Abstract ID: 25401

Health Economic Analysis of a Bivalent HPV Vaccine and the Value of Cross-Protection in a US Female Population

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INTRODUCTION

- In 2010, there were an estimated 12,200 incident cases of cervical cancer and 4,210 cervical cancer deaths in the United States (US)[1]
- The annual cost of cervical cancer in the US in 2009 was estimated at $172 million[2,3]
- Human papillomavirus (HPV) types 16 and 18 account for ~70% of cervical cancer cases; 10 other high-risk (10-OHR) types account for the majority of the remaining cases[4]
- A bivalent HPV vaccine has been established as being highly efficacious in preventing HPV infections caused by types 16 and 18 that may subsequently evolve into cervical disease[5]
- Clinical trial data for the bivalent vaccine indicate additional cross-protection (XP) efficacy against 10-OHR types (31,33,35,39,45,51,52,56,58,59)[5-7]
- Previous studies have shown HPV vaccination to be cost-effective in 12-year-old girls[8,9]

OBJECTIVE

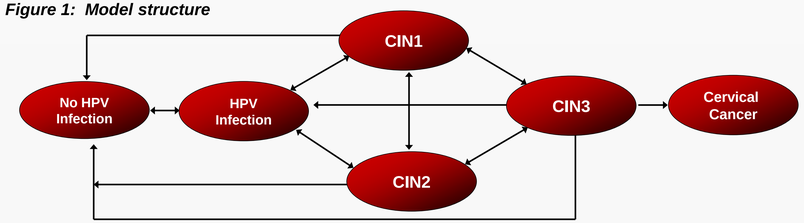
- Use a mathematical model of cervical cancer to evaluate the benefits of HPV vaccination and to estimate the additional value of cross-protection in 18-year-old women in the US

METHODS

Model Overview

- A lifetime Markov model was developed to simulate the natural history of HPV infection and cervical disease (Figure 1)
- Model transition probabilities were calibrated using age-specific cervical screening, cervical cancer incidence, and mortality data
- Cervical screening rates, cervical screening test characteristics, diagnostic and treatment costs, and utilities were estimated from published literature; selected inputs are displayed in Table 1
- Disease health states had utility decrements associated with them; utility values range from 0 (death) to 1 (perfect health)
- Clinical outcomes include lifetime numbers of abnormal Papanicolaou (Pap) smears, detected cervical intraepithelial neoplasia (CIN) lesions grades 1-3, and cervical cancer cases and deaths
- Economic outcomes include total costs, total quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratios (ICERs)

Figure 1: Model structure



HPV=human papillomavirus; CIN=cervical intraepithelial neoplasia

Funding for this study was provided by GlaxoSmithKline USA

METHODS (CONTINUED)

Analysis

- Model outcomes were assessed for two populations of 100,000 18-year-old women distinguished by HPV status (Table 2)
- For both populations, outcomes were assessed for cohorts of unvaccinated women and vaccinated women, assuming full vaccination coverage (3 doses)
- Bivalent and cross-protection CIN2+ vaccine efficacies (using HPV infection as a proxy) were applied in accordance with clinical trial results;[5-7] in the more recent end of study analysis, higher vaccine efficacy estimates have been observed[10]
- QALYs were calculated by multiplying the time spent in the health state by the age-specific general utility and multiplying that by the health state utility
- Cost ($US2009) and QALY outcomes are discounted at a rate of 3% per annum

Table 1: Selected model inputs

Model Parameter	Estimate
Costs	
HPV vaccination[11,12]	
Vaccine dose	$129
Administrative fee (per dose)	$19
Diagnostic[13,14]	
Liquid-based cytology	$116
Colposcopy	$192
Biopsy	$171
Treatment[13,15]	
CIN1	$1,820
CIN2/3	$4,080
Stage 1 cervical cancer	$31,012
Stage 2/3 cervical cancer	$33,191
Stage 4 cervical cancer	$53,161

Model Parameter	Estimate
Utilities	
General population[16]	0.72-1.00
Detected CIN1-3[17]	0.97
Treatment state[9]	
Stage 1 cervical cancer	0.65
Stages 2/3 cervical cancer	0.56
Stage 4 cervical cancer	0.48
Post-treatment follow-up[9]	
Stage 1 cervical cancer	0.97
Stages 2/3 cervical cancer	0.90
Stage 4 cervical cancer	0.62

Table 2: Study population characteristics

Population	HPV Status	Description of HPV Status	CIN2+ Vaccine Efficacy (Bivalent and XP)
HPV naïve	Naïve	Negative HPV DNA test & seronegative	98.4% against 16/18[5] 68.4% against 10-OHR[6]
General	Naïve & non-naïve	Regardless of HPV DNA test result or serostatus	92.4% against 16/18[7] 47.3% against 10-OHR[7]

HPV=human papillomavirus; CIN=cervical intraepithelial neoplasia; 10-OHR=10 other high-risk HPV types

RESULTS

Table 3: Economic results with and without HPV vaccination for the HPV naïve and general populations

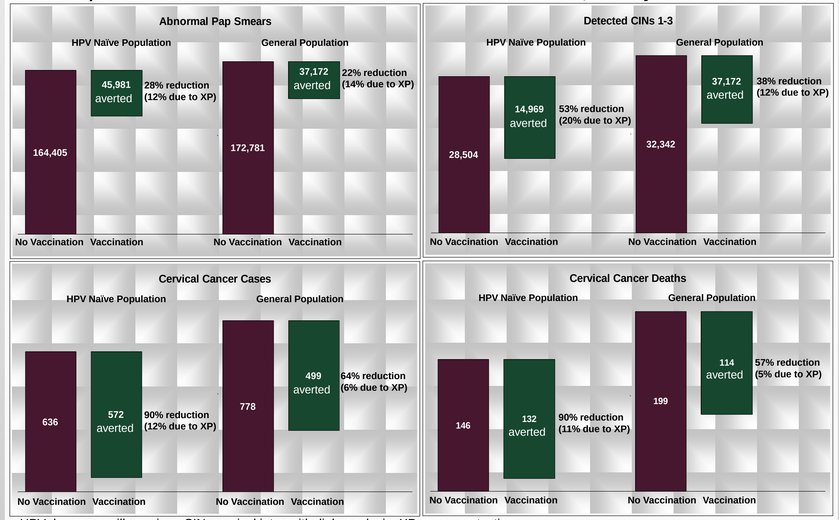
Scenario	Total Cost per Woman	Total QALY per Woman	Cost per QALY
HPV Naïve Population			
No vaccination	$2,352	23.9922	--
Bivalent vaccine	$2,469	24.0004	$14,400
Bivalent vaccine with XP	$2,289	24.0019	Dominant
General Population			
No vaccination	$2,526	23.9876	--
Bivalent vaccine	$2,675	23.9948	$20,500
Bivalent vaccine with XP	$2,557	23.9958	$3,800

HPV=human papillomavirus; XP=cross-protection. Vaccination strategies are compared with no vaccination.

- The bivalent vaccine with cross-protection is dominant (less costly and more effective) compared with no vaccination in a population of HPV naïve 18-year-old women (Table 3)
- In a general population of 18-year-old women, the bivalent vaccine with cross-protection has an ICER of $3,800 compared with no vaccination

RESULTS (CONTINUED)

Figure 2: Estimated lifetime number of clinical events with no HPV vaccination and events averted and percent reductions with vaccination vs. no vaccination for 100,000 18-year-old women



HPV=human papillomavirus; CIN=cervical intraepithelial neoplasia; XP=cross-protection

- HPV vaccination may result in significant reductions across all cervical event types for both the HPV naïve and general populations (Figure 2)
- The bivalent HPV vaccine with cross-protection against 10 other high-risk types could prevent an additional 5-20% of cervical disease events compared with the bivalent vaccine

CONCLUSIONS

- HPV vaccination with cross protection may offer substantial clinical and economic benefits in 18-year-old US women
- Model results suggest that HPV vaccination of 18-year-olds is cost-effective by generally accepted criteria such as <$50,000 per QALY in both HPV naïve and general populations
- A mathematical model of cervical cancer indicates that cross-protection vaccine efficacy further amplifies the clinical and economic benefits of the bivalent vaccine

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