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学位論文題名

# 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)

## 学位論文内容の要旨

### 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 vaccine is essential. For this reason, many studies on parental attitudes towards and acceptance of 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: H-city, which has cervical cancer screening rates of around 55%, and L-city, 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 H-city and 18 elementary (n=914) and 11 junior high schools (n=971) in L-city between October and December 2010. Participants were randomized to receive either the survey instrument alone, or the survey instrument and a detailed “HPV Information Sheet” about HPV and cervical cancer. Independent predictors of parental HPV vaccine acceptability were determined and the effect of the information sheet assessed.

#### **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 ¥40,000. 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 significantly increased acceptability in L-City from 83.9% to 90.9% (p=0.03), but not in H-city. Furthermore, while worries about vaccine safety were the main barrier to acceptance in H-City (aOR: 0.28; CI: 0.12-0.53), as hypothesized, not participating in regular screening was the greatest barrier in L-City (aOR: 0.27; CI: 0.12-0.61).

**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 large-sale population based studies are needed to investigate whether lower vaccine acceptance in mothers who do not undergo regular cervical screening is also reflected in actual uptake rates after the introduction of national funding, since widespread disparities in cervical cancer may persist or potentially worsen if vaccination coverage is poor in areas with low screening coverage.

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# 学位論文審査の要旨

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出産適齢期である 20～30 代の日本人女性において最も発症率が高いがんは子宮頸がん（以後、頸がん）であり、近年は増加傾向にあって若年化も認める。その原因の 99%はヒトパピローマウイルス（HPV）で、この HPV に対するワクチン接種により頸がんを約 80%減少させると推定されている。しかしワクチン普及の最大障壁は自立が不十分な思春期女子への接種である。すなわち接種率向上には保護者の理解が鍵となる。そこで、本研究では思春期女子を持つ母親を対象とした頸がん及び HPV ワクチン接種に対する 2つの意識調査を実施して、接種率向上の方策を検討した。調査 1 は 2010 年 7-9 月に札幌市内の小・中学校 19 校の 11-14 歳の女子を持つ母親 2,192 名を対象とした横断的研究で、HPV や頸がんに関する知識や接種に関する自記式質問紙調査である。調査 2 は横断的研究と無作為割付介入研究を同時に実施し、酒田市と北見市を対象地とした。小・中学校の母親 3,471 名に対し 2010 年 10-12 月に調査を行い、対象者を無作為割付により 2 群に分け、一方には HPV や頸がんについて詳細な情報を提供した。接種料金に関する質問では HPV ワクチンの接種が無料なら娘に接種させるとした母親が多かった一方で、全額自己負担でも接種させるとした母親はほとんどいなかった。安全性に対する不安と母親の検診受診歴が無いことは接種の障壁であった。一方医師の勧奨、保健所などからの案内や娘の同級生の接種状況は、意思決定に前向きな影響を与えた。さらにワクチンについて伝聞と効果を納得することもワクチン受容度に関連していた。情報提供による介入は、低受診率の地域では負担なく接種できれば情報提供がワクチン受容度を高めることを示した。すなわち本研究の結果は、接種率向上の要因を明らかにすることに繋がった。

質疑応答で、副査の荒戸教授から、海外ではワクチンの安全性が受容の障壁となってい

るかとの質問と参加者の検診受診率が想定したより高く、選択バイアスがあるのではないかと指摘があった。申請者は、欧米では高学歴の母親は安全性に懸念を持ち、接種に反対する傾向があると述べた。また、選択バイアスに関しては調査1、2ともに母親の平均年齢は40歳前後であり、この年齢層の受診率は全年齢層の平均より高い一方、北見の参加者では確かに未受診者のデータが不足していることを説明した。副査の玉城教授からは2000年以降における頸がんの増加、ワクチン効果の持続性、有効性に関する国別比較、そしてワクチン受容度に関する研究が日本で少ない理由について質問があった。申請者は頸がんの増加は初交年齢の若年化といった性行動の変化やこの年齢層の検診受診率が低いことを理由として挙げた。また引用した研究のワクチン効果は6か月の持続感染を指標に検討されており、他の報告でも同様であると述べた。最後に申請者は日本におけるHPVに関する研究の多くは婦人科医が実施し、焦点が異なることを述べた。副査の櫻木教授は、日本の若年女性の頸がん検診受診率が低い理由とこれを改善する方策について質問された。さらに韓国では検診受診率が上がっていることを指摘して母親の検診受診歴と娘の接種率に関する類似した研究の有無について質問があった。申請者は英国のように受診率の高い国においては若年女性が検診の重要性について学ぶ機会が多いことを説明し、例として高校、母親、GP、若年者向け雑誌を挙げた。加えて日本では母親や教師など教える側が検診について教育を受けておらず、検診の重要性を認知していないため、自分の知識を娘や生徒に教えられないこと、若年者向けの雑誌で検診の重要性が取り上げられないことがないこと、このトピックを扱うような漫画は若年女性の教育に有効な手段になることを述べた。また申請者は韓国ではHPVワクチンへの公的援助がないために接種率が低く、そのため母親の受診歴と娘のワクチンの状況に関する研究が行われていないと述べた。最後に、主査の玉腰教授はHPVワクチンに対する父親の態度について説明するよう助言した。これは学位論文には示されているが口頭試問で触れなかったものである。申請者は父親のワクチン受容度も高いが、HPVと性的行動との関連を娘に話さねばならないことと婦人科を受診しての接種が障壁となることを述べた。さらに、HPVとワクチンについての男性の知識が少ないことから、頸がん予防のための男性への教育の重要性を述べた。これを受け、さらに男性への有効な教育方法について質問があり、申請者はそれに対して中学校と高校での教育が効果的であると述べた。

この論文の一部は英文国際誌に既に掲載されている。また、この成果をもとに今後日本人女性を対象とした頸がん予防事業が広く普及することが期待される。審査員一同は、これらの成果を高く評価し、大学院課程における研鑽や取得単位なども併せ申請者が博士(医学)の学位を受けるのに十分な資格を有するものと判定した。