

## RESEARCH ARTICLE

# HPV Vaccination for Cervical Cancer Prevention is not Cost-Effective in Japan

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### Abstract

**Background:** Our study objectives were to evaluate the medical economics of cervical cancer prevention and thereby contribute to cancer care policy decisions in Japan. **Methods:** Model creation: we created presence-absence models for prevention by designating human papillomavirus (HPV) vaccination for primary prevention of cervical cancer. Cost classification and cost estimates: we divided the costs of cancer care into seven categories (prevention, mass-screening, curative treatment, palliative care, indirect, non-medical, and psychosocial cost) and estimated costs for each model. Cost-benefit analyses: we performed cost-benefit analyses for Japan as a whole. **Results:** HPV vaccination was estimated to cost \$291.5 million, cervical cancer screening \$76.0 million and curative treatment \$12.0 million. The loss due to death was \$251.0 million and the net benefit was -\$128.5 million (negative). **Conclusion:** Cervical cancer prevention was not found to be cost-effective in Japan. While few cost-benefit analyses have been reported in the field of cancer care, these would be essential for Japanese policy determination.

**Keywords:** HPV vaccination, cervical cancer prevention, cost - benefit analysis

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### Introduction

Cost-effectiveness must be assessed before routine prevention or screening if cancer is suspected. In addition to medical costs, those associated with cancer should include overhead costs due to income loss, hospital visits and psychosocial impact. We created presence-absence models for prevention by designating human papillomavirus (HPV) vaccination for the primary prevention for cervical cancer. We then performed cost-benefit analyses.

### Materials and Methods

#### *Model creation*

All cases of cervical cancer result from sustained infection with HPV (Harper et al., 2004). There are more than 100 subtypes of HPV, but approximately 70% of cervical cancer cases are preventable with vaccines to type 16 (Bosch et al., 1995). HPV vaccination is effective in reducing cervical cancer (Rodríguez et al., 2013). However, the mean survival time with stage IIIB cervical cancer is approximately 5 years in Japan (National Cancer Center, 2013). Therefore, we created two models for cervical cancer.

**Model A:** An individual who received HPV vaccination at the age of 14 years. She was screened every year from the age of 30 and was diagnosed with stage 0 cervical

cancer at the age of 40 years; the patient was cured by conization.

**Model B:** An individual who received neither HPV vaccination nor screening. She was diagnosed with stage IIIB cervical cancer at the age of 40 and underwent radical hysterectomy, irradiation, and anticancer drug treatment; however, the patient died 5 years later.

We aimed at age 14 for HPV vaccination the recommended age in Japan (Ministry of Health, Labor and Welfare, 2014). We aimed at age 40, the peak age of cervical cancer onset for examining cervical cancer onset and considered death to occur 5 years later, according to the clinical course of stage IIIB cervical cancer (National Cancer Center, 2013).

#### *Cost classification and estimation*

We converted 100 yen to 1 dollar (the exchange rate in November 2013). Each cost is shown (Table 1). Costs for each model are also shown in Table 2. The totals do not match the sum of costs because of rounding off of figures.

#### *Prevention*

Gardasil® (Merck & Co., Inc., Whitehouse Station, NJ, USA) and Cervarix® (GlaxoSmithKline plc., Brentford, Middlesex, UK) are available for HPV vaccination in Japan. However, both vaccines were beyond National Health Insurance price listings; we estimated the public expenditure to be \$500.0 (Ministry of Health, Labor and

**Mass-screening**

Brush cytology for cervical cancer screening costs \$50.0 (Japan Association of Obstetricians and Gynecologists, 2014). The cervical cancer screening, which would be performed annually from age 30 to 40 years (11 times in total), costs \$550.0.

**Curative treatment**

Conization for stage 0 cervical cancer costs \$2,612.4.

**Palliative care**

Radical hysterectomy, irradiation, and anticancer drugs (cisplatin, a standard adjuvant chemotherapy for progressive cervical cancer in Japan (Japan Society of Gynecologic Oncology, 2011)) for 6 cycles cost \$16,162.5 (Iyaku-Joho-Kenkyujo, 2012; Igakutushinsya, 2014).

**Indirect cost**

Income loss due to absence from work was estimated by the wage general survey. Lost earnings after premature death are calculated as follows:

$$\text{Lost earnings} = I \times (1 - R) \times C$$

where I is basic annual income, -R is a living subtraction rate which is generally 30% in Japan (NICHIBENREN, 2013) and C is a middle interest subtraction coefficient. We adopted the Leibniz coefficient as the middle interest subtraction coefficient (Kurata and Miyahara, 2014).

The basic annual income of the 40-44 age group (females only) in 2011 was \$39,414.1 (Ministry of Health, Labor and Welfare, 2014).

**Model A**

Income loss due to absence from work for 2 weeks \$1,642.3

**Model B**

Income loss due to absence from work for 5 years \$197,070.5

Lost earnings after premature death  
 $\$39,414.1 \times (1 - 0.3) \times 13.163 = \$363,165.5$

Total \$560,236.0

**Non-medical cost**

We estimated travel time and costs required for patients with ten types of cancer receiving outpatient treatment (Isshiki et al., 2013). We adopted the travel costs for cervical cancer as non-medical cost. According to the study, the cost for cervical cancer is \$67.46 per round-trip.

**Model A**

after conization weekly, for 2 weeks 2 times  
 $\$67.46 \times 2 = \$134.9$

**Model B**

irradiation 5 times/week, for 5 weeks 25 times  
 anticancer drugs weekly, for 6 weeks 6 times  
 after therapy monthly, for 1st and 2nd year 21 times  
 every 3 months, 12 times  
 for 3rd to 5th year

Total 64 times  
 $\$67.46 \times 64 = \$4,317.2$

**Psychosocial cost**

Boardman et al. (2011) determined the appropriate value of a statistical life (VSL) in the United States to be \$5 million, based on reports and meta-analyses. The value of a life -year (VLY) is the constant annual amount, which, taken over a person's remaining life span, has a discounted value equal to his or her VSL. VLY is calculated as follows:

$$\text{VLY} = \text{VSL}/A (T - a, r)$$

where a is current age and T is the expected age at death; therefore, T - a corresponds to life expectancy. A (T - a, r) is the annuity factor based on the life expectancy and the appropriate discount rate (r).

There were very few similar studies in Japan, but Uchida et al. (2010) calculated that the VLY for a patient with advanced cancer equals \$188,460.0. We adopted this as the VLY of each cancer death model with an annual discount rate of 3.5%.

Model B for 5 years  $(4)\sum_{t=0}^5 (\$188,460.0 \times (1 - 0.035)^t) = \$878,607.3$

**Results**

**Model A**

**Vaccination cost**

Girls aged 14 years in Japan in 2013 (Ministry of Internal Affairs, 2014) 583,000

HPV vaccination cost for each girl \$500.0 (Table 2)

$$583,000 \times \$500.0 = \$291,500,000$$

**Mass-screening cost**

Participation rate in examination is 23.7% (Organization for Economic Co-operation and Development(OECD), 2006).

$$583,000 \times 0.237 = 138,171$$

Cervical cancer examination \$550.0 for each individual (Table 1)

$$138,171 \times \$550.0 = \$75,994,050$$

**Cost of curative treatment**

Incidence of cervical cancer in the under -40 age group in 2008 (National Cancer Center, 2013) 9,095

Cervical cancer prevention rate by vaccination is 70% (Hanley and Konno, 2010)

$$9,095 \times (1 - 0.7) = 2,729$$

Cost of conization for each individual \$2,612.4 (Table 2)

Indirect cost for each individual \$1,642.3 (Table 2)

Non-medical cost for each individual \$134.9 (Table 2)

$$2,729 \times (\$2,612.4 + \$1,642.3 + \$134.9) = \$11,979,218.4$$

**Model B**

**Loss of income due to death**

Number of deaths due to cervical cancer in the under-40 age group in 2011 (National Cancer Center, 2013) 245

Evasion rate of death due to cervical cancer by vaccination is 70%  $245 \times 0.7 = 172$

(Hanley and Konno, 2010)

Loss of income due to death for each individual (Table 2) \$1,459,323.0

$$172 \times \$1,459,323.0 = \$251,003,556.0$$

Net benefit

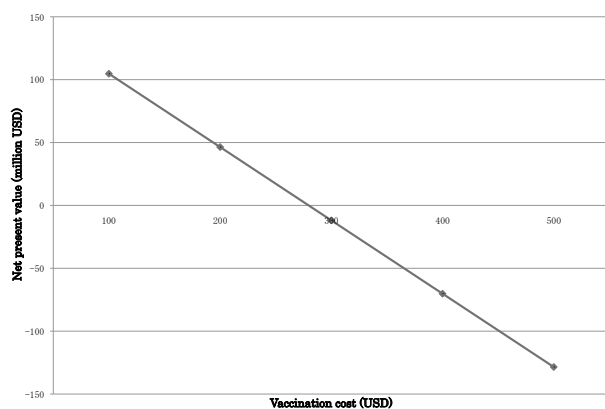
$$\$251,003,556.0 - (\$291,500,000 + \$75,994,050 + \$11,979,218.4) = -\$128,469,712.4$$

**Table 1. Cost Classification and Estimation**

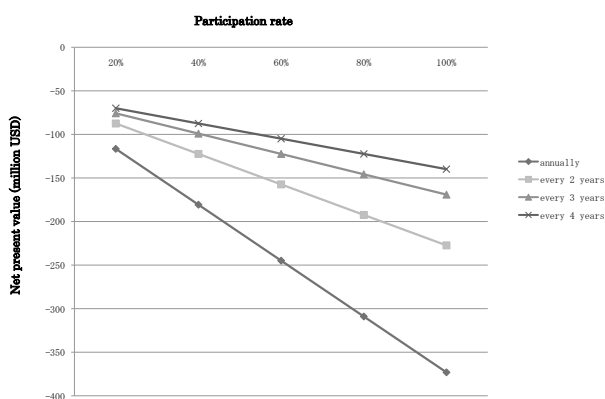
	Model	Remarks	Cost(\$)
Prevention	A	HPV vaccination	500.0
Mass screening	A	Brush cytology	550.0
Curative treatment	A	Conization	2612.4
Palliative care	B	Radical hysterectomy, irradiation, anticancer drugs	16162.5
Indirect cost	A		1642.3
	B		560236.0
Non-medical cost	A	2 times for 2 weeks	134.9
	B	64 times for 5 years	4317.2
Psychosocial cost	B	For 5 years	878607.3

**Table 2. Costs for Each Model**

Cost classification	Model A	Model B
Prevention	500.0	0.0
Mass-screening	550.0	0.0
Curative treatment	2612.4	0.0
Palliative care	0.0	16162.5
Indirect cost	1642.3	560236.0
Non-medical cost	134.9	4317.2
Psychosocial cost	0.0	878607.3
Total cost	5439.6	1459323.0



**Figure 1. Change of The Net Present Value by The Vaccination Cost**



**Figure 2. Change of The Net Present Value by the Participation Rate in Examination**

## Discussion

Premature death due to cancer creates a tremendous economic burden because of the associated large indirect and psychosocial costs. Choi et al. (2014) identified factors associated with catastrophic health expenditures. In that study, change in economic status due to job loss leads to incur catastrophic health expenditure. Our study draws attention to the need for cost-effective public health and screening measures to prevent cancer and improve early detection.

Prasad and Hill (2008) conducted a cost-benefit analysis study in Kentucky, USA, and demonstrated that HPV vaccination was cost-effective. However, HPV vaccination was not found to be cost-effective in Japan due to the high vaccination costs. We estimated that a net benefit could be generated if the cost of HPV vaccination was reduced to \$280 (Figure 1). Furthermore, the participation rate in cervical cancer screening was as low as 23.7% in Japan (OECD, 2006). Ghotbi and Anai (2012) also emphasized on the need to increase awareness among Japanese female adolescents. If this rate increased to approximately 100%, the estimation would be more precise. In that case, mass-screening performed every 3 or 4 years would cost as much as it costs at present (Figure 2).

While few cost-benefit analyses have been reported in the field of cancer care, especially in Japan, these data contribute to public health and policy intelligence, which is required to set up affordable cancer care systems and effectively allocate public research funds. Our study also provides evidence that could be used to assess whether cancer prevention measures such as public awareness campaigns and screening programs to improve early detection are cost-effective.

Importantly, our study had several limitations. First, this study was conducted based on the latest data. Our results are for 2013, the time when declining birthrates became a problem in Japan. Changes in future demographic statistics may affect our estimations.

Second, only surgical treatments, anticancer drugs, and irradiation were included in the curative and palliative costs. We did not include other drugs typically prescribed to patients with cancer (e.g., antibiotics, growth factors, opioids, and antiemetic drugs) because information about the proportion of these drugs prescribed to patients with cancer was insufficient.

Third, we adopted the travel costs of our previous study (Isshiki et al., 2013) as the non-medical cost. Although this is a unique study, it was performed in a single institution and coverage was limited to the metropolitan area. A multi-institution study covering all of Japan should be conducted.

Finally, additional research is necessary to assess the costs incurred by working people with cancer returning to their workplaces. However, it is difficult to estimate diminished productivity due to illness.

Despite these important data limitations, we believe that our study is the first to estimate the economic burden of cancer in Japan and will be essential in Japanese policy determination.

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