Modelling the Impact of Spread of Human Papillomavirus Infections under Vaccination in Kenya

Miriam Malia, Isaac Chepkwony, and David Malonza

***Abstract* — Human Papillomavirus (HPV), a sexually transmitted virus is a collection of more than 40 types of viruses, some of which are linked to several cancers. HPV type 16 and HPV type 18 are accountable for 70% of cervical cancer cause. Besides cervical cancer, HPV has been linked to several cancers such as anal cancer, oropharyngeal cancer and neck cancer. Mathematical models have been used in the evaluation of control strategies and making of health policies. Very few mathematical models have been developed on HPV awareness in Kenya. In this study we developed a deterministic model on the impact of HPV infection under vaccination. In this model we incorporated an ineffective media awareness. We computed the equilibrium points of the model and local and global stability analysis was conducted on the reproduction number. The numerical simulation results show that the HPV infections continue to stay in the community due to the ineffective mass media awareness. Sensitivity analysis show that the infection contact rate β_1_1 and negative attitudes influencing condom use rate δ_c are parameters that contribute to the persistence of HPV infections in the community.**

***Keywords* — Human Papillomavirus (HPV), Latin Hypercube Sampling (LHS), Partial Rank Correlation Coefficient (PRCC).**

I. Introduction

Cervical cancer is the abnormal growth of cells in the cervix. It is the 2nd highest frequent cancer after breast cancer among women in Kenya [1]. It has caused an estimated 46000 deaths in women aged 15-49 years in developing countries [1]. Cervical cancer is caused by a virus called Human papillomavirus (HPV). There are about 40 types of HPV [2]. These are classified as high-risks as they are oncogenic that is cancer causing and low risk strains which are non-oncogenic. The high-risk strains of HPV are 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 66 [1]. HPV 16 and 18 are accountable for 90% of cervical cancer cause [3]. HPV 16 is also found in 90% of neck and head related cancers [4]. HPV infections are asymptomatic and may clear within one year, especially if the host has a strong immune system but some persist for decades and result in cancer cells [5]. Mass media is any mode of transmitting information so it gets to as many people as possible. There are four categories of mass media which include print media, broadcast media, outdoor media and digital media [6]. Controlling the spread of HPV to minimize the increase in infections is a crucial mandate in the health sector. This can be attained by getting vaccinated and effective media awareness [7]. The media campaigns will educate people about HPV, the diseases that it causes and how one can contract it. Research studies done on media awareness and healthy behavior have found out that media awareness bring forth a good change in behavior and even put a stop to undesirable behavior change in people [8].It has also been observed that the details and facts about a disease passed on by the media is a crucial factor that ascertains if an immunization campaign will be successful or not [9]. Pervasive broadcasting of societal challenges by the media could result to desensitization to media reports that is a decreased reaction to a detrimental stimulus after frequent exposure [10]. Reference [11] analysed the effect of media crusades on the transmission of illness in a population that kept fluctuating due to migration. They modelled media awareness as a separate compartment. This model showed that the disease-fee equilibrium is stable when the reproduction number R_o<1 and becomes unstable when R_0>1.Their analysis showed that endemic equilibrium was locally and also nonlinearly stable under defined circumstances. They concluded that the media awareness crusades are valuable in reducing the transmission of infectious diseases by secluding a proportion of susceptible from those infected. Reference [12] did research on the repercussions of media coverage on the transmission of influenza. They proposed a deterministic transmission and

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vaccination model where the population was divided into different categories depending on their disease status. In the model they included the impact of media coverage on reporting the number of infections together with the number of people vaccinated successfully. They found out that the media can set off an immunization fear if the vaccine is flawed and messages that were simplified resulted to the immunized interacting with the infected with no concern to disease risk. They concluded that simplified understandings of disease epidemiology propagated through media, make the spread of the epidemic worse. Reference [13] presented a study on the analysis of interrelation between two processes accounting for the spreading of a disease and the spreading of information awareness to prevent its infection. They included immunization and presence of a mass media awareness in their model. They found out that the immediacy of awareness when infected has no effect on the dynamics; the other two factors namely degree of immunization of aware individuals and mass media did change the critical aspects of disease spreading. Reference [14] investigated how the spread of awareness caused by a first-hand contact with a disease affects the spread of the disease. They showed that in a social network, the spread of awareness and the resulting reduction in susceptibility doesn't lower the incidence of the disease but in some cases can prevent onset of epidemics implying that awareness can act as an effective measure of disease control. Reference [15] conducted a study to compare two strategies for controlling the spread of HPV in the American population. The research is conducted via a cost analysis of a mandatory vaccination policy with individual-based awareness versus a voluntary vaccination with a mass media awareness campaign. For the latter strategy they modelled it as compartments for aware and unaware individuals in each disease state. They came to the conclusion that a high transmission rate and a high reproduction rate require a high efficacy of media awareness and high vaccine coverage to eliminate the HPV virus. A research study on the impact of awareness on dynamics of infectious diseases was carried out by [16]. They divided the overall population into six compartments: unaware susceptible, unaware infected, unaware recovered, aware susceptible, aware infected and aware recovered. They included two types of awareness in the model namely private awareness and public awareness. The private awareness was associated with direct contacts between unaware and aware populations whereas public awareness involved mass media awareness campaigns. The results obtained showed that both private and public awareness have the capacity to reduce the spread of disease by increasing the threshold for onset of a stable endemic steady state characterized by persistent infection. The faster people lose awareness (that is the larger is the unaware population), the higher is the overall rate of infection as manifested by the disease endemic state. The presence of awareness causes corresponding behavioral change in the population which in turn causes the reduction in the size of disease outbreaks. The spread of private awareness or public awareness helps to control or minimize the spread of diseases. A number of mathematical models have been proposed to analyse the effects of information and awareness on the spread of epidemics. Some of these models have modelled awareness explicitly as a separate compartment while others have incorporated it as a direct modification of the disease transmission rate [16].

To the best of the author's knowledge, very limited attention has been given to study the impact of HPV infections under vaccination in Kenya. Therefore, motivated by the above studies, this paper is focused on that. We use a slightly different approach used by [16] where we introduce distinct compartments for unaware and aware individuals in susceptible, infected and vaccinated disease states. In this paper, we propose a deterministic model on the impact of HPV infections under vaccination in Kenya in the presence of an ineffective mass-media awareness.

II. Model Formulation

We formulate a deterministic model with seven compartments. These are: S-Susceptibles,individuals who do not have the infection and are unaware of the infection, S_a −Individuals who don't have the infection but are aware of existence of HPV infection,V_a −Individuals who are vaccinated and aware,V −Individuals who are vaccinated and have no awareness as it has worn off, I −Infected, they have the infection and are unaware of the infection, I_a −Infected and aware, T −Treatment, they undergoing treatment. In the susceptible class S we have persons joining at the rate Λ the natural birth rate and they are unaware of HPV infections as they haven't heard of it. Some of the susceptible become aware about the disease from the media, seek treatment options such as undergoing for cancer screenings and they join S_a at the rate $\phi_2 T$.The ones who responded to the media awareness campaigns get themselves vaccinated and join class V_a at the rate γ. Once this awareness "wears off", some women will move to the V class at the rate λ_1 and back to V_a at the rate ϕ_1. We also assume that some susceptibles heeded to the media campaigns and they reduced sexual activity (have one faithful partner), however they did not get vaccinated perhaps because they cannot afford the cost of the vaccine hence, they remain in S_a. Once the awareness wears off, the aware susceptibles move back to class S at the rate λ_2. Those who are neither vaccinated nor aware may get infected through interactions with people from both the classes I and I_a ; and they move to I class at

the rate β. The aware susceptible S_a also may get infected and move to I at the rate β. The incidence contact rate β are given as

$$\beta = \frac{\beta_1(I+\delta_c I_a)}{N} \quad (1)$$

where β_1 is the average contact rate and δ_c is the negative attitudes towards condom use rate.

Condom use rate reduces the spread of the disease by the individuals in I_a. However due to negative attitudes affecting efficacy of condom use by the aware infected, they help move the susceptibles to the infected compartment. These negative attitudes include religion and peer influence [17]. The infected who become aware move to class I_a. Once the awareness wears off, they may revert to doing the practices that encourage further spread of the HPV infections thus they move back to class I. From the ongoing media campaigns, those infected in class I_a may go to hospitals to get screened for cancer. If they happen to have cancer and it is detected early, they proceed to class T at the rate τ_1. If they die from the HPV infection then they leave the infected class at rate α. All individuals that die from natural death leave the classes at the rate μ. HPV virus has no cure. However, the disease/ infections that arise from HPV, their manifestations can be treated for a better quality of life. Therefore, the treatment class is for treating the disastrous manifestations of HPV and not cure it. Once these manifestations of HPV are treated, the individuals recover and move back to class I_a at the rate τ_2.

A. Model Equations

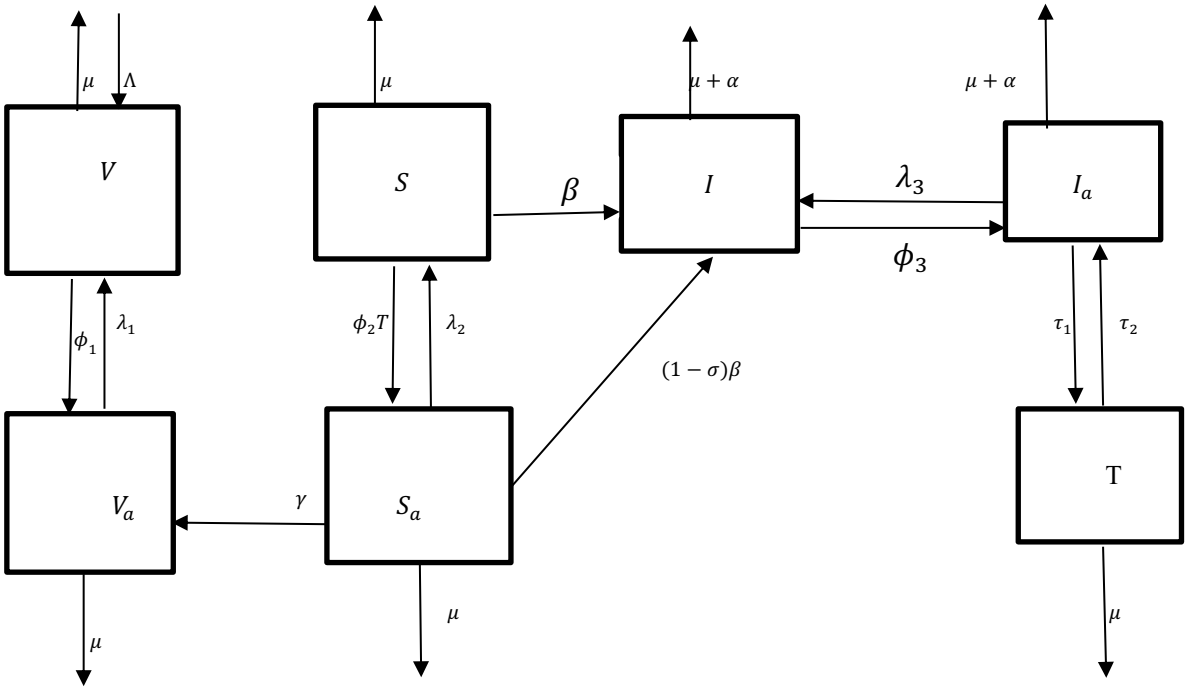

Fig.1. Flow chart of HPV infections under vaccination.

B. Model Assumptions

The assumptions for this model are:

- There is a homogeneous mixing of people and individuals become infected with HPV after contact with a person from the infected classes.
- There is a vaccination programme being carried out by the government.
- When an individual who does not have the HPV infection is vaccinated, they automatically become immune to the virus. Vaccinating infected individuals gives no immunity to the virus.
- HPV infections that we deal with in this research are the ones caused by HPV 16 and 18.
- The ongoing mass-media awareness is not effective ($\sigma = 0$) thus some aware susceptibles get infected with HPV and join the infected class.
- The population in model is restricted to a female population.

The equations that describe this model are:

$$\frac{dS}{dt} = \Lambda + \lambda_2 S_a - \phi_2 TS - \beta S - \mu S$$
$$\frac{dS_a}{dt} = \phi_2 TS - \beta S_a - \eta_1 S_a$$
$$\frac{dI}{dt} = \beta S + \beta S_a + \lambda_3 I_a - \eta_2 I$$

$$\frac{dI_a}{dt} = \phi_3 \mathrm{I} + \tau_2 \mathrm{T} - \eta_3 I_a \quad (2)$$
$$\frac{dV}{dt} = \lambda_1 V_a - \eta_4 V$$
$$\frac{dV_E}{dt} = \gamma S_a + \phi_1 V - \eta_5 V_a$$
$$\frac{dT}{dt} = \tau_1 I_a - (\mu + \tau_2) T$$

where we let $\eta_1 = \lambda_2 + \gamma + \mu$, $\eta_2 = \phi_3 + \mu + \alpha$, $\eta_3 = \lambda_3 + \tau_1 + \mu + \alpha$, $\eta_4 = \phi_1 + \mu$ and $\eta_5 = \lambda_1 + \mu$.

III. Positivity of Solutions

We use the theorem below to show the positivity of the model

Theorem 3.3.2. Let the initial data be given as $\{S(0) > 0, S_a(0) > 0, I(0) > 0, I_a(0) > 0, V(0) > 0, V_a(0) > 0, T(0) > 0\}$. Then the solutions of the model system (4.1) are nonnegative for all $t > 0$.

Proof

We begin with our first equation of model system (2) which is given by

$$\frac{dS}{dt} = \Lambda + \lambda_2 S_a - \phi_2 TS - \beta S - \mu S$$

With $\lambda_2 S_a \geq 0$ for all $t \geq 0$ and thus the above equation becomes

$$\frac{dS}{dt} \leq \Lambda - \phi_2 TS - \beta S - \mu S \quad (3)$$

(3) can be rewritten as

$$\frac{dS}{dt}\left\{S(t) exp\left[\left(\int_0^{t_1}\left(\beta(\zeta) + \phi_2 T(\zeta)\right)d\zeta + \mu t\right)\right]\right\} \leq \Lambda \exp\left[\int_0^{t_1}(\beta(\zeta) + \phi_2 T(\zeta) d\zeta + \mu t\right] \quad (4)$$

Hence

$$S(t) < S(0)\exp\left[-\int_0^{t_1}(\beta(\zeta) + \phi_2 T(\zeta) d\zeta + \mu t_1\right] + \exp\left[-\left(\int_0^{t_1}(\beta(\zeta) + \phi_2 T(\zeta) d\zeta + \mu t_1\right)\right]\left[\int_0^{t_1} \Lambda \exp\left[\left(\int_0^{p}(\beta(\zeta) + \phi_2 T(\zeta) d\zeta + \mu p\right)\right] dp\right] > 0 \quad (5)$$

Since the right-hand side of (5) was positive, the solution $S(t)$ would always remain positive for all $t > 0$. Similarly, it can be shown that S_a, I, I_a, V, V_a, T are positive for all $t > 0$. This completes our proof.

IV. HPV Reproduction Number

From the model system (2) we consider the infectious compartments below.

$$\frac{dI}{dt} = \beta S + \beta S_a + \lambda_3 I_a - (\phi_3 + \mu + \alpha) I$$
$$\frac{dI_a}{dt} = \phi_3 \mathrm{I} - (\lambda_3 + \tau_1 + \mu + \alpha) I_a \quad (6)$$

Using the notation in [18], the matrices that represent new cases of infections,F and transfer of infections, V are given by

$$F = \begin{pmatrix} \frac{\beta_1 \Lambda}{\mu} & \frac{\beta_1 \delta_c \Lambda}{\mu} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} \eta_2 & -\lambda_3 & 0 \\ -\phi_3 & \eta_3 & 0 \\ 0 & -\tau_1 & (\mu + \tau_2) \end{pmatrix}$$

The reproduction number is the largest eigen value of the matrix FV^{-1} and that is

$$R_0 = \frac{\beta_1 \Lambda(\eta_3 + \delta_c \phi_3)}{\mu(\eta_2 \eta_3 - \lambda_3 \phi_3)} \quad (7)$$
$$R_0 = R_I + R_{I_a}$$

R_I is the reproduction number of the infected individuals and R_{I_a} is the reproduction of the infected aware individuals where $R_{I_a} = \frac{\Lambda \beta_1 \delta_c \phi_3}{\mu \eta_2 \eta_3 (1-\kappa)}$, $R_I = \frac{\Lambda \beta_1}{\mu \eta_2 (1-\kappa)}$ and $\kappa = \frac{\lambda_3}{(\lambda_3 + \tau_1 + \mu + \alpha)} \frac{\phi_3}{(\phi_3 + \mu + \alpha)}$.

V. HPV Free Equilibrium Points and Its Stability

We determined the HPV free equilibrium point as $H^0 = \left(\frac{\Lambda}{\mu}, 0,0,0,0,0,0\right)$.

Theorem 1: The HPV free equilibrium H^0 is locally asymptotically stable if $R_0 < 1$.

Proof

The Jacobian matrix of the system of equations (1) at H^0 is given as,

$$J_{H'} = \begin{bmatrix} -\mu & \lambda_2 & -\frac{\beta_1\Lambda}{\mu} & -\frac{\beta_1\Lambda\delta_c}{\mu} & 0 & 0 & -\frac{\phi_2\Lambda}{\mu} \\ 0 & -\eta_1 & 0 & 0 & 0 & 0 & -\frac{\phi_2\Lambda}{\mu} \\ 0 & 0 & \frac{\beta_1\Lambda}{\mu} - \eta_2 & \frac{\beta_1\Lambda\delta_c}{\mu} + \lambda_3 & 0 & 0 & 0 \\ 0 & 0 & \phi_3 & -\eta_3 & 0 & 0 & \tau_2 \\ 0 & 0 & 0 & 0 & -\eta_4 & \lambda_1 & 0 \\ 0 & 0 & 0 & 0 & \phi_1 & -\eta_5 & 0 \\ 0 & 0 & 0 & \tau_1 & 0 & 0 & -(\mu+\tau_2) \end{bmatrix}$$

The characteristic polynomial of the matrix J_{H^0} is given by;

$$b^3 + C_1 b^2 + C_2 b + C_3 = 0 \tag{8}$$

$$C_1 = -\frac{\beta_1\Lambda}{\mu} + \eta_2 + \eta_3 + \eta_4$$

$$C_2 = -\frac{\beta_1\Lambda}{\mu}\eta_3 - \frac{\beta_1\Lambda}{\mu}\eta_4 + \eta_2\eta_3 + \eta_2\eta_4 + \eta_3\eta_4 - \frac{\beta_1\Lambda\delta_c\phi_3}{\mu} - \phi_3\lambda_3$$

$$C_3 = -\frac{\beta_1\Lambda\eta_3\eta_4}{\mu} + \eta_2\eta_3\eta_4 - \frac{\beta_1\Lambda\delta_c\phi_3\eta_4}{\mu} - \lambda_3\phi_3\eta_4$$

Rewriting C_3 in terms of R_0 we obtain,

$$C_3 = \eta_2\eta_3\eta_4 - \lambda_3\phi_3\eta_4 - \frac{\beta_1\Lambda\eta_3\eta_4}{\mu} - \frac{\beta_1\Lambda\delta_c\phi_3\eta_4}{\mu} = \eta_4(1 - R_0) \tag{9}$$

We use Routh-Hurwitz criterion to determine the conditions for the roots of (7) to have negative eigen values. The Routh—Hurwitz criterion of stability of HPV free equilibrium is given by

$$D_1 = C_1 \qquad D_2 = \begin{pmatrix} C_1 & 1 \\ C_3 & C_2 \end{pmatrix} \qquad D_3 = \begin{pmatrix} C_1 & 1 & 0 \\ C_3 & C_2 & C_1 \\ 0 & 0 & C_3 \end{pmatrix} \tag{10}$$

$$D_1 = -\frac{\beta_1\Lambda}{\mu} + \eta_2 + \eta_3 + \eta_4$$

$$D_2 = C_1C_2 - C_3 = \left(-\frac{\beta_1\Lambda}{\mu} + \eta_2 + \eta_3 + \eta_4\right)\left(-\frac{\beta_1\Lambda}{\mu}\eta_3 - \frac{\beta_1\Lambda}{\mu}\eta_4 + \eta_2\eta_3 + \eta_2\eta_4 + \eta_3\eta_4 - \frac{\beta_1\Lambda\delta_c\phi_3}{\mu} - \phi_3\lambda_3\right) - (\eta_4(1 - R_0))$$

$$D_3 = C_1C_2C_3 - C_3^2 = \left(-\frac{\beta_1\Lambda}{\mu} + \eta_2 + \eta_3 + \eta_4\right)\left(-\frac{\beta_1\Lambda}{\mu}\eta_3 - \frac{\beta_1\Lambda}{\mu}\eta_4 + \eta_2\eta_3 + \eta_2\eta_4 + \eta_3\eta_4 - \frac{\beta_1\Lambda\delta_c\phi_3}{\mu} - \phi_3\lambda_3\right) - \eta_4^2(1 - R_0)^2$$

The above result shows that we have $D_2 > 0, D_3 > 0$ if and only if $R_0 < 1$. Thus, we conclude that the HPV free equilibrium is locally asymptotically stable whenever $R_0 < 1$. This theorem implies that if $R_0 < 1$ it means that every individual infected can pass the HPV infection to less than one new person hence the HPV infection cannot develop in the population.

The global stability of HPV free equilibrium of system (1) is investigated using the Castillo-Chavez approach [19] which is described in the theorem below.

Theorem 2: The HPV free equilibrium point $H^0 = (X^0, 0) = (\frac{\Lambda}{\mu}, 0,0,0,0,0,0)$ of model 1 is globally asymptotically stable if

$R_0 < 1$ and the following conditions are satisfied;

1. $\frac{dX}{dt} = F(X, 0)$, X^0 is globally asymptotically stable.
2. $G(X, Z) = AZ - \hat{G}(X, Z)$, $G(X, Z) \geq 0$

for $(X, Z) \in R_+^7$ where $A = D_Z G(X, Z)$ is an M-matrix (the off diagonal element of A is non-negative) and R_+^7 is the region where the equations of the model make epidemiological sense.

Proof

The system of equations (1) is written as

$$\frac{dX}{dt} = F(X, Z), \ \frac{dZ}{dt} = G(X, Z), \ G(X, 0) = 0 \tag{11}$$

Where $X = (S, S_a, V, V_a)$ represents the HPV free classes and $Z = (I, I_a, T)$ are the HPV infected classes. $\frac{dX}{dt} = F(X, 0)$ can be written as $\frac{dS}{dt} = \Lambda - \mu S$. Thus, we have,

$$\Lambda - \mu S(t) = [\Lambda - \mu S(0)]e^{-\mu t} \tag{12}$$

$$S(t) = \frac{[\Lambda - \mu S(0)]e^{-\mu t}}{\mu}, \ S(t) \to \frac{\Lambda}{\mu} \quad \text{as} \ \ t \to \infty$$

Hence condition (1) is satisfied consequently. For the second condition we have,

$$\hat{G}(X, Z) = AZ - G(X, Z) \tag{13}$$

where $G(X, Z) = \begin{pmatrix} \beta S + \lambda_3 I_a - \eta_2 \\ \phi_3 I - \eta_3 I_a \\ \tau_1 I_a - (\mu + \tau_2)T \end{pmatrix}$ $\qquad AZ = \begin{pmatrix} (\beta_1 S^0 - \eta_2)I + (\beta_1\delta_c S^0 + \lambda_3)I_a \\ \phi_3 I - \eta_3 I_a \\ \tau_1 I_a - (\mu + \tau_2)T \end{pmatrix}$

$$\hat{G}(X,Z)=\begin{pmatrix}\beta_1(I+\delta_c I_a)(S^0-S)\\0\\0\end{pmatrix}=\begin{pmatrix}\beta_1(I+\delta_c I_a)(1-\frac{S}{S^0})\\0\\0\end{pmatrix}=\begin{pmatrix}\beta_1(I+\delta_c I_a)(1-\frac{S}{N})\\0\\0\end{pmatrix} \quad (14)$$

Since $S\le N, \frac{S}{N}\le 1$ then it is clear that $\hat{G}(X,Z)\ge 0$. Thus condition 2 is satisfied. Therefore, the HPV free equilibrium point is globally asymptotically stable. The epidemiological indication of HPV free equilibrium being asymptotically stable means that the HPV infections will be eliminated from the community if the reproduction number is reduced to and /or maintained at a value below one.

VI. HPV Endemic Equilibrium Points and Its Stability

The HPV endemic equilibrium point $E'=(S^*,S_a^*,I^*,I_a^*,V^*,V_a^*,T^*)\ is$ obtained by equating the right hand side of (2) to zero and solving it in terms of I^*. Thus, we have;

$$\begin{aligned}
I_a^* &= \frac{\phi_3(\mu+\tau_2)}{\eta_3(\mu+\tau_2)-\tau_2\tau_1}I^*\\
T^* &= \frac{\tau_1}{\mu+\tau_2}I_a^*\\
S_a^* &= \frac{\phi_2\Lambda T^*}{(\beta_1 I^*+\beta_1\delta_c I_a^*+\eta_1)(\phi_2 T^*+\beta_1 I^*+\beta_1\delta_c I_a^*+\mu)-\lambda_2\phi_2 T^*}\\
S^* &= \frac{(\beta_1 I^*+\beta_1\delta_c I_a^*+\eta_1)\Lambda}{(\beta_1 I^*+\beta_1\delta_c I_a^*+\eta_1)(\phi_2 T^*+\beta_1 I^*+\beta_1\delta_c I_a^*+\mu)-\lambda_2\phi_2 T^*}\\
V^* &= \frac{\lambda_1\gamma\phi_2\Lambda T^*}{(\eta_4\eta_5-\phi_1\lambda_1)[(\beta_1 I^*+\beta_1\delta_c I_a^*+\eta_1)(\phi_2 T^*+\beta_1 I^*+\beta_1\delta_c I_a^*+\mu)-\lambda_2\phi_2 T^*]}\\
V_a^* &= \frac{\eta_4\gamma\phi_2\Lambda T^*}{(\eta_4\eta_5-\phi_1\lambda_1)[(\beta_1 I^*+\beta_1\delta_c I_a^*+\eta_1)(\phi_2 T^*+\beta_1 I^*+\beta_1\delta_c I_a^*+\mu)-\lambda_2\phi_2 T^*]}
\end{aligned} \quad (15)$$

Substituting the solutions of the variables in (15) into the third equation of (2) we obtain;

$$A_3 I^{*2}+A_2 I^*+A_1=0 \quad (16)$$

$$A_3=\mu\beta_1(\eta_3+\delta_c\phi_3)\big(\phi_2\tau_1\phi_3+\mu\eta_3(\beta_1(\eta_3+\delta_c\phi_3)+1)\big)(\eta_2\eta_3+\lambda_3\phi_3)$$

$$A_2=\beta_1(\eta_3+\delta_c\phi_3)\big(\mu\eta_3\Lambda\beta_1(\eta_3+\delta_c\phi_3)+\Lambda\tau_1\phi_3\phi_2+\mu(\eta_2\eta_3-\lambda_3\phi_3)\big)+(\tau_1\phi_3\phi_2+\mu\eta_3\beta_1((\eta_3+\delta_c\phi_3)+1))\mu\eta_3(\lambda_3\phi_3-\eta_2^2)$$

$$A_1=\Big(\eta_1\beta_1\Lambda(\eta_3+\delta_c\phi_3)-\frac{\lambda_2\phi_2\tau_1\phi_3}{\mu}\Big)(1-R_0)$$

We observe that $A_1>0$ when $R_0<1$, $A_1=0$ when $R_0=1$ and $A_1<1$ when $R_0>1$.When $A_1<0$, $\Delta=A_2^2-4A_3A_1>0$ the polynomial (15) has a unique positive solution. Consequently, system (1) has a unique HPV endemic equilibrium. On the other hand, when $R_0<1$ then $A_1>0$ and bringing another condition that $A_2<0$ and $\Delta>0$, it results to two positive real roots suggesting the existence of two positive equilibria. If $R_0=1$, and $A_1=0$ then there exists a unique positive non-zero root of the polynomial (15) if and only if $A_2<0$. Thus, we have the following on the existence of endemic equilibria of the model;

i) If $R_0>1$ then the system (1) has a unique HPV endemic equilibrium (14) which is unstable.

ii) There is no HPV endemic equilibrium if $R_0<R_0^c$ where R_0^c is the critical R_0 and is given by

$$R_0^c=1-\frac{A_2^2}{4A_3\Big(\eta_1\beta_1\Lambda(\eta_3+\delta_c\phi_3)-\frac{\lambda_2\phi_2\tau_1\phi_3}{\mu}\Big)} \quad (16)$$

R_0^c is obtained after equating the discriminant $\Delta=0$ and making $R_0$the subject of the equation.

iii) There are two HPV endemic equilibrium if $A_2<0$ and $\Delta>0$.

iv) If $R_0<1$ then the system (1) has an HPV free equilibrium which is locally asymptotically stable.

We use the center manifold theory as described in [21] to investigate the nature of bifurcation. We find that the model undergoes a forward bifurcation at $R_0=1$.

VII. Results

We present the numerical simulations of the model system (2) in this section. We use MATLAB software and the parameters in Table I to come up with the numerical simulations.

TABLE I: Parameters and Their Description

Parameter	Description	Value	Source
Λ	Natural birth rate	0.02639	[20]
μ	Natural mortality rate	0.00501	[20]
τ_1	Rate at which aware infected individual seeks treatment.	0.035	[21]
τ_2	Rate at which an individual recover.	0.0028	Assumed
γ	Vaccination rate.	0.25	[22]
β_1	Infection contact rate.	0.000194	[22]
δ	Death rate due to HPV infection	0.61	[22]
ϕ_1	Rate at which vaccinated individuals become aware.	0.045	Assumed

TABLE I: PARAMETERS AND THEIR DESCRIPTION *(CONT)*

ϕ_2	Rate at which a susceptible individual becomes aware.	0.035	Assumed
ϕ_3	Rate at which an infected individual becomes aware.	0.035	Assumed
λ_1	Rate at which vaccinated individuals lose awareness	0.65	Assumed
λ_2	Rate at which susceptible individuals lose awareness	0.055	Assumed
λ_3	Rate at which infected individuals lose awareness	0.075	Assumed
δ_c	Negative attitude rates influencing condom use rates.	0.36	[23]
σ	Efficiency of awareness.	0-1	Assumed

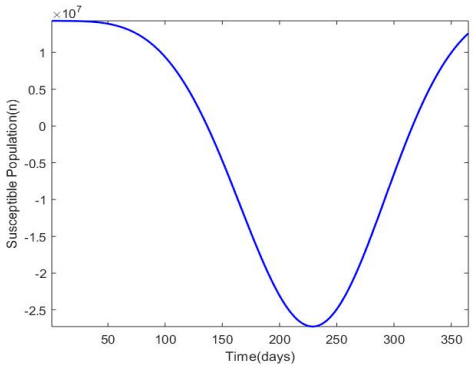

Fig. 2. Susceptible population.

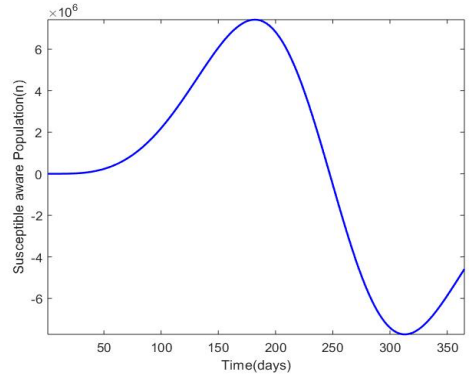

Fig. 3. Susceptible aware population.

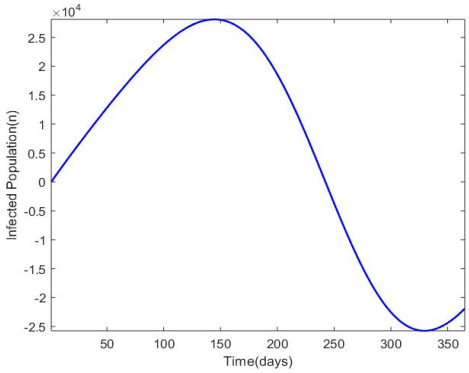

Fig. 4. Infected Population.

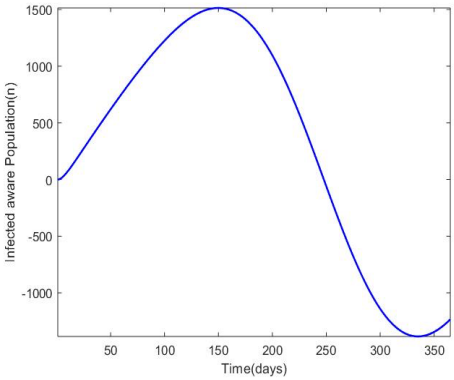

Fig. 5. Infected Aware Population

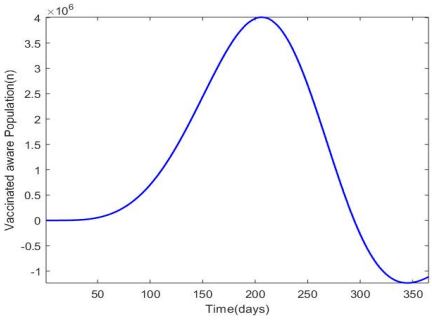

Fig. 6. Vaccinated aware population.

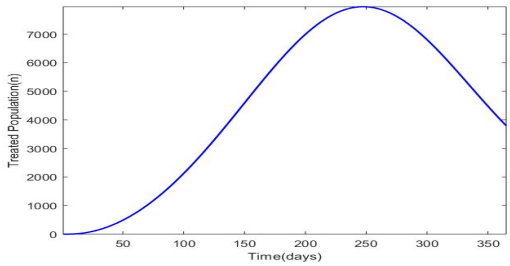

Fig. 7. Treated population.

Fig. 2 represents susceptible population over time. The population decreases at first then it increases again. This is because this population is joining the susceptible aware class hence the decreasing number and it increases as the susceptible aware population is reverting back to the susceptible class as they have forgot the awareness they had acquired earlier on.

Fig. 3 represents the susceptible aware population which increases steadily for a few days then decreases for about a hundred days then increases again. The increase is due to the movement from the susceptible class to the susceptible aware class as a result of the media awareness about the virus. It decreases as a result of the susceptible aware getting vaccinated and also losing their awareness hence moving back to the susceptible class. It increases again because the susceptibles become aware about the virus since the media awareness is ongoing thus move back to susceptible aware class.

Fig. 4 represent the infected population which increases in the first one hundred and fifty days. This is due to susceptibles who are becoming infected as the media awareness has not caught up with them. The population then decreases for the next a hundred and sixty days and then increases again. This is because the infected population join the infected aware group after the media awareness. However, it increases again as the infected aware group rejoin the infected class.

Fig. 5 shows the infected aware population increases in the then reduces afterwards and then increases again. The increase is due to the influx of the infected people joining the infected aware population. The reduction is due to the infected aware group is joining the treatment class as they are seeking for treatment options as the media awareness campaigns encourage that. The other reason this population is decreasing is due to ineffective media awareness so they are going back to the infected class as the awareness has worn out. It increases again as the infected become aware about the virus through the ongoing media awareness therefore join the infected aware population.

Fig. 6 shows the vaccinated educated population which increases in the next two hundred days and then decreases. This is because at first the aware susceptibles are getting themselves vaccinated against HPV as the media awareness campaigns are encouraging that. However, the population decreases due to the ineffective media awareness (for instance misinformation about the vaccine) as the numbers of susceptibles getting vaccinated goes down.

Fig. 7 represents the population undergoing treatment. This population increases in the next two hundred and fifty days and this is because majority of the infected aware individuals are going to hospitals to seek for treatment options. After the two hundred and fifty days this population decreases as the awareness about the disease has worn out due to ineffective campaigns as a result, they are not seeking treatment options.

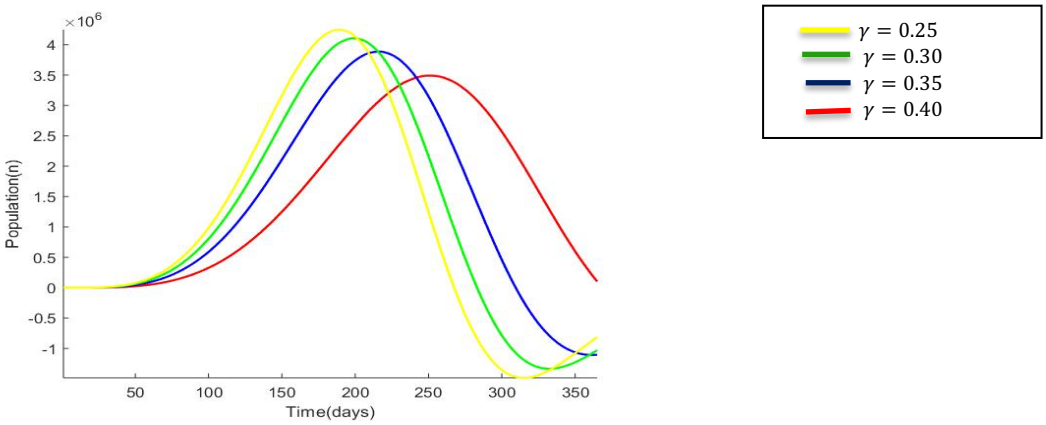

Fig.8. Effect on population on varying the rates of vaccination.

In Fig. 8 we observe the effect on the population upon increasing the rate of vaccination from 0.25, 0.30, 0.35, 0.40. Increasing the rate of vaccination leads to an increasing number of girls and women who get themselves vaccinated against HPV in the first few days. Despite this, the number of vaccinated individuals started to decrease later and this is attributed to there being an ineffective media awareness.

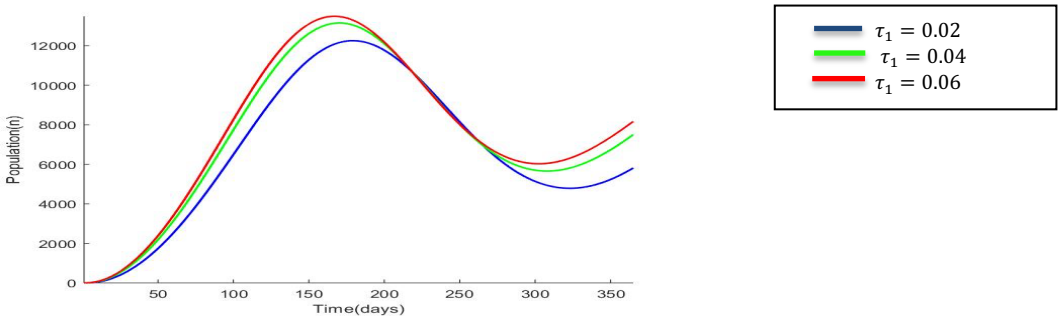

Fig. 9. Simulation results on varying rate of treatment on population.

Fig. 9 is produced as a result of variation of the rate of treatment on the population. We observe that increasing this rate leads to more people seeking treatment in the initial days. However, this number decreases in the coming latter days and this is due to the presence of an ineffective media awareness. Table II shows the sensitivity indices of parameters in the reproduction number.

VIII. Sensitivity Analysis

Sensitivity analysis is performed on the parameters of the model in an effort to determine the critical parameters that influence the model outcome [24]. In order to achieve this, we use the Latin Hypercube Sampling/Partial Rank Correlation Coefficient method. The results presented in Table II show that τ_1, the rate of seeking treatment is a critical parameter that is contributing the most variability in R_0. The infection contact rate β_1, the negative attitudes influencing the condom use rates δ_c are also influential parameters in the variability of R_0. Therefore, the parameters λ_3, β_1 and δ_c have the capability to make HPV infections

increase. To the contrary, the rate of seeking treatment τ_1,the rate of gaining awareness among the infected ϕ_3 and rate of getting vaccinated γ parameters have capability of controlling HPV infections spread when increased.

TABLE II: SENSITIVITY INDICES OF THE REPRODUCTION NUMBER AGAINST MENTIONED PARAMETERS

Parameter	Sensitivity index value	Parameter	Sensitivity index value
Λ	0.023621359	λ_3	0.526416351
β_1	0.894672530	α	0.289106381
μ	-0.219143113	δ_c	0.621808964
ϕ_3	-0.428736542	τ_1	-0.732723659

IX. CONCLUSION

This paper has analysed the impact of HPV infections under vaccination in Kenya. We incorporated movement from the susceptible aware class to infected class. This movement was to show that the mass media awareness campaigns were ineffective. We carried out an analysis on the model in regards to the invariant region and we concluded that the solutions of the model were uniformly bounded in the region Ω for all future time. The reproduction number of the model was determined and it represented the sum of the reproduction number of infected individuals R_I and of infected aware individuals R_{I_a}. We performed a stability analysis on the equilibrium points of the model. The HPV free equilibrium point for this model was locally asymptotically stable and globally asymptotically stable when $R_0 < 1$. The endemic equilibrium point for this model was found to exist under several conditions. If $R_0 > 1$, then the HPV endemic equilibrium was unique and unstable; if $R_0 < 1$ then the HPV endemic equilibrium was locally asymptotically stable. The nature of bifurcation was investigated using Castillo-Chavez theory. It was concluded that the model 1 has a forward bifurcation at $R_0 = 1$. The sensitivity analysis using LHS-PRCC show that the infection contact rate β_1 and negative attitudes influencing condom use rate δ_c are parameters that contribute to the persistence of HPV infections in the community. From the numerical simulation results, we conclude that the HPV infections continue to stay in the community due to the ineffective mass media awareness campaigns. The results presented in Fig. 7 and Fig. 8 showed the impact of vaccination and treatment on HPV infections. The simulations showed that increasing treatment levels and vaccination rates results to a reduction in the number of infected people and an increase in the number of vaccinated people respectively. Sensitivity analysis also confirms that increasing τ_1 the rate of treatment would help control HPV infections spread. In the future, the authors would like to extend the system (2) by considering an effective mass media awareness variable to control the spread of HPV infection in the community.

CONFLICT OF INTEREST

Authors declare that they do not have any conflict of interest.

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