Mathematical Modelling of Cervical Cancer Vaccination and Treatment Effectiveness

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Mathematical Modelling of Cervical Cancer Vaccination and Treatment Effectiveness

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Abstract

After breast cancer, cervical cancer is the second most frequent cancer in women globally. The Human Papillomavirus is the most common cause of cervical cancer. In this paper, we used a nonlinear ordinary differential equation system to build a mathematical model of cervical cancer with six compartments (the number of susceptible women, vaccinations of susceptible women, the infected women with HPV, the number of infected with cervical cancer, treatment individual, and recovery class). The model is examined using the existence of bounded and positive solutions, numerical analysis, sensitivity analysis, and stability analysis of disease free and endemic equilibrium point as a function of R_0 values. The numerical simulations of the system are carried out using the ODE45 subroutine of MATLAB, and the results are revealed using graphs and biologically interpreted. Using numerical simulation, applying vaccination and increasing treatment for everyone can help to reduce and control the spread of cervical cancer.

Keywords: Basic reproduction number, Cervical cancer, Equilibrium Point,

Numerical Simulation, Sensitivity analysis, Stability Analysis.

1 Introduction

Uterine cervical cancer is a global health issue, but it is particularly concerning in developing countries. The main cause of cervical cancer is infection with HPV [1]. Breast cancer (30.2%), cervix cancer (13.4%), and colorectal cancer are the three most common cancers in Ethiopia's adult population (5.7%)[2] . Women account for around two-thirds of all cancer deaths each year. It is either the first or second most common type of cancer in women. There are over 100 different types of HPV, the majority of which are harmless.The types of HPV that are very common in cases of cervical cancer are types 16 and 18, which is more than 70% of all cervical cancers reported [3],

Behavioral, biological, environmental, and genetic risk factors of cancer. Tobacco usage, harmful alcohol consumption, a poor diet, and physical inactivity are all behavioral risk factors. Overweight, obesity, age, the individual's sex, and genetic or inherited make-up are all biological factors. Exposure to carcinogens in the environment, such as chemicals, radiation, and infectious agents, is a concern (including certain viruses) [4]. Low levels of awareness, a lack of effective screening programs, being overshadowed by other health priorities (such as AIDS, tuberculosis, and malaria), and a lack of attention to women's health are all plausible reasons for the country's higher cervical cancer incidence rate[5]. Blood spots or light bleeding between or following periods, bleeding after intercourse, douching, increased vaginal discharge, pain during sexual intercourse, bleeding after menopause, and unexplained persistent pelvic and back pain are all symptoms of cervical cancer[4].

About 40% of cancers can be prevented through primary prevention, which is also the most cost-effective method of fighting cancer. Hysterectomy, Cone

biopsy, Radical trachelectomy, Lymph node removal, chemoradiation,radiation therapy, surgery, clinical trials and radiation therapy are all used to treatment cervical cancer. [6].

Vaccination provides an alternative or a supplementary intervention for CC prevention. Because neither ÂăscreeningÂă nor vaccinationÂăcan guarantee 100 percent protection against CC, the best prevention plan may comprise a mix of the two [7]. Mathematical modeling is an abstract that uses mathematical language to explain system behavior and portrays the behavior of real devices and things in mathematical terms. [8]. In this study, we created a compartment model called SVI_vCTR and analyze it to explore cervical cancer utilizing stability analysis, sensitivity analysis and the ODE45 numerical simulation approach.

2 Mathematical Formulation

In this work, we divided the model into six sections to create a model for cervical cancer. The number of susceptible women S(t), women vaccinated V(t), the number of women infected with HPV I_v(t), the number of women infected cervical cancer C(t), the number of women treated for HPV and infected cervical cancer T(t), and the number of women recovered from disease R(t) are the variables. To create the model, we used the following basic assumptions.

- After the age of 15, the susceptible population consists of all females.
- The recruiting rate, natural death rate, and cervical cancer death rate are all taken into account.
- The total population is equal to the sum of all variables, that is, $N(t) = S(t) + V(t) + I_v(t) + C(t) + T(t) + R(t)$.
- Individual vaccination rates are proportionate to the number of people

who are at risk.

- Infected women with HPV and infected women with cervical cancer receive individualized treatment.

The new model's flow chart depicts the disease of cervical cancer as it spreads through the population:

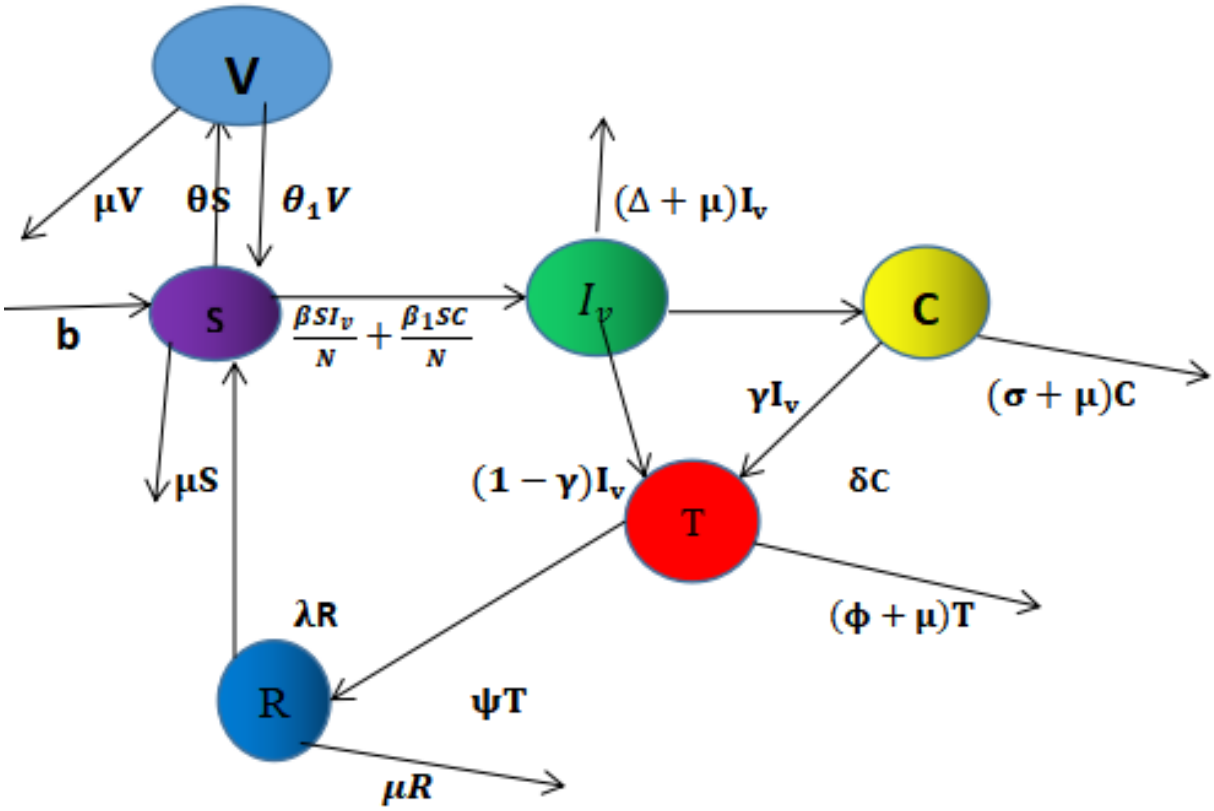

Figure 1: The flow chart of the Compartment model

The following systems of ordinary differential equations are used in the model equation of the above flow char[2], [3],[9] and [10].

$$
\begin{aligned}
\frac{dS}{dt} &= b - \frac{S\beta I_v}{N} - \frac{S\beta_1 C}{N} - \mu S + \theta_1 V - \theta S + \lambda R, \\
\frac{dV}{dt} &= \theta S - \theta_1 V - \mu V, \\
\frac{dI_v}{dt} &= \frac{S\beta I_v}{N} + \frac{S\beta_1 C}{N} - (\Delta + \mu) I_v - (1-\gamma) I_v - \gamma I_v, \\
\frac{dC}{dt} &= \gamma I_v - (\sigma + \mu) C - \delta C, \\
\frac{dT}{dt} &= \delta C + (1-\gamma) I_v - (\phi + \mu) T - \psi T, \\
\frac{dR}{dt} &= \psi T - \mu R - \lambda R,
\end{aligned}
\tag{1}
$$

With $S(t) > 0, V(t) \geq 0, I_v(t) \geq 0, C(t) \geq 0, T(t) \geq 0, R(t) \geq 0,$

Description of variables

S(t)	At time t, denotes the vulnerable population of women over the age of 15.
V(t)	Vaccination individual at time t.
$I_v(t)$	People that were infected with HPV at time t .
C(t)	People who infected with cervical cancer at time t.
T(t)	Treatment individual at time t.
R(t)	At time t, the individual is recovering..

Description of parameters

b	The rate of recruitment in the vulnerable population.
μ	The natural death rate per year for each variable .
θ_1	Failure rate of vaccination
θ	Vaccination rate
β	The transition from HPV-susceptible to HPV-infected.
β_1	The transition from HPV-susceptible to HPV-infected.
δ	The proportion of infected cervical cancer patients in each therapy group.
γ	The percentage of people with cervical cancer who are infected and who are recei
β_1	The transition from HPV-susceptible to cervical cancer-infected..
σ	Infected cervical cancer has a high mortality rate.
Δ	The number of people who die as a result of being infected with HPV is on the rise
ϕ	Treatment-related death rate.
ψ	The rate of treatment individual to recovery.
λ	The percentage of people who have been shifted to the susceptible class.

3 Analysis of The Model

3.1 Positivity and boundedness of the model's solution

Theorem 1:

The biological importance of the model system (1) lies on the region $\Omega = \{(S,V,I_v,C,T,R)\text{in } R^6 : 0 \leq S+V+I_v+C+T+R = N, N < \frac{b}{\mu}\}$.

Proof:

From the first equation of system (1), $\frac{dS}{dt} = b - \frac{S\beta I_v}{N} - \frac{S\beta_1 C}{N} - \mu S + \theta_1 V - \theta S + \lambda R$, we can be expressed as a form of inequality $\frac{dS}{dt} \geq -\frac{S\beta I_v}{N} - \frac{S\beta_1 C}{N} - \mu S - \theta S$. We obtain after some simplifications, $S(t) > S_0 e^{-\left(\frac{\beta I_v + \beta_1 C + \mu + \theta}{N}\right)t} \geq 0$. Here, The starting population of susceptible is $S(0)$, which is an integral constant and

indicates a positive amount with the limit $t \to \infty$, resulting in $S(t) > 0$. As a result, S(t) is always a positive number.

From the second equation of system (1), $\frac{dV}{dt} = \theta S - \theta_1 V - \mu V$, expressed as type of inequality, $\frac{dV}{dt} \geq -\theta_1 V - \mu V$. We got, $V(t) > V_0 e^{-(\theta_1+\mu)t} \geq 0$. Here, V_0 is an integral constant, the initial population of the vaccine individual, and a positive amount with a limit $t \to \infty$ which leads to $V(t) > 0$. Hence, $V(t)$ is always a positive number.

Based on third equation of system (1), $\frac{dI_v}{dt} = \frac{S\beta I_v}{N} + \frac{S\beta_1 C}{N} - (\Delta + \mu) I_v - (1-\gamma) I_v - \gamma I_v$, it can be expressed as form of inequality as $\frac{dI_v}{dt} \geq -(\Delta+\mu) I_v - (1-\gamma) I_v - \gamma I_v$. The analytic solution $I_v(t) > I_v(0) e^{-(\Delta+\mu+1)t} \geq 0$. Since, $I_v(0)$ represents the initial population of HPV-infected people, an integral constant, and a positive value. $t \to \infty$ leads to $I_v(t) > 0$. Hence, $I_v(t)$ is always positive.

Based on fourth equation of system (1)„ $\frac{dC}{dt} = \gamma I_v - (\sigma + \mu) C - \delta C$, which can express as an inequality form $\frac{dC}{dt} \geq -(\sigma + \mu) C - \delta C$. The solution is $C(t) > C_0 e^{-(\sigma+\mu+\delta)t} \geq 0$. This shows that, $C(0)$ is constant and initial population of the People who infected with cervical cancer and positive quantity with the limit $t \to \infty$ and the solution leads to $C(t) > 0$. Here, $C(t)$ is always positive.

Based on fifth equation of system (1)„ $\frac{dT}{dt} = \delta C + (1-\gamma) I_v - (\phi + \mu) T - \psi T$, which can express as an inequality form $\frac{dT}{dt} \geq -(\phi + \mu) T - \psi T$. The solution is $T(t) > C_0 e^{-(\phi+\mu+\psi)t} \geq 0$. This shows that, $T(0)$ constant, initial population of the treatment compartment and positive quantity with the limit $t \to \infty$ and the solution leads to $T(t) > 0$. Here, $T(t)$ is always a positive number.

Finally, the last equation of system (1), , $\frac{dR}{dt} = \psi T - \mu R - \lambda R$, we can express as an inequality form $\frac{dR}{dt} \geq -\mu R - \lambda R$. Then, the analytical solution is $R(t) > R_0 e^{-(\mu+\lambda)t} \geq 0$. As a result„ $R(0)$ is an integral constant that reflects the initial population of the recovered or removed compartment, and it has a positive

value with the limit $t \to \infty$ resulting in $R(t) > 0$. Here, $R(t)$ is always positive in this case.

Since, $\frac{dN}{dt} = b - \mu N - \Delta I_v - \sigma C - \phi T \leq b - \mu N$. Now, $N(t) \leq \frac{b}{\mu} + e^{-\mu t}\left(N(0) - \frac{b}{\mu}\right)$. Consider initial condition such that $0 \leq N(0) \leq \frac{b}{\mu}$ by Gronwall inequality, $0 \leq N(t) \leq \frac{b}{\mu}$.

Now, human population is now non-zero and bounded. Theorem (1) states that if a uniquely boundedness solution exists, the significance domain Ω is positively invariant.

3.1 Equilibrium Point

Disease Free Equilibrium Point

The right-hand side of equations (1) through (6) can be zero, and the variables' values can be calculated. In this situation, in the long run, every human population is mathematically susceptible, which indicates that the human population's susceptibility is not zero and can be represented as $(S, V, I_v, C, T, R) = (S, 0, 0, 0, 0, 0)$. To simplify things, we can write $(S, V, I_v, C, T, R) = (\frac{b}{\mu+\theta}, 0, 0, 0, 0, 0)$. As a result, the disease-free equilibrium point is $E_0 = (\frac{b}{\mu+\theta}, 0, 0, 0, 0, 0)$.

Endemic Equilibrium Point

The endemic equilibrium point occurs when a disease can't be completely eradicated but still exists in the human population. Let's start with equation (4),$\frac{dC}{dt} = \gamma I_v - (\sigma + \mu + \delta)C = 0$,to determine the endemic equilibrium point designated by E_1, $C^* = \frac{\gamma I_v}{\sigma+\mu+\delta}$.

From the third equation of system (1), $\frac{dI_v}{dt} = S\left(\frac{\beta I_v + \beta_1 C}{N}\right) - \left(\Delta + \mu + (1-\gamma) + \gamma\right) I_v = 0$. By simplifying this equation, I have

$S^* = \frac{(\Delta+\mu+1)\left(N(\sigma+\mu+\delta)\right) - \beta_1\gamma)N}{\beta N(\sigma+\mu+\delta)}$.

Since from the second equation of system (1),$\frac{dV}{dt} = \theta S - \theta_1 V - \mu V = 0$ and solving we get,

$V^* = \frac{\theta S}{\theta_1+\mu}$.

Starting from equation (6) from system (1), $\frac{dR}{dt} = \psi T - \mu R - \lambda R = 0$. After some simplifications and the value of $T^* = \frac{(\mu+\lambda)R}{\psi}$.

Equation (5) from system (1), $\frac{dT}{dt} = \delta C + (1-\gamma) I_v - \phi T - \mu T - \psi T = 0$. After some simplifications and the value of $I_v^* = \frac{(\phi+\mu+\psi)(\sigma+\mu+\delta)(\mu+\lambda)R}{\psi(\delta\gamma+(1-\gamma)(\sigma+\mu+\delta))}$.

From the equation (1) in system (1), to substitute the value of $C^*, S^*, T^*, V^* I_v*$ and simplify $\frac{dS}{dt} = b - S\left((\frac{\beta I_v+\beta_1 C}{N}\right) - \mu S + \theta_1 V - \theta S + \lambda R = 0$ and the value of R^* is

$R^* = \frac{-bN+\beta_1 C+S^*(\beta I_v^*+N\mu+N\theta)-\theta_1 V^* N}{\lambda N}$

Then the endemic equilibrium point $E_1 = (S^*, V^*, I_v^*, C^*, T^*, R^*)$, since

$S^* = \frac{(\Delta+\mu+1)(N(\sigma+\mu+\delta))-\beta_1\gamma)N}{\beta N(\sigma+\mu+\delta)}$.

$V^* = \frac{\theta S}{\theta_1+\mu}$.

$I_v^* = \frac{(\phi+\mu+\psi)(\sigma+\mu+\delta)(\mu+\lambda)R}{\psi(\delta\gamma+(1-\gamma)(\sigma+\mu+\delta))}$.

$C^* = \frac{\gamma I_v}{\sigma+\mu+\delta}$

$T^* = \frac{(\mu+\lambda)R}{\psi}$.

$R^* = \frac{-bN+\beta_1 C+S^*(\beta I_v^*+N\mu+N\theta)-\theta_1 V^* N}{\lambda N}$.

Basic Reproduction Number R_0

The basic reproduction number, R_0, is calculated using the next generation matrix approach, $R_0 = P(FV^-1)$,where P is the largest eigenvalue, F is the fresh infection accuracy rate in the compartment model, and V is the individual transfer out and in the compartment model. Infected compartment I_v and C are then the only ones we consider. Let fI_v denote the appearance of new infectious into I_v and $fI_v = S\left(\frac{\beta I_v+\beta_1 C}{N}\right)$ and $fC = 0$.

$$\begin{bmatrix} fI_v \\ fC \end{bmatrix} = \begin{bmatrix} S\left(\frac{\beta I_v+\beta_1 C}{N}\right) \\ 0 \end{bmatrix},$$

Then, using the Jacobian matrix as a linearizer,

$$F = \begin{bmatrix} \frac{\partial f I_v(E_0)}{\partial I_v} & \frac{\partial f I_v(E_0)}{\partial C} \\ \frac{\partial f C(E_0)}{\partial I_v} & \frac{\partial f C(E_0)}{\partial C} \end{bmatrix} = \begin{bmatrix} \frac{\beta S}{N} & \frac{\beta_1 S}{N} \\ 0 & 0 \end{bmatrix}, \text{ since } S = N$$

$$F = \begin{bmatrix} \beta & \beta_1 \\ 0 & 0 \end{bmatrix}$$

Find the value of V, we consider $VI_v = (\Delta+\mu+1)I_v$ and $VC = -\gamma I_v + (\sigma+\mu+\delta)C$.

Then,

$$\begin{bmatrix} VI_v \\ VC \end{bmatrix} = \begin{bmatrix} (\Delta+\mu+1)I_v \\ -\gamma I_v + (\sigma+\mu+\delta)C \end{bmatrix},, \text{ the linearization using the Jacobian matrix}$$

is ,

$$V = \begin{bmatrix} \frac{\partial V I_v(E_0)}{\partial I_v} & \frac{\partial V I_v(E_0)}{\partial C} \\ \frac{\partial V C(E_0)}{\partial I_v} & \frac{\partial V C(E_0)}{\partial C} \end{bmatrix} = \begin{bmatrix} \Delta+\mu+1 & 0 \\ -\gamma & \sigma+\mu+\delta \end{bmatrix} \text{ and}$$

$$V^-1 = \begin{bmatrix} \frac{1}{\Delta+\mu+1} & 0 \\ \frac{\gamma}{(\Delta+\mu+1)(\sigma+\mu+\delta)} & \frac{1}{\sigma+\mu+\delta} \end{bmatrix}$$

Then the next generation matrix method is given by

$$R_0 = maxP(FV^-1) = maxP(\begin{bmatrix} \beta & \beta_1 \\ 0 & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{\Delta+\mu+1} & 0 \\ \frac{\gamma}{(\Delta+\mu+1)(\sigma+\mu+\delta)} & \frac{1}{\sigma+\mu+\delta} \end{bmatrix})$$

$$=\max \mathrm{P}(\begin{bmatrix} \frac{\beta}{\Delta+\mu+1} + \frac{\delta\gamma}{(\Delta+\mu+1)(\sigma+\mu+\delta)} & \frac{\beta_1}{\sigma+\mu+\delta} \\ 0 & 0 \end{bmatrix})$$

Then find the value of P by using eigenvalue λ_1 of this equation and we have to get

$$\lambda_1 \left(\lambda_1 - \frac{\beta(\sigma+\mu+\delta)+\delta\gamma)}{(\Delta+\mu+1)(\sigma+\mu+\delta)}\right) = 0.$$

Which implies that, $\lambda_1 = 0$ or $\lambda_1 = \frac{\beta(\sigma+\mu+\delta)+\delta\gamma}{(\Delta+\mu+1)(\sigma+\mu+\delta)}$.

Then $R_0 = \frac{\beta(\sigma+\mu+\delta)+\delta\gamma)}{(\Delta+\mu+1)(\sigma+\mu+\delta)}$.

3.2 Stability Analysis

Stability of Disease Free Equilibrium Point E_0

Theorem 2:

When $R_0 < 1$, the disease-free equilibrium point denoted by E_0 in the model equation (1) through equation (6) is locally asymptotically stable, while E_0 is unstable when $R_0 > 1$.

Proof:

The sign of eigenvalue of the related Jacobi matrix is used to analyze the local stability behavior of equilibrium points. To put it another way, if the eigenvalues are negative and the real component is negative, the system is stable; otherwise, it is unstable. The following formula give the Jacobian matrix of non linear differential equations.

$$J(S,V,I_v,C,T,R) = \begin{bmatrix} \frac{dS}{\partial S} & \frac{dS}{\partial V} & \frac{dS}{\partial I_v} & \frac{dS}{\partial C} & \frac{dS}{\partial T} & \frac{dS}{\partial R} \\ \frac{dV}{\partial S} & \frac{dV}{\partial V} & \frac{dV}{\partial I_v} & \frac{dV}{\partial C} & \frac{dV}{\partial T} & \frac{dV}{\partial R} \\ \frac{dI_v}{\partial S} & \frac{dI_v}{\partial V} & \frac{dI_v}{\partial I_v} & \frac{dI_v}{\partial C} & \frac{dI_v}{\partial T} & \frac{dI_v}{\partial R} \\ \frac{dC}{\partial S} & \frac{dC}{\partial V} & \frac{dC}{\partial I_v} & \frac{dC}{\partial C} & \frac{dC}{\partial T} & \frac{dC}{\partial R} \\ \frac{dT}{\partial S} & \frac{dT}{\partial V} & \frac{dT}{\partial I_v} & \frac{dT}{\partial C} & \frac{dT}{\partial T} & \frac{dT}{\partial R} \\ \frac{dR}{\partial S} & \frac{dR}{\partial V} & \frac{dR}{\partial I_v} & \frac{dR}{\partial C} & \frac{dR}{\partial T} & \frac{dR}{\partial R} \end{bmatrix}, \tag{2}$$

The Jacobian matrix of system (1) are given by,

$$J(S,V,I_v,C,T,R) = \begin{bmatrix} \frac{-\beta I_v - \beta_1 C}{N} - \mu - \theta & \theta_1 & \frac{-S\beta}{N} & \frac{-S\beta_1}{N} & 0 \\ \theta & -\theta_1 - \mu & 0 & 0 & 0 \\ \frac{\beta I_v + \beta_1 C}{N} & 0 & \frac{S\beta}{N} - (\Delta + \mu + 1) & \frac{S\beta_1}{N} & 0 \\ 0 & 0 & \gamma & -\sigma - \mu - \delta & 0 \\ 0 & 0 & 1-\gamma & \delta & -\phi - \mu - \psi \\ 0 & 0 & 0 & 0 & \psi \end{bmatrix} \tag{3}$$

The disease free equilibrium point, $E_0\left(\frac{b}{\mu+\theta}, 0, 0, 0, 0, 0\right)$ can be substitute into equation (3) we have get,

$$J\left(\frac{b}{\mu+\theta},0,0,0,0,0\right)=\begin{bmatrix} -\mu-\theta & \theta_1 & -\frac{b\beta}{(\mu+\theta)N} & -\frac{b\beta_1}{(\mu+\theta)N} & 0 \\ \theta & -\theta_1-\mu & 0 & 0 & 0 \\ 0 & 0 & \frac{-b\beta}{N(\mu+\theta)}-(\Delta+\mu+1) & \frac{b\beta_1}{(\mu+\theta)N} & 0 \\ 0 & 0 & \gamma & -\sigma-\mu-\delta & 0 \\ 0 & 0 & 1-\gamma & \delta & -\phi-\mu-\psi \\ 0 & 0 & 0 & 0 & \psi \end{bmatrix} \quad (4)$$

To find the Eigen value, solve the characteristic equation for equation (4), which is given by the formulas below.

$$Det(J-cI)=\begin{vmatrix} -\mu-\theta-c & \theta_1 & -\frac{b\beta}{(\mu+\theta)N} & -\frac{b\beta_1}{(\mu+\theta)N} & 0 & \lambda \\ \theta & -\theta_1-\mu-c & 0 & 0 & 0 & 0 \\ 0 & 0 & \alpha & \frac{b\beta_1}{(\mu+\theta)N} & 0 & 0 \\ 0 & 0 & \gamma & \omega & 0 & 0 \\ 0 & 0 & 1-\gamma & \delta & -\phi-\mu-\psi-c) & 0 \\ 0 & 0 & 0 & 0 & \psi & -\mu-\lambda-c \end{vmatrix} = \quad (5)$$

Where, $\alpha=\frac{-b\beta}{N(\mu+\theta)}-\Delta-\mu-1-c$ and $\omega=-\sigma-\mu-\delta-c$

The characteristics equation of equation (5) are,

$\Rightarrow(-\mu-\theta-c)(-\theta_1-\mu-c)(\frac{-b\beta}{N(\mu+\theta)}-(\Delta+\mu+1)-c)(-\sigma-\mu-\delta-c)(-\phi-\mu-\psi-c)(-\mu-\lambda-c)=0,$

As a result, we have the following to find the Eigenvalue c. $\Rightarrow -\mu-\theta-c=0,\Rightarrow c_1=-(\mu+\theta)<0.$

$\Rightarrow -\theta_1-\mu-c=0,\Rightarrow c_2=-(\theta_1+\mu)<0.$

$\Rightarrow \frac{-b\beta}{N(\mu+\theta)}-(\Delta+\mu+1)-c=0,\Rightarrow c_3=-(\frac{b\beta}{N(\mu+\theta)}+(\Delta+\mu+1))<0.$

$\Rightarrow -\sigma-\mu-\delta-c=0,\Rightarrow c_4=-(\sigma+\mu+\delta)<0.$

$\Rightarrow -\phi-\mu-\psi-c=0,\Rightarrow c_5=-(\phi+\mu+\psi)<0.$

$\Rightarrow -\mu-\lambda-c=0, \Rightarrow c_6=-(\mu+\lambda)<0.$

We can determine the nature of illness free equilibrium point based on the algebraic sign of Eigenvalue $c_1, c_2, c_3, c_4, c_5, c_6$ of jacobian matrix. Because all of the eigenvalues are negative or less than zero, the disease-free equilibrium point is locally asymptotically stable whenever $R_0<1$.

Theorem 3:

The disease free equilibrium point of equation (1) to equation (6) is globally asymptotically stable whenever $R_0<1$ and E_0 is unstable if $R_0>1$.

Proof:

We consider the following Lyapunov function

$$W=a_1 I_v+a_2 C \tag{6}$$

Differentiate this equation with respect to time gives,

$$\frac{dW}{dt}=a_1\frac{dI_v}{dt}+a_2\frac{dC}{dt}, \tag{7}$$

Substitute $\frac{dI_v}{dt}$ and $\frac{dC}{dt}$ into equation (5), we have

$$\frac{dW}{dt}=a_1\left(\frac{S\beta I_v}{N}+\frac{S\beta_1 C}{N}-(\Delta+\mu)I_v-(1-\gamma)I_v-\gamma I_v\right)+a_2\left(\gamma I_v-(\sigma+\mu)C-\delta C\right), \tag{8}$$

$$\frac{dW}{dt}=a_1\left(\frac{S\beta I_v}{N}+\frac{S\beta_1 C}{N}-(\Delta+\mu+1)I_v\right)+a_2\left(\gamma I_v-(\sigma+\mu)C-\delta C\right), \tag{9}$$

$$\frac{dW}{dt}=\frac{a_1 S\beta_1 C}{N}-a_2(\sigma+\mu+\delta)C+a_1\left(\frac{\delta\beta}{N}-(\Delta+\mu+1)+a_2\gamma\right)I_v, \tag{10}$$

Here, $a_1\left(\frac{S\beta}{N}-(\Delta+\mu+1)\right)=-a_2\gamma$. Now,

$$a_2=\frac{-\left(\frac{S\beta}{N}-(\Delta+\mu+1)\right)a_1}{\gamma}, \tag{11}$$

$$\frac{dW}{dt} = \frac{a_1 S\beta_1 C}{N} + \frac{\left(\frac{S\beta}{N} - (\Delta+\mu+1)\right)a_1}{\gamma}(\sigma+\mu+\delta)Ca_1, \tag{12}$$

$$= \frac{\left(S\beta_1\gamma + S\beta - N(\Delta+\mu+1)(\sigma+\mu+\delta)\right)Ca_1}{N\gamma}, \tag{13}$$

Let, $S = N$ and taking $a_1 = 1$ and substitute R_0, we have

$$\frac{dW}{dt} \leq \frac{(\Delta+\mu+1)(\sigma+\mu+\delta)(R_0-1)C}{\gamma}, \tag{14}$$

Since, $\frac{dW}{dt} \leq 0$ for $R_0 < 1$. This means that the only $\frac{dW}{dt} \leq 0$, E_0 is globally asymptotically stable whenever $R_0 < 1$, according to Lasalles invariant principle.

Stability of E_1

Theorem 4:

Endemic equilibrium point $E_1 = (S^*, V^*, I_v^*, C^*, T^*, R^*)$ of the systems (1) to (6) are locally asymptotically stable, if $R_0 > 1$.

Proof

Let E^* are transformation into $S = S^* + s, V = V^* + v, I_v = I_v^* + i, C = C^* + c$, $T = T^* + t$ and $R = R^* + r$, where s, v, i, c, t and r are small perturbations.

using positive definite function,

$$M = \frac{1}{2}\left(n_1 s^2 + n_2 v^2 + n_3 i^2 + n_4 c^2 + n_5 t^2 + n_6 r^2\right) \tag{15}$$

Differentiate equation (15) with respect to time, we have,

$$\frac{dM}{dt} = n_1 s\frac{dS}{dt} + n_2 v\frac{dV}{dt} + n_3 i\frac{I_v}{dt} + n_4 c\frac{dC}{dt} + n_5 t\frac{dT}{dt} + n_6 r\frac{dR}{dt} \tag{16}$$

Now, substitute the values $\frac{dS}{dt}, \frac{dV}{dt}, \frac{dI_v}{dt}, \frac{dC}{dt}, \frac{dT}{dt}, \frac{dR}{dt}$ into equation (16) gives,

$$\frac{dM}{dt} = n_1 s\left(b - \frac{S\beta I_v}{N} - \frac{S\beta_1 C}{N} - \mu S + \theta_1 V - \theta S + \lambda R\right) + n_2 v\left(\theta S - \theta_1 V - \mu V\right) \tag{17}$$

$$+ n_3 i\left(\frac{S\beta I_v}{N} + \frac{S\beta_1 C}{N} - (\Delta+\mu)I_v - (1-\gamma)I_v - \gamma I_v\right) + n_4 c\left(\gamma I_v - (\sigma+\mu)C - \delta C\right)$$

$$+n_5 t\left(\delta C+(1-\gamma) I_v-(\phi+\mu) T-\psi T\right)+n_6 r\left(\psi T-\mu R-\lambda R\right)$$

$$\frac{dM}{dt}=-n_1\left(\mu+\theta\right)s^2-n_2\left(\theta_1+\mu\right)v^2-n_3\left(\Delta+\mu+1\right)i^2-n_4\left(\sigma+\mu+\delta)\right)c^2-n_5\left(\phi+\mu+\psi\right)t^2 \tag{18}$$

$$-n_6\left(\mu+\lambda\right)r^2-n_1\left(\frac{\beta}{N}s^2 i+\frac{\beta_1}{N}s^2 c-\lambda sr-bs\right)+n_3\left(\frac{\beta}{N}i^2 s+\frac{\beta_1}{N}sic\right)+n_4\gamma ic+\delta tc-$$

$$n_5\left(\gamma-1\right)it+n_6\psi tr$$

Let choosing $n_1=n_2=n_3=n_4=n_5=n_6=1$

$$\frac{dM}{dt}=-\left(\mu+\theta\right)s^2-\left(\theta_1+\mu\right)v^2-\left((\Delta+\mu+1)\right)i^2-\left(\sigma+\mu+\delta)\right)c^2-\left(\phi+\mu+\psi\right)t^2 \tag{19}$$

$$-\left(\mu+\lambda\right)r^2-\left(\frac{\beta}{N}s^2 i+\frac{\beta_1}{N}s^2 c-\lambda sr-bs\right)+\left(\frac{\beta}{N}i^2 s+\frac{\beta_1}{N}sic\right)+\gamma ic+n_5\delta tc-\left(\gamma-1\right)it+$$

$$\psi tr$$

Because, $\frac{dM}{dt}\leq 0$ is negative definite within the attraction area Ω. As a result, endemic if $R_0>1$, the endemic equilibrium point E_1 is locally asymptotically stable.

Theorem 5 :

Endemic equilibrium point $E_1=(S^*,V^*,I_v^*,C^*,T^*,R^*)$ of the systems (1) to (6) are globally asymptotically stable, if $R_0>1$.

Proof

Since to show that E^* is globally asymptotically stable, we have consider Lyapunov function as

$$M=(S-S^*-S\ln\tfrac{S}{S^*})+(I_v-I_v^*-I_v\ln(\tfrac{I_v}{I_v^*}))+c_0(V-V^*-V\ln\tfrac{V}{V^*})+c_1(C-C^*-$$

$$C\ln\tfrac{C}{C^*})+c_2(T-T^*-T\ln\tfrac{T}{T^*})+c_3(R-R^*-R\ln\tfrac{R}{R^*}),$$

where c_0, c_1, $c_2$and c_3 are constants and positive numbers I selected appropriately. The lyapunov function above is positive definite if and only if

$$M=(S-S^*-S\ln\tfrac{S}{S^*})+(I_v-I_v^*-I_v\ln\tfrac{I_v}{I_v^*})+c_0(V-V^*-V\ln\tfrac{V}{V^*})+c_1(C-C^*-C\ln\tfrac{C}{C^*})+$$

$$c_2(T-T^*-T\ln\tfrac{T}{T^*})+c_3(R-R^*-R\ln\tfrac{R}{R^*})>0,$$

Differentiating this equation with respect to t , we obtain;

$\frac{dM}{dt} = (S-S^*)\frac{\dot{S}}{S} + (I_v - I_v^*)\frac{\dot{I}_v}{I_v} + (V-V^*)\frac{\dot{V}}{V} + (C-C^*)\frac{\dot{C}}{C} + (T-T^*)\frac{\dot{T}}{T} + (R-R^*)\frac{\dot{R}}{R}$

Substitute the value of $\dot{S}$, $\dot{I}_v$, $\dot{V}$,$\dot{C}$, $\dot{T}$ and $\dot{R}$ into this equation we have,

$\frac{dM}{dt} = c_0(\frac{S-S^*}{S})(b - \frac{S\beta I_v}{N} - \frac{S\beta_1 C}{N} - \mu S + \theta_1 V - \theta S + \lambda R) + c_1(\frac{V-V^*}{V})(\theta S - \theta_1 V - \mu V +$

$c_2(\frac{I_v - I_v^*}{I_v})(\frac{S\beta I_v}{N} + \frac{S\beta_1 C}{N} - (\Delta+\mu)I_v - (1-\gamma)I_v - \gamma I_v) + c_3(\frac{C-C^*}{C})(\gamma I_v - (\sigma+\mu)C - \delta C) +$

$c_4(\frac{T-T^*}{T})(\delta C + (1-\gamma)I_v - (\phi+\mu)T - \psi T) + c_5(\frac{R-R^*}{R})(\psi T - \mu R - \lambda R)$

After some simplifications, we get

$\frac{dM}{dt} = -c_0(\mu+\theta)(S-S^*)^2 - c_1(\theta_1+\mu)(V-V^*)^2 - c_2(\Delta+\mu+1)(I_v - I_v^*)^2 - c_3(\sigma+\mu+$

$\delta)(C-C^*)^2 - c_4(\phi+\mu+\psi)(T-T^*)^2 - c_5(\mu+\lambda)(R-R^*)^2 + (c_0 b(S-S^*) + c_0\theta_1(V-$

$V^*)(S-S^*) + c_0\lambda(S-S^*)(R-R^*)$

$+c_1\theta(V-V^*)(S-S^*) + c_3\gamma(I_v - I_v^*)(C-C^*) + c_4\delta(T-T^*)(C-C^*) + c_4(1-\gamma)(I_v -$

$I_v^*)(T-T^*) + c_5\psi(T-T^*)(R-R^*))$.

Now, if $c_0 b(S-S^*) + c_0\theta_1(V-V^*)(S-S^*) + c_0\lambda(S-S^*)(R-R^*) + c_1\theta(V-V^*)(S-$

$S^*) + c_3\gamma(I_v - I_v^*)(C-C^*) + c_4\delta(T-T^*)(C-C^*) + c_4(1-\gamma)(I_v - I_v^*)(T-T^*) + c_5\psi(T-$

$T^*)(R-R^*)) < 0$, then, $\frac{dM}{dt} < 0$ and $R_0 > 1$. This show that endemic equilibrium point $E_1 = (S^*, V^*, I_v^*, C^*, T^*, R^*)$ of the systems (1) to (6) are globally asymptotically stable.

3.3 Sensitivity Analysis

The normalized forward sensitivity index of a variable $R_0 = R$ that depends differentiable on parameter P is defined as $\Lambda_P^R = \frac{\partial R_0}{\partial P} \times \frac{P}{R_0}$. All of the basic parameters are displayed when you type for parameter p.

Here, $R_0 = \frac{\beta(\sigma+\mu+\delta)+\delta\gamma)}{(\Delta+\mu+1)(\sigma+\mu+\delta}$ for the sensitive index of R_0 to the parameters such as $\beta, \delta, \sigma, \Delta, \mu, \gamma$ as follows:

Now, $\Lambda_\beta^R = \frac{\partial R_0}{\partial \beta} \times \frac{\beta}{R_0} = \frac{(\sigma+\mu+\delta)}{(\sigma+\mu+\delta)(\Delta+\mu+1)} \times \frac{\beta(\sigma+\mu+\delta)(\Delta+\mu+1)}{\beta(\sigma+\mu+\delta)+\delta\gamma} = \frac{\beta(\sigma+\mu+\delta)}{\beta(\sigma+\mu+\delta)+\delta\gamma} > 0$

For parameter δ, $\Lambda_\delta^R = \frac{\partial R_0}{\partial \delta} \times \frac{\delta}{R_0} = \frac{\beta+\gamma(\sigma+\mu+\delta)-\beta(\sigma+\mu+\delta)+\delta\gamma}{(\sigma+\mu+\delta)(\Delta+\mu+1)} \times \frac{\delta(\sigma+\mu+\delta)(\Delta+\mu+1)}{\beta(\sigma+\mu+\delta)+\delta\gamma}$

$= \frac{\delta\left((\beta+\gamma)(\sigma+\mu+\delta)-\beta(\sigma+\mu+\delta)+\delta\gamma\right)}{(\sigma+\mu+\delta)(\sigma+\mu+\delta+\delta\gamma)} > 0$

For parameter σ, $\Lambda_{\sigma}^{R} = \frac{\partial R_0}{\partial \sigma} \times \frac{\sigma}{R_0} = \frac{\beta(\sigma+\mu+\delta)-\beta(\sigma+\mu+\delta)+\delta\gamma}{(\sigma+\mu+\delta)(\Delta+\mu+1)} \times \frac{\sigma(\sigma+\mu+\delta)(\Delta+\mu+1)}{\beta(\sigma+\mu+\delta)+\delta\gamma}$

$= \frac{\beta(\sigma+\mu+\delta)-\beta(\sigma+\mu+\delta)+\delta\gamma)}{(\sigma+\mu+\delta)\beta(\sigma+\mu+\delta)+\delta\gamma} = \frac{-\delta\gamma}{(\sigma+\mu+\delta)\beta(\sigma+\mu+\delta)+\delta\gamma} < 0.$

For parameter γ, $\Lambda_{\gamma}^{R} = \frac{\partial R_0}{\partial \gamma} \times \frac{\gamma}{R_0} = \frac{\delta}{(\sigma+\mu+\delta)(\Delta+\mu+1)} \times \frac{\gamma(\sigma+\mu+\delta)(\Delta+\mu+1)}{\beta(\sigma+\mu+\delta)+\delta\gamma}$

$= \frac{\delta\gamma}{\beta(\sigma+\mu+\delta)+\delta\gamma} > 0.$

For parameter Δ, $\Lambda_{\Delta}^{R} = \frac{\partial R_0}{\partial \Delta} \times \frac{\Delta}{R_0} = -\frac{\beta(\sigma+\mu+\delta)+\delta\gamma}{(\Delta+\mu+1)^2(\sigma+\mu+\delta)} \times \frac{\Delta(\sigma+\mu+\delta)(\Delta+\mu+1)}{\beta(\sigma+\mu+\delta)+\delta\gamma}$

$= \frac{-\Delta}{(\mu+\Delta+1)} < 0.$

For parameter μ, $\Lambda_{\mu}^{R} = \frac{\partial R_0}{\partial \mu} \times \frac{\mu}{R_0} = \frac{\beta(\sigma+\mu+\delta)(\Delta+\mu+1)-\beta(\sigma+\mu+\delta)+\delta\gamma(\delta+\Delta+2\mu+\sigma+1)}{(\Delta+\mu+1)^2(\sigma+\mu+\delta)^2} \times \frac{\mu(\sigma+\mu+\delta)(\Delta+\mu+1)}{\beta(\sigma+\mu+\delta)+\delta\gamma}$

$= \frac{\beta\mu}{\beta(\sigma+\mu+\delta)+\delta\gamma} - \frac{\mu(\delta+\Delta+2\mu+\sigma+1)}{(\Delta+\mu+1)(\sigma+\delta+\mu)} > 0.$

Positive indexes for factors like μ, γ, δ, and β indicate that if their values are rising, they have a major impact on the spread of cervical cancer in their community.. As their values increase, those factors with negative sensitivity indices, such as σ and Δ have an effect of reducing the burden of cervical cancer in the community. Then we must reduce the positive indices of parameters while increasing the negative indices.

4 Result and Discussion

To generate numerical simulations of the system (1), the MATLAB function ODE45 is utilized. The stability study of the provided system of nonlinear ordinary differential equations (1) is performed by altering the following parameter values in Table (1), and then the supplied model is systematically computed.

Parameters	Value(per year)	Source	Parameters	Value(per year)	Source
b	288802, 16,821,072	[2], [10]	ψ	0.0576	Assumed
β	0.8	[10]	ϕ	0.0576	Assumed
β_1	0.248	[10]	δ	0.576	Assumed
μ	0.0162	[2]	σ	0.8	[3],[10]
θ_1	0.1	[2]	γ	0.85	[10]
θ	0.8	[9], [2]	Δ	0.0576	[10]
λ	0.032	Assumed			

Table 1: The parameter values of the model

Based on the above data in table (1), we found that $R_0 = \frac{\beta(\sigma+\mu+\delta)+\delta\gamma)}{(\Delta+\mu+1)(\sigma+\mu+\delta)} = \frac{0.8(0.8+0.0162+0.576)+0.576(0.85)}{(0.032+0.0162+1)(0.8+0.0162+0.576)} = 1.0987 > 1$. This shows that the disease-free equilibrium point is asymptotically unstable both locally and globally, but the endemic equilibrium point is asymptotically stable both locally and globally, meaning that cervical cancer is propagated or transmitted in the population.

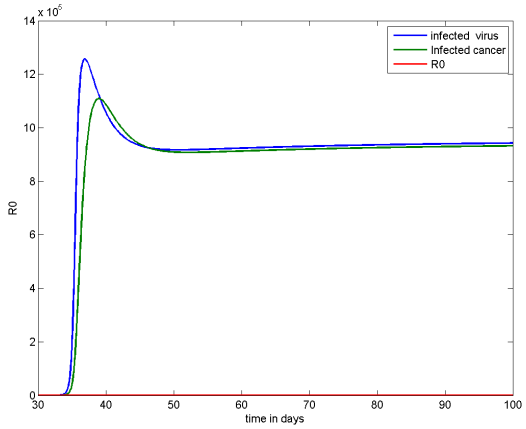

Figure 2: Infected virus and cervical cancer population for the R_0

In Figure 2, the infected virus, the cervical cancer population, and R_0 do not intersect. This indicates that the basic reproduction number is insecure, implying that cervical cancer was spreading throughout the community.

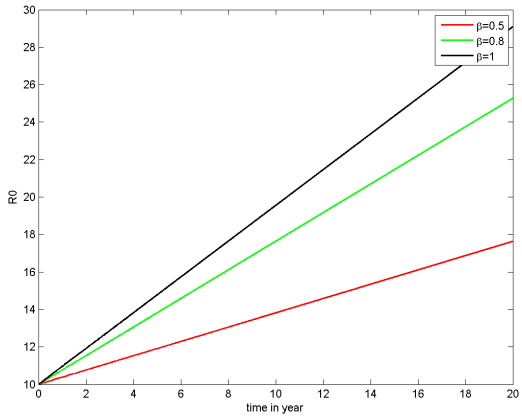

Figure 3: Infected HPV population with different value of treatment

As seen in Figure 3, the fundamental reproduction number R_0 grows as the parameter β increases. When the fundamental reproduction number R_0 rises, the endemic equilibrium point stabilizes, indicating that cervical cancer is widely distributed in the community. As a result, we must use various strategies, such as vaccination, to adjust the parameters of β.

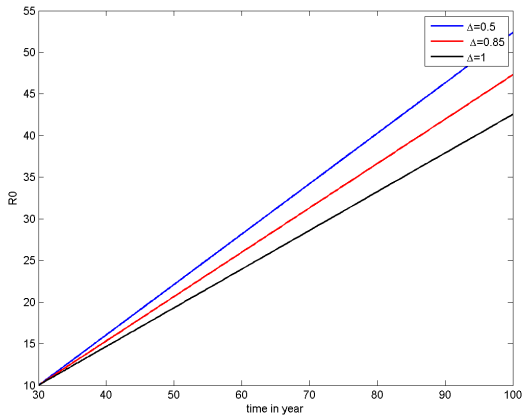

Figure 4: Infected HPV population with different value of treatment

Figure 4 shows that until the parameter of Δ grows, the fundamental reproduction number R_0 falls. When R_0 falls, the endemic equilibrium point becomes unstable, while the disease-free equilibrium point remains stable, indicating that cervical cancer is rapidly dying out. As a result, we must use various strategies such as immunization and treatment to improve the parameters of Δ.

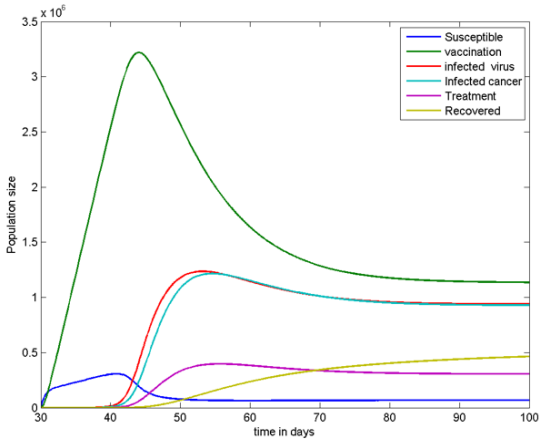

Figure 5: value of vaccination $\theta = 0.5$

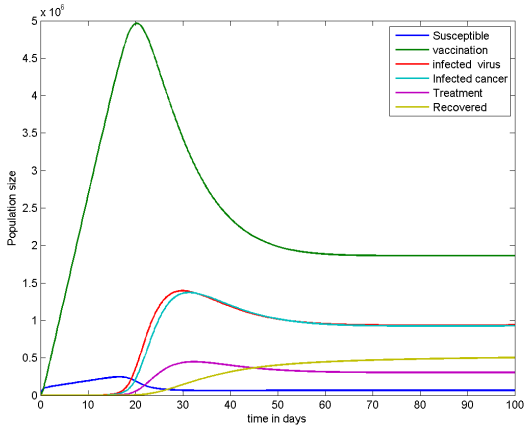

Figure 6: Susceptible,Infected HPV , infected cancer, treatment and recovery with value of vaccination $\theta = 1$

In Figure 5 and 6 shows that, vaccination is administered to the parameter $\theta = 0.5$ and $\theta = 1$ vulnerable population, resulting in a rapid decline in the number of people infected with HPV. As a result, the number of uninfected HPV rises while the number of infected cervical cancer decreases.

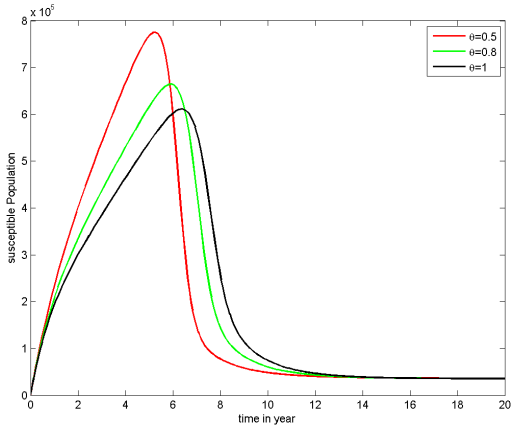

Figure 7: Susceptible with different value of vaccination

Figure 7 shows how the susceptible population decreases rapidly as the number of vaccinations administered to the population rises. People who get vaccinated gain immunity before becoming infected with HPV, and the number of people infected with cervical cancer decreases as the number of people who get vaccinated rises. As a result, immunization plays a critical role in preventing HPV-related cancers.

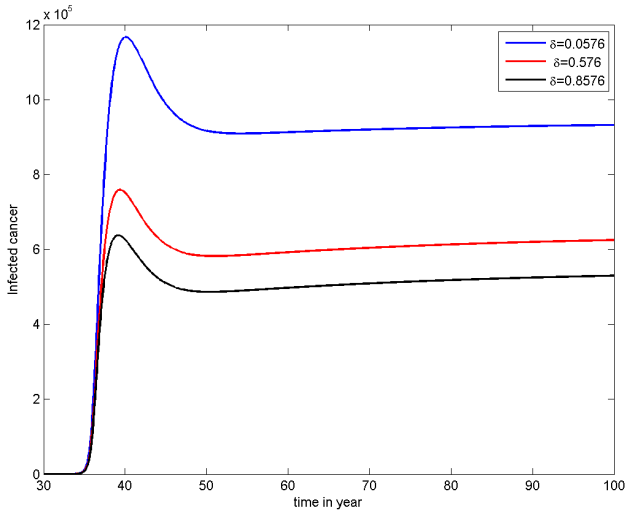

Figure 8: Infected cancer with different value of treatment

As shown in Figure 8, the number of people infected with cervical cancer decreases as the number of treatments offered to the community rises. As

the number of people treated for cervical cancer rises, the number of people infected with the disease decreases. As a result, therapy plays a critical role in cancer control .

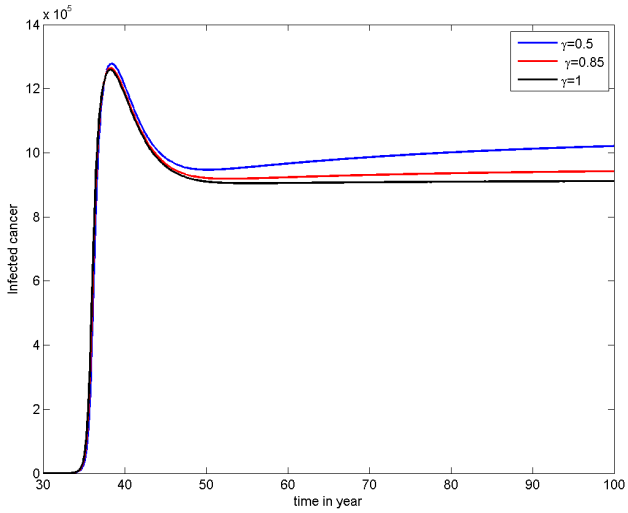

Figure 9: Infected HPV with different value of treatment

As seen in Figure 9, the number of HPV-infected people decreases as the number of treatments administered to the community rises. As the number of people treated for HPV decreases, the number of those infected with the virus decreases. As a result, therapy plays a critical role in preventing HPV-related cancers.

5 Conclusions

In this paper, we developed a $SVIvCTR$ model for the propagation of cervical cancer transmission disease. A mathematical model that examines the cervical cancer transmission illness in the presence of vaccination and treatment. The model properties such as positive, boundedness, sensitivity analysis, existence of stability of disease free equilibrium points as well as endemic equilibrium point, and basic reproduction number R_0 are computed, indicating that the model is mathematically well-posed and epidemiological meaningful.

The disease-free equilibrium point is globally asymptotically unstable, according to stability analysis, because the basic reproduction number $R_0 = 1.0987 > 1$. The sickness does not progress and eventually dies out in this situation. The endemic equilibrium point is locally asymptotically stable due to the basic reproduction number $R_0 = 1.0987 > 1$ and globally asymptotically stable because all trajectories originating inside the region of attraction are approaching the equilibrium values $(S^*, V^*, I_v^*, C^*, T^*, R^*)$. In this instance, each existing infection results in the emergence of several new infections. It was discovered that the model has an endemic equilibrium that exists when $R_0 = 1.0987 > 1$.

We studied four most influential parameters such as β, δ, γ, and μ to make the basic reproduction number R_0 less than one using sensitivity analysis to increases the spread of cervical cancer. We must control the spread of cervical cancer disease by increasing the parameter value of Δ and σ.

When a vaccination is administered to a susceptible population, that group develops immunity against HPV, which is responsible for 80% of cervical cancer cases. Vaccines, in general, have an important role in reducing and controlling disease.

Data availability statement

We are pleased to announce that the manuscript's materials, including all essential raw data, will be made freely available to any scientist who desires to use them for non-commercial purposes while maintaining participant confidentiality.

Authors contributions

MDG came up with the paper's main idea and produced the first draft of the manuscript. MFE changed and double-checked every stage of the solutions in this study. The writers read and approved the final manuscript.

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