



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RESEARCH PAPER

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# Health consciousness and cervical cancer screening rates in HPV-unvaccinated girls: comparison from HPV-recommended and HPV-recommendation-suspended program periods

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## ABSTRACT

In Japan, the vast majority of females between 13 and 24 are now unvaccinated for HPV and thus unprotected from HPV-caused cervical cancer. We analyzed the differences among these unvaccinated females regarding their understanding of the HPV vaccine, its role in cervical cancer prevention, and their need for cervical cancer screening – based on whether they refused vaccination when their government's recommendation for HPV vaccination was still in effect (*vaccination-recommended group*) – or during the last 7 years, while the government suspension was in effect (*recommendation-suspended group*). The *vaccination-recommended group* understood more about the HPV vaccine and the best timing for HPV vaccination than the *recommendation-suspended group* ( $p < .0001$  and  $p = .002$ , respectively). We found that girls in the *vaccination-recommended group* had more chances to talk with the family about cervical cancer and they were more afraid of acquiring the disease ( $p < .0001$  and  $p < .0001$ , respectively). The girls in the *recommendation-suspended group* tended to feel more inhibited from talking about cervical cancer with friends and acquaintances ( $p = .0262$ ). The cervical cancer screening rate of the *vaccination-recommended group* was significantly higher ( $p = .014$ ).

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## Introduction

The vast majority of cervical cancers are caused by one of the several oncogenic strains of the human papillomavirus (HPV),<sup>1,2</sup> thus HPV vaccines are expected to be one of the two powerful preventive tools against cervical cancer; the other being routine cervical cancer screening. In other countries, HPV vaccination is trusted and recommended for all girls. In the United States it is recommended for all girls 9–12 years of age, in Australia girls 12–13 years of age, and in Canada girls 11–14 years of age.<sup>3</sup> On the other hand, trial with the quadrivalent vaccine had shown efficacy against infection and disease in men who had sex with women and/or men preventing HPV 16 and 11 genital warts and HPV 6, 11, 16 and 18 anal intraepithelial neoplasia in 2011. Based on the result, HPV vaccination was recommended for boys in the U.S. from 2011, in Australia from 2013, in Canada from 2017.<sup>4,5</sup> The gender-neutral HPV vaccination is recommended in 33 countries now.<sup>6</sup>

Japan's own national HPV vaccination program began in 2010. By April of 2013, the scheduling of HPV vaccination for girls aged 12–16 had become part of its national routine. However, in June 2013, a small number of highly publicized reports that alleged adverse medical events, such as chronic pain and motor impairment, had occurred in several young girls following their HPV immunization. The Japanese Ministry of Health, Labor, and Welfare (MHLW) almost immediately suspended its previous official recommendation

for HPV vaccination.<sup>7</sup> As a consequence, the vaccination rate in Japan plummeted, from approximately 70% the year before (2012), to 1% or less that year, where the rate still resides today, seven years later.<sup>8</sup> There has recently been a trend for increasing cervical cancer rates at ever younger ages, potentially linked to this ongoing lapse in vaccination protection.

Cervical cancer screening is yet another powerful preventive measure against cervical cancer. However, the cervical cancer screening rate in Japanese females, at less than 40% of all eligible women, is unusually low relative to similarly advanced countries. Most notably, the cervical screening rate among Japanese women in their early twenties is only 10%.<sup>9</sup>

We report here on the differences we found in young HPV-unvaccinated Japanese women regarding their understanding of HPV vaccine, cervical cancer and cervical cancer screening – that was linked to whether they were teenagers during the government's pro-HPV vaccination recommendation period or during the later recommendation-suspension period.

## Methods

From March 19 to 21 of 2020, under Internal Review Board approval, we conducted an online survey of Japanese 18–19 year-old girls who were members of an internet survey panel. These girls made up the *recommendation-suspended*

group. Informed consent was obtained from all participants and their mothers.

Valid survey answers were obtained from 184 girls. They are all HPV-unvaccinated at the time of our survey. A self-administered questionnaire was given. The girls were asked about their understanding regarding cervical cancer and HPV vaccination and whether or not they were having cervical cancer screenings. They were asked about their family's socio-demographic characteristics, such as employment and civil status, and total household income. Questions also probed their knowledge concerning the HPV vaccine, about the best timing for vaccination or having a cervical cancer screening, about having talks with family about cervical cancer, and whether they worried about being affected with cervical cancer.

For comparison of our current results in those of women who grew of age during the golden period of pro-vaccination policies, we pulled up the results of an internet survey we had conducted in February 2015 of unvaccinated girls in the *vaccination-recommended group*. That survey had been conducted among 16 ~ 39 year-old women and investigated their thinking about cervical cancer prevention. We extracted the responses of 251 unvaccinated 18–19 year-old girls from the self-administered questionnaire for those questions which were the same as in the most recent questionnaire we gave to the *recommendation-suspended group*. We evaluated for differences in understandings about the HPV vaccine and cervical cancer, and about rates of cervical cancer screening between the *vaccination-recommended group* and the *recommendation-suspended group* of unvaccinated females.

## Statistics

Using StatsModels, differences between the two groups were calculated by the chi-square test and the logistic regression test for categorical variables. The level of statistical significance was set at  $p = .05$ .

## Results

### Characteristics of the survey responders

The relevant characteristics of the responders are shown in Table 1. Women in the *vaccination-recommended group* were much more likely to be married ( $p = .0021$ ), and were more likely to be stay-at-home wives ( $p = .0049$ ) (Table 1).

### Awareness regarding the HPV vaccine

In reference to the question of awareness of the HPV vaccine, 98.8% (248/251) of the *vaccination-recommended group* knew about the HPV vaccine, whereas in the *recommendation-suspended group*, only 60.3% (111/184) knew about the vaccine (Table 2). In reference to the question regarding recognition that the best timing for HPV vaccination was before having her first sexual relationship, in the *vaccination-recommended group*, 18.7% knew the fact well, 13.1% knew it a little bit, and 68.2% did not know the fact. In the *recommendation-suspended group*, 7.1% knew the fact well, 16.3% knew a little, and 76.6% did not know this fact (Table 2). In reference to the

**Table 1.** Characteristics of the internet survey responders.

Responder Characteristics			
Subjects	Recommended	Suspended	p-value
Resident area	251	184	n.s.
Hokkaido	15 (6.0%)	7 (3.8%)	
Touhoku	15 (6.0%)	10 (5.4%)	
Kantou	81 (32.3%)	69 (37.5%)	
Chubu	45 (17.9%)	27 (14.7%)	
Kinki	54 (21.5%)	35 (19.0%)	
Chugoku	13 (5.2%)	12 (6.5%)	
Shikoku	4 (1.6%)	2 (1.1%)	
Kyushu/Okinawa	24 (9.5%)	22 (12.0%)	
Civil status			<0.001
Unmarried	227 (90.4%)	182 (98.9%)	
Married	24 (9.6%)	2 (1.1%)	
Employment status			0.005
Company employee (others)	4 (1.6%)	2 (1.1%)	
Stay-at-home	24 (9.6%)	2 (1.1%)	
Part-time staff	10 (4.0%)	9 (4.9%)	
Student	208 (82.8%)	164 (89.1%)	
Other	5 (2.0%)	7 (3.8%)	
Household income			n.s.
<2 million yen	31 (12.3%)	16 (8.7%)	
2–4 million yen	24 (9.5%)	8 (4.3%)	
4–6 million yen	13 (5.2%)	7 (3.8%)	
6–8 million yen	10 (4.0%)	8 (4.3%)	
8–10 million yen	6 (2.4%)	8 (4.3%)	
>10 million yen	3 (1.2%)	7 (3.8%)	
Unknown	89 (35.5%)	59 (32.1%)	
NA	75 (29.9%)	71 (38.7%)	

**Table 2.** Recognition of HPV vaccine.

	Yes	Maybe	No
Do you know HPV vaccine?			
Recommended	248 (98.8%)		3 (1.2%)
Suspended	111 (60.3%)		73 (39.7%)
$p < .001$			
Do you know the best timing of HPV vaccination was before having first sexual relationship?			
Recommended	47 (18.7%)	33 (13.1%)	171 (68.2%)
Suspended	13 (7.1%)	30 (16.3%)	141 (76.6%)
$p = .002$			
Do you know the preventive effect for cervical cancer?			
Recommended	26 (10.4%)	69 (27.5%)	156 (62.1%)
Suspended	19 (10.3%)	46 (25.0%)	119 (64.7%)
$p = .66$			

question of recognition of the cervical cancer preventative effects of the HPV vaccine, we found no significant differences in the answers from the girls in the two groups (Table 2).

### Understanding of cervical cancer

We questioned the women regarding several topics relating to cervical cancer and HPV: cervical cancer being caused by HPV infection, HPV being acquired from sexual relations, the number of cervical cancer cases that have been increasing in women in their 20s, how cervical cancer has an effect on fertility, and how she may lose her life due to cervical cancer. We found no significant differences in the answers given by the girls in the two groups (Table 3).

However, in reference to a question about having conversations with family members about cervical cancer, of 251 responses from the *vaccination-recommended group*, 44.6%

**Table 3.** Knowledge of cervical cancer.

	Yes	Maybe	No
Do you know that cervical cancer is caused by HPV?			
Recommended	26 (10.4%)	39 (15.5%)	186 (74.1%)
Suspended	16 (8.7%)	38 (20.6%)	130 (70.7%)
$p = .3593$			
Do you know that HPV is acquired from sexual relations?			
Recommended	38 (15.2%)	51 (20.3%)	162 (64.5%)
Suspended	24 (13.0%)	35 (19.0%)	125 (68.0%)
$p = .7398$			
Do you know that cervical cancer cases are increasing for women in their 20s?			
Recommended	46 (18.3%)	79 (31.5%)	126 (50.2%)
Suspended	30 (16.3%)	67 (36.4%)	87 (47.3%)
$p = .5475$			
Do you know that cervical cancer has an effect on your fertility?			
Recommended	121 (48.2%)	77 (30.7%)	53 (21.1%)
Suspended	98 (53.3%)	47 (25.5%)	39 (21.2%)
$p = .4675$			
Do you know you may lose your life from cervical cancer?			
Recommended	79 (31.5%)	80 (31.9%)	92 (36.6%)
Suspended	65 (35.3%)	54 (29.4%)	65 (35.3%)
$p = .6882$			

had talked with their families, 43.8% had not, and 11.6% did not remember. In the *recommendation-suspended group*, only 25.0% had talked with their families about cervical cancer, 64.1% did not, and 10.9% did not remember. The girls in the *vaccination-recommended group* were much more likely to have talked with their families about cervical cancer ( $p < .0001$ ) (Table 4).

When asked if they worried about acquiring cervical cancer, in the *vaccination-recommended group*, 32.7% worried a lot, 41.8% worried somewhat, 19.9% worried only a little, and 5.6% did not worry at all. In the *recommendation-suspended group*, 9.7% worried a lot, 46.2% worried somewhat, 37.0% worried a little, and 7.1% did not worry at all. The girls in the *vaccination-recommended group* worried more about acquiring cervical cancer ( $p < .0001$ ) (Table 4).

In reference to the question about feeling resistant toward talking about cervical cancer with her friends and acquaintances, in the *vaccination-recommended group* 29.9% said they felt resistant, 23.9% said they did not feel resistant, and 46.2% were unsure if they were hesitant. In the

**Table 4.** Perceptions about cervical cancer.

	Yes	No	Unknown	
Did you ever talk with your family about cervical cancer?				
Recommended	112 (44.6%)	110 (43.8%)	29 (11.6%)	
Suspended	46 (25.0%)	118 (64.1%)	20 (10.9%)	
$p < .001$				
How worried are you about acquiring cervical cancer?				
	Very much	Somewhat	A little	Not at all
Recommended	82 (32.7%)	105 (41.8%)	50 (19.9%)	14 (5.6%)
Suspended	18 (9.8%)	85 (46.2%)	68 (37.0%)	13 (7.0%)
$p < .001$				
Do you feel resistance in talking about cervical cancer?				
	Yes	No	Unknown	
Recommended	75 (29.9%)	60 (23.9%)	116 (46.2%)	
Suspended	63 (34.2%)	59 (23.9%)	62 (33.7%)	
$p = .026$				

*recommendation-suspended group*, 34.2% felt resistant, 23.9% did not feel resistant, and 33.7% were unsure. The girls in the *recommendation-suspended group* were more likely to feel resistance (34.2% vs 29.9%) toward talking about cervical cancer with their friends and acquaintances ( $p = .0262$ ) (Table 4).

### Cervical cancer screening

In reference to having cervical cancer screening, in the *vaccination-recommended group*, 1% (2 women) had a regularly scheduled screening, 11.6% had been several times, and 87.4% had never been screened. In the *recommendation-suspended group*, 1.1% (2 women) had screenings on a regular schedule, 3.8% had been screened several times, and 95.1% had never been screened. The girls growing up in the *vaccination-recommended group* had cervical screenings more often than the girls in the *recommendation-suspended group* ( $p = .014$ ). (Table 5).

### Discussion

In the *recommendation-suspended group*, 39.7% of the girls answered they had never heard of the HPV vaccine. They learned about HPV vaccine in this survey and asked her mother about HPV vaccine and her own vaccine status to answer our questions. On the other hand, 98.8% of the girls in the *vaccination-recommended group* had heard of the HPV vaccine. The girls in the *vaccination-recommended group* were significantly more aware of the HPV vaccine than the girls in the *recommendation-suspended group*, even though none of the girls in either group were HPV-vaccinated. The girls in the *vaccination-recommended group* were also more cognizant that the best timing for HPV vaccination was before having first her sexual relationship. However, more than 60% of the girls in the *vaccination-recommended group* did not know very much about the specific preventative effect of the HPV vaccine for cervical cancer. We assumed that the reason for this knowledge gap was that they either were never told, forgot, or they did not fully understand the concept of cervical cancer at age 12–16 when their family talked to them about getting the HPV vaccine.

We did not find a significant difference for knowledge about cervical cancer between girls in the two groups. The girls in the *vaccination-recommended group* had talked more about cervical cancer with their families and they felt less hesitant in talking about cervical cancer with their friends and acquaintances, and they were more concerned about getting cervical cancer than the girls in the *recommendation-suspended group* (Table 4). We presume that the increased concern was the result of conversations with the family that gave them more accurate knowledge about cervical cancer,

**Table 5.** Cervical cancer screening.

	Regularly	Several times	Never
Have you ever had cervical cancer screening?			
Recommended	2 (0.8%)	29 (11.6%)	220 (87.6%)
Suspended	2 (1.1%)	7 (3.8%)	175 (95.1%)
$p = .015$			

allowing them to recognize that cervical cancer is a real disease threat, and a far more common disease than they might have expected. Hence, they worried more about acquiring the disease. This group also felt less resistance to talking about cervical cancer with friends and acquaintances, perhaps a benefit of the accurate information gained through talking with family. On the other hand, the girls in the *recommendation-suspended group* did not recognize the risk of cervical cancer well. They felt hesitant in talking about cervical cancer with friends and acquaintances, perhaps because they know that cervical cancer was related to having sexual relations and were embarrassed to admit they were engaging in sex. The girls in the *recommendation-suspended group* did not worry as much about getting cervical cancer, perhaps living up to the old motto: Ignorance is bliss.

Not only governmental recommendation but also the news about adverse events was possible to be a background factor. The news about adverse events after HPV vaccination was more often reported in 2015 than in 2020. The girls who responded in 2015 should have heard about the news more than the girls who responded in 2020. The girls who had heard of the news could ask her family about HPV vaccine and cervical cancer.

Significantly more girls in the *vaccination-recommended group* than in the *recommendation-suspended group* already had cervical cancer screenings at the time of our survey of the 19–20 year olds. Screening is expected to be almost as powerful a preventative measure against cervical cancer as the HPV vaccine itself. It has been reported that the cervical cancer screening rate is higher among U.S. women who received the HPV vaccine than unvaccinated women,<sup>3</sup> but here we are analyzing two groups of women, who were never vaccinated, for their thinking. We assume that the reason for the higher screening levels for the unvaccinated women who came of age for HPV-vaccination during the pro-vaccine years was the result of them at least talking about the vaccine and cervical cancer with their families – even though they did not get vaccinated for whatever reason at the time – and these conversations at least made the girls and their mothers more aware of the disease, increasing the likelihood of the daughter later developing the good habit of routinely visiting a gynecologic clinic.

In a previous study, we explored the cervical cancer screening rates among HPV-vaccinated and unvaccinated Japanese women. The cervical cancer screening rate among HPV-vaccinated women at age 20 was 6.4%, the rate for unvaccinated women was 3.9%.<sup>10</sup> However, in this current study, we are comparing only unvaccinated to other unvaccinated women. The women in both surveys were all 18–19 years old when surveyed, but the surveys were taken years apart. The one group of unvaccinated women, the *vaccination-recommended group*, were teenagers through a time when the government, and society in general, was proactive toward HPV vaccination. The second group were teenagers during a time of anti-vaccine paranoia. There was a significant positive difference in the first group's knowledge about the HPV vaccine and cervical cancer, and in their cancer screening rates. This was a remarkable outcome because the only major difference between the two groups of unvaccinated women was that, when they were teenagers, the local government was, or was not, actively recommending HPV vaccination.

Under normal circumstances, all women should have a routine of thorough cancer screening. It has been suggested

that the cervical cancer screening rate would be lower in the *recommendation-suspended group* of girls. We have shown here that the adverse effects from 7 years of suspending HPV vaccination have also clearly included reducing the preventive effects of cervical cancer screening. These deficiencies will have important future consequences for preventing cancer in Japanese women.

We theorize that one problem with the suspension of the government's recommendation for the HPV vaccination is that it precludes one of the good chances a young girl might have for talking about the HPV vaccine, cervical cancer, and future cervical cancer screening with her family. Because the HPV vaccine is no longer state-recommended, Japanese mothers now seldom talk to their teenage daughters about HPV vaccination or about cervical cancer. Sex education classes in Japan are a little better. However, if HPV vaccination becomes once again recommended by our government, most mothers would be much more likely to consider HPV vaccination for their daughters and they would try to talk about it with their daughters. Mothers would learn more about the HPV vaccine and cervical cancer, they would involve their husbands more in the decision-making process, they would give their daughters more accurate information about the HPV vaccine, cervical cancer, and sexual education. Their daughters would improve their understanding of the HPV vaccine and cervical cancer through these conversations, would think of the disease as a real threat, and they would learn to fear the disease enough to try harder to prevent the acquiring of it.

Mothers in Japan play a pivotal role in their daughters' vaccination decision-making. In our previous study, we found that, under the hypothetical scenario of a restart of the government's recommendation for the vaccine, the percentage of mothers who would be thereafter willing to encourage their daughters to get the HPV vaccine increased significantly, from 12.1% to 21.0% ( $p < .001$ ). Educating mothers about the HPV vaccine and about HPV-caused cancers positively changed their attitude toward the HPV vaccine and raised the rate of likely vaccination encouragement to 27.3%.<sup>11</sup>

We also previously found that the father's participation in the family decision-making concerning vaccination was significantly associated with increased vaccination of his daughter (odds ratio: 3.9, 95%CI: 2.35–6.46). When the father had a positive attitude toward HPV vaccination, the relationship between the father's participation in decision-making and their daughter's inoculation was even more enhanced (odds ratio: 10.51, 95%CI: 5.16–21.62) (Shindo *et al.* submitted).

Mothers also play a significant role in their daughters' cervical cancer screening decision-making. In our previous study, 20-year-old girls who had not yet received their first cervical cancer screening were randomized into two study groups. One group received only a personalized daughter-directed reminder leaflet for cervical cancer screening. In the second group, both the daughters and their mothers received a combination package containing the same reminder leaflet as did the first group, plus an additional informational leaflet for the mother, which requested that the mother recommends that her daughter undergoes cervical cancer screening. The cervical cancer screening rate of 20-year-old women whose mothers received an information leaflet was significantly higher than that for women who received only a leaflet for themselves (11% vs 9%,  $p = .0049$ ).<sup>12</sup>

Considering the above, talking about the HPV vaccine and cervical cancer with their families is very important for promoting HPV vaccination and cervical cancer screening. But the suspension of the government's recommendation for the HPV vaccination program has removed one of the best opportunities for families to have these discussions. Hence, we think the governmental recommendation should be resumed as soon as possible.

Our study has some limitations. Firstly, there were more married women in the *vaccination-recommended group* than the girls in the *recommendation-suspended group*. The married girls could have more chances to have cervical cancer screening before they had gotten married although our survey revealed that the girls growing up in the *vaccination-recommended group* had cervical screenings more often than the girls in the *recommendation-suspended group*. Secondly, we selected 18–19 year-old girls for our survey, although the recommended age to begin cervical cancer screening is 20 and up in Japan. Hence, when they become 20-year-olds and receive their cervical cancer screening reminder leaflet, it is unclear whether they actually attend a cancer screening. The actual recognition regarding cervical cancer and the actual cancer screening rate may not correlate with the rate found in this investigation. However, these girls will soon be 20, and we expect that it will be possible for us to recommend cancer screening to them in better ways, based on the knowledge and information obtained in this investigation.

## Conclusions

The girls in the *vaccination-recommended group* know more about the HPV vaccine and cervical cancer and had cervical cancer screening more often than the girls in the *recommendation-suspended group*. Talking about the HPV vaccine and cervical cancer with their families is a critical means for promoting HPV vaccination and cervical cancer screening. But the continued suspension of the government's recommendation for the HPV vaccination program steals a key opportunity for young girls of recommendation age talking about these matters with their family.

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## Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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