



## Short communication

## Cervical cancer screening rate differs by HPV vaccination status: An interim analysis



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## ABSTRACT

**Background:** The incidence of cervical cancer has been increasing, especially in younger generation, in Japan. The females born between 1994 and 1999, who achieved rates of HPV vaccination approaching 70%, have become the target of cervical cancer screening programs. Here, we have analyzed the cervical cancer screening rates among the vaccinated and unvaccinated women.

**Methods:** The survey data for cervical cancer screening at age 20 in FY 2015 was derived from two cities, Toyonaka and Iwaki.

**Results:** Among 2,727 females, in Toyonaka and Iwaki, who were born in FY 1995 and targeted in FY 2015 at age 20 for cervical cancer screening, their HPV vaccination rate was 64.2% (1,753/2,727). The screening rate was 6.4% (112/1,753) in the vaccinated and 3.9% (38/974) in the unvaccinated. This difference was statistically significant ( $p < 0.01$ ).

**Conclusions:** We have demonstrated that HPV-vaccinated females tended to be effectively protected from future cervical cancer than the unvaccinated.

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## 1. Background

Worldwide, among the female cancers, the frequency and death rates of cervical cancer are the fourth highest [1], with 530,000 newly contracting this disease in 2012, and making up 7.5% of all cancer deaths among women [2].

In Japan, a trend for significantly decreasing the age-adjusted incidence of cervical cancer began in 1976, but that downward trend reversed after 2000; the incidence has been increasing significantly ever since [3], especially in young generation. In the Japan, the estimated number of new cases of cervical cancer among females aged 20–49 in 2014 was 5,002, with 656 of these cases leading to death [4]. To counter this trend, females in Japan aged 20 and older are recommended to receive cervical cancer screening every two years; however, despite that recommendation, the cervical cancer screening rate is extremely low, especially for young women 20–24 years-old, where the screening rate is currently only

around 10% [5]. The screening rate is only around 10–20% in females aged 25–29 and around 10–30% in those aged 30–39 [5].

Public subsidies and governmental recommendation for human papillomavirus (HPV) vaccination in Japan started in fiscal year (FY) 2010. Girls aged 13–16 could be immunized with only a small out-of-pocket fee. The combination of government recommendation and subsidy soon resulted in a high vaccination rate country-wide, even though it was not a school-based program. Females born between 1994 and 1999 enjoyed rates of vaccination protection approaching 70% [6–9].

Beginning in April of 2013, the HPV vaccine officially became a free routine national immunization for girls aged 12–16. However, soon thereafter, sensational media reports of alleged adverse vaccination events began to circulate. In response to the negative publicity, the Japanese Ministry of Health, Labor and Welfare (MHLW) suspended its recommendation for the HPV vaccine, a policy of suspension that has continued now for approaching six years.

Nevertheless, that cohort of females born between 1994 and 1999, who achieved rates of HPV vaccination protection approaching 70%, have recently been coming of age (20 and older) where they have become the target of cervical cancer screening programs.

**Abbreviations:** FY, fiscal year; HPV, human papillomavirus; MHLW, Ministry of Health, Labor and Welfare.

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This means that two groups of females that grew up during the high vaccination period of 2010–2013, 70% of whom were vaccinated and 30% of whom were unvaccinated, are now, or soon will be, eligible for cervical cancer screening. It has not been clear whether the rate of cervical cancer screening is going to be different between the two groups, vaccinated versus unvaccinated. An internet survey we conducted previously found that vaccinated females are more aware of their health needs than unvaccinated females (submitted). Here, we have analyzed the cervical cancer screening rates among this discreet cohort of vaccinated and unvaccinated women. This information will be important to guide development of future strategies for cervical cancer prevention related to HPV vaccination and screening.

## 2. Methods

The survey data for cervical cancer screening at age 20 in FY 2015 was derived from two Japanese cities, Toyonaka (population: around 400,000) in Osaka Prefecture, the metropolitan area, and Iwaki (population: around 340,000) in Fukushima Prefecture, a local area as an interim analysis. In Japan, females aged 20 or older who miss their subsidy-targeted year for screening can still undergo the subsidized exam the next year, so, for females who missed screening at age 20, their results from age 21 were included. Because a previous study demonstrated that between 10 and 20% of women mistakenly remember whether or not they had been vaccinated for HPV [10], HPV vaccination status was confirmed from public records in the present study. It is reasonable to assume that there might be some females who have moved into the two survey cities from other cities. For them, immunization records were not available where they now were to receive cervical cancer screening. Therefore, this analysis excluded those who transferred in after reaching 12 years of age, the minimum age for vaccination. The cervical cancer screening rates for the vaccinated and unvaccinated were compared by Fisher's exact test and the level of statistical significance was set at  $p = 0.05$ .

## 3. Results

In the city of Toyonaka, there were 1,461 females born in FY 1995 who, at age 20 in FY 2015, were the potential targets for cervical cancer screening. This excluded girls who had moved to Toyonaka after reaching the age of 12. Of the potential targets, 940 (64.3%) had a record of HPV vaccination, 521 (35.7%) did not. Among all targets, 31 vaccinated females and 10 unvaccinated females (3.3% versus 1.9%, respectively) received their recommended cervical cancer screening at the age 20. Likewise, in Iwaki, among 1,266 potential targets, 813 were vaccinated (64.2%) and 453 (35.8%) were not. Among the targets, 81 vaccinated (10.0%) and 28 unvaccinated females (6.2%) received cervical cancer screening (Table 1).

**Table 1**  
Cervical cancer screening rates for FY 2015 in Toyonaka and Iwaki, Japan, for females age 20 who had or had not received the HPV vaccine.

	Target of screening	Received screening	p-value
Toyonaka city			
Vaccinated	940	31(3.3%)	0.14
Unvaccinated	521	10(1.9%)	
Iwaki city			
Vaccinated	813	81(10.0%)	0.022
Unvaccinated	453	28(6.2%)	
Total			
Vaccinated	1753	112(6.4%)	0.0064
Unvaccinated	974	38(3.9%)	

When combined, the cervical cancer screening rate in these two cities for females born in FY 1995 was 6.4% (112/1,753) for those vaccinated and 3.9% (38/974) in the unvaccinated. This difference was statistically significant ( $p = 0.0064$ , Fisher's exact test).

## 4. Conclusions

Cervical cancer can now be effectively prevented by the combination of timely HPV vaccination and cervical cancer screening. Following the introduction of the HPV vaccine, there was justified concern among physicians that vaccinated females would not undertake needed cervical cancer screening later in life because they might be under the misconception that the risk of cervical cancer was completely prevented by their taking the HPV vaccine. Although the bivalent/quadrivalent HPV vaccines approved in Japan do effectively prevent most HPV infections and thus dramatically reduces the overall risk of cervical cancer by around 60–70% [11,12], that still leaves 30–40% of cervical cancers unprotected from. According to our previous internet survey, vaccinated females were found to have a relatively higher awareness of their own health condition, and were thus more inclined towards receiving cervical cancer screening (submitted). However, their actual health behavior, *i.e.*, receiving cervical cancer screening, has yet to be analyzed.

In a previous study conducted in U.S.A., the screening rate among women aged 21–30 (already much higher than in Japan) was significantly higher in the vaccinated females (67.5%) than in the unvaccinated (52.8%) [13]. However, in their study, age distribution was significantly different between the vaccinated and the unvaccinated ( $p < 0.001$ ). The unvaccinated group was significantly older than the vaccinated one. Generally, among the younger generation, the older the women were, the higher the screening rate was.

In the present study, excluding any age bias, we have demonstrated that HPV-vaccinated females tended to be effectively protected from all forms of future cervical cancer than the unvaccinated because of the combination of being vaccinated and their subsequent higher rates of cervical cancer screening. Vaccinated females appear to have a higher health consciousness than the unvaccinated, resulting in a positive health disparity.

Clearly, unvaccinated females should be receiving enhanced health behavior counseling, including promoting effective cervical cancer screening. However, this seems to be a very difficult challenge. In one of our previous studies, we found that the rate of women who received screening for gastric cancer, which is high in Japanese, was 81% among those who had received cervical cancer screening within the 2-year window prior to our survey (group A), and only 45% among those who had not received cervical cancer screening (Group B). The rate for receiving screening for colon cancer was 78% in group A and 44% in group B, and for breast cancer it was 93% in group A and 51% in group B. Overall, for these and other cancers, past cancer screening rates were significantly higher for the mothers in group A than for mothers in group B ( $p < 0.001$ ) [14]. Overall good health behaviors seem to be linked. Our previous internet survey showed that daughters who received HPV vaccine tended to talk about cervical cancer and cancer screening with their parents more frequently than those who did not receive HPV vaccine (unpublished). Vaccination is possibly a phenomenon of general healthcare seeking behavior.

Although the cervical cancer screening rate for vaccinated females is significantly higher than for the unvaccinated, even it is still only 6.4%. One of the reasons for non-participation in cervical cancer screening was not aware of cervical cancer screening [15]. A nationwide improvement in cervical cancer screening rates is absolutely essential for both the unvaccinated and the vacci-

nated. Our project-in-progress focuses on improving the screening rates by distributing leaflets specifically targeted to the vaccinated or to the unvaccinated. In the leaflet targeted to the already vaccinated, the rational and well-reasoned necessity for cancer screening will be the appeal; in the leaflet for the unvaccinated, fear of the dire consequences of cervical cancer will be the focus.

After 2020, the girls who failed to get immunized from 2013 onward due to our government's suspension of its recommendation for HPV vaccination will become of age to be the target of cervical cancer screening, starting at age 20. Our next major problem will be how to persuade this large population of unprotected women to begin receiving critical life-saving regular cervical cancer screening.

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### Declaration of Competing Interest

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