## 学位論文内容の要旨 (Summary of dissertation)

博士の専攻分野の名称 博士(医学)

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学位論文題名 (Title of dissertation)

Barriers to and Predictors of Human Papillomavirus (HPV) Vaccine Acceptance in Parents of Adolescent Girls: Maximizing the Public Health Impact of HPV Vaccination in Japan

(思春期の娘を持つ親の子宮頸がん予防 HPV ワクチンに対する認知と受容:

接種率向上のための要因解明)

## Introduction:

Cervical cancer, caused by persistent infection with an oncogenic human papillomavirus (HPV), is highly preventable, yet it claims the life of 275,100 women annually. Two highly effective prophylactic HPV vaccines have been developed. Both contain antigens against HPV types 16 and 18, responsible for around 70% of cervical cancers worldwide. HPV vaccines offer promising new options in future cervical cancer prevention programs. However, for the public health impact to be fully realized, high uptake is necessary. Since HPV is transmitted sexually, the vaccine should ideally be administered before sexual debut. Consequently, the primary target age group for vaccination is pre/adolescent girls. In this age group most countries require parental consent, so understanding parental attitudes towards HPV vaccination have taken place, both in Europe/North America and Asia. However, no such study has taken place in Japan.

In Japan, cervical cancer is the most common cancer in women aged 20-39yrs and the incidence is increasing. In women aged 20-29yrs and 30-39yrs, HPV 16 and 18 are responsible for 90% and 76% of all cervical cancer cases, respectively. Thus HPV vaccines offer a unique opportunity to reduce morbidity and mortality associated with cervical cancer in Japanese women of reproductive age. However, for high uptake rates to be achieved, the vaccine must be both affordable and acceptable to those who influence uptake most. Consequently, this study was designed to: (i) determine attitudes towards and knowledge of HPV and HPV vaccines, as well as the overall acceptance of HPV vaccination in Japanese parents, (ii) evaluate the influence of written educational information about HPV on parental acceptability of HPV vaccination, particularly in areas of low cervical screening uptake and (iii) identify socio-demographic and attitudinal predictors associated with HPV vaccine acceptance, in particular mothers cervical cancer screening history. **Materials and Methods:** 

**Study 1** A 103-item survey instrument that assessed parental attitudes towards childhood vaccinations, socio-demographic factors, knowledge about and attitudes towards cervical cancer, HPV and the HPV vaccination, willingness to pay for HPV vaccine, as well as information on cervical screening history and HPV related diseases was distributed to 2192 primary caregivers with daughters aged 11–14yrs, attending 5 elementary (n=560) and 14 junior high schools (n=1632) in Sapporo between July and September 2010. Surveys were sent out via the schools and returned to the main researcher by post. Independent predictors

of parental HPV vaccine acceptability were determined using multivariable logistic regression models.

**Study 2:** A randomized intervention study within a cross-sectional survey was conducted in two cities: Sakata in Yamagata prefecture which has cervical cancer screening rates of around 55% and Kitami, Hokkaido, which has cervical cancer screening rates of around 7%. Subjects were 3471 primary caregivers with daughters aged 11–14yrs, attending 15 elementary (n=769) and 7 junior high schools (n=817) in Sakata and 18 elementary (n=914) and 11 junior high schools (n=971) in Kitami between October and December 2010. In addition to the survey instrument used in study 1, a random half of participants received a detailed "HPV Information Sheet" about HPV and cervical cancer. Independent predictors of parental HPV vaccine acceptability were determined using multivariable logistic regression models. **Results:** 

Since 98.5% of respondents were mothers, data from mothers and fathers was analyzed separately.

**Results 1 (Study 1, mothers):** Responses from 862 participants were analyzed. Around 93% of mothers would accept the vaccine for their daughter if free, but only 1.5% was willing to pay the minimum recommended price of  $\pm40,000$ . Vaccine acceptance was higher in mothers who had heard of HPV vaccine (aOR:2.58; CI:1.47–4.53), and who believed susceptibility to (aOR:2.30; CI:1.34–3.92) and severity of (aOR:3.73; CI:1.41–9.88) HPV to be high. Recommendations from a doctor (aOR:12.60; CI :7.06–21.48) were also positively associated with increased HPV vaccine acceptance. Concerns about side effects of both the HPV vaccine (aOR:0.03; CI:0.01–0.08) and routine childhood vaccines in general (aOR:0.11; CI :0.02–0.78) emerged as barriers to vaccination. Not participating in routine cervical screening also emerged as a deterrent (aOR:0.49; CI:0.27–0.91).

**Results 2 (Study 2, mothers):** Responses from 1032 participants were analyzed. Vaccine acceptability was similar to that of survey 1, around 92% if offered for free and 1.5% at the recommended price. Providing written educational material did not increase acceptability. Furthermore, participating in regular cervical screening (aOR:1.89; CI:1.10-3.25) was associated with positive acceptance of HPV vaccination and concerns about vaccine safety (aOR:0.57; CI:0.36-0.91) was a barrier. However, the greatest barrier to HPV vaccination acceptance was living in an area with low cervical screening uptake (aOR:0.51; CI:0.31-0.84).

**Results 3 (Studies 1 and 2, fathers):** Responses from 27 fathers (16 divorced, widowed or single; 11 married or cohabiting) were analyzed. Only one (3.7%) participant believed he had been previously been infected with HPV and most (81.4%) believed their future risk was low. No differences existed according to marital status. However, single fathers were significantly more likely than married fathers to believe their daughter was at risk for HPV (87.5% versus 36.4%; p=0.01) and cervical cancer (75.0% versus 27.3%; p=0.02). Acceptability of free HPV vaccination was similar to that of mothers at 92% with no difference according to marital status. However single fathers were significantly more likely (p=0.005) to pay more when vaccination came at a cost. Concerns specific to single fathers included explaining the sexual nature of HPV and having to take a daughter to a gynecologist to be vaccinated.

## **Conclusions:**

The results of this first study investigating attitudes towards and acceptance of HPV vaccination in Japanese parents of adolescent girls are encouraging. Acceptance is high, when cost is not a barrier. They suggest that if physicians actively address safety concerns and are aware of issues specific to single fathers, high uptake can be achieved in a publically funded HPV vaccination program. They do also indicate, however, that further research is needed to investigate whether lower vaccine acceptance in mothers who do not undergo regular cervical screening is also reflected in actual uptake rates, since widespread disparities in cervical cancer could result.

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