The Dynamic Optimal Control Model for Analyzing the Cost-effectiveness of Cervical Cancer Prevention in South-Asian Developing Countries

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Introduction: Cervical cancer

- Fourth most frequent cancer in women
  - “Every two minutes, somewhere in the world, one woman will lose her life to the disease.” (*WHO, 2018*)
  - Estimated 530,000 incident cases in 2012, representing 7.9% of all female cancers (*WHO 2012*)
- 80% of the 274,000 deaths from cervical cancer each year occurred in developing countries *(Agosti and Goldie, 2007*)
- Poverty trap

Background: HPV vaccine

- Human papilloma virus (HPV) infection is the major cause of cervical cancer (*Schiffman, et al, 1993; Walboomers, et al, 1999; Bosch, et al, 2002; ACS, 2017*)
- HPV vaccine can prevent certain types of HPV which can further prevent cervical cancer (*Saslow, et al, 2007*)
- Types of HPV vaccine
  - Cervarix: type 16 and 18
  - Gardasil: type 6, 11, 16 and 18
  - Gardasil 9: types 6, 11, 16, 18, 31, 33, 45, 52, and 58
- Price of the vaccine: $4.55/dose ~$40/dose (*Campos, et al, 2016*)

Background: Screening

- Vaccine does not eliminate the need for regular screening (*WHO*)
  - The vaccines do not protect against all high risk HPV types
  - Non-vaccinated girls continue to be at risk
- Types of screening
  - Visual Inspection with Acetic Acid (VIA)
  - Pap Smear test
  - HPV DNA test

Research Question

- What is the most cost-effective HPV vaccination rate and screening rate in developing countries?
- Can fully coverage rate be cost-effective?

Theoretical Model

Health Behavior Decision Tree

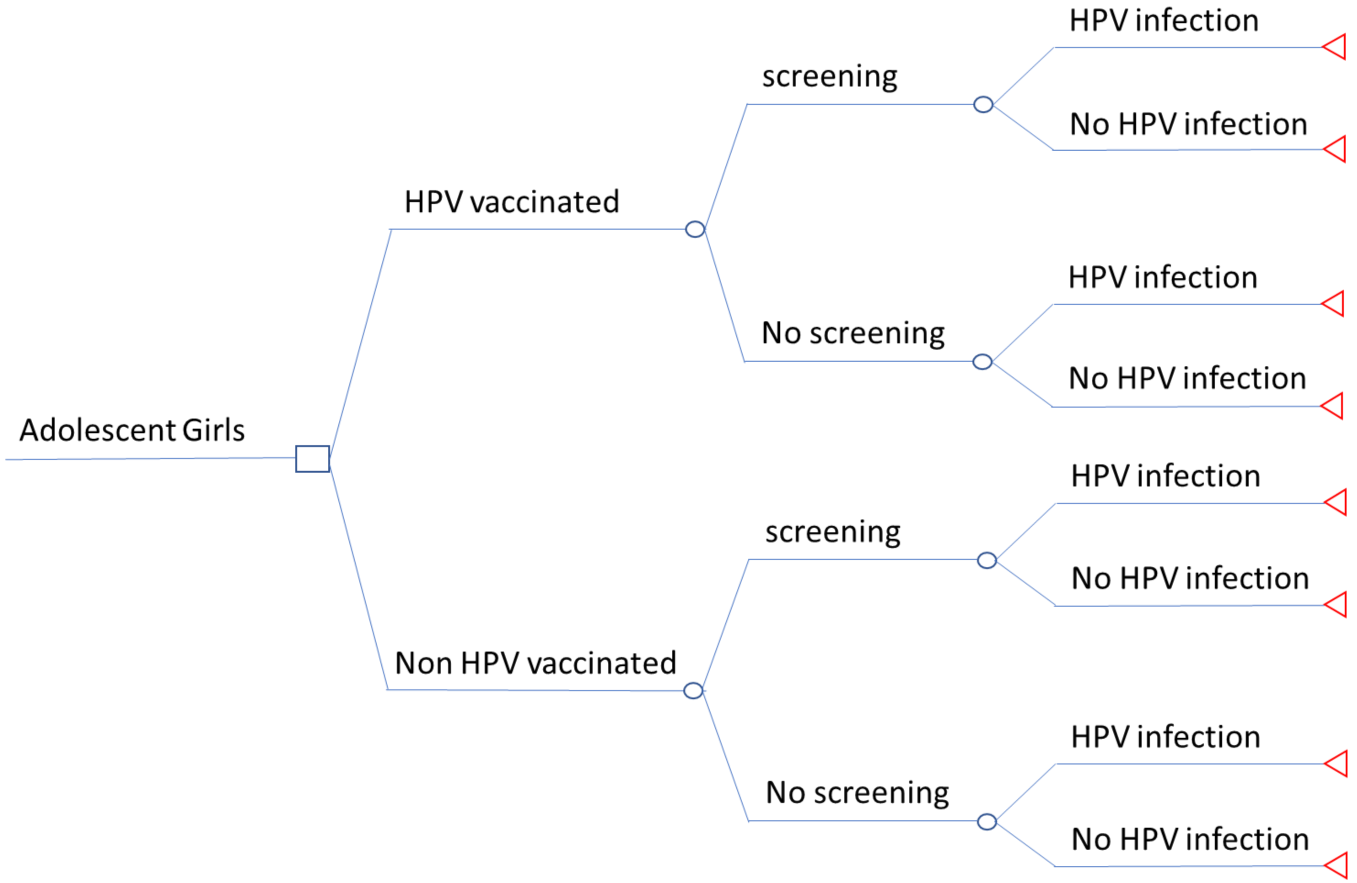


Figure 1 The health behavior decision tree of HPV vaccine and cervical cancer screening

Theoretical Model

Cohort Markov Model

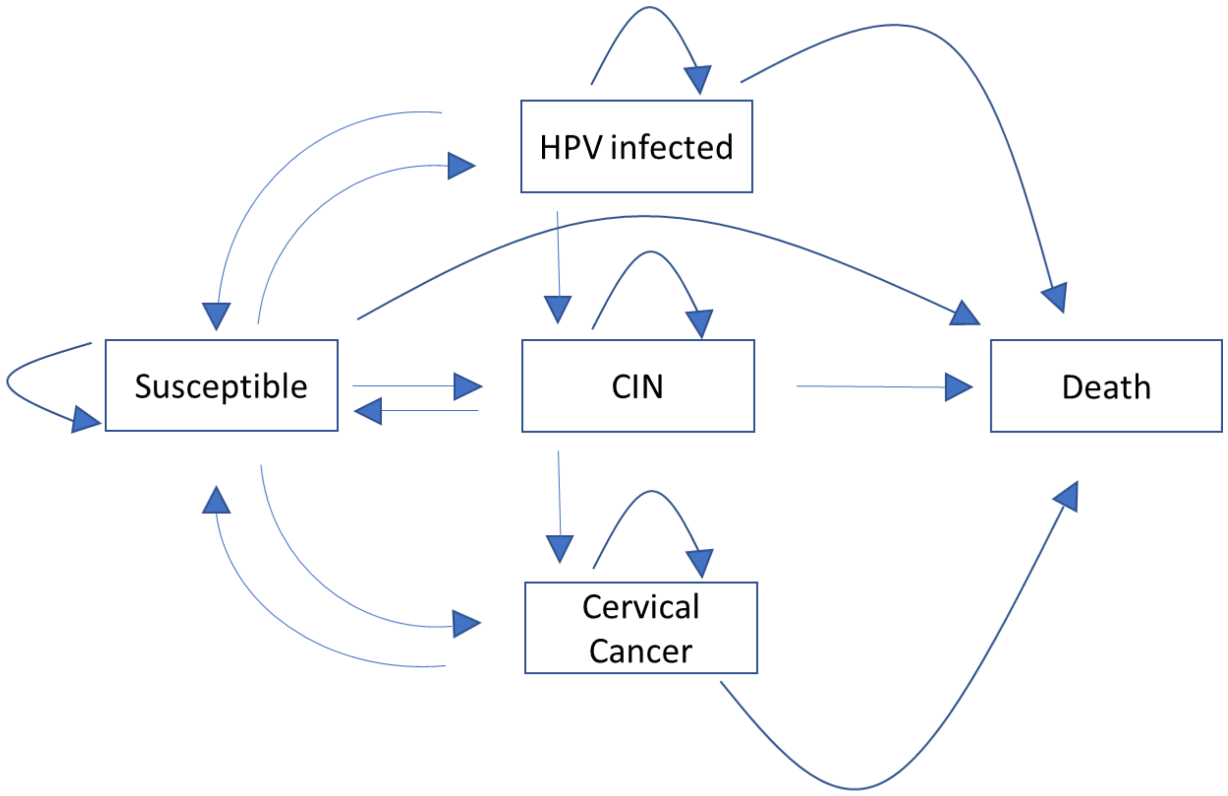


Figure 2 Transition of stages with the HPV

Theoretical Model

SIS Model
Ribassin-Majed and Lounes 2010

- Non-vaccinated Susceptible women
  - $\frac{dXs}{dt} = (1 - \varphi(t))\Lambda - \gamma Xs + \delta Xi - \mu Xs$
- Non-vaccinated Infected women
  - $\frac{dXi}{dt} = \gamma Xs - (\delta + \mu)\, Xi$
- Vaccinated Susceptible women
  - $\frac{dVs}{dt} = \varphi(t)\Lambda - (1 - \tau)\gamma Vs + \delta Vi - \mu Vs$
- Vaccinated Infected women
  - $\frac{dVi}{dt} = (1 - \tau)\gamma Vs - (\delta + \mu)Vi$

Theoretical Model

SIS Model (cont'd)

- Population size (only women in this case)

$$N_f = X_s + X_i + V_s + V_i$$

$$\dot{N}_f = \Lambda - \mu N_f \longrightarrow N^* = \frac{\Lambda}{\mu}$$

$$\mathrm{M} = \{(X_s, X_i, V_s, V_i) \in \mathbb{R}_+^4, X_s + X_i + V_s + V_i \leq \frac{\Lambda}{\mu}\}.$$

- Screening population

$$\dot{S} = \omega(t)\, \dot{N}_f$$

Dynamic Optimal Control Model

- Objective function:
  - Minimize the total social welfare cost (*Brown and White, 2011*):
    - The cost of the vaccine
    - The cost of the screening
    - The cost of HPV infection treatment
    - The cost of precancerous stage (CIN) and cervical cancer treatment

$$\min_{v(t),\omega(t)} C = \int_0^T [A(V_s + V_i) + B(\omega(t)N_f) + C(X_i + V_i) + D + E]\, \mathrm{dt}$$

Dynamic Optimal Control Model

$$\min_{v(t),\omega(t)} C = \int_0^T [A(V_s + V_i) + B(\omega(t)N_f) + C(X_i + V_i) + D + E]\, \mathrm{dt}$$

s.t.:

$$\frac{dXs}{dt} = (1 - \varphi(t))\Lambda - \gamma Xs + \delta Xi - \mu Xs$$

$$\frac{dXi}{dt} = \gamma Xs - (\delta + \mu)\, Xi$$

$$\frac{dVs}{dt} = \varphi(t)\Lambda - (1 - \tau)\gamma Vs + \delta Vi - \mu Vs$$

$$\frac{dVi}{dt} = (1 - \tau)\gamma Vs - (\delta + \mu) Vi$$

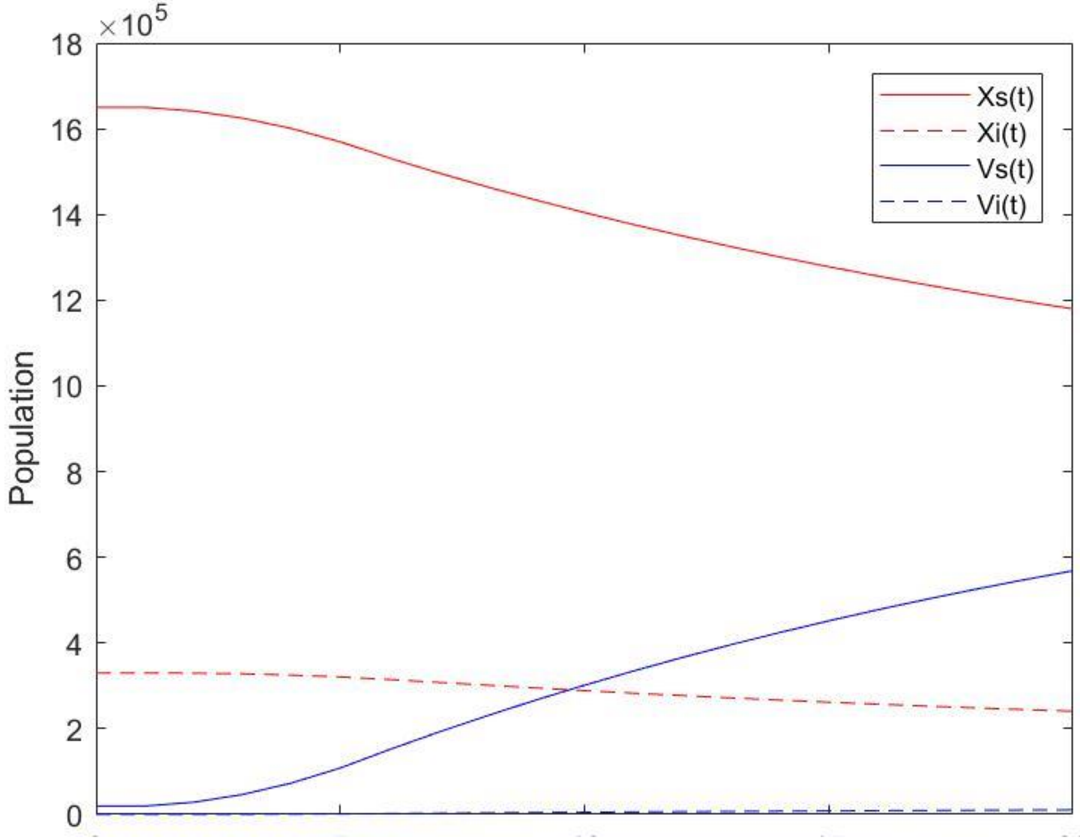
To solve the model, we need to set up the initial conditions for the state variables, which lead us to do the simulation with real world data.

Simulation: Facts and assumptions

- Low-income country scenario:
  - Vaccine: *2 doses for the 10 years old girls*
  - Screening: *screen every 5 years for the women age from 25 to 65*
- Costs do not change for the time period
- Time period: *10 years*
- HPV vaccine effectiveness of protection: *90% and lifetime*

Discussion: Simulation

- Use APMoniter with Matlab



Discussion: Add two more variables

- Precancerous-stage (CIN) population:
  - $\frac{dCp}{d\varphi} < 0$
  - $\frac{dCp}{d\omega} \frac{\leq}{>} 0$?
- Cervical cancer patient population
  - $\frac{dCc}{d\varphi} < 0$
  - $\frac{dCp}{d\omega} < 0$

Future work

- Extend the model with dynamic CIN population and cervical cancer population, as well as variate Λ (the new population enter sexual activity)
- Apply data from different south-Asian countries (Nepal, Bangladesh, Pakistan, etc.) to find the optimal vaccination and screening rates
- Compare the cost-effectiveness of vaccination and screening for developing countries by calculating the disability-adjusted life years (DALYs) and incremental cost-effectiveness ratios (ICERs) separately for vaccination and screening, then compare ICERs to the countries’ per capita gross domestic product

Thank you!