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Modelling the Impact of an Effective Mass Media Awareness Campaigns on the Spread of HPV Infections

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Abstract

Cancer is a menace to public health globally. Human Papillomavirus (HPV) is a sexually transmitted virus and has been linked to several cancers such as cervical cancer, anal cancer, oropharyngeal cancer and neck cancer. In this research a mathematical model based on a system of ordinary differential equations is formulated to study the impact of an effective mass media awareness campaigns on the spread of HPV infections under vaccination in Kenya. The basic reproduction number is computed using the next generation matrix method. The equilibrium points of the model are determined and their stability investigated. The results of stability analysis show that the HPV free equilibrium is locally asymptotically stable when $R_0 < 1$ and the endemic equilibrium point existed if $R_0 < 1$. We used the center manifold theory to investigate the nature of bifurcation. The investigation identified that the bifurcation parameter θ changes from negative to positive, changes its stability from stable to unstable thus a negative unstable equilibrium becomes positive and locally asymptotically stable. Sensitivity analysis shows that the prevalence of HPV infection can be reduced by reducing the contact rate between the susceptibles and infected β, increasing the rate of treatment τ_1 and increasing vaccination rate γ. Moreover, the relapse from the susceptible aware and infected aware to susceptible and infected classes respectively that is λ_2 and λ_3 respectively increase the spread of HPV in the community. The results from the numerical simulations validated the fact that an effective mass media awareness campaigns brought the numbers of HPV infections to equilibrium.

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Keywords: Human papillomavirus; mass-media awareness; reproduction number; sensitivity analysis;, bifurcation; numerical simulation.

1 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]. 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]. Human Papilloma Virus is highly transmissible and is now thought as the most occurring sexually transmitted infection (CDC, 2011a). It is generally passed on from one individual to another through intimate skin-to-skin contact and not through body fluids. Advancement of HPV infection to cervical cancer takes long time that is more than 25 years. Technically this slow pace of progression provides a chance for early diagnosis [5]. There are three HPV vaccines which are present on the market now. They are namely Gardasil, Gardasil 9 and Cervarix [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. It will also educate people on the methods of protecting themselves from this infection that is through using condoms and having faithful sexual partner [8]. In addition to these it will educate people about the several factors that lead HPV infections to progress to cancer; these factors include prolonged use of contraceptives, smoking of tobacco and having multiple births [8] Last but not least these media campaigns will emphasize on the need for people to go and have cancer screenings in order to detect the cancer early [5]. Granell et al., [9] 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 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. Kan et al., (2016) found out that the introduction of awareness in the population could lower the density of the infection. A research study on the impact of awareness on dynamics of infectious diseases was carried out by Agaba et al., [10]. 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 [11-14]. The spread of private awareness or public awareness helps to control or minimize the spread of diseases [15,16]. Muthuri et al., (2021) determined the effects of targeted mass media campaigns and treatment on alcohol abuse in Kenya. In this research they a developed deterministic mode for alcohol abuse driven by the light and heavy drinkers taking into consideration the influence of pre exposure to mass media campaigns. The results showed that mass media campaign against alcohol consumption reduces alcohol abuse. The study concluded that alcohol addiction would reduce in the community if there was an emphasis on alcohol treatment and the mass media campaigns were regulated.

2 Model Formulation

In this model the human population is categorized into seven compartments at any time $t > 0$. 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 the infection,V_a −Individuals who are vaccinated and are aware from the media awareness, V −Individuals who are vaccinated and have no knowledge of the infection as the awareness has worn off, I −Infected, they have the infection and are unaware of the infection, I_a −Infected aware, they have the infection and are aware of it, T −Treatment,they have the infection and are 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 from the media and they join S_a at the rate $\phi_2 T$ as some will seek for treatment options such as undergoing for cancer screenings. The ones

who respond to the media awareness campaigns get themselves vaccinated and join class V_a at the rate γ. Since the campaign also encourages women to reduce sexual activity or have one sexual partner, we can assume that those who get vaccinated will adhere to that. Once this awareness "wears off", women will then move to the V class at the rate λ_1 and back to V_a at the rate ϕ_1.Movement between the V_a and V classes will continue in both directions due to the fact that the campaign is ongoing and the women may get aware again.

We also assume that some susceptibles heeded to the media campaigns and they reduced sexual activity (have one sexual 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

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

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

Condom use rate reduces the disease spread by the individuals in I_a. However due to negative attitudes affecting efficacy of condom use by the infected aware people, they help move the susceptibles to the infected compartment. These negative attitudes include religion and peer influence (Karei et al 2012).

The infected through the media awareness campaigns are encouraged to have one faithful or use protection so they do not pass the infection to others and also, they protect themselves from contracting other strains of HPV. The infected who get this information will move to class I_a. Once the education 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 hospital 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.

2.1 Model assumptions

The assumptions for this model are:

- There is homogeneous mixing of people in Kenya 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.
- There is an ongoing effective mass-media awareness campaigns that back up the vaccination.
- When an individual who does not have the HPV infection is vaccinated, they automatically become immune to the virus.
- Vaccinating infected individuals has no effect.
- Immunity obtained from the vaccine is one that is life-long (it protects the individual from HPV for the rest of his/her life).
- HPV infections that we dealt with in this research are those that are caused by HPV 16 and 18.
- Due to the effective mass-media awareness ($\sigma = 1$) the aware susceptibles (individuals in S_a) did not get infected with HPV.

2.2 Model flow charts and equations of model

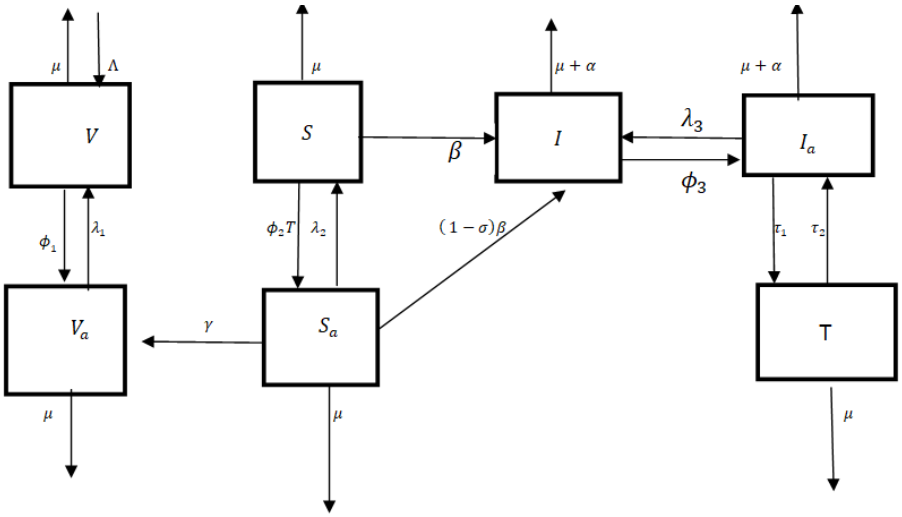


Fig. 1. Flow chart

The model description, model assumptions and Fig. 1 result in the following system of ordinary differential equations

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda + \lambda_2 S_a - \phi_2 TS - \beta S - \mu S \\
\frac{dS_a}{dt} &= \phi_2 TS - (\lambda_2 + \gamma + \mu) S_a \\
\frac{dI}{dt} &= \beta S + \lambda_3 I_a - (\phi_3 + \mu + \alpha) I \\
\frac{dI_a}{dt} &= \phi_3 \mathrm{I} + \tau_2 \mathrm{T} - \lambda_3 I_a + -\tau_1 I_a - (\mu + \alpha) I_a \\
\frac{dV}{dt} &= \lambda_1 V_a - \phi_1 V - \mu V \\
\frac{dV_a}{dt} &= \gamma S_a + \phi_1 V - \lambda_1 V_a - \mu V_a \\
\frac{dT}{dt} &= \tau_1 I_a - (\mu + \tau_2) T
\end{aligned} \tag{1}$$

where $\beta = \beta_1(I + \delta_c I_a)$ and we let $k_1 = \lambda_2 + \gamma + \mu$, $k_2 = \phi_3 + \mu + \alpha$, $k_3 = \lambda_3 + \tau_1 + \mu + \alpha$

3 Model Analysis

This analysis involves ascertaining the invariant region, HPV infection-free equilibrium, reproduction number, local and global stability analysis on HPV infection free equilibrium, endemic equilibrium analysis, bifurcation and sensitivity analysis on the model parameters.

3.1 Invariant region

Theorem 1

The solutions of model system (1) are uniformly bounded in a set

$$\Omega_1 = \left\{(S, S_a, I, I_a, V, V_a, T) \in \square_7^+ \mid \mathrm{N}(0) \leq N < \frac{\Lambda}{\mu}\right\} \tag{2}$$

Proof

Given that system (1) is a finite dimensional dynamical system, its initial and boundary conditions need to be constrained to Ω. Let $(S, S_a, I, I_a, V, V_a, T)$ be the solution to system (1) and $S(0) > 0$, $S_a(0) > 0$, $I(0) > 0$, $I_a(0) > 0$, $V(0) > 0$, $V_a(0) > 0$, $T(0) > 0$ be the initial conditions. Adding all the equations of (1) we obtain,

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dS_a}{dt} + \frac{dI}{dt} + \frac{dI_a}{dt} + \frac{dV}{dt} + \frac{dV_a}{dt} + \frac{dT}{dt} = \Lambda - \mu N - \alpha(I + I_a) \tag{3}$$

Where $N = S + S_a + I + I_a + V + V_a + T$

In the absence of mortality rate due to HPV infection (that is $= 0$) equation (3) becomes,

$$\frac{dN}{dt} = \Lambda - \mu N$$

On integrating and taking $t \to \infty$, the limit of $N(t)$ is,

$$\lim_{t\to\infty} N(t) < \frac{\Lambda}{\mu} \tag{4}$$

From (4) it is clear that $N(t)$ is bounded, consequently all solutions are bounded with an upper bound $N = max\left\{\frac{\Lambda}{\mu}\right\}$. Therefore, all feasible solutions of system (1) enter and remain in region Ω_2.

3.2 Positivity of the model

Theorem 2

Let $\Omega_1 = \left\{(S, S_a, I, I_a, V, V_a, T) \in \square_7^+ \mid N \leq \frac{\Lambda}{\mu}\right\}$ with the initial conditions

$\{S(0) > 0, S_a(0) > 0, I(0) > 0, I_a(0) > 0, V(0) > 0, V_a(0) > 0, T(0) > 0\} \in \Omega_2$ then the solution set $\{(S, S_a, I, I_a, V, V_a, T)\}$ of system of (1) exists, is unique and positive for all $t > 0$.

Proof

We begin with our first equation in (1) which is given by

$$\frac{dS}{dt} = \Lambda + \lambda_2 S_a - \phi_2 TS - \beta S - \mu S$$
$$\frac{dS}{dt} \geq -(\phi_2 T + \beta + \mu)S \tag{5}$$

We let $\phi_2 T + \beta = \varepsilon_1$, thus equation (5) becomes

$$\frac{dS}{dt} \geq -(\varepsilon_1 + \mu)S \tag{6}$$

Separating the variables and integrating with respect to time t we get,

$$In\, S(t) \geq -\int_0^t (\varepsilon_1 + \mu)dt + c \tag{7}$$

Where c is a constant of integration. Introducing the exponential function on both sides we have,

$$S(t) \geq e^{-\left(\int_0^t (\varepsilon_1 + \mu)dt + c\right)} \tag{8}$$

Substituting the initial condition $t = 0$ and solving for c we get,

$$S(0) \geq e^0 \cdot e^c \text{ , hence } e^c = S(0) \tag{9}$$

Thus, our solution now is,

$$S(t) \geq S(0)e^{-\left(\int_0^t (\varepsilon_1+\mu)dt\right)} > 0 \tag{10}$$

Equation (10) is positive for all time t. We do the same to the other differential equations in system (1) which all turn out to be positive for all time t. This completes our proof.

3.3 HPV free equilibrium and Reproduction number

The HPV free equilibrium of the system is denoted by $H^0 = (S^0, S_a^0, I^0, I_a^0, V^0, V_a^0, T^0)$. To obtain H^0 we equate the right hand side of (1) to zero and set $S_a = I = I_a = V = V_a = T = 0$. By doing so we obtain,

$$H^0 = \left(\frac{\Lambda}{\mu}, 0,0,0,0,0,0\right) \tag{11}$$

The reproduction number R_0 is the average number of secondary infections caused by an infected individual during its infectious period. We use the next generation matrix method which is given by FD^{-1} to obtain the HPV infection reproduction number R_0 where the matrix F is the Jacobian matrix of new infections and D is the Jacobian matrix of transition of infections at H^0. We consider the infectious compartments below from the model system (1)

$$\begin{aligned} \frac{dI}{dt} &= \beta S + \lambda_3 I_a - k_2 I \\ \frac{dI_a}{dt} &= \phi_3 \mathrm{I} - k_3 I_a \\ \frac{dT}{dt} &= \tau_1 I_a - \mu T \end{aligned} \tag{12}$$

We obtain the appearance of new infections as F_i and transfer of infections as D_i,

$$F_i = \begin{pmatrix} \beta S \\ 0 \\ 0 \end{pmatrix} \qquad \text{and} \qquad D_i = \begin{pmatrix} \lambda_3 I_a - k_2 I \\ \phi_3 \mathrm{I} - k_3 I_a \\ \tau_1 I_a - (\mu + \tau_2) T \end{pmatrix}$$

This results into the Jacobian matrix of the new infection rates F and Jacobian matrix of transition of infections D respectively at H^0 as,

$$F = \begin{bmatrix} \frac{\beta_1 \Lambda}{\mu} & \frac{\beta_1 \delta_c \Lambda}{\mu} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \qquad D = \begin{bmatrix} k_2 & -\lambda_3 & 0 \\ -\phi_3 & k_3 & 0 \\ 0 & -\tau_1 & \mu + \tau_2 \end{bmatrix}$$

The reproduction number of the model is the largest eigen-value of the matrix FD^{-1} where D^{-1} is the inverse of D. Matrix FD^{-1} is given by

$$FD^{-1} = \begin{bmatrix} \frac{\beta_1 \Lambda k_3 + \beta_1 \Lambda \delta_c \phi_3}{\mu(k_2 k_3 - \lambda_3 \phi_3)} & \frac{\beta_1 \Lambda \lambda_3 + \beta_1 \Lambda \delta_c k_2}{\mu(k_2 k_3 - \lambda_3 \phi_3)} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

The reproduction number R_0 is therefore given by

$$R_0 = \frac{\beta_1 \Lambda k_3 + \beta_1 \Lambda \delta_c \phi_3}{\mu(k_2 k_3 - \lambda_3 \phi_3)} \tag{13}$$

3.4 Local Stability of HPV free equilibrium

Theorem 3

The HPV free equilibrium (H^0) is locally asymptotically stable if $R_0 < 1$ and unstable otherwise.

Proof

Evaluating the Jacobian matrix of the system (1) at H^0.

$$J_{H^0} = \begin{bmatrix} -\mu & \lambda_2 & \frac{\beta_1\Lambda}{\mu} & \frac{\beta_1\Lambda\delta_c}{\mu} & 0 & 0 & -\frac{\phi_2\Lambda}{\mu} \\ 0 & -k_1 & 0 & 0 & 0 & 0 & \frac{\phi_2\Lambda\delta_c}{\mu} \\ 0 & 0 & \frac{\beta_1\Lambda}{\mu} - k_2 & \frac{\beta_1\Lambda\delta_c}{\mu} + \lambda_3 & 0 & 0 & 0 \\ 0 & 0 & \phi_3 & -k_3 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -(\phi_1 + \mu) & \lambda_1 & 0 \\ 0 & 0 & 0 & 0 & \phi_1 & -(\lambda_1 + \mu) & 0 \\ 0 & 0 & \tau_1 & \tau_2 & 0 & 0 & -\mu - \tau_2 \end{bmatrix}$$

The first three eigen values are $-\mu, -k_1$ and $-\mu - \tau_2$. The other eigenvalues are determined from the reduced matrix given below.

$$\begin{bmatrix} \frac{\beta_1\Lambda}{\mu} - k_2 & \frac{\beta_1\Lambda\delta_c}{\mu} + \lambda_3 & 0 \\ \phi_3 & -k_3 & 0 \\ 0 & 0 & -(\phi_1 + \mu) \end{bmatrix}$$

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

$$a^3 + P_1 a^2 + P_2 a + P_3 = 0 \tag{14}$$

Where

$$P_1 = -\frac{\beta_1\Lambda}{\mu} + k_2 + k_3 + \phi_1 + \mu$$
$$P_2 = -\frac{\beta_1\Lambda}{\mu}k_3 - \frac{\beta_1\Lambda}{\mu}\phi_1 - \beta_1\Lambda + k_2k_3 + k_2\phi_1 + k_2\mu + k_3\phi_1 + k_3\mu - \frac{\beta_1\Lambda\delta_c}{\mu} - \lambda_3$$
$$P_3 = k_2k_3\phi_1 + k_2k_3\mu - \frac{\beta_1\Lambda k_3\phi_1}{\mu} - \frac{\beta_1\Lambda\mu k_3}{\mu} - \frac{\beta_1\Lambda\delta_c\phi_3\phi_1}{\mu} - \frac{\beta_1\Lambda\mu\delta_c\phi_3}{\mu} - \lambda_3\phi_3\phi_1 - \mu\lambda_3\phi_3$$

Using Routh-Hurwitz criteria equation (14) has a negative root if and only if $P_1 > 0$, $P_2 > 0$, $P_3 > 0$ and $P_1P_2 > P_3$. When $R_1 < 1$, then $P_1P_2 > P_3$. Therefore, HPV free equilibrium point is locally asymptotically stable whenever $R_1 < 1$.

3.5 Global Stability analysis of HPV-free equilibrium

Theorem 4

The HPV free equilibrium is globally asymptotically stable if $2\Lambda - \frac{\Lambda^2}{\mu S} - \mu S = 0$.

Proof

We propose the following Lyapunov function

$$L(S, S_a, I, I_a, V, V_a, T) = S - S^0 - S^0 In\frac{S}{S^0} + G_1S_a + G_2I + G_3I_a + G_4V + G_5V_a + G_6T$$

Which satisfies the conditions

1. $L(S^0, S_a^0, I^0, I_a^0, V^0, V_a^0, T^0) = 0$
2. $L(S, S_a, I, I_a, V, V_a, T) > 0$
3. $\frac{dL(S^0, S_a^0, I^0, I_a^0, V^0, V_a^0, T^0)}{dt} = 0$
4. $\frac{dL(S, S_a, I, I_a, V, V_a, T)}{dt} < 0$

where G_i where $i = 1,2,3,4,5$ and 6 are positive parameters that are determined.

The HPV free equilibrium point for our system is $H^0 = (S^0, S_a^0, I^0, I_a^0, V^0, V_a^0, T^0)$. Thus, we have,

$$L(S^0, S_a^0, I^0, I_a^0, V^0, V_a^0, T^0) = S^0 - S^0 - In\frac{S^0}{S^0} + G_1 S_a^0 + G_2 I^0 + G_3 I_a^0 + G_4 V^0 + G_5 V_a^0 + G_6 T^0 = 0$$

Thus condition 1 is satisfied.

$$L(S, S_a, I, I_a, V, V_a, T) = S - S^0 - S^0 In\frac{S}{S^0} + G_1 S_a + G_2 I + G_3 I_a + G_4 V + G_5 V_a + G_6 T > 0$$

Hence the condition 2 is satisfied.

$$\frac{dL(S^0, S_a^0, I^0, I_a^0, V^0, V_a^0, T^0)}{dt} = \left(1 - \frac{S^0}{S^0}\right)\frac{dS^0}{dt} + G_1\frac{dS_a^0}{dt} + G_2\frac{dI^0}{dt} + G_3\frac{dI_a^0}{dt} + G_4\frac{dV^0}{dt} + G_5\frac{dV_a^0}{dt} + G_6\frac{dT^0}{dt}$$

Since $S_a^0 = I^0 = I_a^0 = V^0 = V_a^0 = T^0 = 0$ and $S^0 = \frac{\Lambda}{\mu}$, then the above equation is reduced to

$$\frac{dL(S^0, S_a^0, I^0, I_a^0, V^0, V_a^0, T^0)}{dt} = 0$$

thus, condition 3 becomes satisfied.

$$\frac{dL(S, S_a, I, I_a, V, V_a, T)}{dt} = \left(1 - \frac{S^0}{S}\right)\frac{dS}{dt} + G_1\frac{dS_a}{dt} + G_2\frac{dI}{dt} + G_3\frac{dI_a}{dt} + G_4\frac{dV}{dt} + G_5\frac{dV_a}{dt} + G_6\frac{dT}{dt}$$

$$= \left(1 - \frac{S^0}{S}\right)(\Lambda + \lambda_2 S_a - \phi_2 TS - \beta S - \mu S) + G_1(\phi_2 TS - \sigma\beta S_a - \lambda_2 S_a - \gamma S_a - \mu S_a) + G_2(\beta S + \lambda_3 I_a - k_2 I) + G_3(\phi_3 I - k_3 I_a) + G_4(\lambda_1 V_a - \phi_1 V - \mu V) + G_5(\gamma S_a + \phi_1 V - \lambda_1 V_a - \mu V_a) + G_6(\tau_1 I + \tau_2 I_a - \mu T)$$

$$= \Lambda + \lambda_2 S_a - \phi_2 TS - \beta S - \mu S - \Lambda\frac{S^0}{S} - \lambda_2 S_a\frac{S^0}{S} + \phi_2 TS^0 + \beta S^0 + \mu S^0 + G_1(\phi_2 TS - \sigma\beta S_a - \lambda_2 S_a - \gamma S_a - \mu S_a) + G_2(\beta S + \lambda_3 I_a - k_2 I) + G_3(\phi_3 I - k_3 I_a) + G_4(\lambda_1 V_a - \phi_1 V - \mu V) + G_5(\gamma S_a + \phi_1 V - \lambda_1 V_a - \mu V_a) + G_6(\tau_1 I + \tau_2 I_a - \mu T)$$

At HPV free equilibrium point we have $S^0 = \frac{\Lambda}{\mu}$, substituting it in the above equation and simplifying we obtain,

$$= 2\Lambda - \frac{\Lambda^2}{\mu S} - \mu S + (G_1 - 1)\phi_2 TS + (G_2 - 1)\beta S + \left(G_5\gamma - \frac{\lambda_2\Lambda}{\mu} - G_1 k_1 + \lambda_2\right)S_a + (G_3\phi_3 - G_2 k_2 + G_6\tau_1)I + (G_2\lambda_3 - G_3 k_3 + G_6\tau_2)I_a + (G_5\phi_1 - G_4\phi_1 - G_4\mu)V + (G_4\lambda_1 - G_5\lambda_1 - G_5\mu)V_a + \left(\frac{\Lambda\phi_2}{\mu} - G_6\mu\right)T \quad (15)$$

Equating the non-linear terms in equation (15) to zero we obtain,

$$G_1 = 1,\ G_2 = 1,\ G_3 = \frac{1}{\phi_3}\left(k_2 - \frac{\tau_1\Lambda\phi_2}{\mu^2}\right),\ G_4 = \frac{1}{\gamma},\quad G_5 = \frac{(\lambda_1 + \mu)}{\lambda_1}\left(\frac{\lambda_2\Lambda}{\mu} + k_1 - \lambda_2\right),\ G_6 = \frac{\Lambda\phi_2}{\mu^2}$$

Thus $\frac{dL(S,S_a,I,I_a,V,V_a,T)}{dt} < 0$, hence satisfying condition 4 since $2\Lambda - \frac{\Lambda^2}{\mu S} - \mu S < 0$ and all parameters are positive. Since the above conditions have been satisfied for HPV free equilibrium point, we concluded that the HPV free equilibrium point to be globally asymptotically stable. This completes the proof.

3.6 Endemic equilibrium point

In our model, this is the point when the HPV infection persists in the community. We let

$E_0^* = (S^*, S_a^*, I^*, I_a^*, V^*, V_a^*, T^*)$ be the endemic equilibrium point

Setting the right-hand side of system of equations (1) to zero we get,

$$\begin{aligned}
S^* &= \xi_3 \\
S_a^* &= \frac{\xi_4(\Lambda-\mu\xi_3)}{\{\beta_1(1+\delta_c\xi_1)+\phi_2\xi_2\xi_3-\lambda_2\xi_4\}} \\
I^* &= \frac{(\Lambda-\mu\xi_3)}{\{\beta_1(1+\delta_c\xi_1)+\phi_2\xi_2\xi_3-\lambda_2\xi_4\}} \\
I_a^* &= \frac{\xi_1(\Lambda-\mu\xi_3)}{\{\beta_1(1+\delta_c\xi_1)+\phi_2\xi_2\xi_3-\lambda_2\xi_4\}} \\
V^* &= \frac{\lambda_1\gamma\xi_4(\Lambda-\mu\xi_3)}{\mu(\phi_1+\lambda_1+\mu)\{\beta_1(1+\delta_c\xi_1)+\phi_2\xi_2\xi_3-\lambda_2\xi_4\}} \\
V_a^* &= \frac{\gamma\xi_4(\Lambda-\mu\xi_3)[\mu(\phi_1+\lambda_1+\mu)+\phi_1\lambda_1]}{\mu(\lambda_1+\mu)(\phi_1+\lambda_1+\mu)\{\beta_1(1+\delta_c\xi_1)+\phi_2\xi_2\xi_3-\lambda_2\xi_4\}} \\
T^* &= \frac{\xi_2(\Lambda-\mu\xi_3)}{\{\beta_1(1+\delta_c\xi_1)+\phi_2\xi_2\xi_3-\lambda_2\xi_4\}}
\end{aligned} \tag{16}$$

where $\xi_1 = \frac{\phi_3}{k_3}$, $\xi_2 = \frac{\tau_1\xi_1}{\mu+\tau_2}$, $\xi_3 = \frac{(k_2-\lambda_3\xi_1)}{\beta_1(1+\delta_c\xi_1)}$, $\xi_4 = \frac{\xi_2\xi_3\phi_2}{k_1}$

Rewriting equation (13) in terms of β_1 we have,

$$\beta_1 = \frac{R_1\mu(k_2k_3-\lambda_3\phi_3)}{\Lambda(k_3+\delta_c\phi_3)} \tag{17}$$

Substituting the value of β_1 into equation (16) we get,

$$\begin{aligned}
S^* &= \frac{\Lambda}{\mu R_1} \\
S_a^* &= \frac{\Lambda^3\xi_2\phi_2(R_1-1)}{\mu^2R_1^2k_1(k_2k_3-\lambda_3\phi_3)+\Lambda^2\phi_2\xi_2(k_1-\lambda_2)} \\
I^* &= \frac{\mu\Lambda^2k_1(R_1-1)}{\mu^2R_1^2k_1(k_2k_3-\lambda_3\phi_3)+\Lambda^2\phi_2\xi_2(k_1-\lambda_2)} \\
I_a^* &= \frac{\xi_1\mu\Lambda^2k_1(R_1-1)}{\mu^2R_1^2k_1(k_2k_3-\lambda_3\phi_3)+\Lambda^2\phi_2\xi_2(k_1-\lambda_2)} \\
T^* &= \frac{\xi_2\mu\Lambda^2k_1(R_1-1)}{\mu^2R_1^2k_1(k_2k_3-\lambda_3\phi_3)+\Lambda^2\phi_2\xi_2(k_1-\lambda_2)} \\
V^* &= \frac{\gamma\xi_2\phi_2\Lambda^3\lambda_1(R_1-1)}{\mu R_1(\lambda_1+\mu)(\phi_1+\lambda_1+\mu)\{\mu^2R_1^2k_1(k_2k_3-\lambda_3\phi_3)+\Lambda^2\phi_2\xi_2(k_1-\lambda_2)\}} \\
V_a^* &= \frac{\gamma\xi_2\phi_2\Lambda^3(R_1-1)\{\mu(\phi_1+\lambda_1+\mu)+\phi_1\lambda_1\}}{\mu^2R_1(\lambda_1+\mu)(\phi_1+\lambda_1+\mu)\{\mu^2R_1^2k_1(k_2k_3-\lambda_3\phi_3)+\Lambda^2\phi_2\xi_2(k_1-\lambda_2)\}}
\end{aligned}$$

From the above, we came to the conclusion that endemic equilibrium exists if $R_1 > 1$.

3.7 Bifurcation of model 2

Choosing $\theta = \beta_1^*$ as the bifurcation parameter and investigating the case when $R_0 = 1$ we have,

$$\beta_1^* = \frac{\mu(k_2k_3-\lambda_3\phi_3)}{\Lambda(k_2+\delta_c\phi_3)} \tag{18}$$

The system (1) with the bifurcation point θ, has a simple zero eigen value therefore we can use the Center Manifold theory to analyse the stability of the system (1) near $\beta_1^* = \theta$. The Jacobian of the model at $\theta = \beta_1^*$ has a right eigen vector $w = (w_1, w_2, w_3, w_4, w_5, w_6, w_7)^t$ given by

$$\begin{bmatrix} -\mu & \lambda_2 & -g_1 & -g_2 & 0 & 0 & -g_2 \\ 0 & -k_1 & 0 & 0 & 0 & 0 & -g_2 \\ 0 & 0 & -(k_2 - g_{1)} & g_2 + \lambda_3 & 0 & 0 & 0 \\ 0 & 0 & \phi_3 & -k_3 & 0 & 0 & \tau_2 \\ 0 & 0 & 0 & 0 & -(\phi_1 + \mu) & \lambda_1 & 0 \\ 0 & 0 & 0 & 0 & \phi_1 & -(\lambda_1 + \mu) & 0 \\ 0 & 0 & \tau_1 & \tau_2 & 0 & 0 & -\mu - \tau_2 \end{bmatrix} \begin{bmatrix} w_1 \\ w_2 \\ w_3 \\ w_4 \\ w_5 \\ w_6 \\ w_7 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix} \tag{19}$$

Where $g_1 = \frac{\beta_1 \Lambda}{\mu}$, $g_2 = \frac{\beta_1 \Lambda \delta_c}{\mu}$. Solving equation (19) we get,

$$w_1 = -\frac{(g_1 w_3 + g_2 w_4 + g_2 w_7 - \lambda_2 w_2)}{\mu} < 0\,, \quad w_2 = \frac{g_2 w_7}{k_1} > 0\,, w_3 = \frac{(g_2 + \lambda_3) w_4}{(k_2 - g_1)} > 0\,, \tag{20}$$

$$w_4 = \frac{\phi_3 w_3 + \tau_2 w_7}{k_3} > 0 \qquad w_5 = \frac{w_6}{(\phi_1 + \mu)} > 0, \quad w_6 = \frac{\phi_1 w_5}{(\lambda_1 + \mu)} > 0\,, \; w_7 = \frac{(\tau_1 w_3 + \tau_2 w_4)}{\mu} > 0$$

The Jacobian matrix has a left eigen vector denoted by $v = (v_1, v_2, v_3, v_4, v_5, v_6, v_7)^t$. The components of the left eigen vector are given as

$$v_1 = v_2 = 0, \quad v_3 = \frac{\phi_3 v_4 + (\tau_1 v_7}{(k_2 - g_1)} > 0, \quad v_4 = \frac{(g_2 + \lambda_3) v_3 + \tau_2 v_7}{k_3} > 0,$$

$$v_5 = \frac{\phi_1 v_6}{(\phi_1 + \mu)} > 0\,, \quad v_6 = \frac{\lambda_1 v_5}{(\lambda_1 + \mu)} > 0, \quad v_7 = 0 \tag{21}$$

We now compute $\boldsymbol{a}$ and **b** as outlined in (Castillo-Chavez and Song, 2004)

$$\boldsymbol{a} = 2 v_3 w_1 \theta (w_3 + w_4 \delta_c) < 0 \tag{22}$$

$$\boldsymbol{b} = v_3 \frac{\Lambda}{\mu} (w_3 + w_4 \delta_c) > 0$$

Thus θ changes from negative to pos itive, 0 changes its stability from stable to unstable therefore a negative unstable equilibrium becomes positive and locally asymptotically stable.

4 Results and Discussion

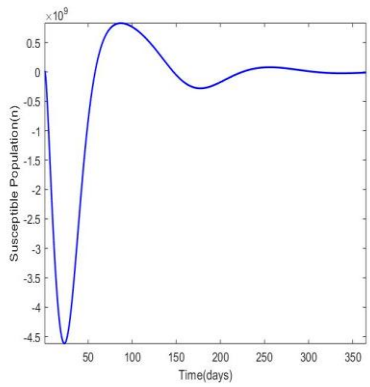
4.1 Numerical simulations

We present the numerical simulations of the model system (1) in this section. We use MATLAB software and the parameters in Table 1 to come up with the numerical simulations.

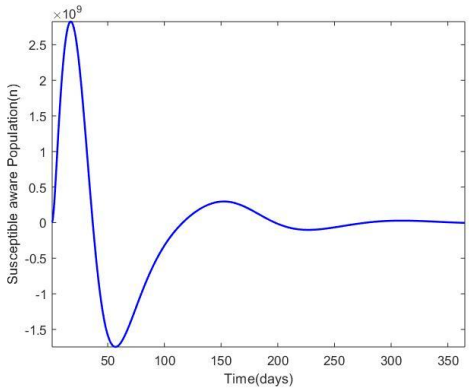
Table 1. Parameters and their description

Parameter	Description	Value	Source
Λ	Natural birth rate	0.02639	CIA [17]
μ	Natural mortality rate	0.00501	CIA [17]
τ_1	Rate at which aware infected individual seeks treatment.	0.035	ICO [18]
τ_2	Rate at which an individual recovers	0.0028	Assumed
γ	Vaccination rate	0.25	Bruni et al. [19]

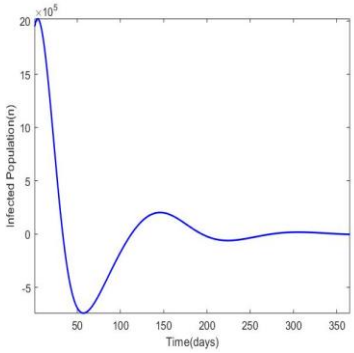
Parameter	Description	Value	Source
β_1	Infection contact rate	0.000194	Bruni et al. [19]
δ	Death rate due to HPV infection	0.61	Bruni et al. [19]
ϕ_1	Rate at which vaccinated individuals become aware	0.045	Assumed
ϕ_2	Rate at which a susceptible individual becomes aware	0.035	Assumed
ϕ_3	Rate at which 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	Ronoh et al. [20]
σ	Efficiency of awareness	0-1	Assumed



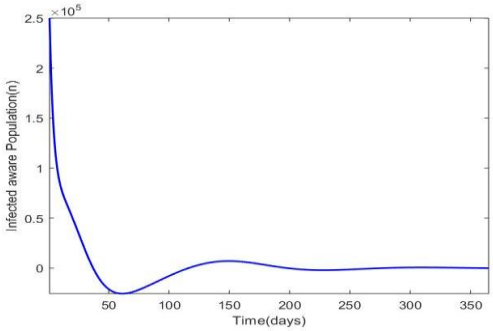
(a) Susceptible population



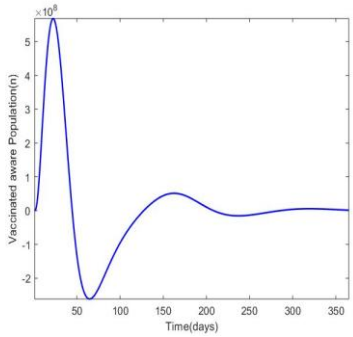
(b) Susceptible aware population



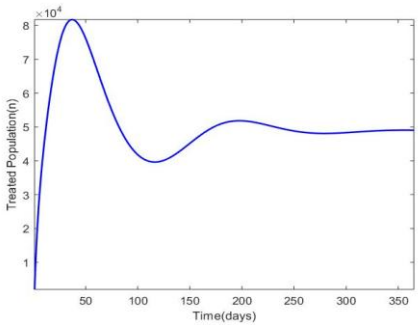
(c) Infected population



(d) Infected aware population



(e) Vaccinated aware population



(f) Treated Population

Fig. 2. Population plots of model 2

Fig. 2 shows the population plots of model 2. In Fig. 2(a) the susceptible population class decreases and then increases in the first sixty days. The decrease is because of the susceptible population has become aware of the virus and they are moving to the susceptible aware class. The increase which happens in few days is attributed to the wearing out of awareness from the susceptible aware thus moving back to the susceptible class. After that the population stabilizes as it moves to the susceptible aware class and this is due to the effective mass media awareness.

In Fig. 2(b), the susceptible aware class population increases and then decreases in the first fifty days. The increase is attributed to the influx of susceptible population that is joining the susceptible aware class after getting exposed to the mass media awareness campaigns on the virus. The decrease is due to the movement to the vaccinated aware class where the susceptible aware population are heeding to the message from awareness groups that they should get vaccinated against HPV. The population then increases again and this is still because of more susceptible individuals becoming aware of the virus and then stabilizes afterwards. There are a number of reasons why this population becomes stable and they include shortage in the number of vaccines available and the cost of the vaccine; many people may be unable to afford it. Despite of this the population remains in this class as the mass media awareness is effective. In Fig. 2(c), the infected population decreases for some days and this is brought up by mass media awareness as they join the infected aware class. It then increases and becomes steady. This is as a result of the infected aware population class moving to the infected class due to wearing out however this comes to a stop and this population becomes steady.

In Fig. 2(d), the infected aware population decreases in the first fifty days due to movement to treatment and increases for some time as some infected aware lose awareness and move back to infected class. However due to the effective media awareness campaigns this population increases to an equilibrium point.

In Fig. 2(e), the vaccinated aware population increases for the first forty days. This is due to the inflow from the susceptible aware class who are getting vaccinated. However, these numbers decrease for another thirty days. This is due to the low turnout of susceptible aware individuals who are getting vaccinated due to the negative false opinions they have regarding the HPV vaccine or high cost of the vaccine. After some days the population increases to become steady due to effective media awareness campaigns.

In Fig. 2(f), the treatment class increases with time due to the individuals being encouraged to go to hospitals and get cancer screening tests among other various treatment options. However, it decreases and then increases to a steady point. The decrease is associated with the number of infected aware who leave the treatment class after seeking treatment options. Also, it is attributed to the deaths that occur due to HPV-related complications.

The findings in Fig. 3 show that increasing the τ, rate of seeking treatment leads to an increase in the number of individuals seeking for treatment (a reduction in the number of infected aware individuals). Increasing the rate of vaccination also leads to an increase in the number of individuals getting vaccinated (thus a reduction in the number of susceptible aware individuals) as shown in Fig. 4. The findings imply that provided the media awareness campaigns on HPV are effective and the rate of seeking treatment and vaccination rate remain high then the community will be able to eradicate/ maintain low numbers of HPV infections.

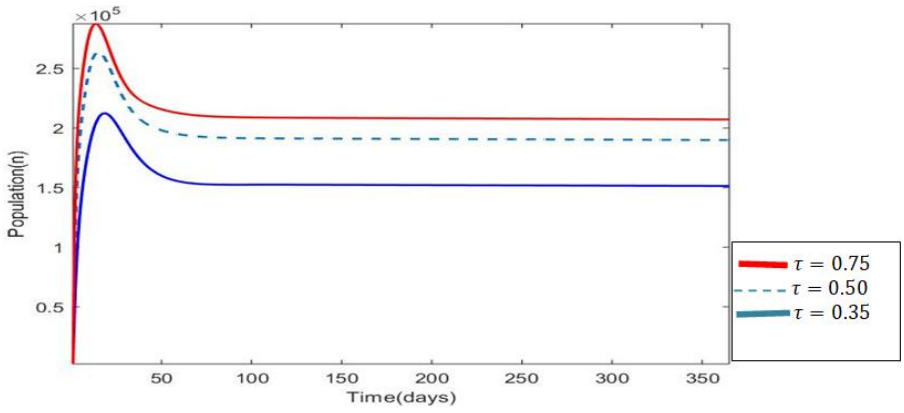


Fig. 3. Effect on population on varying the rates of treatment

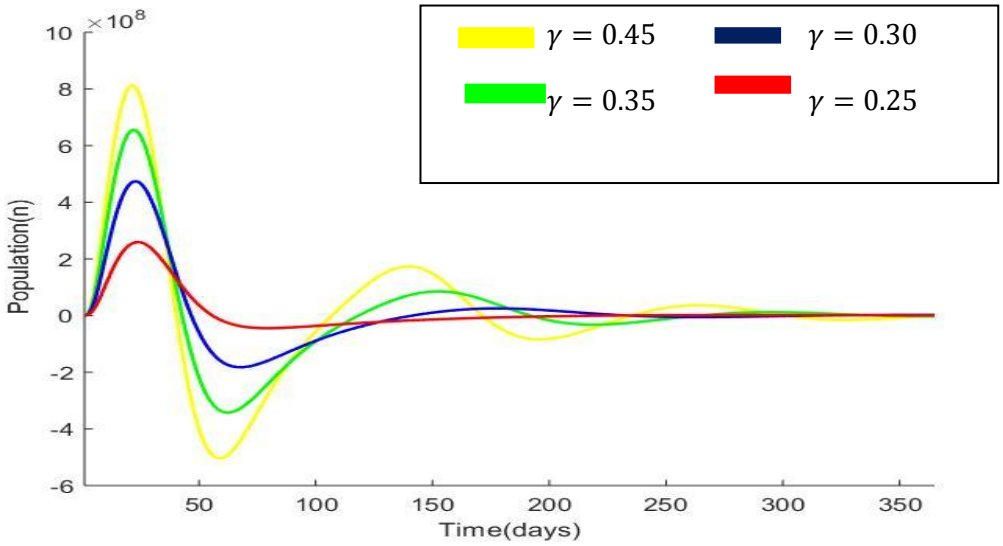


Fig. 4. Effect on population on varying the rates of vaccination

4.2 Sensitivity analysis

This is a technique of ascertaining how uncertainty in the output of a model can be distributed to different sources of uncertainty in the model parameters, (Schneeweiss, 2006). The goal of this technique is to determine which parameters have the highest influence on the model. We use the Latin Hypercube Sampling-Partial Rank Correlation Coefficient (LHS-PRCC) method which is a coherent tool used to carry out sensitivity analysis in our model. It involves a combination of two statistical techniques, Latin Hypercube Sampling and Partial Rank Correlation Coefficient analysis [21,22].

Table 2. Sensitivity indices of the reproduction number against mentioned parameters

Parameter	Sensitivity index value	Parameter	Sensitivity index value
Λ	0.013121359	λ_3	0.534875624
β_1	0.675110785	α	0.257927851
μ	0.120124752	δ_c	0.598521356
ϕ_3	-0.547785203	τ_1	-0.672534560

The parameter with the most positive impact on the reproduction number according to the PRCC values is β_1 which is followed by δ_c λ_3 ,α, λ_2 and λ_1. This means that increasing these parameters increases the reproduction number and decreasing them reduces the R_0. The parameters τ_1, ϕ_3, γ, have the greatest negative influence on R_0. That is increasing them results to a decrease in R_0.

5 Conclusion

In this paper, we formulated a mathematical model of an effective mass media awareness campaigns on the spread of HPV infections in Kenya.

We investigated the local and global stabilities of HPV free endemic equilibrium using the Routh-Hurwitz criteria and established that the HPV free equilibrium point was locally asymptotically stable if $R_1 < 1$. When it came to global stability, we came up with a Lyapunov function and drew the conclusion that the HPV equilibrium point was globally asymptotically stable. The endemic equilibrium point existed if $R_1 > 1$. We analyzed the nature of bifurcation and found out that θ changes from negative to positive, changes its stability from stable to unstable thus the negative unstable equilibrium becomes positive and locally asymptotically stable. Sensitivity analysis confirms that the relapse from the susceptible aware and infected aware to

susceptible and infected classes respectively that is λ_2 and λ_3 respectively increase the spread of HPV in the community. However, the numerical simulations of this model show that an effective mass media awareness campaigns bring the numbers of HPV infections to a certain equilibrium which in turn would lead to the eradication of HPV infections in the community [23-25]. The results in Fig. 4 showed the impact of vaccination whereby increasing the rates of vaccinations resulted to an increase in the number of vaccinated (thus a decrease in the number of susceptible aware individuals). This signifies that increasing the rate of vaccination will help in reducing the spread of HPV among the susceptible individuals. Therefore, we conclude that if HPV vaccination and treatment is stressed on and an effective mass media awareness is being carried out then HPV spread in the community will be decreased [26-29]. Further research can be carried on the impact of implementing HPV education in the curriculum of primary school on the spread of HPV infection.

Competing Interests

Authors have declared that no competing interests exist.

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