stage of infection to the asymptomatic and symptomatic stages of infection, respectively. This implies that if concerted efforts are not put in place to check the progression rate, it will trigger an increase in the number of monkeypox cases in the population. In Figures 8 and 9, increasing the vaccination rate for the susceptibles and the rate at which symptomatic individuals are promptly moved to the isolation centre for treatment, respectively, decreases the effective reproduction number. If the results in Figures 8 and 9 are put to practice, it will help in controlling the spread of monkeypox infection in the population.

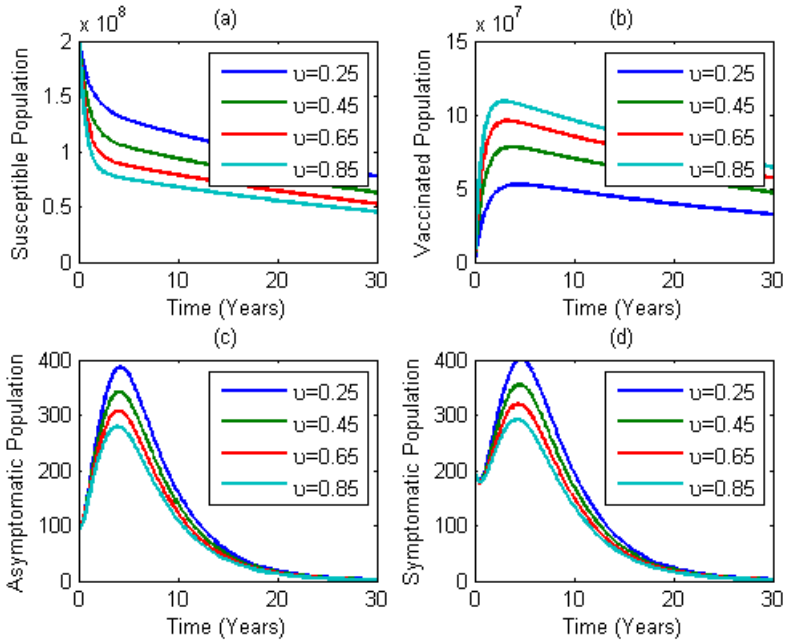

Figure 3: Simulation of model (4) showing the population of susceptible, vaccinated, asymptomatic and symptomatic individuals. Here, the effective vaccination rate, υ is varied from 0.25 to 0.85.

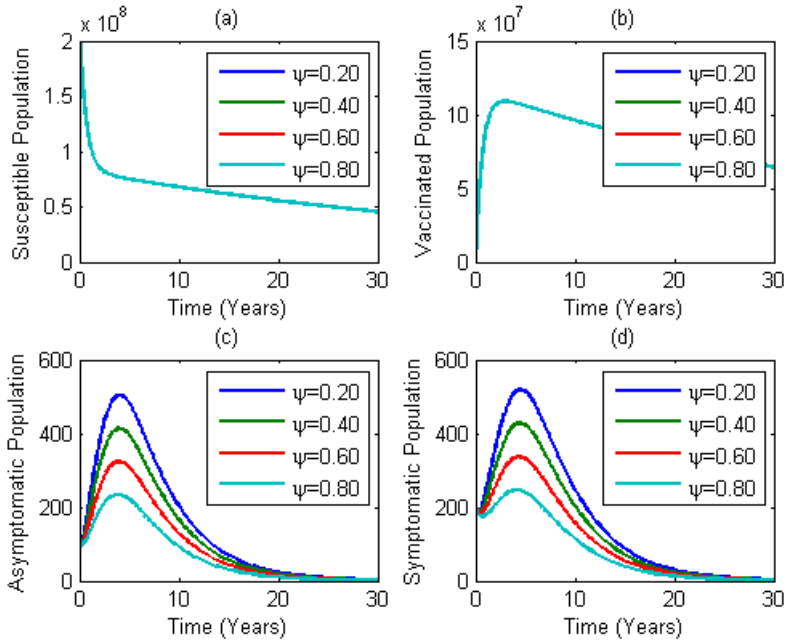

Figure 4: Simulation of model (4) showing the population of susceptible, vaccinated, asymptomatic and symptomatic individuals. Here, the efficacy rate of public awareness campaign, ψ is varied from 0.20 to 0.80.

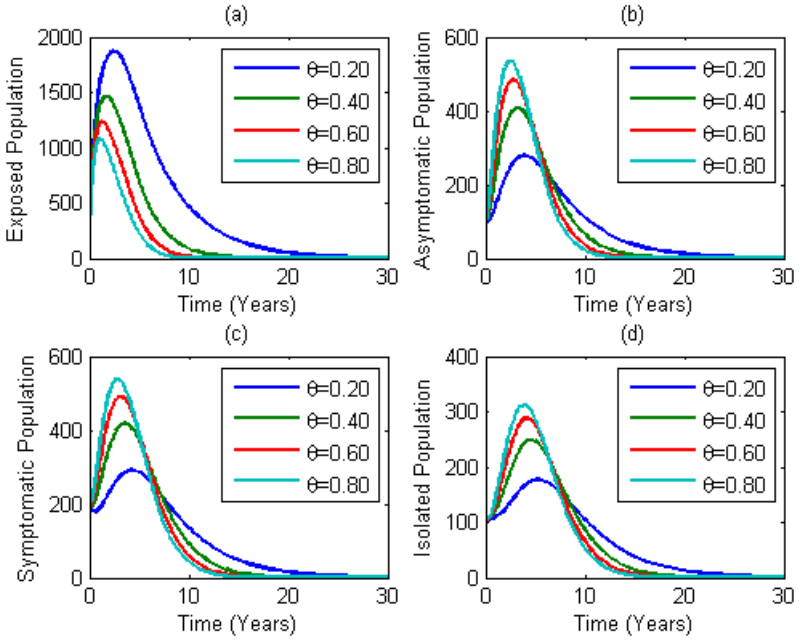

Figure 5: Simulation of model (4) showing the population of exposed, asymptomatic, symptomatic and the isolated individuals. Here, the progression rate, θ is varied from 0.20 to 0.80.

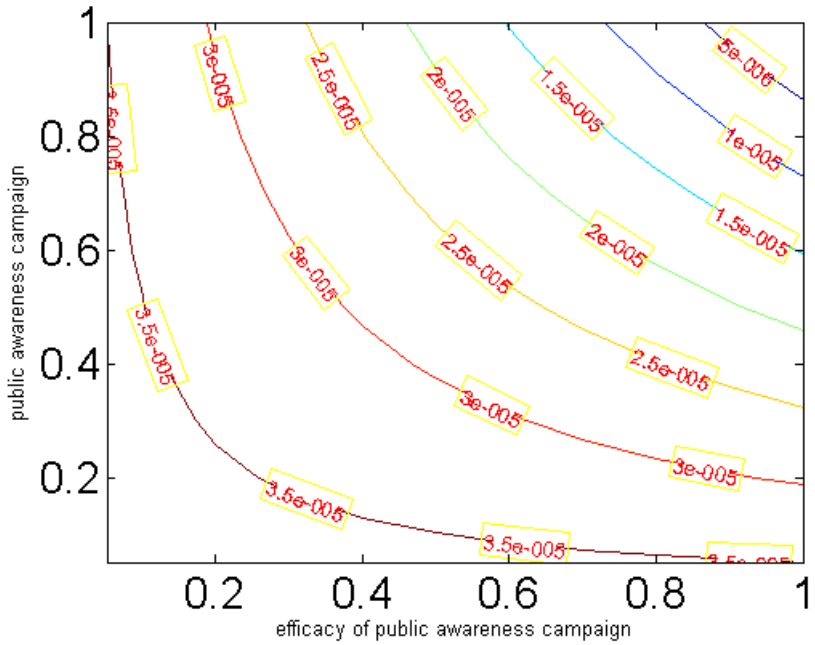

Figure 6: Contour plot of the human reproduction number, R_{0h} as a function of public awareness campaign, ε and efficacy rate of public awareness campaign, ψ.

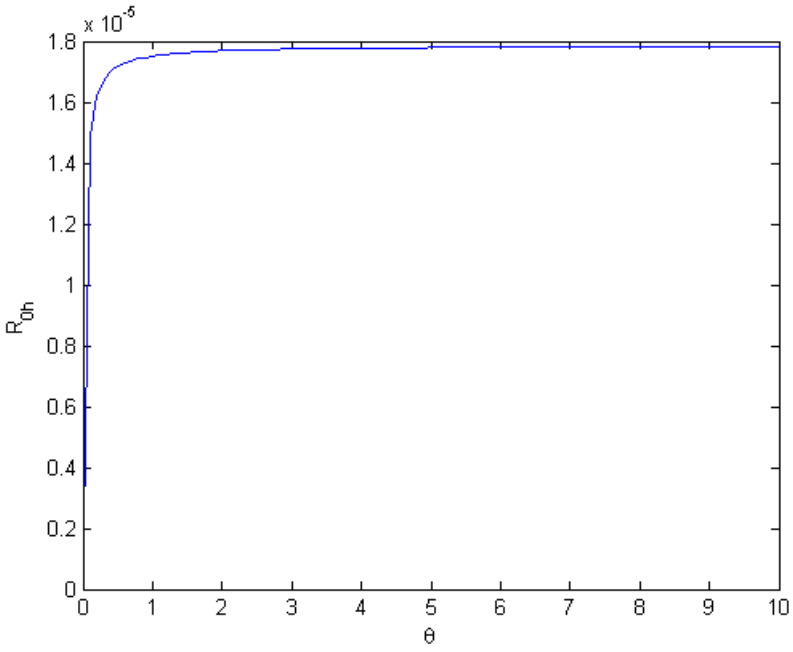

Figure 7: Plot of the human reproduction number, R_{0h} as a function of progression rate, θ Parameter values used are as in Table 2.

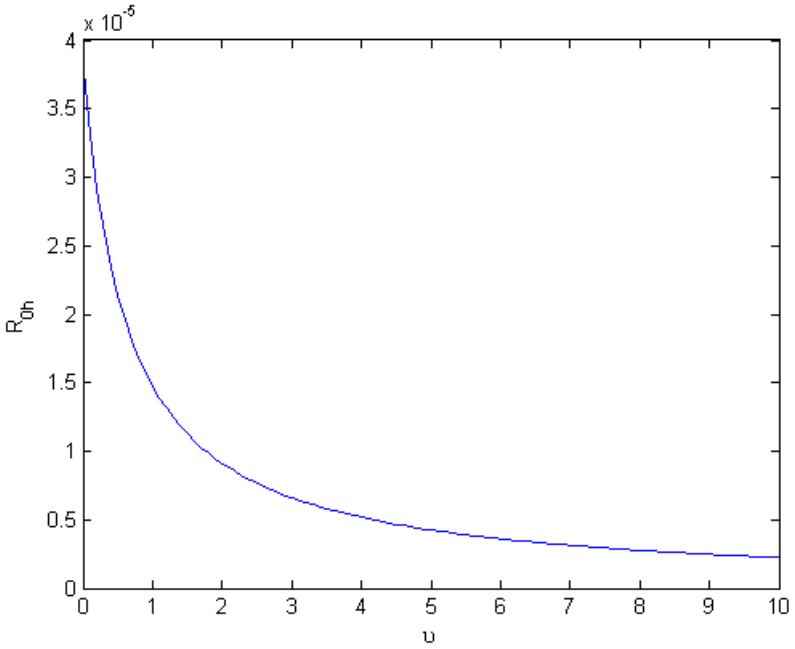

Figure 8: Plot of the human reproduction number, R_{0h} as a function of effective vaccination rate, υ Parameter values used are as in Table 2.

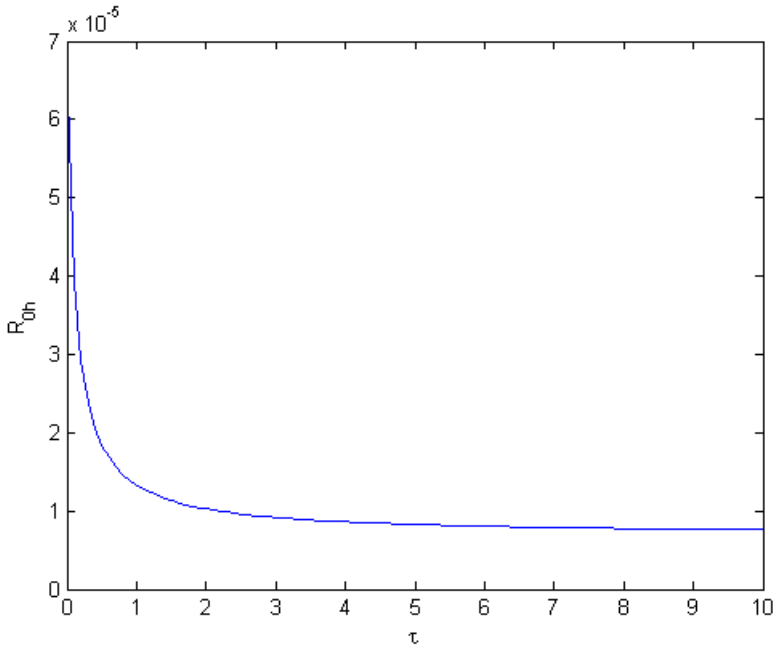

Figure 9: Plot of the human reproduction number, R_{0h} as a function of treatment rate of the symptomatic individuals, τ Parameter values used are as in Table 2.

6 Conclusion

This study presents a new deterministic mathematical model for gaining insights into the transmission dynamics of monkeypox infection in a population with treatment, vaccination and public awareness campaign as control strategies. The disease-free equilibrium (DFE) of model (4) is locally asymptotically stable whenever the associated reproduction number is less than unity. Rigorous qualitative analysis of model (4) show that it undergoes the phenomenon of backward bifurcation, where a stable DFE coexits with a stable endemic equilibrium. In a backward bifurcation situation, the effective monkeypox control is dependent on the initial sizes of the sub-population of the model. The implication is that, the presence of backward bifurcation in the transmission dynamics of monkeypox makes its control challenging. In the absence of this phenomenon (that is for the special case, $\upsilon = \omega = \phi = \beta_a = 0$ where there is only human-to-human transmission of the disease), the disease-free equilibrium of the model (4) is shown to be globally-asymptotically stable (GAS) when the associated reproduction number, $\widehat{R_0} \leq 1$. Using a non-linear Lyapunov function for the same special case as above, we showed that the unique endemic equilibrium point of the model is globally asymptotically stable when the associated reproduction number, $\widehat{R_0} > 1$. Results from the sensitivity analysis of the model, using the human reproduction number number, R_{0h}, show that, the most sensitive parameters are the monkeypox transmission rate from human-to-human (β_h), efficacy of public awareness campaign (ψ), vaccination rate for the susceptible individuals (υ), waning rate of the monkeypox vaccine (ω) and the treatment rate for the symptomatic individuals (τ). The epidemiological implication of these results is that, public awareness campaign in the population should be strenghtened by the government and other critical stakeholders in order to educate the populace on the need to be vaccinated against monkeypox infection, get to a health facility immediately when blisters show up on their body and the need to develop vaccines that will not wane within a short period of time

Numerical simulations results reveal that, increasing the rate of vaccination of the susceptible individuals, the efficacy rate of the public awareness campaign and the movement rate of the symptomatic individuals to the isolation centre for treatment, respectively, could help in the reduction of monkeypox cases in the population. So far, few mathematical models have been formulated to study the transmission dynamics, prevention and control of monkeypox. In view of this, we suggest the following extensions of our model for further study:

i. Carry out optimal control and cost-effectiveness analysis of the control strategies.

ii. Further theoretical results, such as the global asymptotic stability of the disease-free and unique endemic equilibrium, which exists for $R_{0a} > 1$ (for the special case of animal-to-human transmission), can be explored.

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Competing interests

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