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Cost and Effectiveness Evaluation of Prophylactic HPV Vaccine in Developing Countries

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ABSTRACT

Background: Approximately 80% of cervical cancer cases occur in developing countries. In Thailand, cervical cancer has been the leading cancer in females, with an incidence of 24.7 cases per 100,000 individuals per year. **Objectives:** We constructed a decision model to simulate the lifetime economic impact for women in the context of human papillomavirus (HPV) infection prevention. HPV-related diseases were of interest: cervical cancer, cervical intraepithelial neoplasia, and genital warts. The two strategies used were 1) current practice and 2) prophylactic quadrivalent vaccine against HPV types 6, 11, 16, and 18. **Methods:** We developed a Markov simulation model to evaluate the incremental cost-effectiveness ratio of prophylactic HPV vaccine. Women transition through a model either healthy or developing HPV or its related diseases, or die from cervical cancer or from other causes according to transitional probabilities under the Thai health-care context. Costs from a provider perspective were obtained from King Chulalongkorn Memorial Hospital. Costs and benefits were discounted at 3% annually. **Results:** Compared with no prophylactic HPV vaccine, the incremental cost-effectiveness ratio was 160,649.50 baht per quality-adjusted life-year. The mortality rate was reduced by 54.8%. The incidence of cervical cancer, cervical intraepithelial neoplasia grade 1, cervical intraepithelial neoplasia grade 2/3, and genital warts was reduced by up to 55.1%. **Conclusion:** Compared with commonly accepted standard thresholds recommended by the World Health Organization Commission on Macroeconomics and Health, the nationwide coverage of HPV vaccination in girls is likely to be cost-effective in Thailand.

Keywords: cost-effectiveness, developing countries, HPV vaccine.

Introduction

Cervical cancer is the second most common female malignancy worldwide. Approximately 80% of all cases occur in developing countries and predominantly in low socioeconomic populations [1–4]. Results from many studies suggest that infection with human papillomavirus (HPV) is the first step in the development of cervical cancer [5–7]. There are more than 100 types of papilloma viruses (HPVs) that infect humans. Types 16 and 18 were the most common types identified in patients with cervical cancer in Western countries (70%–85% of cases) [8–13].

In Thailand, cervical cancer has been the leading cancer in females, accounting for 24.7 new cases per 100,000 individuals per year [14,15]. Furthermore, cervical cancer has been identified as a national public-health problem [16,17]. Among a population of 32.2 million women in 2008, there were an estimated 8000 new cases and about 2178 deaths [18,19]. HPV types 16 and 18 account for 52% and 19% of cervical cancers, respectively [20]. HPV type 16 was detected in 48% and type 18 in 16% of individuals with cervical intraepithelial neoplasia (CIN) grade 3 [21].

On the basis of this evidence, great effort has been undertaken to develop effective HPV vaccines [22]. Currently, HPV vaccines have been approved worldwide for preventing cervical cancer and other HPV-related diseases [23]. Several mathematical models based on the natural history of HPV diseases have been published to evaluate the cost-effectiveness of the HPV vaccine [12,24–33]. This study used a different approach. We modeled a treatment algorithm reflecting standard practice for individuals with genital warts, CIN1, CIN2/3, as well as cervical cancer and compared the effect that vaccine would have on the population of patients who did and did not receive prophylactic HPV vaccination.

Objectives

We therefore aimed to perform a cost-effectiveness evaluation of a prophylactic HPV (6, 11, 16, 18) vaccination program compared with current management from a care provider perspective under the Thai health-care management setting as the nominated comparator.

Methods

Simulation model

We developed a mutually exclusive state-transition Markov model [34,35] to clearly depict the clinical management algorithm of treatments for genital warts, CIN, and various stages of cervical cancer (Fig. 1) as defined by the Federation of Gynaecology and

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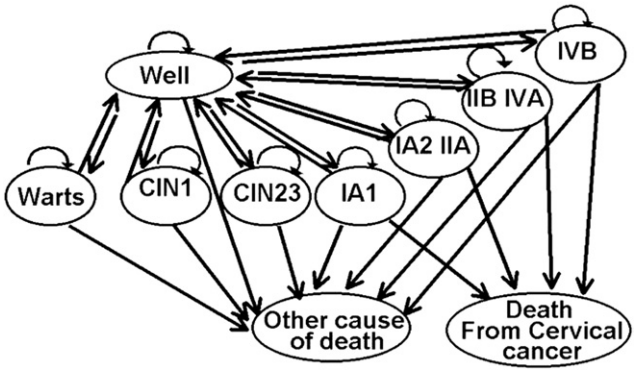

Fig. 1 – Simple schematic model to portray the algorithm of treatments of genital warts, cervical intraepithelial neoplasia (CIN), and stages for cervical cancer. CIN, cervical intraepithelial neoplasia; IA1, cervical cancer stage IA1; IA2–IIA, cervical cancer stage IA2–IIA; IIB–IVA, cervical cancer stage IIB–IVA; IVB, cervical cancer stage IVB.

Obstetrics using the TreeAge software (TreeAge software, Inc., Williamstown, MA). Our hypothetical longitudinal entire lifetime cohort was 12-year-old girls who never had sexual intercourse. The cohort was followed through different health states until age 100 years. In yearly cycles, each girl had her own outcome and moved through health states. Women could transition healthy or develop HPV and its related diseases as a result of diagnosis, or they could die from cervical cancer or other causes according to transitional probabilities. In an attempt to decrease bias and improve the quality of the data used to calculate the transition probabilities required by the model, the authors reviewed the literature thoroughly and systematically for data on Thai health outcomes. When adequate Thai data were not available, we used data from the Asia-Pacific or other regions and experts' opinion.

The age-specific incidence of cervical cancer was obtained from the National Cancer Institute, Ministry of Public Health (MoPH), Thailand. The number of noncervical cancer deaths was estimated by using Thai female lifetable statistics [36]. Data are shown in Table 1.

Assumptions

The main assumptions of the model were as follows:

1. Vaccination was at the age of 12 years.
2. The proportion of women taking immunization was 100% and varied in the sensitivity analysis.
3. The duration of vaccine protection was lifelong, with a vaccination cost of 6189 Thai baht per three-dose course.
4. The efficacy of the quadrivalent vaccine against HPV types 6, 11, 16, and 18, based on literature review, was estimated at 97% [53]. In the sensitivity analyses, alternative assumptions were investigated by varying this efficacy from 90% to 99.9% and cross-protection between types was not taken into account.
5. Because the Markov Model did not have the ability to remember prior events, we assumed that women who were treated and were cured returned to the healthy state and had a probability of redeveloping a disease similar to those of women without prior disease.
6. The Federation of Gynaecology and Obstetrics stages classification and treatment algorithm would not change over time.

Cost of care

To assess the costs of care, we conducted the analysis from the perspective of a health-care provider. Costs, expressed in Thai

Table 1 – Baseline values in the model.

Variable	Base case	Reference
Annual probability of death (from all causes)		[36]
10–14*	0.001	
50–54	0.0134	
95–99	0.8103	
Annual incidence of cervical cancer	24.7 per 100,000	[37]
15–19*	1 per 100,000	
50–54	74 per 100,000	
70–74	61 per 100,000	
Annual incidence of CIN1	120 per 100,000	[38]
15–19*	160 per 100,000	
20–24	510 per 100,000	
>70	20 per 100,000	
Annual incidence of CIN2/3	80 per 100,000	[38]
15–19*	90 per 100,000	
25–29	380 per 100,000	
>70	1 per 100,000	
Annual incidence of genital warts	231 per 100,000	[39]
10–14*	10 per 100,000	
20–24	861 per 100,000	
>45	48 per 100,000	
5-y cancer survival (%)		
Stage IA1	94.3	[40]
Survival of recurrence	93.7	[41]
Stage IA2, IB, IIA	88.8	[42]
Survival of recurrence	83.3	[41]
Stage IIB–IVA	67.6	[43]
Survival of recurrence	53.0	[43]
Stage IVB	22	[44]
5-y progression-free survival (%)		
Stage IA1	92	Assumed
Stage IA2, IB, IIA	80	[45]
Stage IIB–IVA	6	Assumed
Median progression-free survival: Stage IVB (mo)	3.8	[46]
Annual recurrence rate: CIN1 (%)	9	[47]
Annual recurrence rate: CIN2/3 (%)	11.9	[48]
Annual recurrence rate: genital warts (%)	39	[49]
Prevalence of HPV16 or 18 in CIN (%)	75	[21]
Prevalence of HPV16 or 18 in cervical cancer (%)	85.5	[50]
Prevalence of HPV6 or 11 in genital warts (%)	80	[51]
Quality of life of patients with	Mean (SD)	[52]
Genital warts	0.743 (0.12)	
CIN1	0.787 (0.09)	
CIN2/3	0.776 (0.13)	
IA1	0.784 (0.13)	
IA2, IB, IIA	0.788 (0.13)	
IIB–IVA	0.776 (0.13)	
IVB	0.814 (0.12)	

CIN, cervical intraepithelial neoplasia; IA1, cervical cancer stage IA1; IA2, cervical cancer stage IA2; IB, cervical cancer stage IB; IIA, cervical cancer stage IIA; IIB–IVA, cervical cancer stage IIB–IVA; IVB, cervical cancer stage IVB.

* Calculate in 5-y age categories; only lowest, middle, and highest age groups were showed.