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

Mengqi Liu (Mandy), Alok K. Bohara
Economics Department, University of New Mexico
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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

- 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

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

Figure 2 Transition of stages with the HPV
Theoretical Model

- Non-vaccinated Susceptible women
  \[ \frac{dx_s}{dt} = (1 - \varphi(t))\Lambda - \gamma Xs + \delta Xi - \mu Xs \]
- Non-vaccinated Infected women
  \[ \frac{dx_i}{dt} = \gamma Xs - (\delta + \mu) Xi \]
- Vaccinated Susceptible women
  \[ \frac{dv_s}{dt} = \varphi(t)\Lambda - (1 - \tau)\gamma Vs + \delta Vi - \mu Vs \]
- Vaccinated Infected women
  \[ \frac{dv_i}{dt} = (1 - \tau)\gamma Vs - (\delta + \mu) Vi \]
Theoretical Model

• Population size (only women in this case)

\[ N_f = X_s + X_i + V_s + V_i \]

\[ \dot{N}_f = \Lambda - \mu N_f \quad \Rightarrow \quad N^* = \frac{\Lambda}{\mu} \]

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

• 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

\[
\min_{\nu(t), \omega(t)} C = \int_0^T [A(V_s + V_i) + B(\omega(t)N_f) + C(X_i + V_i) + D + E] \, dt
\]
Dynamic Optimal Control Model

\[
\min_{\nu(t), \omega(t)} \quad C = \int_0^T \left[ A(V_s + V_i) + B(\omega(t)N_f) + C(X_i + V_i) + D + E \right] \, dt
\]

s.t.: \[
\begin{align*}
\frac{dX_s}{dt} &= (1 - \varphi(t))A - \gamma X_s + \delta X_i - \mu X_s \\
\frac{dX_i}{dt} &= \gamma X_s - (\delta + \mu) X_i \\
\frac{dV_s}{dt} &= \varphi(t)A - (1 - \tau)\gamma V_s + \delta V_i - \mu V_s \\
\frac{dV_i}{dt} &= (1 - \tau)\gamma V_s - (\delta + \mu)V_i
\end{align*}
\]

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:
  - \( \frac{dC_p}{d\phi} < 0 \)
  - \( \frac{dC_p}{d\omega} > 0 ? \)

- Cervical cancer patient population
  - \( \frac{dCc}{d\phi} < 0 \)
  - \( \frac{dC_p}{d\omega} < 0 \)
Future work

• Extend the model with dynamic CIN population and cervical cancer population, as well as variate $\Lambda$ (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!