

Research Article

How adolescent Japanese girls arrive at HPV vaccination: a semi-structured interview study

***Running title:** HPV vaccination process in Japanese girls

Rie Wakimizu PhD^{1,8*}, Kaori Nishigaki PhD^{2,8}, Hiroshi Fujioka MSc^{3,8}, Koji Maehara MD^{4,8}, Haruo

Kuroki MD^{5,8}, Tadashi Saito MD^{6,8}, Katsuya Uduki MD^{7,8}

1 Faculty of Medicine, University of Tsukuba

2 Faculty of Health Sciences, Tokyo Healthcare University

3 Faculty of Health Sciences, Tsukuba International University

4 MAEHARA Pediatric Clinic

5 SOTOBO Children's Clinic

6 Department of Pediatrics, TAKO Central Hospital

7 SHIROAMU Pediatric Clinic

8 Investigative commission of qualitative study, Society of Ambulatory and General Pediatrics of

Japan

***Address Correspondence to:** Dr. Rie Wakimizu, Associate Professor, Department of Child Health

Care and Nursing, Division of Health Innovation and Nursing, Faculty of Medicine, University of

Tsukuba, 1-1-1, Tennodai, Tsukuba-city, 305-8575, Japan.

E-mail: riewaki@md.tsukuba.ac.jp

Tel & Fax: 029-853-3427

Number of text pages (from INTRODUCTION to CONTRIBUTIONS):32

reference pages:6

tables:1

figures:1

Abstract

We examined the HPV vaccination process in adolescent Japanese girls, including protective and obstructive factors to develop and practice enlightenment activities and educational interventions for promoting HPV vaccination to adolescent Japanese girls and their families. We conducted semi-structured interview with 20 adolescent Japanese girls who lived in the wider Tokyo area, Japan. To analyze the interview data, we adopted the modified grounded theory approach. We identified three stages in the vaccination process: first encounter with cervical cancer and HPV vaccine, thoughts about vaccination, and adjustment with parents toward vaccination. The girls “knew” their knowledge and information on cervical cancer and the HPV vaccine from experts, parents, and friends, “considered and discussed” HPV vaccination in their own way or with parents, and “arranged” actual vaccination. This process was influenced by the promoting/obstructive factors in each stage. Health care providers should understand the experiences and feelings of adolescent girls who were confronted with HPV vaccination in the context of their vaccination process and conduct enlightenment activities to promote vaccination, keeping the promoting and obstructive factors suggested in this study in mind.

Key words

adolescent girls, HPV vaccination, Japan, qualitative study, semi-structured interview

INTRODUCTION

Annually, 8474 persons are affected by cervical cancer (CC) in Japan, and 2519 persons die of the disease per year (Health, Labour & Welfare Ministry, 2011). The age-related structure shows an increase in morbidity at 20-24 years of age and rises rapidly after 25 years until peaking at around 40 (Health, Labour & Welfare Ministry, 2011). CC is the primary cause of morbidity in women in their 20s to 30s (Study Group to Protect a Woman from Cervical Cancer, 2008). It is not only life threatening, but can deprive women of the possibility of pregnancy and childbirth, and inflicts much pain and suffering on young women, physically and psychologically.

CC is caused by human papilloma virus (HPV) (Walboomers *et al.*, 1999). To prevent infection with HPV in women, HPV vaccine has recently been developed (Lehtinen *et al.*, 1996). Bivalent vaccine (Cervarix®) and quadrivalent vaccine (Gardasil®) have been approved and are available in 96 and 123 countries, respectively (Garland *et al.*, 2007; Paavonen *et al.*, 2009). In Japan, marketing approval was given to Cervarix in 2009 and Gardasil in 2011, and these vaccines have been available since 2010 and 2011, respectively.

The official HPV vaccination rate is not released on a national level because public funding programs for vaccination are administered by local governments in Japan. However, there are some reports on vaccination rates compiled by local governments that focus on mass vaccination (Hayashi

et al., 2012; Kobayashi *et al.*, 2012). Compared with routine vaccination, the vaccination rate of optional vaccines is clearly low. To determine the introduction of the HPV vaccine in Japan, health economic modeling was used to analyze the aspect of vaccination cost. In November 2010, the Ministry of Health, Labour and Welfare issued the “Notification on the implementation of urgent vaccination program of CC etc.” Following the notification, public financial support was expanded in local governments across Japan in 2012. In this program, the national and local governments bore half of the vaccination cost for girls of 13 to 16 years old until the end of March 2012. Later, the extension of public funding program was decided by the cabinet up to the end of March 2013. The HPV vaccination rate, however, did not increase. Actually, the HPV vaccination rate in young women of age out of public financial support was only 5.4%, according to a local government report (Miyagi, 2011).

LITERATURE REVIEW

The number of survey reports about HPV vaccination has recently been increasing, and they mainly demonstrated; a) impact by HPV vaccines introduction; b) factors related to HPV vaccination rates in adolescent girls; c) discussions regarding HPV vaccination between parents and their daughters; and d) the association between HPV vaccination and girls’ sexual behavior.

a) Impact of HPV vaccines introduction

Tabrizi *et al.* (2012) and Markowitz *et al.* (2013) reported the reduction in human papillomavirus (HPV) prevalence among young women following HPV vaccine introduction in each country. In Australia, Ali *et al.* (2013) showed that the significant declines in the proportion of young women and heterosexual men having genital warts five years into national HPV program from national surveillance data and Brotherton *et al.* (2013) reported the decrease in incidence of high-grade cervical abnormalities within 3 years after the implementation of a population-wide HPV vaccination program. Declining rates of high-grade cervical lesions in young women due to HPV vaccines was also reported in the United States by Niccolai *et al.* (2013).

b) Factors related to HPV vaccination rates.

Hughes *et al.* (2009) reported women and wealthy families are more likely to collect information about HPV vaccinations from Internet or advertisements and have more knowledge about HPV vaccinations than men and the needy families. Their study also showed parents who had more knowledge of HPV and HPV vaccine were more likely to have their daughters vaccinated against HPV than parents who had less knowledge. Additionally, McRee *et al.* (2012, a) reported having learned about HPV vaccine via the Internet was associated with parents' higher knowledge, positive perceptions of HPV vaccine, and HPV vaccination willingness. Marchand *et al.* (2012) showed that sharing vaccination experience of vaccinated women with unvaccinated women was one of the factors that improved awareness of HPV vaccination in a survey of female college students.

They also described that learning about HPV in health-related major in college or having family members who have health-related work were significantly associated with the acceptance of the HPV vaccine. Overall, it has been shown that the higher levels of awareness and parents' and their daughters' knowledge of HPV and HPV vaccination lead to higher HPV vaccination rates.

On the other hand, according to Darden *et al.* (2013), the most frequent reasons why some adolescents will not receive vaccination against HPV were reported that "Not recommended", "Not needed or not necessary", "Not sexually active", and "Safety concerns/Side effects". It has been also shown that the most common reason why parents and their daughters refused HPV vaccination was uncertainty about vaccine safety or concern about potential adverse events (Kester *et al.*, 2012; Sotiriadis *et al.*, 2012). Relating to this, Zimet *et al.* (2013) stated that most fears related to HPV vaccine are more related to myth than reality and HPV vaccines are quite safe, and they can no longer be considered "new". Teitelman *et al.* (2011) reported that beliefs that their health insurance does not cover the HPV vaccine, a long wait to get an appointment, and limited availability of appointments are the barriers to vaccination for some women. Chou *et al.* (2011) reported that the combination of younger age and practice location was strongly associated with completion rates: 11-17 years-old-girls or patients who initiated vaccination at urban practice locations were associated with very low likelihood of completing HPV vaccination. Liddon *et al.* (2013) investigated the parental underestimation of child's sexual debut and suggested waiting until a parent

thinks a child is sexually active could result in missed opportunities for prevention and implications for HPV Vaccine Uptake at age 11 or 12 years.

c) Discussion about HPV vaccination between parents and their daughters.

Colgrove *et al.* (2010) argued that vaccines against sexual transmitted infections (STI) might threaten teenage abstinence, and that having discussions on STI with girls 11 or 12 years of age was difficult in their study. Thus, they are taking a cautious stance toward HPV vaccine for teenagers. On the other hand, McRee *et al.* (2010,b) concluded that discussions about sex between mothers and 11-14 year-old daughters who are in the ages most likely to be influenced by sexual activities is meaningful and that HPV vaccination discussions provide opportunities for promoting mother-daughter communication about sex.

d) The association between HPV vaccination and girls' sexual behavior.

Bednarczyk *et al.* (2012) showed that HPV vaccination in the recommended ages was not associated with increased sexual activity–related outcome rates in adolescent girls in a cohort study. Liddon *et al.* (2012) highlighted disparities in HPV vaccine initiation by insurance status among girls/women aged 15-24 years and by race/ethnicity among women aged >19 years and showed that no association was found between HPV vaccination and risky sexual behavior.

Thus, previous studies have reported promoting or inhibitory factors and the discussion about HPV vaccination between parents and their daughters. However, there is no study that clarified the

process of girls' HPV initiation including the way how parents and girls collected information about HPV vaccine and how they made decisions. It is assumed that the further elucidation and consideration of the process for girls being vaccinated against HPV may be very useful to review the intervention time, locations, and measures for vaccination promotion in clinical practice.

STUDY AIM

The aim of the study was to examine the process of Japanese adolescent girls to receive HPV vaccine and factors influencing these decisions and implementations. The findings of this study are very important for healthcare providers to develop and practice enlightenment activities and educational interventions for promoting HPV vaccination to adolescent Japanese girls and their families.

METHODS

Study design

We conducted a qualitative study by using the modified grounded theory approach (M-GTA) (Kinoshita, 2003). As part of the study, we interviewed participants inductively, and analyzed their narratives.

Participants

The participants were recruited from three pediatric clinics in the Tokyo metropolitan area. The interviewers did not engage in the professional health-care practices in these clinics.

The criteria for inclusion in the study were as follows : (a) girls who are 10 to 19 years and received at least one HPV vaccination that was started in December 2009, or (b) girls who are 10 to 19 years and knew about the HPV vaccine, but decided not to undergo vaccination; (i) living with family in the community; (ii) assessed their mental and intellectual status by pediatricians to determine their fitness for participation in the study; (iii) able to give informed consent; and (iv) able to participate in an interview in Japanese.

For recruitment purposes, we asked the physicians to recruit those adolescent girls whom the physician believed had met the inclusion criteria. If adolescent girls were interested in the study, the interviewers had permission to contact their caregivers and them by telephone. A meeting was then held with the potential participants, and they were provided with information about the study and on ethical issues. Twenty-one adolescent girls agreed to participate in this study. A girl was excluded from the study due to failure to set the schedule.

Data collection

We used theoretical sampling to recruit the participants (Glaser & Strauss, 1967). In theoretical

sampling, the participants who are likely to provide data similar to or in contrast to the existing data are sampled. For example, with the physicians' help, we recruited adolescent girls who received HPV vaccination by their private expense without government support after collecting a certain amount of data on the adolescent girls who received HPV vaccination with government support.

We contacted 21 adolescent girls, 20 of whom agreed to participate in the study. The data were collected in the period of 2011summer–2012spring, using narrative interviews (Oda *et al.*, 2002). Each of the 20 participants was interviewed once. We prepared an interview guide so that the interviews would be conducted along the purpose. To ensure the quality of the guide, we discussed it with specialists who were engaged directly in providing professional health-care practices to children and their families. During the interviews, participants were asked about the factors they considered in making their decision about HPV vaccination, difficulties associated with the decision-making process, and the reasons why they decided in favor of or against getting the HPV vaccine. Participants who did not get vaccinated for HPV were asked if they would consider the possibility of the vaccination in the future. Additional information such as demographic data and other vaccination history was collected from their parents. The framework of the interview comprised two dimensions:

1. Level of knowledge on CC and the HPV vaccine

- 1) When and how did you find out about the HPV vaccine?

2) Do you know the purpose of HPV vaccination?

i) Do you know what it is for? ii) When and how did you find out about it?

3) (Questionnaire) Read A) to G) texts below and choose Correct, Wrong, or Unknown.

A) CC is mainly caused by infection with HPV (human papilloma virus)

B) HPV infection is transmitted primarily by sexual intercourse

C) About 80% of adult women have been infected with HPV at least once

D) CC is increasing in women in their 20s and 30s in Japan

E) HPV vaccine can prevent about 60% of CC

F) CC can be cured 100% and does not affect pregnancy or delivery if detected early

G) Even if you receive HPV vaccination, you have to undergo CC screening

2. Expression of attitudes and behaviors

1) Did you want to have HPV vaccination? Why or Why not?

2) What do you think about the HPV vaccine being available in Japan for cancer prevention?

3) Is HPV vaccination necessary for you? Why or Why not?

4) Were you anxious about or afraid of having HPV vaccination? Describe specifically.

(For those vaccinated) What did you feel when you were vaccinated?

5) Before you received HPV vaccination, did you talk about it with your family or friends? What did you talk about?

6) What was the attitude of your family and friends regarding HPV vaccination?

We posed open-ended questions (except questions about CC and the HPV vaccine). The answers to the questions were checked after the interview. When the subject of vaccination expense came up in conversation during the interview, the interviewer asked about participants' preferred amount of self-pay and public financial support.

The interviews were conducted in a private room at institutions. The mean duration of the interviews was 45 min (the time ranged from 39 to 66 min). With the participants' permission, interviews were tape-recorded and transcribed verbatim by the principal author.

Data analysis

To analyze the data, we used the Modified Grounded Theory Approach (M-GTA) (Kinoshita, 2003), which was developed on the basis of methodology that was formulated by Glaser and Strauss (1967) on the GTA. When using the M-GTA, data analysis is conducted in several stages. Initially, the transcript of one of the participants is read a number of times, with the focus of attention being the theme of the study. Then, as the result of interpretive analysis, concepts are created. Unlike the GTA, the concept in the M-GTA is the minimum analytical unit, and each concept is derived from several pieces of data. When a concept is being created, data that are similar or antithetical to the concept also are examined in order to pre-empt an arbitrary interpretation by the analyst. Several

concepts are created, and the relationships among them are determined. Then, the concepts are categorized. Finally, the phenomenon being studied is explained by using the categories and concepts that have been developed. In this study, data collection and data analysis were reiterated until theoretical saturation was reached.

We analyzed the verbatim data in Japanese. All of the categories, concepts, and quotations that were provided by the participants' narratives, which appear in this article, were also originally in Japanese. We translated these into English (they were edited and proofread by a professional) so that they could be read by international researchers. To ensure the accuracy and validity of the data analysis, the principal author analyzed the data under constant discussion with other authors.

Furthermore, we sent the results to two participants for member-checking. Their feedback indicated that the categories that were developed by the authors adequately reflected the experiences of the two participants.

Ethical considerations

We received approval for the study through the ethics committee of the Society of Ambulatory and General Pediatrics of Japan. We informed each participant and her mother, both verbally and in writing, about the purpose of the study and assured the participants that their information would be treated confidentially. We also informed them that their participation in the study was voluntary and

that refusal to participate would not disadvantage of the clinical services they receive. We received not only parents' but their daughters' permission to conduct interview with those younger than 20 years of age.

RESULTS

We interviewed 20 vaccinated/unvaccinated adolescent girls of school age between 12-17 years old who attended to high school or junior high school and lived in the wider Tokyo area, Japan. The characteristics of the study participants are shown in Table 1. The mean age of the girls was 14.9 years (standard deviation, SD: 1.5, range: 12-17). The mean age of the mothers was 45.1 years (SD: 5.5, range: 36-57). Eight girls completed all three HPV vaccinations. Another eight girls completed the first or second vaccination with at least one injection left undone. Four girls had no vaccination including pendency.

We identified three stages in the HPV vaccination process for adolescent Japanese girls of school age: i) First encounter with CC and HPV vaccine, ii) Think about and make decision to get HPV vaccine, iii) Adjustment with parents toward actual vaccination (Fig. 1). Each category and concept is described in detail below.

i) First encounter with CC and HPV vaccine

This category consisted of two concepts: [Collect knowledge and information on CC and the HPV vaccine] and [Know experience of vaccinated friends and vaccination state of peers]. This is the stage when girls know CC and the HPV vaccine for the first time and see the vaccination state of their surroundings.

As factors relevant to the HPV vaccination process, amount and quality of knowledge and information on CC and the HPV vaccine given to the adolescent, adolescent's health literacy, and peer pressure were extracted on this concepts.

[Collect knowledge and information on CC and the HPV vaccine]

Most of the participants had acquired knowledge and information on CC and the HPV vaccine through school-sponsored briefings on vaccine with experts or conversation with local health care providers, parents, and friends. Primary information tools included posters, leaflets, television ads, and the Internet. For example:

I heard about the vaccine with my mother by chance when I went to see a doctor for a cold because I met the qualifying age for the vaccine.

I happened to see a commercial for this vaccine on TV. Mother said to me, "See, this is a new vaccine to prevent cervical cancer." I thought "this is amazing, it prevents cancer".

So I searched it straight away on the Internet.

[Know experience of vaccinated friends and vaccination state of peers]

If a participant had friends who had already been vaccinated, she would have heard about their

vaccination experience from them and gained some insight. Participants also knew about the vaccination state of others regarding how far the HPV vaccine was prevalent around them. Adolescent girls who found the vaccination rate to be high in her immediate circle spoke of peer pressure from friends who had been vaccinated. For example:

About half the girls have already had all three-times injections of HPV vaccine in my class. Including those on the way to completion, about 2/3 are receiving injection now.

My friend, who had a vaccination, says “Haven’t you had a shot yet?” or “Are you thinking of your future?” So I became a little impatient.

ii) Think about and make decision to get HPV vaccine

This was core category. The core category is consisted of two categories: <First thoughts and wavering in attitude toward HPV vaccination> and <Discussion with parents>. In this stage, participants who had obtained knowledge and information on CC, HPV vaccine, and surrounding in the former stage considered HPV vaccination in their own way and discussed the matter with parents. In the case of a physically immature girl whose menstruation had not yet started, the girl and her parents recognized the value of vaccination, but decided not to receive it at that moment.

<First thoughts and wavering in attitude toward HPV vaccination>

This category consisted of five concepts: [Fear and desire to escape from CC], [Recognition the value and admiration for HPV vaccine], [Priority of qualifying for public financial support], [Anxiety regarding IM injection], and [Distrust of the HPV vaccine]. Many participants recognized CC as a scary disease specific to women, and valued the HPV vaccine as a great new vaccine with a potential prophylactic effect against the disease. In cases of the recipient of public aid, participants felt that the priority was to obtain public support because the HPV vaccine is expensive. On the other hand, some participants were nervous regarding receiving an intramuscular (IM) injection, and others were wary of receiving a vaccination easily due to the novelty because this vaccine was recently admitted in Japan. The latter participants were wavering in their attitude between desire and fear of the vaccination.

In this category, relevant to HPV vaccination process, protective factors extracted from the data were fear of CC, possibility of developing CC, awareness of preventing CC, future visions and ideal self-image, public financial support system. On the other hand, obstructive factors extracted from the data were financial burden (if the participants is out of age bracket to qualify for public financial support), and voluntary nature of vaccination.

[Fear and desire to escape from CC]

Three out of 20 subjects knew that the main cause (transmission route) of CC was sexual intercourse, and 5 out of 20 subjects knew that about 80% of adult women could be infected with HPV at least once in their life (infection rate). Additional participants had been imagining that girls and women with CC would have poor prognosis.

Participants who had a clear vision of lifestyle as a woman or specific future self-image were more likely to fear CC and have a strong desire to avoid CC. For example:

I know I may lose my womb in the worst case if I get cervical cancer. I want to avoid it at any cost. I want to have a baby in the future. So, I think it is better to take an injection, even though it is burdensome now.

[Recognition the value and admiration for HPV vaccine]

Eighty percent of participants knew that CC could be prevented by the vaccine, but most of them overestimated the prevention rate to be 80 to 100%, which has been estimated to be approximately 70% by Onuki (2009). Participants acknowledged the high value and praised the HPV vaccine in view of CC prevention. For example:

I guessed there has never been such a vaccine to prevent cancer before, so I thought HPV vaccine was an amazing vaccine. I recognize it a high-value vaccine especially for women who really want to have children in the future, like me.

[Priority of qualifying for public financial support]

Qualification for public financial support encouraged vaccination in 11 out of 16 participants who were already being vaccinated. For example:

My friends and mother said to me, “This vaccine is really expensive at the original price, but you can receive it for free now.” I felt lucky to hear that.

[Anxiety regarding IM injection]

Some participants heard the word “intramuscular injection” for the first time. Participants with a higher awareness of their low tolerance for pain felt greater anxiety for IM injection. For example:

I heard from a friend that she received the vaccine, and it was different from an ordinary injection and really painful because it was inserted into muscle. I am very sensitive to pain, so I was afraid that I would not be able to stand it.

[Distrust of the HPV vaccine]

Some participants expressed distrust and concerns for the effect, side effects, and adverse events caused by the HPV vaccine that has only recently been approved for use in Japan. For example:

It will take a long time to know the effect of this vaccine. I do not want to faint or die, at worst, as a result of the injection.

<Discussion with parents>

This category consisted of three concepts: [Tell own thoughts on HPV vaccination to parents], [Share and discuss the knowledge and information on CC and the HPV vaccine with parents], and [Prioritizing parents' thinking on HPV vaccination].

As factors related to this stage, daily parent-daughter relationship/amount of conversation, vaccine-related health literacy of parents, parental attitude to health, adolescents' reliance on parents, and parental influence on the adolescent were extracted.

[Tell own thoughts on HPV vaccination to parents]

In their discussion with the parents, subjects had communicated different ideas as to whether or not they wanted to have the vaccination, or they wanted to postpone the vaccination. This communication generated discussion between the parents and the adolescent. For example:

The night of the day on which I had received the explanation at school, I told my mother and father "I heard about an injection called the HPV vaccine. I want to get it." My father already knew about the vaccine, and told me "Wait until the local government sends us a

notice of financial support.”

Then it came to, “So what are we going to do with the injection?” when I was chatting with my mother. I said, “I don’t want to have the injection yet,” because I have not started my periods. Mother said to me, “O.K. You can receive the injections after you enter high school. We can afford it.”

[Share and discuss the knowledge and information on CC and the HPV vaccine with parents]

Participants communicated the knowledge and information on CC and the HPV vaccine that were provided from the outside to their parents in the discussion. Some adolescent girls reported that more detailed knowledge and information were given by their parents, and parent-daughter discussion was progressed. For example:

My mother told me how cervical cancer could infect me, saying this was a good chance for me to know. I heard the main infection route was sexual intercourse. So I thought it too early for me to get a shot. But, after talking with my mother, finally we decided to have them done now because I will need the vaccine in the future anyway.

[Prioritizing parents’ thinking on HPV vaccination]

In 5 out of 16 participants who were already being vaccinated, the parents advised the daughter to have the vaccination. Finally, after discussion, the daughter gave priority to the parents' thinking and agreed on vaccination. Also in the other 11 participants already vaccinated, the parents' thinking took primacy over that of the daughter when they decided on the timing of vaccination and other schedules. This tendency was more notable in participants with higher "reliance on the parents" and "susceptibility to the parents' influence" For example:

In fact, I did not want to get a shot, but I decided to have it, because my mother and father said I should have the injections while I have the chance. I thought that they told me so because they cared about me.

iii) Adjustment with parents toward actual vaccination

This category consisted of two concepts: [Arrange the vaccination period and schedule with parents] and [Parents make an appointment with hospital]. In this stage, the parents and adolescent girl who have had a positive discussion for vaccination started to make specific plans and act toward receiving the HPV vaccination.

As factors relevant to this stage, schedule adjustment between the parents and adolescents and parents' ability to search local resources were extracted from the data. The obstructive factor extracted from the data was frequent vaccination against busyness of the parents and adolescents or

lack of time.

[Arrange the vaccination period and schedule with parents]

Participants and their parents who wished to have the vaccination had discussed when to start the three doses of vaccination. Taking account their schedules in the near future, the daughters told their parents when they could receive vaccinations without conflicting with preparatory schools or club activities. The parents also discussed their preferred schedules and adjusted the vaccination timeline with each other. Many adolescent girls told of instances when girls were asked to wait for a vaccination or urged to take vaccination by the parents to coordinate with age/periodic limitation of public financial support because HPV vaccination of 13 to 16 years-old-girls had been supported for public money in Japan. Some families were unable to have a daughter start the vaccination due to failure to adjust their schedule, though the parents and girls both wished to have the vaccination. For example:

Parents told me “you should do it while the subsidy is provided if you are going to have the injection.” So I said, “Then I will go to get the first shot next week. Test week is going to begin with the week after that.”

[Parents make an appointment with the hospital]

When the parents and adolescent girls were able to adjust the vaccination period and schedule, the parents then looked for hospitals provided the HPV vaccination service. In all vaccinated cases, parents made an appointment for vaccination and accompanied their daughter on the hospital visit.

For example:

Honestly, I did not want to go to the obstetrics and gynecology hospital to have an injection. So mother looked for another pediatric clinic. She makes the appointment every time. When the time for the injection was coming up, she reminded me, saying “Next injection is XX. Don’t forget.”

DISCUSSION

This study found that subjects “encountered” the knowledge and information on CC and the HPV vaccine through experts/parents/friends, “thought about” HPV vaccination in their own way or with parents, and then “arranged” the vaccination. This process was influenced by the following extracted factors in each stage: the amount and quality of knowledge and information on CC and the HPV vaccine; child’s health literacy on CC and the HPV vaccine; peer-pressure; fear of CC; possibility of developing CC; awareness of preventing CC ; future self-image and visions; public financial support system; parent-child relationship; parental health literacy; parent-child conversation; parental attitude to health; child’s reliance on parents; parental influence; schedule adjustment between parents and child; and parental ability of resource search. As obstructive factors of the process, the following were extracted from the data: financial burden on family with children out of the qualifying age bracket; voluntary nature of vaccination; and difficulty adjusting the vaccination schedule due to the busyness of the child. These include factors previously suggested by the relevant literature (Chou *et al.*, 2011; Hughes *et al.*, 2009; Kester *et al.*, 2012; McRee *et al.*, 2012, a; Marchand *et al.*, 2012; Sotiriadis *et al.*, 2012; Teitelman *et al.*, 2011) and those revealed by the present study for the first time. This study appears to be the first account of the process how adolescent girls arrive at HPV vaccination in Japan.

Stage 1: First encounter with CC and HPV vaccine

The adolescents participated in this study told that she felt a significant impact when they knew about the existence of the HPV vaccine with the potential to prevent cancer. The impact also seems to have been significant for parents. None of the children failed to be informed of “cancer-prevention vaccine” if they were encouraged to have vaccination by parents. As suggested by Hughes *et al.* (2009) and Hamlish *et al.* (2012), the quality of the explanation of the HPV vaccine provided by parents and healthcare providers can have a significant influence on the child’s vaccination. The fact that all participants recognized the HPV vaccine as a “cancer-prevention vaccine” in this study bore out the notion that at least minimum knowledge on the vaccine was transmitted. Kang and Moneyham (2011) reported that adolescent girls were more willing to receive the HPV vaccination if it was recommended by parents or healthcare providers than by friends or teachers. And Huges *et al.* (2011) suggested that the programs to improve HPV vaccine delivery in primary care should focus on promoting effective parent-clinician communication. So it will be essential to focus on the education of health care professionals regarding indications for HPV vaccination and approaches to communicating most effectively with adolescent and parents about the safety and benefits of vaccination and the risks associated with non-vaccination.

In Japan, HPV vaccination of 13 to 16 years-old-girls is supported for public money, based on the national immunization schedule. Meanwhile, some participants were not informed of the

recommended age for the HPV vaccination, public financial support system, and the specific method of vaccination (including pain associated with IM injection and the requirement of three IM injections at intervals). One participant who was in the third year of junior high school and did not know the recommended age said that it was too early for her to be vaccinated. Another participant who received the first vaccination without knowing the specific method of vaccination said that she was shocked by the severe pain of the IM injection and scared of the second and subsequent vaccinations. Another participant said that she, who had thought it would finish in one shot, and lost her motivation at the thought of having to have another two injections. The girls should be informed of the recommended age for HPV vaccination as well as the transmission route of CC. It was found only 3 of 20 subjects knew that HPV, the most common cause of the CC, can be sexually transmitted. Some participants misunderstood that CC would develop spontaneously like other kinds of cancer. The specific method of vaccination must be well communicated beforehand to avoid medical trauma or injection trauma in adolescents. Similar to the findings of Kessels *et al.* (2012), the availability of public funding often prompted participants in this study to have vaccination in most cases. The findings highlighted that full dissemination of financial support information would be required at Stage 1 in addition to vaccine information.

The health literacy of the adolescent daughters and parents is also important in Stage 1. Health literacy in this context means personal ability to search, acquire, understand, and make use of

information required to make a decision on HPV vaccination. Naturally, adolescents are required to gain health literacy as the receivers of the vaccine, but the levels of parental literacy were thought to be various and it actually reflected both the contents and the quality of the explanation from parent to adolescent in this study.

Consistent with the discussion on peer-pressure in a study by Marchand *et al.* (2012), many adolescents in this study were interested in the HPV vaccination state of their peers. Since the HPV vaccine has just been released in Japan, participants were curious about their peers' experience of the HPV vaccination to a clear picture of the vaccination (i.e., modeling). And the participants who got a number of peer reports of syncope due to IM injection had higher levels of anxiety regarding the vaccination.

Stage 2: Think about and make decision to get HPV vaccine

Many adolescents were conflicted about between desire to avoid CC and anxiety regarding HPV vaccination. Their recognition of a "cancer-prevention vaccine" was so strong and their "admiration" for the development of the HPV vaccine was evident. Adolescents who made a realistic estimation of morbidity with clear future visions, intense fear of CC, and higher awareness of prevention were more likely to think about the HPV vaccination in a positive manner. Previous studies have suggested that health awareness and knowledge of vaccine would influence the

consideration of vaccination in adolescents (Kessels *et al.*, 2012; Marchand *et al.*, 2012). As Kessels *et al.* (2012) indicated, professionals are required to accurately inform adolescents of the pathology, prognosis, transmission route of CC, and prevention effects after vaccination.

While the study found that the public financial support system was a positive factor in considering vaccination in 13 to 16 years-old-girls as described in Stage 1, some adolescent girls unqualified for public funding said that the expensive cost of HPV vaccination had been actually an obstacle to vaccination for them and their family. Since Kessels *et al.* (2012) have shown that health insurance coverage of vaccination is a factor that promotes vaccination, the Japanese government is expected to continue the financial support system and broaden the age qualification bracket for funding as a policy.

According to Darden *et al.* (2013), as the most frequent reasons for not vaccinating adolescents, “Safety concerns/Side effects” were reported recently. In our study, anxiety regarding the HPV vaccination was largely divided into worry about the IM injection and distrust of the vaccine itself. Participants said that worry about the vaccination mainly consisted of pain associated with IM injections, distrust of the vaccine consisted of syncope reports, and uncertainty of the effect. The worries and doubts were described by mothers in a study by Kester *et al.* (2012); however, we heard these statements from the children themselves in this study, probably due to much conversation between Japanese parents and their children as described below. Health care providers should

exercise their ingenuity in the IM injection technique to reduce pain and provide the adolescent and family with accurate information on the adverse events and vaccine effect.

Adolescent girls were able to share information on the HPV vaccination with parents and discuss what they thought in conversation with parents. Consequently, exchange of knowledge and information and bilateral improvement in health literacy occurred in the case of parents and adolescents (mothers and daughters, in particular) who had a good relationship and a lot of conversation every day. In case of parents and adolescents with a much better relationship, the topic naturally shifted to the daughters' future and childbearing as they were talking about CC, or woman-specific malignancy, and they seemed to have a positive discussion regarding HPV vaccination. Of two participants whose periods had not yet started, one immediately decided to have vaccinations with the help of the financial support system, and the other decided to have vaccinations when her periods started, both after full discussion between the respective parents and their adolescent daughters. As mentioned here, discussion between parents and their daughters was essential in deciding whether or not to receive the HPV vaccination and to discuss the time of vaccination. Considering that parent- daughter discussion was absent or poor in three of four unvaccinated cases, the maturity levels of parent-daughter discussion could be one of the most crucial factor for promoting HPV vaccination in adolescent girls.

In this study, daughters with a high degree of reliance and susceptibility to their parents tended

to follow their parents' thinking on vaccination. As suggested by Hughes *et al.*(2009) and Hamlish *et al.*(2012), the amount of knowledge and information and literacy level in parents would be reflected in the quality of explanation to children, and furthermore, the vaccination rate. Mullins *et al.*(2013) also stated that HPV vaccine efficacy and safety are important topics to discuss with both girls and mothers; educating mothers is important for health care professionals because parents are a preferred source of vaccine-related information for girls. To achieve high rates of HPV vaccination in Japan, it will be essential to focus on the education of health care professionals regarding indications for HPV vaccination and approaches to communicating most effectively with adolescent and parents about the safety and benefits of vaccination and the risks associated with non-vaccination. We propose holding "school briefings" to provide adolescents and parents with the opportunity to hear and think about the knowledge and information on CC and the HPV vaccine together. It is also preferable if information on public financial support is provided from local government staff on site.

Stage 3: Adjustment with parents toward actual vaccination

Following the discussion in Stage 2, parents, especially mothers, played an important role in having their daughters receive the HPV vaccine. Parents discussed with their daughters who were busy with club activities or at cram school to find suitable times for vaccination, planned the vaccination with the schedule in mind, located the hospital, made appointments, and took their

daughters to the hospital. The ability to make arrangements and the efforts of parents are essential for adolescent Japanese girls to achieve HPV vaccination. Unless parents (guardians) cooperate and play a role, the HPV vaccination process in adolescent girls would never be complete. Health care providers should understand this and focus on enlightening activities on vaccination so that parents (guardians) voluntarily assume the responsibility.

At the same time, interventions are needed to encourage parents to make arrangements and take actions. Teitelman *et al.* (2011) suggested that “inconvenience of making appointments” and “limitation of hours open for appointments” could be a barrier to vaccination. For the same reasons, it took a lot of time to achieve vaccination in some cases in this study. Junior high and high school students living in urban areas of Japan are always busy going to cram school and other lessons every day, even during weekdays. For example, proposing a model vaccination schedule (the first and second injections in summer vacation and the third in winter, etc.) could be one intervention for such busy students. It is also preferable to give parents a list of local medical institutions (pediatrics and internal medicine) providing an HPV vaccination service to save their time and effort searching for a hospital.

Study limitations and implications

We considered recruiting the participants at pediatric clinics as theoretical sampling because

adolescent girls mainly receive HPV vaccine at pediatric clinics in Japan. Therefore, study sample was limited by those who attend the clinic in the present study, which could give the results an unduly large amount of influence. And the response rate of 100% from those who were asked to participate in the study is unusual. Our recruitment method, in which physicians distributed leaflets and introduced the study to those caregivers who the physicians believed met the inclusion criteria, could have influenced those who agreed to participate. Although we had asked the physicians to inform the caregivers that their participation in the study was voluntary and that refusal to participate would not put them at a disadvantage, it is possible that the participants found it difficult to refuse the request of the physicians to participate in the study. This is the first study in Japan that focused on HPV vaccination process and influencing factors in adolescent girls. A wider base of adolescents perhaps from schools may be the next step where this study needs to go to achieve significant results and have power to make conclusions. On the basis of the findings in the present study, we are planning to seek enlightenment of children and their families on HPV vaccination.

CONTRIBUTIONS

Study Design: RW, KN, HF, KM, KH, TS, KU.

Data Collection: RW, KN.

Data Analysis: RW, KN, HF, KM, KH, TS, KU.

Manuscript Writing and Confirmation: RW, KN, HF, KM, KH, TS, KU.

REFERENCES

- Ali H, Donovan B, Wand H, *et al.* Genital warts in young Australians five years into national human papillomavirus vaccination programme: national surveillance data. *BMJ*. 2013 [Epub ahead of print]
- Bednarczyk RA, Davis R, Ault K, Orenstein W, Omer SB. Sexual activity-related outcomes after human papillomavirus vaccination of 11- to 12-year-olds. *Pediatrics*. 2012; **130**:798-805.
- Brotherton JM, Fridman M, May CL, Chappell G, Saville AM, Gertig DM. Early effect of the HPV vaccination programme on cervical abnormalities in Victoria, Australia: an ecological study. *Lancet*. 2011;**377**:2085-2092.
- Chou B, Krill LS, Horton BB, Barat CE, Trimble CL. Disparities in human papillomavirus vaccine completion among vaccine initiators. *Obstet Gynecol*. 2011; **118**:14-20.
- Colgrove J, Abiola S, Mello MM. HPV vaccination mandates--lawmaking amid political and scientific controversy. *N Engl J Med*. 2010; **363**:785-791.
- Darden PM, Thompson DM, Roberts JR, *et al.* Reasons for not vaccinating adolescents: National Immunization Survey of Teens, 2008-2010. *Pediatrics*. 2013; **131**:645-651.

Garland SM, Hernandez-Avila M, Wheeler CM, *et al.* Quadrivalent vaccine against human papillomavirus to prevent anogenital diseases. *N Engl J Med.* 2007; **356**:1928-1943.

Glaser BG, Strauss AL. *The Discovery of Grounded Theory: Strategies for Qualitative Research.* Chicago, IL: Aldine, 1967.

Hamlisch T, Clarke L, Alexander KA. Barriers to HPV immunization for African American adolescent females. *Vaccine.* 2012; **30**:6472-6476.

Hayashi Y, Shimizu Y, Netsu S, Hanley S, Konno R. High HPV vaccination uptake rates for adolescent girls after regional governmental funding in Shiki City, Japan. *Vaccine.* 2012; **30**: 5547-5550.

Health, Labour & Welfare Ministry. *Report from Human papillomavirus (HPV) vaccine Research Group.* 2011.[Cited 25 March 2013]. Available from URL:

<http://www.mhlw.go.jp/stf/shingi/2r98520000014wdd-att/2r98520000016rqg.pdf>.

Hughes CC, Jones AL, Feemster KA, Fiks AG. HPV vaccine decision making in pediatric primary care: a semi-structured interview study. *BMC Pediatr.* 2011;**11**:74. doi:

10.1186/1471-2431-11-74.

Hughes J, Cates JR, Liddon N, Smith JS, Gottlieb SL, Brewer NT. Disparities in how parents are learning about the human papillomavirus vaccine. *Cancer Epidemiol Biomarkers Prev.* 2009;

18:363-372.

- Kang HS, Moneyham L. Attitudes, intentions, and perceived barriers to human papillomavirus vaccination among Korean high school girls and their mothers. *Cancer Nurs.* 2011;**34**:202-208.
- Kessels SJ, Marshall HS, Watson M, Braunack-Mayer AJ, Reuzel R, Tooher RL. Factors associated with HPV vaccine uptake in teenage girls: a systematic review. *Vaccine.* 2012; **30**:3546-3556.
- Kester LM, Zimet GD, Fortenberry JD, Kahn JA, Shew ML. A National Study of HPV Vaccination of Adolescent Girls: Rates, Predictors, and Reason for Non-Vaccination. *J Matern Child Health.* 2012 [Epub ahead of print]
- Kinoshita Y. *Grounded Theory Approach No Jissen.* Tokyo, Koubundou, 2003.
- Kobayashi H, Nakajima Y, Akasaki M. Factors influencing coverage of human papillomavirus vaccination: Questionnaire survey of local governments in Nara prefecture about the HPV vaccination program and communication campaigns to promote the program. *Progress in Medicine.* 2012; **32**: 753-759.
- Lehtinen M, Dillner J, Knekt P, *et al.* Serological diagnosis of human papillomavirus type 16 infection and the risk for subsequent development of cervical carcinoma. *BMJ.* 1996; **312**: 537-539.
- Liddon N, Michael SL, Dittus P, Markowitz LE. Maternal Underestimation of Child's Sexual Experience: Suggested Implications for HPV Vaccine Uptake at Recommended Ages. *J Adolesc Health.* 2013 [Epub ahead of print]

- Liddon NC, Leichliter JS, Markowitz LE. Human papillomavirus vaccine and sexual behavior among adolescent and young women. *Am J Prev Med.* 2012; **42**: 44-52.
- Marchand E, Glenn BA, Bastani R. Low HPV vaccine coverage among female community college students. *J Community Health.* 2012; **37**: 1136-1144.
- Markowitz LE, Hariri S, Lin C, *et al.* Reduction in human papillomavirus (HPV) prevalence among young women following HPV vaccine introduction in the United States, National Health and Nutrition Examination Surveys, 2003-2010. *J Infect Dis.* 2013;**208**:385-393.
- McRee AL, Reiter PL, Brewer NT. Parents' Internet use for information about HPV vaccine. *Vaccine.* 2012,a; **30**: 3757-3762.
- McRee AL, Gottlieb SL, Reiter PL, Dittus PJ, Tucker Halpern C, Brewer NT. Human papillomavirus vaccine discussions: an opportunity for mothers to talk with their daughters about sexual health. *Sex Transm Dis.* 2012,b; **39**: 394-401.
- Miyagi E. *Research report supported by Health and Labour Sciences Research Grant (2011)* [Cited 25 March 2013]. Available from URL: <http://kanagawacc.jp/pdf/23report.pdf>.
- Mullins TL, Griffioen AM, Glynn S, *et al.* Human papillomavirus vaccine communication: Perspectives of 11-12 year-old girls, mothers, and clinicians. *Vaccine.* 2013;**31**:4894-4901.
- Nicolai LM, Julian PJ, Meek JI, *et al.* Declining rates of high-grade cervical lesions in young women in Connecticut, 2008-2011. *Cancer Epidemiol Biomarkers Prev.* 2013;**22**:1446-50.

Oda H, Kasuga T, Yamamoto N, Kasuga T, Miyaji N. *Shitsuteki Kenkyu Nyumon*. Tokyo, Shunjusha, 2002.

Onuki M, Matsumoto K, Satoh T, *et al*. Human papillomavirus infections among Japanese women: age-related prevalence and type-specific risk for cervical cancer. *Cancer Sci*. 2009; **100**:1312-1316.

Paavonen J, Naud P, Salmerón J, *et al*. Efficacy of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine against cervical infection and precancer caused by oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomised study in young women. *Lancet*. 2009; **374**:301-314.

Sotiriadis A, Dagklis T, Siamanta V, Chatzigeorgiou K, Agorastos T; LYSISTRATA Study Group. Increasing fear of adverse effects drops intention to vaccinate after the introduction of prophylactic HPV vaccine. *Journal of Arch Gynecol Obstet*. 2012; **285**: 1719-1724.

Study group to protect a woman from cervical cancer. *Report of survey about the cervical cancer screening*. 2008.[Cited 25 March 2013]. Available from URL: <http://www.cczeropro.jp/kenshin/img/result/result.pdf>.

Tabrizi SN, Brotherton JM, Kaldor JM, *et al*. Fall in human papillomavirus prevalence following a national vaccination program. *J Infect Dis*. 2012 ;**206**:1645-1651.

Teitelman AM, Stringer M, Nguyen GT, Hanlon AL, Averbuch T, Stimpfel AW. Social Cognitive and

Clinical Factors Associated with HPV Vaccine Initiation Among Urban, Economically

Disadvantaged Women. *J Obstet Gynecol Neonatal Nurs.* 2011; **40**: 691-701.

Walboomers JM, Jacobs MV, Manos MM, *et al.* Human papillomavirus is a necessary cause of

invasive cervical cancer worldwide. *J Pathol.* 1999; **189**:12-19.

Zimet GD, Rosberger Z, Fisher WA, Perez S, Stupiansky NW. Beliefs, behaviors and HPV vaccine:

Correcting the myths and the misinformation. *Prev Med.* 2013 [Epub ahead of print]

TABLE and FIGURES

Table 1. Characteristics of the study’s participants

Figure 1. HPV vaccination process and related factors in adolescent Japanese girls

Table 1
Characteristics of study participants

Identification no.	Girl's age (years)	School attended by the girl	Girl's status of HPV vaccination	Girl's health issue	Subsidy from the national and local government	Family situation
1	17	high school	under vaccination (two injections)		None	
2	14	junior high school	completed (all three injections)	asthma	full amount of the expenses	single-female-parent, three-generation family
3	12	junior high school	under vaccination (one injection)	asthma, atopic dermatitis	90% of the expenses	
4	16	high school	completed (all three injections)		None	
5	14	junior high school	under vaccination (one injection)	congenital hypothyroidism	90% of the expenses	
6	13	junior high school	completed (all three injections)		90% of the expenses	
7	14	junior high school	under vaccination (one injection)		90% of the expenses	
8	14	junior high school	completed (all three injections)		None	
9	16	high school	under vaccination (two injections)	asthma	full amount of the expenses	single-female-parent
10	16	high school	completed (all three injections)		full amount of the expenses	three-generation family
11	16	high school	under vaccination (two injections)		full amount of the expenses	
12	17	high school	under vaccination (one injection)		full amount of the expenses	three-generation family
13	14	junior high school	under vaccination (two injections)		full amount of the expenses	three-generation family
14	13	junior high school	under vaccination (one injection)		full amount of the expenses	three-generation family
15	14	junior high school	unvaccinated		90% of the expenses	
16	17	high school	unvaccinated		None	
17	14	junior high school	unvaccinated	asthma	90% of the expenses	single-female-parent, on public assistance
18	17	high school	completed (all three injections)		None	
19	14	junior high school	unvaccinated		90% of the expenses	
20	16	high school	completed (all three injections)		90% of the expenses	

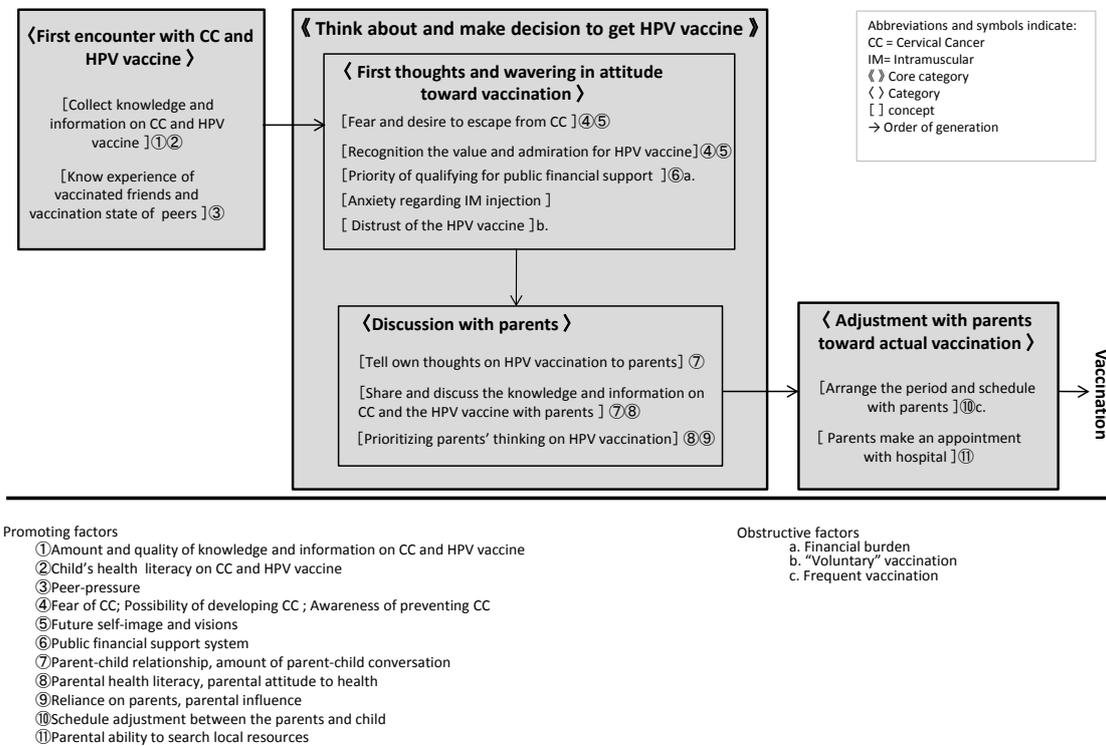


Figure 1 HPV vaccination process and related factors in adolescent Japanese girls.