



Factors Influencing Maternal Acceptance of Human Papillomavirus Vaccination for Their School-Aged Daughters in Fukuoka Prefecture, Japan

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Authors' contributions

This work was carried out in collaboration between all authors. Author YH designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors MN and TS managed the analyses of the study. All authors read and approved the final manuscript.

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ABSTRACT

Aims: The aim of this study was to elucidate the factors that influence maternal acceptance of human papillomavirus (HPV) vaccination for their school-aged daughters.

Study Design: The survey was cross-sectional and conducted using an anonymous self-administered questionnaire.

Place and Duration of Study: Two middle schools and 10 high schools in Fukuoka prefecture, between November 2012 and April 2013.

Methodology: The cross-sectional survey was conducted on mothers (n=1,407) with daughters aged 13-16 years, and an anonymous self-administered questionnaire was used. The items were HPV vaccination status of daughter, knowledge of the HPV vaccine and cervical cancer, attitude

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toward the HPV vaccine and general vaccinations, and communication with daughters about cervical cancer. The questionnaire was distributed and collected through the junior high school students and the high school students. Variables were extracted related to the daughters' state of vaccination, and subsequently multivariate logistic regression analysis was performed.

Results: Eight factors of mothers were extracted related to daughters' HPV vaccination in order of strong influential: attitude placing importance on cost-free vaccination (OR, 9.26; 95% CI, 3.42-25.0), sense of parental obligation (OR, 4.65; 95% CI, 2.30-9.43), trust in the effectiveness of vaccine (OR, 3.91; 95% CI, 2.41-6.34), trust in the government's handling of vaccination (OR, 2.40; 95% CI, 1.49-3.86), communication with daughters (OR, 2.04; 95% CI, 1.28-3.22), trust in the safety of vaccine (OR, 1.81; 95% CI, 1.04-3.15), threat of cervical cancer (OR, 1.80; 95% CI, 1.14-2.86), and knowledge of the HPV vaccine (OR, 1.23; 95% CI, 1.06-1.43).

Conclusion: HPV vaccination of school-aged girls was promoted by passive factors of mothers: attitude toward free vaccination through a public subsidy and a sense of parental obligation. Further enhancement of education for HPV prevention is urgently needed.

Keywords: HPV vaccination; mother; acceptance of HPV vaccination; attitudes; influencing factor.

1. INTRODUCTION

In Japan, more than 2,500 women die annually from cervical cancer. Over 17,000 women are affected when intraepithelial cancer is included. In recent years, there has been an increase in the cervical cancer incidence and mortality in the young age group. Thus, cervical cancer has become a significant health problem in women, including in young women [1,2]. Cervical cancer screening has been used in Japan for approximately 50 years. Since 1983, this screening has been conducted as a national program under the Health and Medical Service Law for the Aged. As a result, the cervical cancer incidence and mortality have declined in middle-aged and elderly women. In contrast, the number of young women who undergo screening has decreased due to inadequate education about cervical cancer, and the cervical cancer incidence and mortality have increased in the young generation [3]. Since 2009, the local governments in Japan have been distributing coupons for free cervical cancer screening for women aged 20 years or older. The local governments have held events to promote cervical cancer screening where periodic screening once every two years has been recommended [1]. However, the percentages of people who undergo screening have only been approximately 20-30% [4].

The human papillomavirus (HPV) vaccine has been approved in this setting, and there is much anticipation that the vaccine will reduce the cervical cancer incidence and will contribute to cost effectiveness [5-8]. There are over 100 genotypes of HPV. At least 16 types are associated with the development of cervical

cancer and are called the "high risk HPV types." In contrast, the low risk HPV types, such as types 6 and 11, cause genital warts with repeated recurrences [9,10]. In Japan, a bivalent vaccine was approved against types 16 and 18 in 2009 and a quadrivalent vaccine was approved against types 6 and 11 in 2011. Presently, one of these two types of HPV vaccines can be selected for vaccination [11].

Vaccination for sexually transmitted HPV infection is targeted at uninfected individuals before sexual debut. After HPV vaccines were approved, many local governments have developed programs to promote vaccination, including free vaccination, in girls aged 13-16 years [12]. Free HPV vaccines have become available to girls aged 13-16 years in all regions of Fukuoka Prefecture since April 2011, and a program to promote vaccination has been developed by each municipality. Since June 2013, adverse reactions such as local pain, syncope, and chronic pain have become recognized as problems. The WHO advisory committee examined the reports on adverse events of HPV vaccines, including those in Japan, and issued a statement that the vaccines are safe [13]. However, the Japanese government has suspended its strong recommendation for HPV vaccination until now [14]. The recommendation by the Japanese Ministry of Health, Labour and Welfare has caused concerns and confusion about HPV vaccination among many healthcare providers and parents. Therefore, it is important to elucidate what factors affect the decision of mothers to have their daughters vaccinated against HPV. Such data will be valuable to improve the HPV vaccination rate and to

examine the approach to increase awareness of cervical cancer prevention in both the mothers and daughters.

However, in Japan, recommendation for HPV vaccines was withdrawn only a little over 3 years after the HPV vaccine was approved. During this period, only a few studies have been reported to elucidate the factors for maternal acceptance of HPV vaccination of their daughters. Our study examined the factors influencing maternal acceptance of HPV vaccination of their daughters. The subjects were mothers with school-aged daughters in the age range recommended for HPV vaccination. It was performed during a period in which HPV vaccination is actively encouraged.

2. MATERIALS AND METHODS

2.1 Conceptual Framework

In the health belief model developed by Becker et al, human health behavior is influenced by not only knowledge but also subjective attitude toward the “difference between the benefits and

burden of the behavior” [15]. The theory of planned behavior proposed by Ajzen explains three attitude factors that determine health behavior in people: “positive or negative attitude toward the behavior,” “one’s own belief and expectation of others,” and “ease of performing the behavior” [15]. The concept of our study was based on the health belief model and the theory of planned behavior (Fig. 1). Our study hypothesized that maternal decision-making about HPV vaccination for their daughters is influenced by the maternal factors: subjective attitude factors, knowledge factors related to the HPV vaccine, and socio-environmental factors. The maternal subjective attitude factors involved the determination of the benefits and burden of HPV vaccination. And the maternal attitude factors were hypothesized to be the “threat of cervical cancer,” “positive or negative attitude toward the HPV vaccine,” and “attitude toward general vaccines. The socio-environmental factors were predicted to be “age, income, marital status, and presence of a reliable healthcare provider.” In our study, race and religion were not used as factors because Japan is mostly racially and religiously homogeneous.

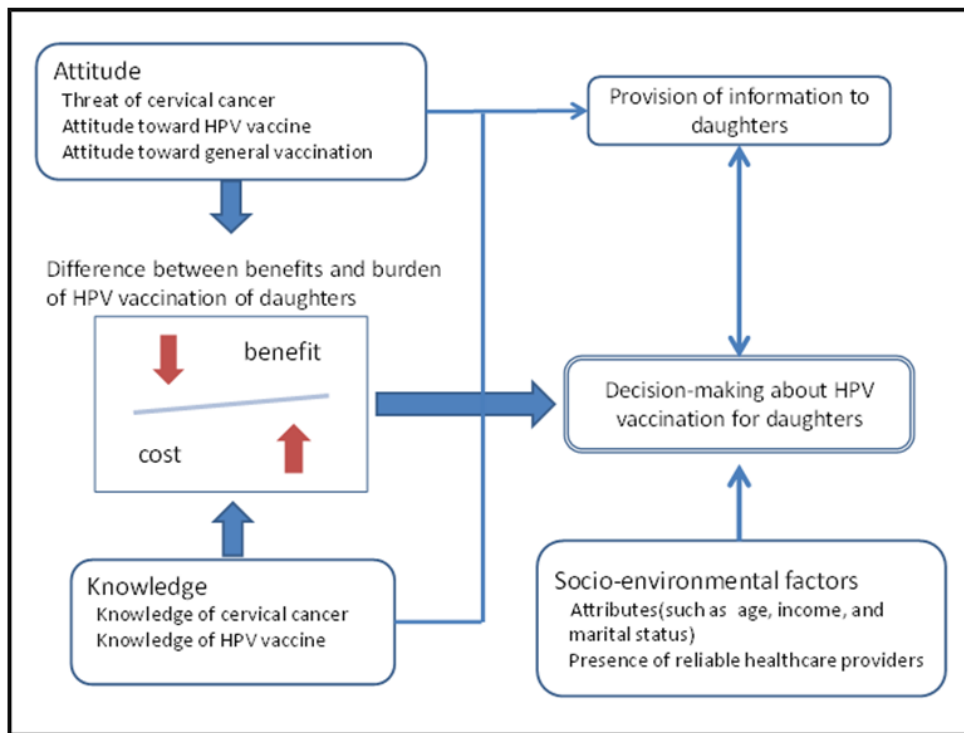


Fig. 1. Factors influencing maternal acceptance of human papillomavirus vaccination for their school-aged daughters: conceptual diagram

2.2 Participants

The questionnaire was distributed to 3,828 guardians with children in the age range (13-16 years) recommended for HPV vaccination (first year in junior high school to first year in high school) in Fukuoka Prefecture. Fukuoka Prefecture is located in the northern region of the island of Kyushu and is an important area for transportation, connecting Kyushu with Honshu. It is close to the Korean peninsula and is an economic region that is more accessible to other Asian countries than other parts of Japan. Fukuoka Prefecture is urban with an area of 4,980 km² and a population exceeding 5 million, the largest population in the Kyushu region.

2.3 Procedure

The survey was cross-sectional and conducted using an anonymous self-administered questionnaire. The questionnaire was distributed to guardians through the junior high school students and the high school students between November 2012 and April 2013. The schools were selected randomly, and 2 middle schools and 10 high schools agreed to participate in the survey. A written information form was included, which explained the purpose of the study and that their personal information will be protected, their participation was voluntary, and non-participation would not have any adverse effects. Their permission was obtained if they submitted their questionnaire. When guardians completed it, they were asked to return the questionnaire in a sealed envelope that was collected through students. Information on cervical cancer prevention was provided after the survey was conducted. A leaflet was used for this purpose and was distributed to the students and their guardians.

2.4 Questionnaires' Items

We conducted an exhaustive literature review to identify potential survey items. And, HPV vaccine investigators external to the study reviewed items to establish content validity. The questionnaire was pretested on small sample from the study population, and subsequently revised.

We examined three measures by computing an internal reliability coefficient (Cronbach's α). For the three measures-attitudes toward the HPV vaccine, attitudes toward general vaccinations, knowledge of the HPV vaccine -that showed

adequate internal reliability ($\alpha > 0.65$). We next examined construct validity using principal factor analysis. A criterion for determining items was set that the factor loading is 0.4 or more. As a result, contribution rate in each factor were knowledge of the HPV vaccine 6 items (38.8), attitudes toward the HPV vaccine 5 items (42.3), and attitudes toward general vaccinations 5 items (49.1). One-dimension structure was confirmed among these three factors.

2.4.1 Background questions

The survey asked the participant about their age, annual household income, employment status, marital status, educational background, and health condition.

This survey was carried out through the school. There was a strong desire to protect the privacy guardian among some schools. Therefore, we needed to use the questionnaire which was excluded educational background, annual household income, marital status, and employment status according to their requirement of school.

2.4.2 HPV vaccination status of daughters

The participants chose one of the six answers regarding their daughters' HPV vaccination status: "my daughter has already completed the 3-shot series," "the plan is to complete the 3-shot series within a year," "my daughter has not begun her vaccination but the plan is to have her vaccinated," "there is no plan to have my daughter vaccinated at this time," "my daughter will not be vaccinated," and "my daughter began her vaccination but it was discontinued."

2.4.3 Threat of cervical cancer

The participants were questioned on their familiarity with cervical cancer and asked to select one of the following 4 answers: "agree," "somewhat agree," "somewhat disagree," and "disagree." We classified 4 answers into two categories: yes or no choice.

2.4.4 Attitudes toward the HPV vaccine

The questions in our study was created based on the "questions that evaluated their perception of the HPV vaccine" of Ragin et al. [16]. In our study, the participants were asked about the following 6 items: "issues of sexuality should be discussed with the adolescents before HPV

vaccination,” “vaccination against HPV may promote unprotected sex in adolescents,” “I have doubts regarding its effectiveness,” “I am concerned about its adverse effects,” “the HPV vaccine should also be given to boys,” and “it is important that the HPV vaccine is free of charge.” The participants responded to these items on a 5-point scale: “strongly agree,” “agree,” “disagree,” “strongly disagree,” and “don’t know.” We divided 5 answers into two categories: yes or others’ choice. The Cronbach’ α coefficient for this questions was 0.66.

2.4.5 Attitudes toward general vaccinations

Questions were created based on the scales developed by Allen [17] and Marlow et al. [18]. Appropriate reliability and validity has also been demonstrated by Allen [17] (Cronbach’s $\alpha=0.76$). In our study, the participants responded to the following 5 items: “vaccination is important to prevent infection,” “it is a parental obligation to have their children vaccinated,” “I trust in the government’s handling of vaccinations,” “I am concerned about the side effects,” and “there are too many types of vaccinations.” The participants responded to these items on a 4-point scale: “agree,” “somewhat agree,” “somewhat disagree,” and “disagree.” We classified 4 answers into two categories: yes or no choice. The Cronbach’s α coefficient for this question was 0.76 in our study.

2.4.6 Knowledge of the HPV vaccine and cervical cancer

The participants’ awareness of cervical cancer was examined by asking them to choose one of the two answers: “I know about cervical cancer,” and “I have heard only of the name of the disease, or I do not know about cervical cancer.” The participants’ knowledge of the HPV vaccine was evaluated using questions created based on the “knowledge assessment of the HPV vaccine” of Ragin et al. [16]. In our study, the participants were asked to respond “yes” or “no” to the following 6 items: “have you heard about the HPV vaccination?”, “HPV vaccination is recommended for individuals who have never been infected,” “HPV vaccination targets women,” “do you know for which age group vaccination is recommended?”, “it is a vaccine that effectively protects against cervical cancer and genital warts,” and “cervical cancer screening is still necessary after vaccination.” The percentages of mothers who answered correctly were calculated. The Cronbach’s α

coefficient for this question was 0.67 in our study, indicating slightly low internal consistency.

2.4.7 Communication with daughter about cervical cancer

The participants were asked whether or not they had communicated with their daughters about cervical cancer and asked about the content of the communication.

2.4.8 Presence of reliable healthcare providers

The participants were asked whether or not they had a healthcare provider whom they can freely consult about vaccination.

2.5 Analysis

A chi-square test and t-test of SPSS ver. 21.0 were used to identify the maternal factors related to the HPV vaccination status of daughters. In addition, the objective variable, the vaccination status, was divided into 2 groups: a vaccination group and a non-vaccination group. Logistic regression analysis was performed using the identified maternal factors as explanatory variables. Logistic regression analysis was performed including no answer of the following 4 items: educational background, annual household income, marital status, and employment status. The objective variables were the vaccination group and non-vaccination group. The entered explanatory variables were 19 items: 5 items of attributes (age, annual income, employment status, marital status, and educational background), knowledge of cervical cancer, knowledge of the HPV vaccine, threat of cervical cancer, 4 items of attitude toward the HPV vaccine (vaccination potentially promoting unprotected sex, doubts about its effectiveness, concerns about its safety, and importance of cost-free vaccination), 5 items of attitude toward general vaccinations (importance of vaccination to prevent infection, parental obligation, trust in the government’s handling of vaccinations, concerns about side effects, and too many types of vaccines), presence of healthcare providers with whom mothers can consult, and communication with daughters. The forced entry method was used for 5 items of attributes, and a stepwise method was used for the other 14 items.

3. RESULTS AND DISCUSSION

3.1 Result

3.1.1 Characteristics of participants

Responses were obtained from a total of 2,097 guardians, consisting of 2,035 mothers and 56 fathers (response rate: 54.9%). There were 1,407 mothers among these participants who had daughters, and the data from these mothers were used for analysis (Table 1). Of these mothers, 77.0% were in their 40s and 70.3% were from a household with income of at least the national average of annual income, 4 million yen. In addition, 75.8% worked full-time or part-time, 12.0% was a single parent, and 93.9% responded that their health condition was "good," "somewhat good," or "fair."

3.1.2 HPV vaccination status of daughter

Mothers with daughters who had already completed the 3-shot series or planned to

complete the 3-shot series within a year accounted for 78.4% of the mothers. If mothers with daughters who planned to be vaccinated were included, 87.7% of the mothers can be speculated to have positive HPV vaccination behavior. These mothers were placed in the vaccination group. In contrast, 12.3% of the mothers had no plans to or would not vaccinate their daughters. These mothers were placed in the non-vaccination group. The total number of mothers was 1,324 in whom the relationship was examined between the daughters' vaccination status and variables of maternal knowledge and attitude. The reason for discontinuance of vaccination was "development of severe side effects such as allergy" (n=3), "scheduling conflict" (n=16), "lack of knowledge about the number of shots and the interval between shots" (n=5), and "unsigned" (n=24). These issues were determined to have occurred unrelated to maternal decision-making. Thus, they were excluded from data analysis.

Table 1. Characteristics of participants (n=1407)

	Number and Percent (%)
Age (n=1,407)	
20-29	1(0.1)
30-39	113(8.0)
40-49	1084(77.0)
50-59	196(13.9)
≥60	5(0.4)
no answer	8(0.6)
Household income (n=863)	
<4,000,000Yen	202(23.4)
≥4,000,000Yen	607(70.3)
no answer	54 (6.3)
Employment status (n=1,104)	
Employed (full-time, part-time, and self-employed)	837(75.8)
Unemployed	255(23.1)
no answer	12(1.1)
Marital status (n=1,104)	
Married	960(87.0)
Divorced/separated/widowed/single	133(12.0)
no answer	11(1.0)
Education (n=863)	
≤ Junior high school	364(42.2)
> Junior high school (College, Junior-College, Vocational school)	319(37.0)
Other	170(19.7)
no answer	10(1.7)
Health condition (n=1,407)	
Good	545(38.7)
Somewhat good	351(24.9)
Fair	427(30.4)
Somewhat poor	68(4.8)
Poor	14(1.0)
no answer	2(0.2)

3.1.3 Knowledge of the HPV vaccine and cervical cancer

The mothers' responses about their knowledge of cervical cancer were: "I know about cervical cancer" in 41.9% of the mothers, "I have heard only of the name of the disease, or I do not know about cervical cancer" in 52.0%. It was shown that over half of the mothers had no information beyond the disease name of cervical cancer. Table 2 shows the percentages of mothers who correctly answered the questions related to knowledge of the HPV vaccine.

The percentages of mothers with correct answers were 65-80% for questions on HPV vaccination targeting women, recommended age group for HPV vaccination, and necessity of cervical cancer screening after vaccination. Only 30% of the mothers knew that the HPV vaccine effectively protects against cervical cancer and genital warts.

3.1.4 Maternal factors associated with vaccination status of their daughters

Table 3 shows the relationship of the daughters' vaccination status with the following maternal factors: knowledge of and attitude toward the HPV vaccine and cervical cancer, attitude toward general vaccinations, presence of reliable healthcare providers, and mother-daughter communication about cervical cancer prevention. The vaccination group had a significantly higher percentage of mothers who knew about the disease cervical cancer compared with the non-vaccination group ($P=0.006$). The vaccination group also had a significantly higher average score of HPV vaccine knowledge ($P<0.001$). The vaccination group had a significantly higher percentage of mothers (68.1%) who were familiar with cervical cancer ($P<0.001$). The reasons that the participants gave for their familiarity were that they had people close to them who had cervical cancer or died from it and that the participants previously had an abnormal Pap test result. Cost-free vaccination was important in 94% of the mothers. This percentage was particularly high among questions on attitude toward the HPV vaccine for adolescent girls. This percentage was significantly higher in the vaccination group than in the non-vaccination group ($P<0.001$). For attitude toward general vaccinations, more than 90% of the mothers overall felt that vaccination was important for prevention of infection and that it was a parental obligation to vaccinate their children. Thus, it was shown that a majority of the mothers had a

positive attitude toward vaccination. There was a relationship between the daughters' vaccination status and all 5 items related to attitude toward general vaccinations ($P<0.001$). Only 53.1% of the mothers had communicated with their daughters about cervical cancer. A higher percentage of mothers had this communication in the vaccination group than in the non-vaccination group ($P<0.001$). The content of the communication consisted of "being able to receive vaccination cost-free if they acted now" in over 70% of the mothers. It was followed by "necessity of cervical cancer screening," "infection route of HPV," and "cervical cancer" in 40% or less of the mothers. Only 52.4% of the mothers had a healthcare provider whom they can freely consult about vaccination. A higher percentage of mothers had a healthcare provider in the vaccination group than in the non-vaccination group ($P<0.001$).

3.1.5 Final multivariable logistic regression model for acceptance of HPV vaccination for daughters

Multivariate logistic regression was performed. The explanatory variables were maternal attributes and variables shown to be related to the HPV vaccination status.

Table 4 shows the resulting 8 variables that were extracted. Following eight maternal factors which promoted to the HPV vaccination of daughters in order of strong influential: attitude placing importance on cost-free vaccination (OR, 9.26; 95% CI, 3.42-25.0), sense of parental obligation (OR, 4.65; 95% CI, 2.30-9.43), trust in the effectiveness of vaccine (OR, 3.91; 95% CI, 2.41-6.34), trust in the government's handling of vaccination (OR, 2.40; 95% CI, 1.49-3.86), communication with daughters (OR, 2.04; 95% CI, 1.28-3.22), trust in the safety of vaccine (OR, 1.81; 95% CI, 1.04-3.15), threat of cervical cancer (OR, 1.80; 95% CI, 1.14-2.86), and knowledge of the HPV vaccine (OR, 1.23; 95% CI, 1.06-1.43).

3.2 Discussion

Our survey showed that 78.4% of the female students had been vaccinated in the age group recommended for HPV vaccination. This percentage is higher than the national average vaccination rate of 67.2% in 2012 [12].

Multiple studies have reported that the HPV vaccination behavior of minors is greatly affected

by psychosocial and knowledge of their mothers, the guardians [17-25]. Some literature articles have been reported that previous abnormal results of Papanicolaou (Pap) test and maternal attitude toward the risk of cervical cancer influenced maternal decision-making about the HPV vaccine for their daughters [17,19,20-22]. It has been reported that parental positive attitude toward vaccine promoted vaccination of their daughters, while their negative attitude toward vaccine caused them to be reluctant about the vaccination [22,23,25]. It has also been reported that parental positive attitude toward general vaccinations promoted daughters' HPV vaccination, including against HPV. In contrast, parental negative attitude was a factor causing parents to refuse vaccination for their daughters [18,22,25]. The maternal knowledge factors related to the HPV vaccine have been described in many studies that examined the relationship between maternal knowledge and decision-making about vaccination for their daughters [16,19,22,23,26,27]. In addition, it has been reported that mothers were more likely to recommend HPV vaccination to their daughters if they had received a recommendation from or had consulted with reliable healthcare providers [26]. In addition, it was reported that there was difference of acceptance to HPV preventive vaccination in accordance with cultural belief among ethnic group [28].

In our study, variables that were found to be significantly associated with HPV vaccination status were the eight maternal factors in our conceptual framework we predicted. Among the conceptual framework, social environment factors associated with mother were not related to vaccination status of daughter. However, cost-free vaccination, a sense of duty as a parent to vaccination, trust the government's handling of vaccination, confidence in the safety of the HPV vaccine, the threat to cervical cancer, and knowledge of the HPV vaccine were expected as

important factors when mother determine whether HPV vaccination to daughter were benefit or not.

Over 90% of the mothers had the attitude placing importance on cost-free vaccination. The attitude was significantly related to vaccination to their daughters against HPV. Haesebaert, et al. [26] showed that the attitude placing on cost-free vaccination did not influence maternal acceptance of HPV vaccination for their daughters. However, in Japan, the out-of-the-pocket cost of HPV vaccination is high at approximately 50,000 yen per person aged 16 or older. Therefore, free vaccination through public subsidies can contribute greatly to the improvement of the vaccination rate. However, one cannot rule out that short-term public subsidies might be promoting vaccination without having mothers obtain sufficient information to make an informed decision about their daughters' vaccination. In the promotion of HPV vaccination, it is necessary to increase the eligible age for public funding of vaccination.

Over 90% of the mothers had the attitude toward general vaccinations that it was a parental obligation and important to vaccinate their children. This attitude was strongly related to HPV vaccination status. Marlow, et al. [18] showed that attitude toward vaccination and past vaccination behavior strongly influenced the parental decision to allow their daughters to receive a new vaccine. Similarly, Haesebaert, et al. [26] showed that the acceptance for other vaccines is related with HPV vaccination. In this analysis, the high vaccination rate likely resulted from a sense of obligation for vaccination pervasive in the generation of the parents and free vaccination through public subsidies. This sense of obligation and free vaccination through public subsidies were thought to have passively promoted the parents to have their daughters who receive the new vaccine.

Table 2. Knowledge assessment of the HPV vaccine (n=1,407)

	Correct answer rate (%)
I have heard about HPV vaccination.	83.3
In Japan, HPV vaccination is targeted to women.	79.6
I know the age group for which HPV vaccine is recommended.	71.9
Cervical cancer screening is still necessary after vaccination.	77.0
HPV vaccination is recommended for individuals who have never been infected.	65.0
It is a vaccine that effectively protects against cervical cancer and genital warts.	29.1

Average score ± SD; 3.82 ± 1.55, range 0-6; 6 items, Cronbach's α =0.67

Table 3. Bivariate relationship between Daughters' HPV vaccination status and maternal knowledge and attitude factors about HPV (n=1,324)

Category	Variables	Levels	Vaccination group (n=1161) n (%)	Non-vaccination group (n=163) n (%)	OR	95%CI	P-value
Knowledge of HPV vaccination and cervical cancer	I know about cervical cancer I know only of the name / I do not know	Yes	593(54.0)	99(6.0)	reference		0.006
		No	506(46.0)	51(34.0)	1.66	1.16 - 2.37	
	Scale score of knowledge about HPV vaccine (Average score±SD)		3.93 ± 1.50	3.19 ± 1.71			<0.001
Attitude toward HPV vaccination and cervical cancer	Cervical cancer is a familiar disease to me.	No	335(29.0)	82(50.6)	reference		<0.001
		Yes	822(71.0)	80(49.4)	2.52	1.81 - 3.51	
	Issues of sexuality should be discussed with the adolescents before HPV vaccination.	No	191(16.6)	32(19.8)	reference		0.38
		Yes	957(83.4)	130(80.2)	1.23	0.81 - 1.87	
	Vaccination against HPV may promote unprotected sex in adolescents.	Yes	200(17.6)	45(28.1)	reference		0.002
		No	939(82.4)	115(71.9)	1.84	1.35 - 2.68	
	I have doubts regarding its effectiveness.	Yes	263(23.1)	100(62.1)	reference		<0.001
		No	876(76.9)	61(37.9)	5.46	3.86 - 7.80	
	I am concerned about its safety	Yes	642(56.3)	131(81.4)	reference		<0.001
		No	498(43.7)	30(18.6)	3.39	2.24 - 5.13	
	The HPV vaccine should be given to boys just as in girls.	No	796(70.3)	114(71.2)	reference		0.881
		Yes	336(29.7)	46(28.8)	1.05	0.73 - 1.51	
It is important that the HPV vaccine is free of charge.	No	16(1.4)	25(16.0)	reference		<0.001	
	Yes	1113(98.6)	131(84.0)	13.3	6.91 - 25.5		
Attitude toward general vaccines	Vaccination is important to prevent infection.	No	10(0.9)	21(13.6)	reference		<0.001
		Yes	1130(99.1)	133(86.4)	17.8	8.23 - 38.7	
	It is a parental obligation to have their children vaccinated.	No	40(3.5)	37(24.0)	reference		<0.001
		Yes	1095(96.5)	117(76.0)	8.66	5.33 - 14.1	
	I trust in the government's handling of vaccinations.	No	214(19.0)	79(51.3)	reference		<0.001
		Yes	913(81.0)	75(48.7)	4.49	3.17 - 6.37	
	I am concerned about the side effects.	Yes	876(77.6)	138(90.8)	reference		<0.001
		No	253(22.4)	14(9.2)	2.85	1.62 - 5.03	
	There are too many types of vaccinations.	Yes	554(49.0)	108(70.1)	reference		<0.001
		No	577(51.0)	46(29.9)	2.44	1.70 - 3.52	
I have a healthcare provider whom I can freely consult about vaccination.	No	471(42.5)	94(62.7)	reference		<0.001	
	Yes	628(57.5)	56(37.3)	2.27	1.60 - 3.23		
Did you have a mother-daughter communication about cervical cancer prevention?	No	496(43.5)	101(63.1)	reference		<0.001	
	Yes	644(56.5)	59(36.9)	2.22	1.58 - 3.12		

Note: Scale score of knowledge were examined by t-tests, all other were examined by chi-square tests.

Table 4. Factor associated with HPV vaccination acceptance among mothers: Multiple logistic regression final model (n=1,122)

Category	Variables	OR (95%CI)	P-value	
Characteristics	Age	≤30	reference	
		31-49	0.52(0.23-1.19)	0.12
		≥50	0.56(0.21-1.49)	0.25
	Household income	< 4,000,000Yen	reference	
		≥4,000,000Yen	1.85(0.94-3.68)	0.76
	Employment status	no answer	0.59(0.19-1.79)	0.35
		Employed	reference	
		Unemployed	1.09(0.61-1.93)	0.78
	Marital state	no answer	3.67(0.74-18.1)	0.11
		Married	reference	
		Divorced/separated/widowed/single	0.68(0.33-1.42)	0.31
	Education	no answer	0.38(0.08-1.81)	0.23
≤Junior high school		reference		
> Junior high school		0.75(0.37-1.34)	0.50	
Attitude toward HPV vaccination and cervical cancer	Threat of cervical cancer	Cervical cancer is a familiar disease to me.	No	reference
		Yes	1.79(1.14-2.86)	0.01
	Doubts about the effectiveness	I have doubts regarding the HPV vaccine effectiveness.	Yes	reference
		No	3.91(2.41-6.34)	<0.001
	Concerns about the safety	I am concerned about the HPV vaccine is safety.	Yes	reference
		No	1.81(1.04-3.15)	0.036
	Importance of free vaccination	It is important that the HPV vaccine is free of charge.	No	reference
			Yes	9.26(3.42-25.0)
Attitude toward general vaccines	Trust in the government	I trust in the government's handling of vaccinations.	No	reference
		Yes	2.40(1.44-3.86)	<0.001
	Sense of parental obligation	It is a parental obligation to have their children vaccinated.	No	reference
			Yes	4.65(2.30-9.43)
Communication with daughters	Did you have a mother-daughter communication about cervical cancer prevention?	No	reference	
		Yes	2.04(1.28-3.22)	0.003
Knowledge of HPV vaccination and cervical cancer	Scale score of knowledge about HPV vaccine		1.23(1.06-1.43)	0.005

Note: This value was examined by multivariate logistic regression modeling

However, when there is passive promotion of HPV vaccination due to parental obligation and free vaccination, its negative effect is predicted to be the unlikelihood of passing on preventive education from mothers to their daughters. In our study, there was hardly any mother-daughter communication about cervical cancer prevention. In addition, less than half of the mothers (41.9%) had the knowledge of cervical cancer. Several studies showed that the lack of knowledge about HPV and HPV vaccinations of the mother led to refraining from vaccination to daughters [23,26,27].

The effectiveness and safety of the HPV vaccine was negatively correlated to the HPV vaccination to daughter. Ogilvie, et al. [19] indicated that concerns about vaccine safety and lack of information were some of the main reasons that the parents gave for not having their daughters receive HPV vaccination. Since June 2013, serious adverse reactions to the HPV vaccine have become a problem in Japan, and the government suspended its strong recommendation for vaccination [14]. It is predicted that parents would be even more conflicted about HPV vaccination for their daughters. As a result, the national average of HPV vaccination rates (2014) plummeted to 8 percent from 72 percent. Cervical cancer screening rate has stagnated at 25%, which was similar to previous rate. Therefore, Japan Association for Gynecology and Obstetrics stated that cervical cancer in Japan may become spread more than before [29]. Gamble et al. [20] showed that healthcare professional's recommendation for HPV vaccination were likely to influence decision making of both parent and adolescent in regard to receiving the vaccine. However, there is no general practitioner system in Japan. As a result, a major issue will likely be provision of sufficient information to mothers and their school-aged children.

We need to be mindful of the importance of periodic cervical cancer screening after vaccination, because the HPV vaccine prevents cervical cancer caused only by genotypes 16 and 18 among carcinogenic HPV genotypes. These 2 genotypes cause approximately 70% of cervical cancers [9]. Among widely known carcinogenic HPV genotypes, type 16 has been detected at a slightly lower frequency in Japan than in other countries. However, types 52 and 58 have been detected at higher frequencies in Japan [30]. The cervical cancer screening rate is low in Japan, and thus, an important issue is to improve the

screening rate in addition to improving the HPV vaccination rate. Therefore, it is necessary not only to recommend HPV vaccination for school-aged girls but also to increase the understanding of individuals regarding HPV infection routes, problem about the effectiveness and safety of the vaccine, timing of screening, and specific methods such as involving screening. Since there are limitations to health education in school [31] and medical settings, parents will play a major role.

Maternal role that can be expected in the home is not the only cervical cancer prevention education. Gamble, et al. [20] reported that a factor of parental acceptance of daughters' HPV vaccination was a discussion of sexuality in the parent-child communication. In particular, many mothers who accepted the vaccination actively spoke to their daughters about contraception and prevention of other sexually transmitted diseases. Similarly, Robert et al. [32] showed that the HPV vaccination rate was high in college students whose mothers approved of the vaccination and whose parents communicated to them about sexuality. When mothers recommend HPV vaccination to their children, it might provide an opportunity not only to communicate about vaccination but also to provide health education about sexuality.

In June 2013, the U.S. Centers for Disease Control and Prevention (CDC) reported high effectiveness of the HPV vaccine based on over 50% reduction in the HPV infection rate in women aged 13-17 years since the HPV vaccine was introduced in 2007 [33]. In the U.S., the HPV vaccination rate in girls in their teens was reported to be only 53.8%, and a factor for this low percentage was that the parents did not allow their daughters to be vaccinated. The main reasons why their daughters would remain unvaccinated were parental "vaccine safety concerns," "lack of knowledge about the vaccine or the disease," and the parental attitude that their "[daughters are] not sexually active" [34]. This result suggests the importance of provision of sufficient information to parents in addition to public subsidy to maintain a vaccination rate in girls before sexual debut. Both additional studies on the safety HPV vaccine and discussion about the preventive education are urgently needed.

3.3 Limitations of the study

This study was a cross-sectional survey. Thus, the causal relationship could not be verified between the factors associated with maternal

acceptance and the daughters' HPV vaccination behavior. This study was conducted in some areas of Fukuoka Prefecture. This results cannot be generalized as the current situation in Japan.

4. CONCLUSION

Eight factors of mothers associated with daughters' HPV vaccination, were in order of strong influential: Attitude placing importance on cost-free vaccination, sense of parental obligation, trust in the effectiveness of vaccine, trust in the government's handling of vaccination, communication with daughters, trust in the safety of vaccine, threat of cervical cancer, and knowledge of the HPV vaccine. HPV vaccination of school-aged girls was related to passive factors of mothers: attitude toward free vaccination through a public subsidy and a sense of parental obligation. Further enhancement of education for HPV prevention is urgently needed.

CONSENT

It is not applicable.

ETHICAL APPROVAL

This study was conducted with the approval of the ethics committee of Junshin Gakuen University.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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