BT 5240 – COMPUTATIONAL SYSTEMS BIOLOGY

COMPARTMENTAL MODEL FOR ANALYZING CERVICAL CANCER SCREENING STRATEGIES IN INDIA

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Abstract

This project aims to develop a compartmental model that analyses cervical cancer prevention strategies in India, a country disproportionately affected by this disease. Here, HPV infection is a substantial health issue, with prevalence double the global average and a diverse impact on different regions and demographics. Existing models like SICR provide a basic framework but lack the detail needed to analyze the actual effect of screening programs in India's diverse population.

Through this project, we aim to bridge this gap by developing a compartmental model that incorporates key population dynamics alongside screening coverage rates. The model will assess the impact of HPV testing on identifying pre-cancerous lesions and preventing cancer progression. By simulating these factors, the model offers valuable insights for public health policymakers. It can quantify the effectiveness of current screening programs and guide resource allocation for optimized program design. This quantitative approach is crucial for determining the most impactful strategies for cervical cancer prevention in the Indian context.

1 Introduction

1.1 HPV infection in India

Human Papillomavirus (HPV) infection is a global health concern, affecting millions of individuals worldwide, with significant implications for public health. In India, HPV infection is a substantial health issue, with a diverse impact on different regions and demographics. The country bears a considerable burden of cervical cancer, primarily attributed to high-risk HPV types. India's vast and diverse population, coupled with variations in healthcare accessibility, contributes to the complexity of HPV's prevalence and impact. Compared to the world, India faces a disproportionate burden of cervical cancer with about 22 per cent of global cases and deaths, the country's HPV prevalence is double the global average

This alarming situation has prompted the Indian government to take action. In the 2024 Interim Budget, Union Finance Minister Nirmala Sitharaman announced plans to focus on vaccination against cervical cancer for girls aged 9 to 14, aiming to proactively combat HPV infection and prevent future cases of cervical cancer. While HPV vaccination offers a powerful preventive approach, its effectiveness must be evaluated alongside existing screening programs. This project proposes a novel compartmental model to analyze the interplay of the impact of screening strategies in the Indian context.

1.2 Objectives

The model specifically focuses on:

- Integrating key population factors that influence cervical cancer risk
- Analyzing the impact of HPV testing on identifying pre-cancerous lesions
- Evaluating the effectiveness of screening programs in preventing cervical cancer progression.

2 Methods

2.1 SICR Compartmental Model

An SICR compartmental model from the research paper by Praveen Kumar Rajan is considered as a base compartmental model to start with.

2.1.1 Model Formulation

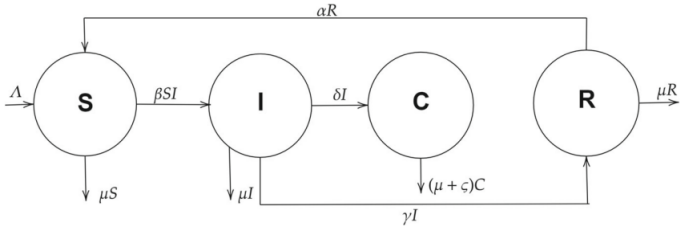


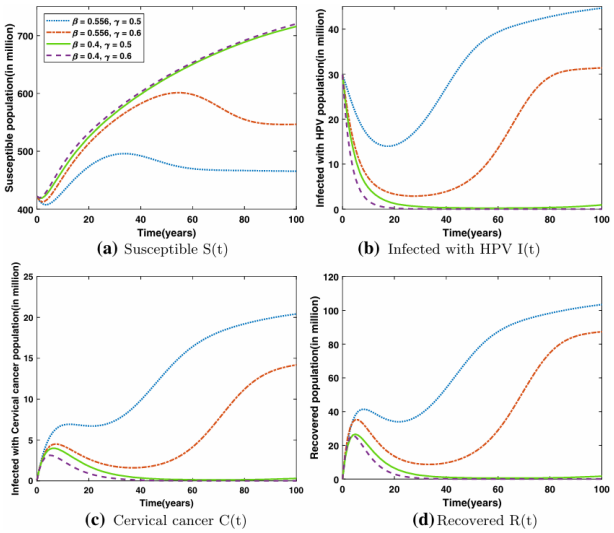
Figure 1: SICR Model

$$\frac{dS}{dt} = \Lambda - \frac{\beta SI}{N} - \mu S + \alpha R$$
$$\frac{dI}{dt} = \frac{\beta SI}{N} - (\delta + \mu + \Upsilon)I$$
$$\frac{dC}{dt} = \delta I - (\varsigma + \mu)C$$
$$\frac{dN}{dt} = \Upsilon I - (\alpha + \mu)R$$

Figure 2: Base Ordinary Differential Equations (ODEs)

2.1.2 Simulation results

Initial conditions: S = 422 million, I = 30 million, C = 99,000, R(0) = 0. We observe the following trends in S,C I and R



(a) Susceptible S(t) **(b)** Infected with HPV I(t)

(c) Cervical cancer C(t) **(d)** Recovered R(t)

Figure 3: SICR Model - Simulation Results

2.2 Updated Compartmental Model

2.2.1 Model Structure

Considering the base compartmental model as the foundation we developed an updated version of the compartmental model including screening and treatment. Based on the screening rate α, the initial susceptible compartment is divided into two smaller compartments: Screened and Not Screened. It is now expected that the Not Screened compartment will carry on similarly to the base compartmental model with Infected and Recovered compartments.

In the Screened compartment we have 2 outcomes Positive and Negative. We have assumed the HPV test as the primary mode of screening and Thermal Ablation as the treatment method as per the WHO recommendations. All patients with positive results in screening are assumed to undergo a colposcopy test to know the stage of infection. As these results are not entirely accurate we expect a fraction of patients ${\beta^3}_{FP}$, i.e false positive patients to go to the Susceptible compartment and the remaining True HPV positive patients are split into 3 categories CIN1, CIN2/3, Cancer based on the HPV Screening for Cervical Cancer in Rural India - N Engl J Med 2009. The False-negative patients in screening are assumed to follow a path similar to that of an unscreened patient thus a certain proportion of them join into the Infected Compartment.

$$\beta^1 = \frac{Sensitivity \times prevalence}{Sensitivity \times prevalence + (1 - Specificity) \times (1 - prevalence)} = \mathbf{0.4}$$

$$\beta^2 = [1 - \frac{Specificity \times (1 - prevalence)}{(1 - Sensitivity) \times prevalence + (Specificity) \times (1 - prevalence)}] = \mathbf{0.013}$$

$$\beta^3_{FP} = [1 - \frac{Sensitivity \times prevalence}{Sensitivity \times prevalence + (1 - Specificity) \times (1 - prevalence)}] = \mathbf{0.6}$$

$$\beta^3_{TN} = \frac{Specificity \times (1 - prevalence)}{(1 - Sensitivity) \times prevalence + (Specificity) \times (1 - prevalence)} = \mathbf{0.987}$$

Prevalence = 10%

HPV Test – Sensitivity: 0.9, Specificity: 0.85

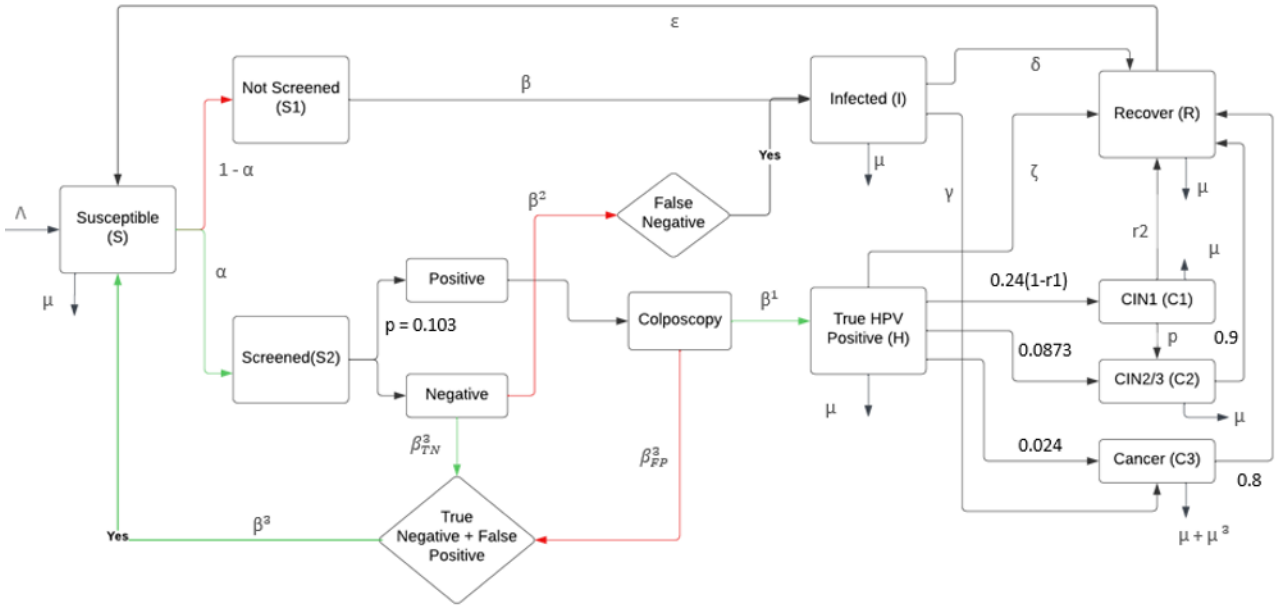


Figure 4: Updated Compartmental Model

Here a few proportion of the Infected population from Not screened stem also join into C3 as generally infected patients get diagnosed in the cancer stage. Patients in CIN2/3 and C3 are assumed to undergo thermal ablation treatment as recommended by the WHO guidelines and the progression and recovery of these compartments is based on the efficacy data of thermal ablation.

The below set of mathematical equations governs the interactions between these groups, considering factors like infection rates, cancer progression, and recovery etc

$$\frac{dS}{dt} = \Lambda + \varepsilon R - S + \eta S1 + \beta^3_{TN} N + \beta^3_{FP} Col - \mu S$$

$$\frac{dS1}{dt} = (1-\alpha)S - (\eta)S1 - \frac{\beta S1 I}{N}$$

$$\frac{dS2}{dt} = \alpha S - S2$$

$$\frac{dI}{dt} = \frac{\beta S1 I}{N} + \beta^2 N - (\delta + \mu + \Upsilon) I$$

$$\frac{dCol}{dt} = pS2 - (\beta^1 + \beta^3_{FP}) Col$$

$$\frac{dN}{dt} = \mathrm{n}S2 - (\beta^2 + \beta^3_{TN}) N$$

$$\frac{dH}{dt} = \beta^1 Col - (0.24(1-r_1) + 0.0873 + 0.024 + \zeta + \mu) H$$

$$\frac{dC1}{dt} = 0.24(1\text{-}r_1)\mathrm{H} - (r_2 + \mathrm{p} + \mu) C1$$

$$\frac{dC2}{dt} = 0.0873\mathrm{H} + \mathrm{pC1} - 0.9\mathrm{C2} - \mu\,\mathrm{C2}$$

$$\frac{dC3}{dt} = 0.024\mathrm{H} - 0.8\mathrm{C3} - (\mu + \mu^3)\mathrm{C3}$$

$$\frac{dR}{dt} = \delta I + \zeta R + r_2 \mathrm{C1} + 0.62\mathrm{C2} + 0.8\mathrm{C3} - (\varepsilon + \mu)\mathrm{R}$$

Figure 5: Updated Ordinary Differential Equations (ODES)

Parameters	Definition	Value
Λ	recruitment rate of susceptible women	9.016 Mil
α	Screening rate	0.7
β	HPV transmission rate	0.556
γ	rate at HPV progress to develop cervical cancer	0.485484
δ	rate of HPV recovering without cancer	0.5
μ	population's normal death rate	0.014516
μ_3	mortality rate of population after cancer	0.108696
ϵ	rate of becoming susceptible again	0.2
r1	rate of clearance from CIN1 but remaining HPV infected	0.13
r2	rate of clearance from both the CIN1 and infection	0.77
p	rate of progression from CIN1 to CIN2	0.065
β^1	True positive rate from Colposcopy	0.4
β^2	False negative rate during screening	0.013
${\beta^3}_{FP}$	False positive rate from Colposcopy	0.6
${\beta^3}_{TN}$	True negative rate during screening	0.987
η	Rate at which not screened people become susceptible again	0.429484
ζ	Recovery rate of HPV patients	0.6799

Figure 6: Parameters

2.3 Parameter Estimation

We have used the base compartmental model results as the base data available and tried to finetune the parameters of our model based on recovered outcome and obtained following results using ODEINT for simulation

2.3.1 Simulation results

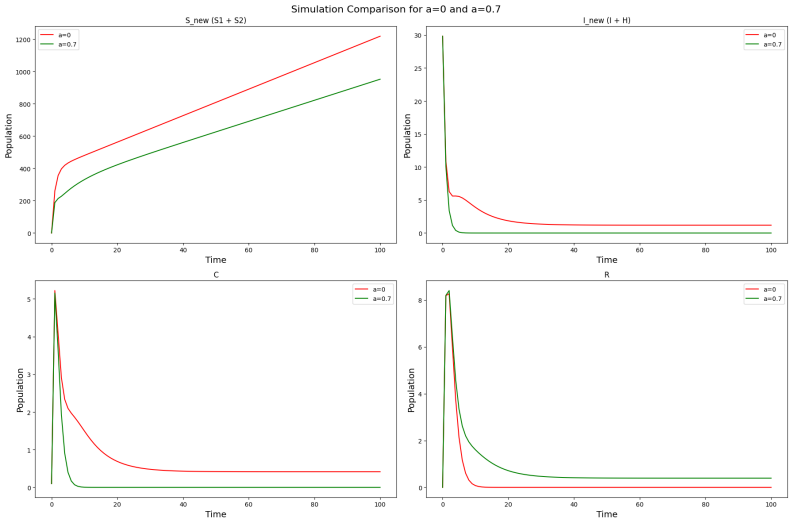


Figure 7: Updated Compartmental Model - Simulation Results

The results showed that as the screening percentage (α) increased, the size of the susceptible pool (S) decreased significantly. This indicates that screening is effective in identifying and removing individuals from the early stages of HPV infection, thereby limiting the spread of the virus. Initially, the number of infected individuals (I) also decreased with increasing screening rates. This suggests that early detection through screening leads to timely interventions and potentially helps clear the infection.

The model also predicts a significant decline in the cancer compartment (C) with increasing screening rates, especially in the long term, preventing the progression of HPV infection to cervical cancer. The number of recovered individuals (R) is expected to rise initially with increased screening. This reflects successful treatment or natural clearance of the infection after being identified through screening.

3 Conclusion

Overall, this model, simulating cervical cancer prevention through screening showed promising results. Increased screening rates effectively reduced the susceptible pool, infections, and cancer cases, highlighting the importance of these programs. However, the model's limitations, such as the convergence of compartments at higher screening, suggest the need for further refinement by incorporating factors like re-infection dynamics and treatment efficacy variability.

The Supplementary Information, which include the codes used for the work is given here.

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