Model for predicting the burden and cost of treatment in cervical cancer and HPV-related diseases in Thailand

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Summary

Purpose: Cervical cancer is a significant health burden in many countries. Long-term cost of care is still not well understood. We aimed to evaluate the long-term burden of illness and healthcare resource utilization associated with cervical cancer, cervical intraepithelial neoplasia (CIN) and genital warts from the care provider perspective. *Method:* We developed a health state-transition Markov model to portray the algorithm of treatment of stages of cervical cancer, CIN and genital warts by tracking a hypothetical lifetime cohort of 12-year-old girls. Costs in this study were unit cost; capital costs and labor costs were included in the unit cost for in-patients and out-patients. *Results:* The highest incidence of CIN and genital warts was observed in women aged 20-30 years old. For cervical cancer, the highest incidence was 45-55 years. Death rate was estimated at 2%, 8%, 84% and 94% in cervical cancer Stage IA1, IA2-IIA, IIB-IVA and IVB, respectively. The estimated mean direct cost per patient with cervical cancer Stage IA1, IA2-IIA, IIB-IVA, IVB, CIN1, CIN2/3 and genital warts were 41,117 Thai Baht ($1,277 US), 97,250 Thai Baht ($3,020 US), 402,683 Thai Baht ($12,506 US), 322,619 Thai Baht ($10,019 US), 5,381 Thai Baht ($167 US), 49,933 Thai Baht ($1.551 US) and 3,585 Thai Baht ($111 US), respectively. Cost for survival or death case was indifferent. The overall lifetime costs from the provider perspective were evaluated at 859.1 million Baht ($26.7 million US) per a cohort of 100,000 women which corresponds to approximately 4,244 million Baht ($131.8 million US) for the current number of Thai 12-year-old girls. *Conclusions:* HPV-related diseases impose health and cost burdens in Thailand. The national immunization programme to reduce this burden as well as further research to evaluate the impact is keenly expected.

Key words: Cost; Cervical cancer; HPV-related diseases.

Introduction

Cervical cancer is a significant health burden in many countries. Approximately 80% of all cases occur in developing countries and predominantly in people of low socio-economic status [1-4]. The death rate is approximately 50% worldwide[5].

In Thailand cervical cancer is identified as a key public health problem [6]. About 8,000 Thai women develop cervical cancer each year [7-9]. Age standardized incidence rate is 24.7 per 100,000 women [10].

A number of clinical studies have shown that the cause of cervical cancer is attributable to the infection with human papillomavirus (HPV) [11-15]. On basis of this evidence, effort is undergoing to develop vaccines that prevent HPV infection. Both of the licenced HPV vaccines can protect women from HPV type 16 and 18 that cause majority of cervical cancer. While quadrivalent vaccine can also protect against HPV type 6 and 11 which mostly cause genital warts [16]. Several mathematical models have been published to evaluate the cost effectiveness of new vaccines [17-27]. One of the important factors for the evaluation of cost-effectiveness is reliable long-term treatment cost. Many studies on cost estimation were carried out in Western countries [28-32]. A study on cost of care in Thailand was evaluated five years after completion of treatment, but did not represent lifetime costs of treatment [33].

Given less understanding in the long-term situation of HPV-related disease, we, therefore, aimed at evaluating the lifetime burden of illness and healthcare resource utilization associated with cervical cancer, cervical intraepithelial neoplasia (CIN) and genital warts from a care provider perspective.

Method

We developed a health state-transition Markov model [34, 35] to portray the algorithm of treatment of stages of cervical cancer, CIN and genital warts using TreeAge software (TreeAge software. Inc., Williamstown, MA, USA). In the model, we simulated a hypothetical lifetime cohort of 12-year-old girls until age 100 years (Figure 1). Costs in this study were unit cost (capital costs and labor costs were included in the unit cost) for in-patients and out-patients at King Chulalongkorn Memorial Hospital (Table 1). Costs were expressed in Thai Baht with the conversion rate of 35 Baht per US dollar. Probabilities at each chance node were systematically reviewed from the Thai healthcare context if available, otherwise data from other regions were used under substantial consensus by three authors with expertise in oncology gynecology (Table 2) [36-42].

Sensitivity analysis

Beta and Gamma distribution were applied to any probabilities and to unit costs in probabilistic sensitivity analysis, respectively. Monte Carlo simulation was performed to obtain the

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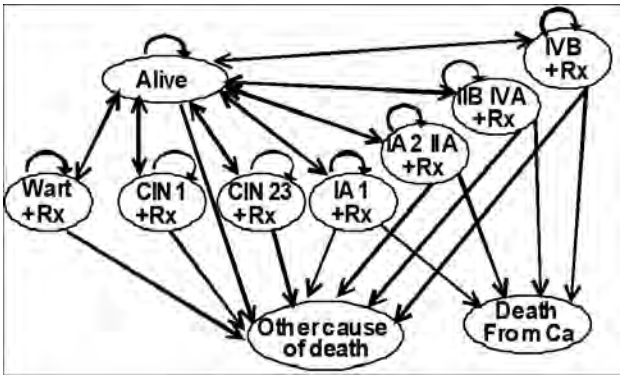

Figure 1. — Model to portray the algorithm of treatment of HPV-related diseases.

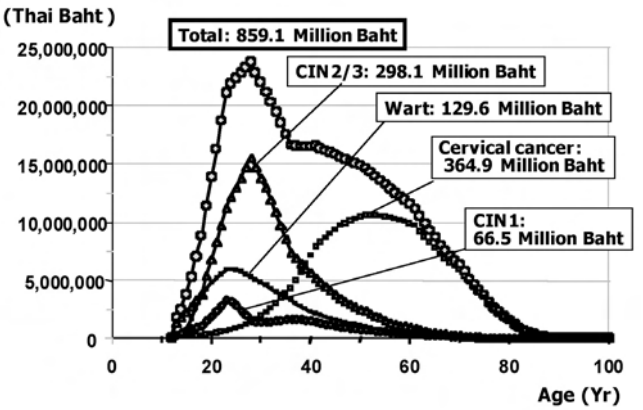

Figure 2. — Results from the model: cost of treatment of HPV-related diseases per cohort of 100,000 12-year-old girls classified by age group.

upper and lower boundary of the estimation. In one probabilistic sensitivity analysis, 10,000 model simulations were completed.

Results

Model validation

The incidence rate according to the model was 24.3/100,000 which is comparable to the incidence rate given by the National Cancer Institute of Thailand of 24.7/100,000 [10]. The cervical cancer mortality rate from the model was 7.99/100,000 which is slightly more than the crude death rate given by the Ministry of Public Health of 5.2/100,000 for the year 2007.

Results from model
Estimated number of HPV related cases and death

Our calculation suggested that in a lifetime cohort of 100,000 women, there would be 56,621 women with HPV-related disease including genital warts, CIN1, CIN2/3 and cervical cancer, of which 632 would die from cervical cancer (Table 3).

Estimated individual cost of treatment

An individual lifetime cost of treatment is shown in Table 4. Minimum and maximum boundaries are also displayed, using the Monte Carlo simulation technique. Costs per cervical cancer death seem to be indifferent from cost per case.

Estimated lifetime cost of treatment

Overall treatment costs of HPV-related diseases were approximately 859.1 million Thai Baht per a lifetime cohort of 100,000 women. The trend was to increase rapidly from the age of 12 years and peaked at the age of 30 years. After age 30 years, this burden was dominated by cervical cancer treatment costs (Figure 2).

Table 1. — *Unit cost for treatment of genital warts, CIN and cervical cancer*.

Procedure	Unit cost (Baht)
Medical treatment of warts	3348.24
Surgical treatment of warts	5,941.56
Cryotherapy	638.10
Conization	33,805.70
TAH	39,842.29
Radical Hysterectomy	101,830.80
Vaginectomy	39,156.97
Chemotherapy	270,857.28
Radiation	52,575.45
Palliative care	66,142.96

Table 2. — *Selected baseline values used in the model*.

Variable	Base case	Ref.
Annual probability of death (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	[10]
Annual incidence of CIN1	120 per 100,000	[37]
Annual incidence of CIN 2/3	80 per 100,000	[37]
Annual incidence of genital warts	231 per 100,000	[31]
5-year cancer survival		
Stage IA1	94.3%	[38]
(survival of recurrence)	93.7%	[39]
Stage IA2, IB, IIA	88.8%	[40]
(survival of recurrence)	83.3%	[39]
Stage IIB-IVA	67.6%	[41]
(survival of recurrence)	53.0%	[41]
Stage IVB	22%	[42]

* Calculated in 5-year age catagories; only lowest, middle and highest age groups are shown.

Discussion

Treatment costs are essential for healthcare policy authorities in assessing benefits such as HPV testing [23] or the national immunization program [43-45]. To our knowledge this was the first attempt to portray lifetime information concerning cervical cancer, CIN and genital wart patients in terms of burden of illness and healthcare

Table 3. — *Results from the model: Lifetime cases per cohort of 100,000 12-year-old girls*.

	Number of cases	Death (%)
Warts	36,150	
CIN1	12,358	
CIN2/3	5,970	
IA1	591	12 (2)
IA2-IIA	909	73 (8)
IIB-IVA	559	468 (84)
IVB	84	79 (94)

Table 4. — *Results from the model: Cost of treatment for individual cases and death (Thai Baht)*.

Disease	Cost of treatment per individual case	Min-Max	Cost of treatment per 1 death
Warts	3,585	558-11,989	
CIN1	5,381	2,136-5,884	
CIN2/3	49,933	39,434-132,963	
IA1	42,220	40,681-80,804	41,157
IA2-IIA	101,673	94,276-456,093	97,583
IIB-IVA	571,712	254,085-2,900,791	421,772
IVB	320,906	262,125-692,184	316,323

Table 5. — *Comparison among HPV-related disease costs*.

Diseases	Country	Cost/1 case	Ref.	Estimation cost/ 1 case from our model
Genital warts	USA	$ 404 US	[30]	3,585 Thai Baht ($102 US)
Genital warts	Germany	euro 378	[29]	
Genital warts	Australia	A$ 386	[31]	
CIN1	Italy	euro 226	[46]	5,381 Thai Baht ($154 US)
CIN2	Italy	euro 1,348		49,933 Thai Baht ($1,427 US)
CIN3	Italy	euro 1,919		
Stage IB2 cervical cancer	USA	$ 5,508 US (radiation) $ 8,316 US (Hysterectomy)	[47]	IAI 42,220 Thai Baht ($1,206 US)
FIGO Stage I	Italy	euro 6,024	[32]	IA2-IIA
FIGO Stage II	Italy	euro 10,572		101,673 Thai Baht
FIGO Stage III	Italy	euro 11,367		($ 2,905 US)
FIGO Stage IV	Italy	euro 8,707		
FIGO Stage I	France	euro 9,164	[28]	IIB-IVA 571,712 Thai
FIGO Stage II	France	euro 15,999		Baht ($16,335 US)
FIGO Stage III	France	euro 22,697		
FIGO Stage IV	France	euro 26,886		IVB 320,906 Thai Baht ($9,169 US)

resource use based on a care provider perspective in Thailand.

Our study estimated 36,150 wart cases per a cohort of 100,000 12-year-old girls (Table 3). The incidence started in younger women with the peak at age 22 years. The cost estimation of 3,585 Thai Baht per wart case (Table 4), and, the lifetime monetary burden of 129.6 million Thai Baht per cohort of 100,000 12-year-old girls (Figure 2), imposed nearly one-third of cervical cancer costs.

Table 4 shows more than a 9-fold increase in cost from CIN1 (5,381 Thai Baht) to CIN2/3 (49,933 Thai Baht). A study in Italy also reported similar findings, although the difference was not as large as in our study [46, 47] (Table 5).

As expected, this study also showed increasing cost of care with increasing severity of cervical cancer (Table 4). These estimates were consistent with figures reported by Ricciardi *et al*. [32] in 2009 and Arveux *et al*. [28] in 2007 (Table 5). In those studies, there was a 75% increase in treatment costs for Stage II compared to Stage I disease, where as our study showed more than a twofold increase in such stages (Table 4).

Our estimated costs of treatment were substantially less expensive when compared to other countries (Table 5). These might not be due to differencies in physician practices but may be dominated by the difference in cost of living. However, this expenditure appeared to be inadequate in relation to our average family income of 226,320 Thai Baht per year [48]. According to the National Statistic Office in Thailand, there were 494,053 individual 12-year-old girls, which accounted for our estimated cases of 279,738 HPV-related diseases as well as corresponding to 4,244 million Thai Baht for direct medical care costs.

It should be noted that there are some limitations of this study. First, cost information was achieved from the unit cost of King Chulalongkorn Memorial Hospital, a tertiary government teaching university hospital. This may be an under-estimation when compared to private hospitals or an over-estimate when compared to secondary or primary hospitals. However, we used the Monte Carlo simulation to display the spread of expected values in terms of minimum and maximum.

Second, due to the lack of country information on age-specific incidence of genital warts and CIN, an alternative approach was to adopt previous studies from other countries. Over- or under-estimation of the true incidence of diseases may have occurred.

Lastly, diagnosis costs, follow-up costs, indirect costs and psychological costs were not taken into account. Therefore, from a provider perspective, all costs in this study should be considered as the lower boundany of the overall costs. Estimates from this study may lay a baseline for further study of cost-effectiveness analysis.

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