HPV 100: HPV Epidemiology, Economic Modeling and Influence on Availability of Therapies for Global Prevention of Cervical Cancer

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Outline

- Incidence of HPV–Induced Cervical Cancer
- Cost-Effectiveness Analysis (CEA) of HPV Vaccines
- CEA of HPV Vaccines in Developing Countries
- Policy Implications

HPV Diseases

- Cervical cancer
- Oropharyngeal cancer
- Vulvar cancer
- Bowen's disease
- Vaginal cancer
- Bowenoid papulosis
- Anorectal cancers
- Genital warts
- Penile cancer

Introduction

- Persistent infection with oncogenic human papillomavirus (HPV):
  - Majority of squamous cell cervical cancer
  - Histologic precursor lesions, cervical intraepithelial neoplasia (CIN)
- Multiple HPV strains cause varying degrees of invasive cervical cancer (ICC) and its CIN precursors
  - HPV strains 16 and 18 cause 70% of all cervical cancers

Incidence

- Worldwide, the incidence of cervical cancer was 529,000 new cases in 2008
  - 288,000 deaths per year according to the World Health Organization
  - Third most common cancer in women
  - Second-leading cause of cancer deaths

Rates of Cervical Cancer by Region

- Women in developing countries most at risk
  - Highest incidence rates
    - Eastern and Western Africa (ASR>33 per 100,000)
    - South-Central Asia (24.6 per 100,000)
    - South America (23.9 per 100,000)
- Risks are lowest in Western Asia (ASR 4.5 per 100,000), North America (5.7 per 100,000) and Australia/New Zealand (5.0 per 100,000)

5-Year Cervical Cancer Survival Rates

- Developed nations: 66%
- Developing countries: <50%
- For every 5-year delay in cervical cancer prevention/detection program, additional 1.5-2.0 million deaths

Incidence in US

- Approximately 12,000 new cases of ICC were diagnosed and about 4200 deaths in women were expected from ICC in 2010
- HPV most common sexually-transmitted disease in US

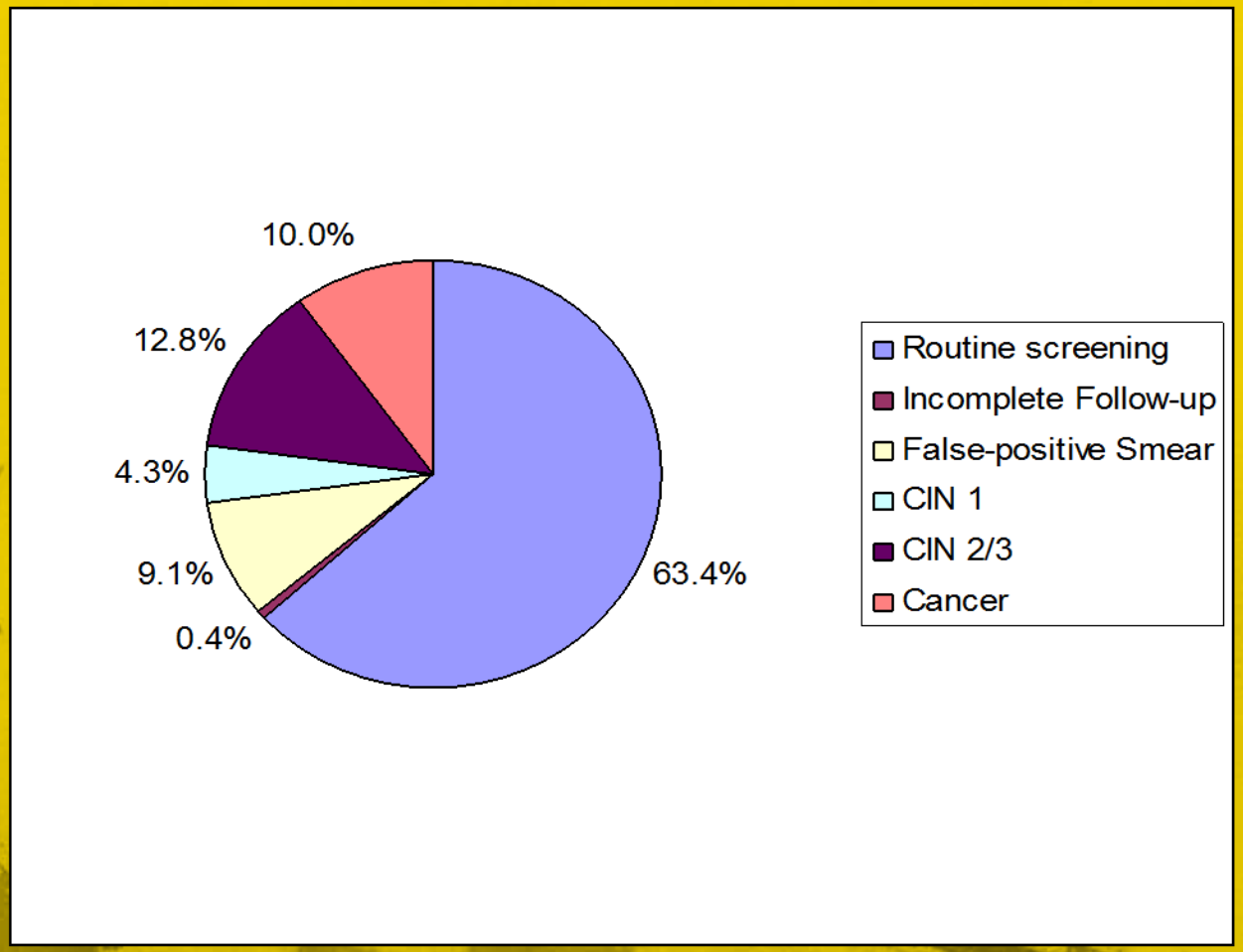
Slowed Decline in ICC Incidence/Mortality

- Poor sensitivity of cervical cytology
- Anxiety and morbidity of screening investigations
- Poor access to and attendance of screening programs
- Falling screening coverage
- Poor predictive value for adenocarcinoma

Estimated US Population Costs

- US$3.4 billion to $5 billion direct
  - Medical: hospital care, physician fees, drug costs, costs of adverse events
  - Nonmedical: transportation costs
- US$1.3 billion indirect (productivity)

Cost Component Distribution



Two Vaccines Currently Available

- Gardasil (Merck)
- Cervarix (GlaxoSmithKline)

Cost will be key factor

Arguments About Vaccine

Pro

- Virtually 100% of cervical cancer is due to HPV
- Cervical cancer is deadly, especially in developing countries
- Poor access to screening programs globally
- Treatment of cervical cancer very expensive
- Boys and men?
  - Reduce transmission; de novo cancers

Con

- Don't know which patients will progress from cervical dysplasia to ICC or spontaneously regress (generally self-limiting)
- Cost
- Vaccine cost-effective only if screen less frequently
- Vaccines don't offer full protection
- 70% of girls need to be vaccinated ("herd immunity")

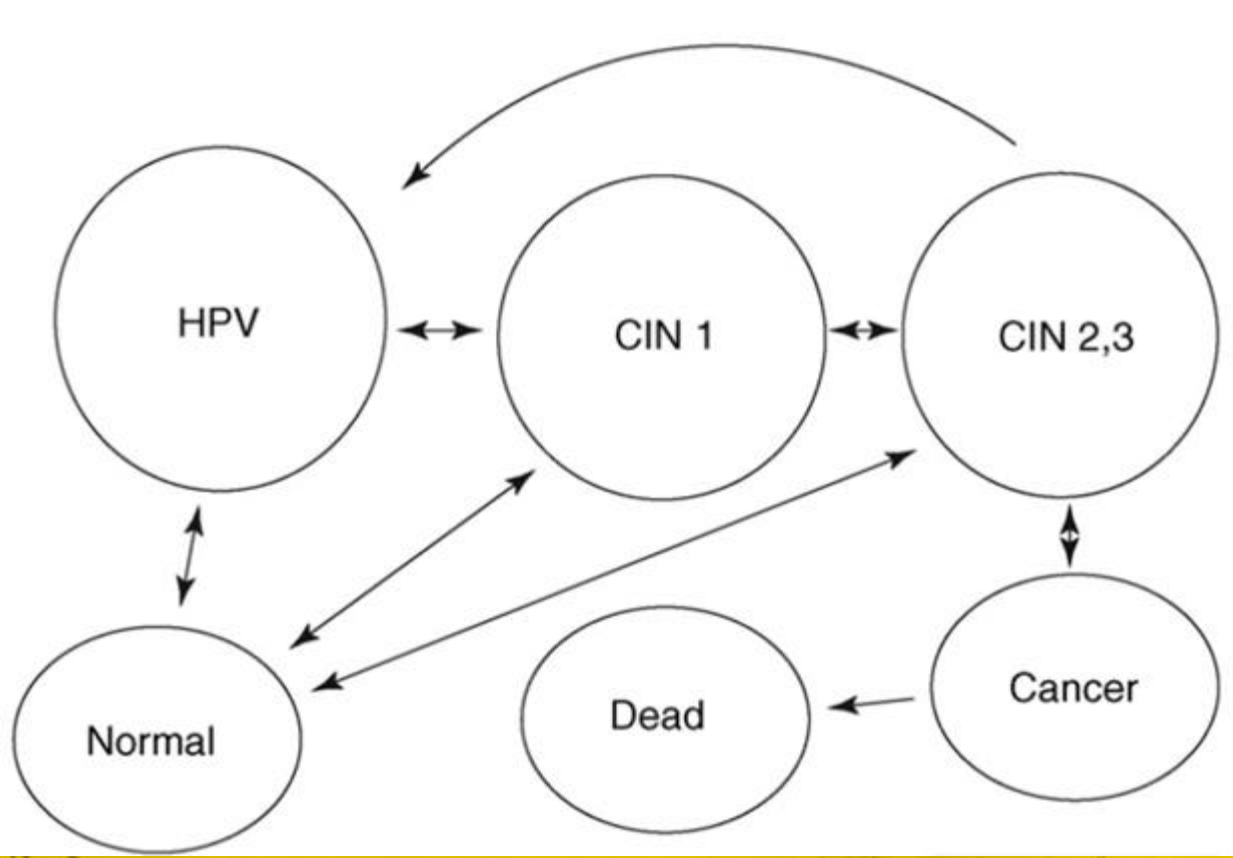
Incremental Cost-Effectiveness Ratio (ICER)

$$\text{Incremental C/E Ratio} = \frac{\text{Cost A - Cost B}}{\text{Effect (A-B)}}$$

Cost-Utility Analysis

- Specific type of CEA:
  - Consequences: life-years gained or lost adjusted by quality factor based on patient preference or on the quality of the health care outcome
  - Often measured as Quality-adjusted life-years (QALYs)

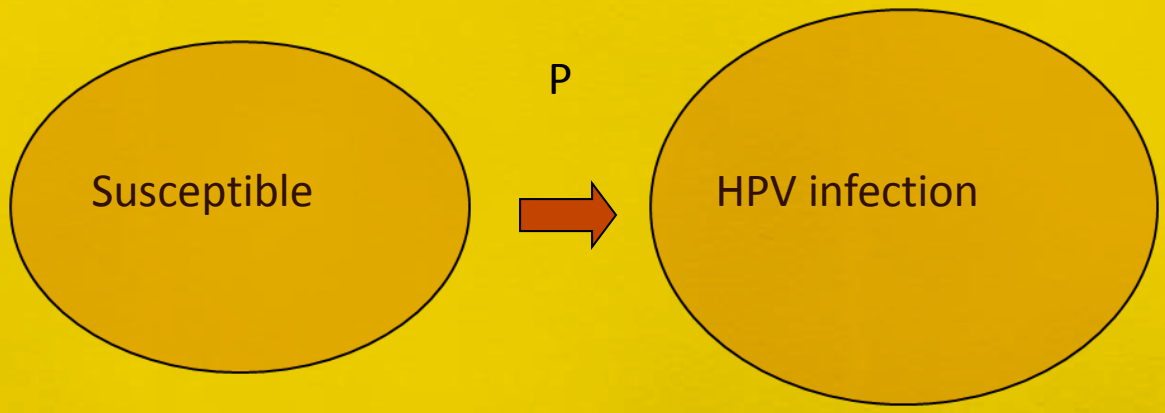
Cost-Effectiveness Models



Types of HPV CE Models

- 3 types thus far
  - Cohort (Markov/health state transition)
    - Majority of models
  - Population dynamic
  - Hybrid

Dynamic Model



Model Comparison

Study	Model type	ICER per QALY gained
IOM*	Cohort	$4,000-6,000
Sanders and Taira	Cohort	22,755-52,398
Kulasingam and Myers	Cohort	44,889-236,250 (LYG)
Taira et al	Hybrid	14,500-442,039
Goldie	Cohort	12,300-4,863,000

*prioritization of vaccine development

Model Outcomes

- All models predicted HPV vaccination result in reduction in HPV infection and/or reduction in cervical precancers and cancer
- Magnitude of reduction influenced by:
  - Duration of protection by vaccine
  - Vaccine effectiveness
  - Screening effectiveness
  - Whether or not HPV types interacted
  - Duration of model follow-up
  - Transmission of infection
  - Health utilities

Model Outcomes (cont'd.)

- Vaccinating females cost-effective
- More cost-effective if vaccine used to increase screening interval and/or delay start of screening
- Vaccinating males only cost-effective if female vaccination rate <30%

Preventive Methods

- Screening using visual inspection with acetic acid (VIA)
- Vaccine
  - Each country should undertake a cost-effectiveness analysis to compare with available methods in their country
  - According to the GAVI Alliance in 2010, Merck and GSK have committed to offering vaccine in developing world <US$ 10

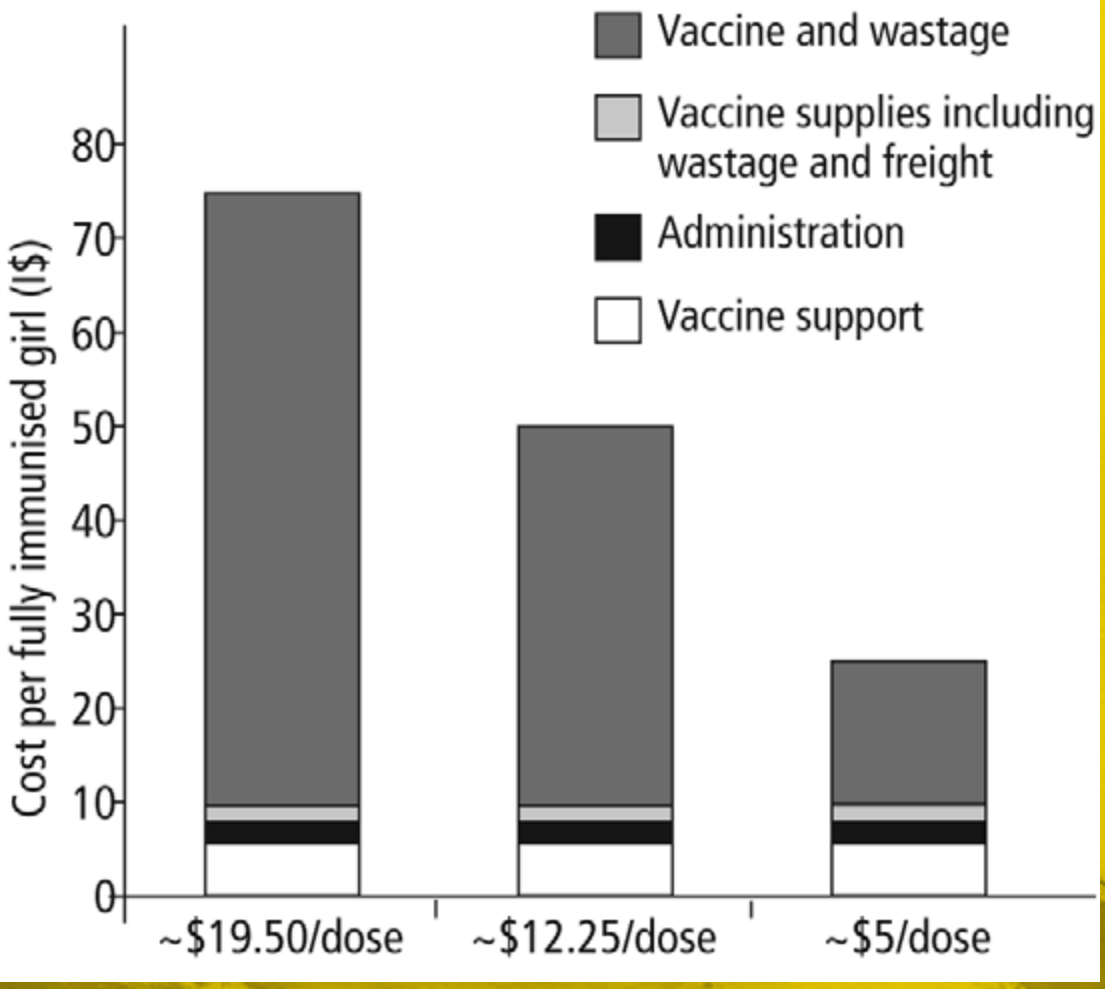
CEA in Developing Countries

- Accessibility to 70% of young adolescent girls in 72 of poorest GAVI-eligible countries + China, Thailand and all of Latin America and Caribbean, could prevent deaths of >4M women over next decade
- Vaccine cost-effective, even in relatively poor countries, if cost per vaccinated girl <I$10-25

Goldie et al, 2008. Reproductive Health Matters.

Cost Per Vaccinated Girl

Figure 1. Schematic of vaccine component costs



Results

- Assuming 70% coverage
  - Mean reduction in lifetime risk of cancer 40-50%
    - <40% in Nigeria, Ghana, Chile
    - >50% in India, Uganda, Argentina
  - Absolute reduction influenced by cervical cancer incidence, population age structure, vaccination coverage
  - Relative reduction also depended on fraction of cancer caused by HPV types 16 and 18

Policy Implications

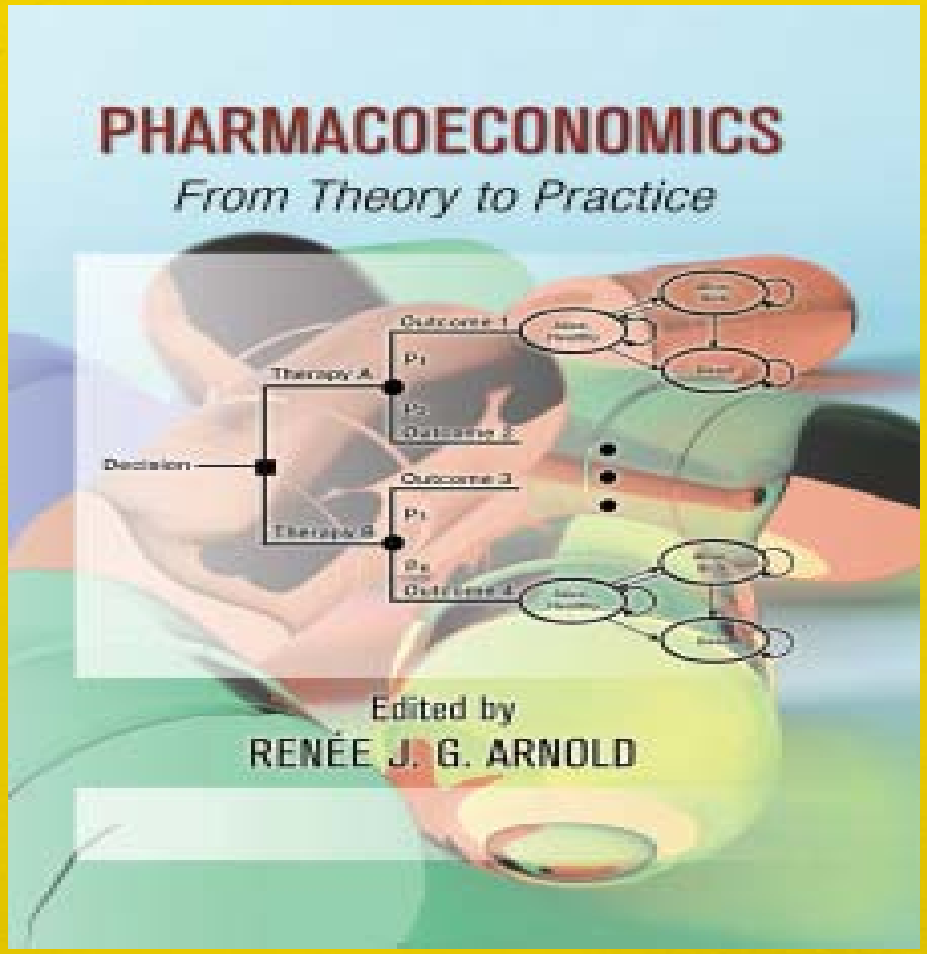
- Countries with highest rates (ASR) of cervical cancer accounted for lower rates of absolute deaths than countries with moderate ASR and large populations
- Approximately 57% of averted deaths in the WHO Southeast Asia region (41% in India alone)
- Countries in Africa would comprise an additional 30%

Implementation

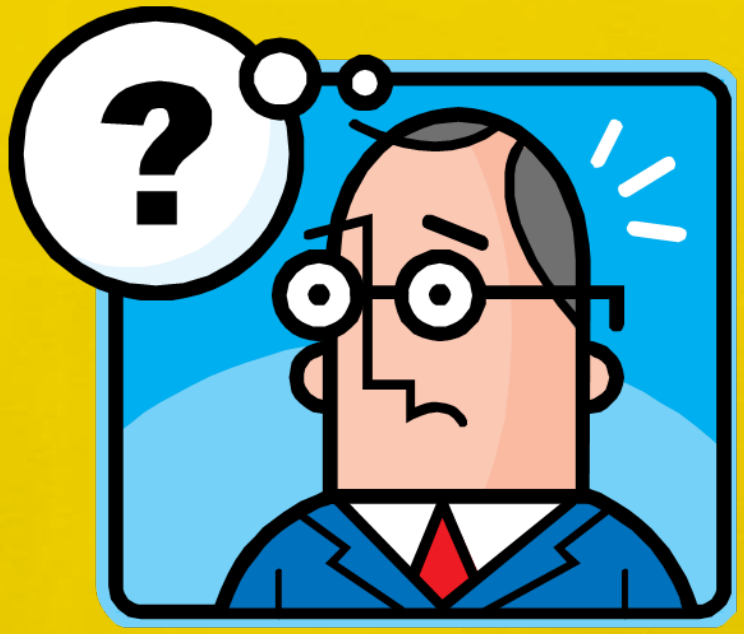
- Regional universal vaccination approach most effective in reducing overall global burden
- Adolescent immunization program
- Country-specific data using standardized costing instruments needed to evaluate alternative program and delivery options, cost of scale-up and efficiencies when combined with other adolescent programs

Other Considerations

- Distributional effects/equity
- Sustainability
- Cultural acceptability
- Political support



http://www.amazon.com/Pharmacoeconomics-Theory-Practice-Drug-Discovery/dp/1420084224/ref=sr_1_1?ie=UTF8&s=books&qid=1255114368&sr=8-1



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