

## Characters of Local Governments as Predictors for Improving the HPV Vaccination Rate in Japan

Nobuko Takahashi,<sup>1</sup> Ken Ishitani,<sup>1,2</sup> and Satoru Shimizu<sup>3</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, School of Medicine, Tokyo Women's Medical University, Tokyo, Japan

<sup>2</sup>Department of Gynecology, Kitasato University Kitasato Institute Hospital, Tokyo, Japan

<sup>3</sup>Department of Medical Education, School of Medicine, Tokyo Women's Medical University, Tokyo, Japan

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We conducted a nationwide questionnaire survey of 500 randomly sampled municipalities to calculate the public-funded human papilloma virus (HPV) vaccination rates in fiscal years 2011-2013. The characteristics of different municipalities were determined from the national statistical data, including those for all the municipalities in Japan. Based on the questionnaire results, we divided the fiscal 2012 HPV vaccination rate into two groups using the median value as the threshold: objective variable and municipality characteristics (29 items) as explanatory variables. Univariate and multivariate regression analyses were performed using the Akaike Information Criterion (AIC) scoring system to examine the valid explanatory variables. Univariate analysis of data from 150 municipalities indicated that the model was good because among 29 explanatory variables, AIC values were the lowest for “number of kindergartens” (AIC: -22.35), followed by “population” (AIC: -11.32), and the two-dimensional cross tables suggested that these explanatory variables were negatively correlated with HPV vaccination rates. Multivariate analysis showed that the combination of “number of kindergartens” and “number of households” (AIC: -30.29) had the smallest AIC values and were the optimal model for explaining HPV vaccination rates in local municipalities. The predictors for improved HPV vaccination rates suggested that these rates were high in municipalities characterized by a small population, large proportion of the elderly, and increased financial stability.

**Key Words:** HPV vaccine, Japan, questionnaire

### Introduction

The human papilloma virus (HPV) vaccine for the prevention of cervical cancer is used in more than 100 countries because it has been proven to be highly effective and safe in clinical studies worldwide, including Japan.<sup>1-3</sup> In addition, HPV vaccines are available under public

funding for adolescent girls in the Western countries, and the initiation of HPV vaccination in developing countries is following an upward trend.<sup>4</sup> In Japan, however, the Ministry of Health, Labor, and Welfare has not actively recommended HPV vaccination from June 2013 to date because of ongoing investigations for its adverse reactions; hence, the HPV vaccination rate in Japan has dras-

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Corresponding Author: Nobuko Takahashi, Department of Obstetrics and Gynecology, School of Medicine, Tokyo Women's Medical University, 8-1 Kawada-cho, Shinjuku-ku, Tokyo 162-8666, Japan. takahashi.nobuko@twmu.ac.jp

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tically decreased.<sup>5</sup> Meanwhile, various reports on HPV vaccines have improved the perceptions of obstetricians and gynecologists in Japan regarding HPV vaccination,<sup>5</sup> and the Ministry of Health, Labor, and Welfare, Japan, is expected to resume active recommendation of the routine use of HPV vaccines soon. Based on these circumstances in Japan and worldwide, we elucidated the factors associated with public-funded HPV vaccination rates.

Many studies have reported the factors associated with HPV vaccination rates.<sup>6</sup> The HPV vaccination rate has been relatively low in developed countries; the following four goals have been proposed by the United States based on a data analysis comparing states with low (12.1%) and high (57.7%) vaccination rates<sup>7</sup>: to reduce missed clinical opportunities to recommend and administer vaccines; to increase the acceptance of parents, caregivers, and adolescents toward HPV vaccines; to maximize the access to HPV vaccination services; and to promote global HPV vaccine uptake. Information–motivation–behavioral skills (IMB) model analysis, in which information, motivation, and behavioral skills are considered essential personal factors affecting the spread of the use of HPV vaccines, is a known analytical method, and macro-level environmental factors, such as healthcare services, economic status, and ethnicity, indirectly affect personal factors.<sup>8</sup> The Andersen’s Behavioral Model of Health Services Use has shown that important factors affecting the use of services include not only personal factors but also local municipality characteristics, which represent an environmental factor.<sup>9</sup> However, municipality characteristics have not been studied in Japan as factors associated with public-funded HPV vaccination rates.

In this study, we conducted a nationwide questionnaire survey on the actual status of vaccination in municipalities that subsidized HPV vaccination to determine the factors that improved the HPV vaccination rate.

## Methods

Municipalities in Japan at 2012 were divided into five groups according to their population (<10,000; 10,000 to <30,000; 30,000 to <100,000; 100,000 to <200,000; and ≥200,000). The public-funded HPV vaccination rates in fiscal years 2011–2013 were investigated through a questionnaire survey (mailed, self-completed or telephone or

visits) of 500 municipalities<sup>10</sup> (100 per population-based group), which were randomly sampled using a random number table. Ten numbers are extracted from any point of the table of random numbers by three columns to the right. And we repeated it ten times. When a number more than the same number and number of each groups upper limit was extracted, we deleted the number and selected the next number.

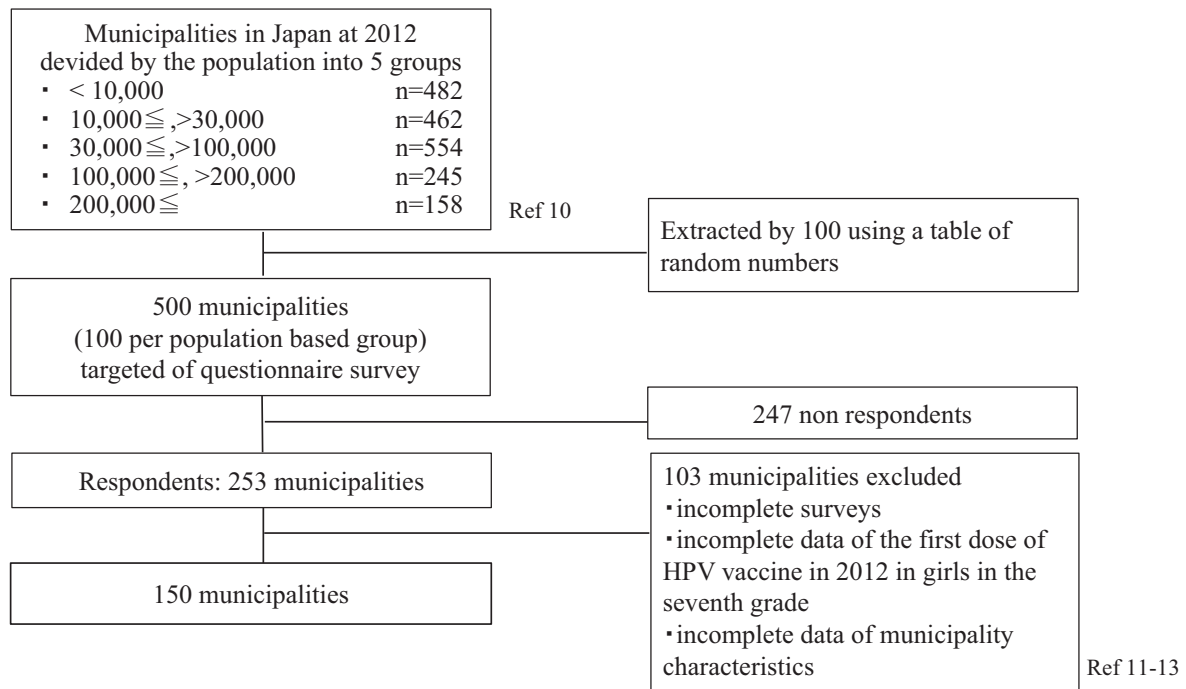
Responses were collected via mail, fax, or telephone. The survey included questions on the school grade(s) of girls eligible for public-funded vaccination, subsidy rates, vaccination rates in fiscal years 2011–2013, number of eligible girls in each school grade, and number of girls who were administered the first vaccination dose. The survey was conducted during the start of HPV vaccination programs across Japan (2012–2013); therefore, the vaccination rates of different fiscal years considerably varied, and some girls were vaccinated in multiple years. Therefore, the vaccination rate was determined as the number of girls who were administered the first dose divided by the number of eligible girls in the seventh grade (first year of middle school in Japan).

The objective variable was the HPV vaccination rate of girls in the seventh grade who were administered the first vaccination dose in fiscal year 2012; it was further divided into two groups (high and low vaccination rate groups) using the median (76.5%) as the threshold. For the explanatory variables, 29 items excluding items without data loss were evaluated from the characteristics of the municipalities obtained from nationwide statistical data obtained from local governments (municipalities; i.e., 2010 census,<sup>10</sup> 2012 basic resident registry,<sup>11</sup> municipality financial status survey,<sup>12</sup> basic school survey,<sup>13</sup> etc.). (Figure 1).

This study was approved by the Ethics Committee of Tokyo Women’s Medical University (approval no. 2485).

## Statistics

We conducted univariate and multivariate regression analyses of the rates of administration of the first dose of HPV vaccine in fiscal year 2012 in girls in the seventh grade in selected municipalities across Japan, which were obtained through the questionnaire survey and municipi-



**Figure 1** Flow diagram of study selection procedure. HPV, human papilloma virus.

pality characteristics (city, town, and village units) to determine and assess Akaike information criterion (AIC) scores for effective explanatory variables and their combinations.

AIC represents the volume of information to evaluate a combination of explanatory variables with objective variables. A lower AIC score indicates that the volume of information is large (better model) and that the explanatory variable is more effective.

To select reliable variables, the Categorical Data Analysis Program (CATDAP)-02 was developed by the Institute of Statistical Mathematics in Japan, using AIC.<sup>14-16</sup> This program selected reliable variables by automatically analyzing all the cases of categorization among the variables. Next, statistical association between variables was determined using the  $\chi^2$  test. Continuous variables were categorized into 4-5 intervals and then analyzed using CATDAP-02.

In order to select a valid explanatory variable to be included in the regression model, it is necessary to evaluate the explanatory variable candidate in some way. When the number of explanatory variables (independent variables) for the objective variable is set as  $k$ , the combinations are calculated as approximately 2 to the power of  $k$ , but there are information quantity criteria such as residual sum of squares,  $R^2$  squared value, AIC, etc., to evalu-

ate the combinations. However, the residual sum of squares and  $R^2$  squared values are limited to approximately 5 or 6 for explanatory variables<sup>16</sup>. Therefore, in order to evaluate the combinations, the authors used CATDAP-02, which can evaluate explanatory variables with AIC.

We are aware that, by also adopting the stepwise method in logistic analysis, it is possible to select combinations of optimal explanatory variables from many explanatory variable candidates, but the evaluation method is based on information quantity criteria such as  $p$  value,  $R^2$  value, or AIC of each explanatory variable. The  $p$  value is “material” for probabilistic determined, and size should not be compared. As mentioned above, because the explanatory variables are limited to 5 and 6, the information quantity criterion was adopted in the present study. Therefore, we adopted CATDAP-02, which has been published, but we believe that it is beyond the scope of this research to discuss which of the proposed information criteria is optimal.

$P$ -value  $< 0.05$  were considered evidence of statistical significance. The JMP 13.0.0 software program (2016 SAS Institute Inc. Japan) was used to perform the statistical analysis.

**Table 1** Characteristics of subject: background information of 150 municipalities.

Characters of Subject	Average±SD	Range
HPV vaccination rate 2012 (%)	71.8±19.3	9-100
HPV vaccinated people 2012	513.4±750.8	1-4,979
Population	164,437.1±237,905.3	2,404-1,409,297
Household	69,080.4±107,350.3	932-676,022
Male to female ratio	1.05±0.05	0.91-1.19
Percentage of elderly population (%)	24.8±5.03	14.7-36.2
Percentage of young population (%)	13.2±1.80	19.5-8.7
Percentage of productive population (%)	61.9±3.66	53.5-70.1
Birth rate (%)	7.74±1.91	2.8-15.2
Basic medical examination rate (%)	9.13±13.6	0.2-100
Uterine cancer examination rate (%)	26.9±11.2	7.7-68.8
Total number of health examinee of the municipality	10,337.3±14,875.0	13-99,163
Total number of participant of group health education	3,550.5±4,921.9	76-31,961
Total number of receiver of Health consultation	1,545.5±2,300.0	10-14,182
Total number of receiver of visit instruction	256.0±389.2	1-2,263
Local allocation tax	9,135,139±9,400,809	39,474-46,408,303
Local tax	24,876,851±42,843,832	117,309-287,127,225
Financial index	0.62±0.27	0.09-1.25
National treasury disbursements	10,185,486±18,832,144	73,009-126,172,073
Prefectural endorsement	3,529,295±4,065,534	160,600-25,262,412
Property income (thousand yen)	309,713.8±627,612.2	3,324-4,364,998
Local bond	682,632±13,003,524	0.01-81,102,900
Total expenditure	65,349,135.9±106,269,874	2,185,826-771,171,614
Council members	29.2±63.5	6-789
Municipality staff	1,107.4±1,530.0	52-10,185
Municipal inhabitants tax	10,807,672±18,870,098	43,937-129,663,031
Fixed property tax	10,926,035±17,609,286	56,131-115,588,131
Kindergartens	16.7±21.2	1-128
Elementary schools	24.6±27.2	1-150
Junior high schools	12.3±14.6	1- 83
Nursery school	26.6±33.7	1-206

HPV, human papilloma virus.

## Results

We conducted the questionnaire survey via post, telephone and visits. Of approximately 1,700 municipalities in Japan, we randomly selected 500 to administer the questionnaire, of which 233 municipalities provided questionnaire responses in writing or via mail or fax. After excluding the municipalities with incomplete data regarding municipality characteristics, we enrolled 150 municipalities in this study (**Table 1**).

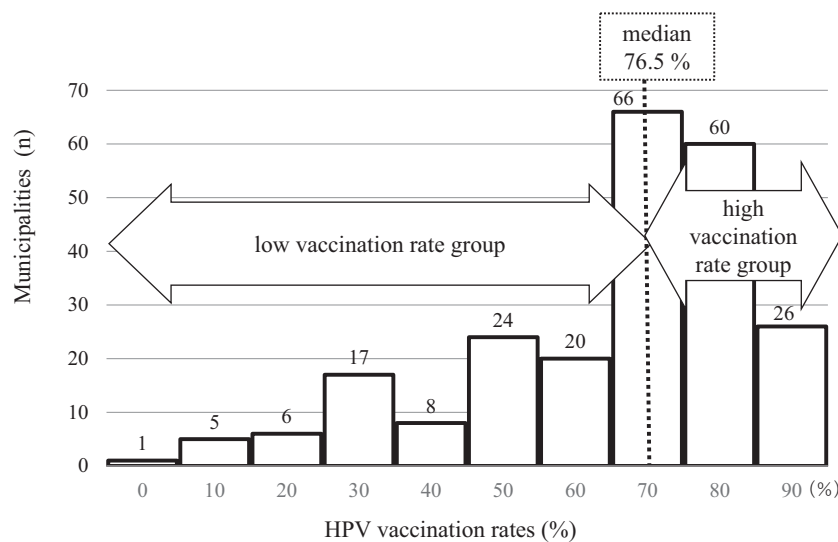
**Figure 2** shows the distribution of HPV vaccination rates in these municipalities. We divided the municipalities into high and low HPV vaccination rate groups based on the median rate of 76.5% and used them as objective variables.

We divided 233 responding municipalities into five groups depending on their population to compare the

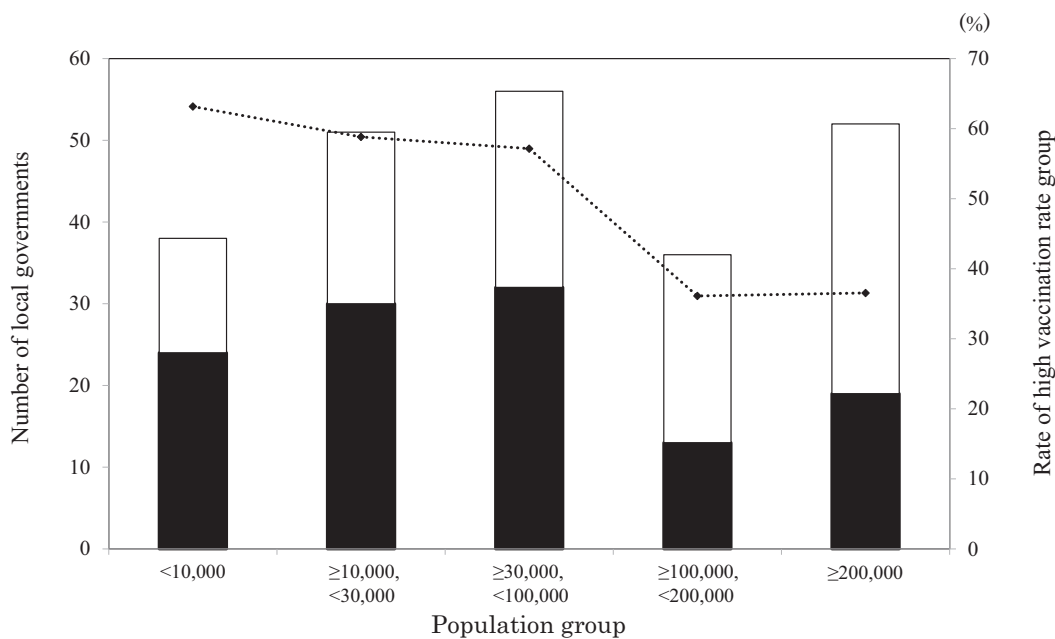
HPV vaccination rates. The percentage of municipalities with HPV vaccination rate higher than the median in each group (in the ascending order of population) was 63.2%, 58.8%, 57.1%, 36.1%, and 36.5%, respectively, suggesting that the vaccination rate tended to be higher in municipalities with a smaller population (**Figure 3**).

We performed both univariate and multivariate regression analyses using the AIC scoring system, with the HPV vaccination rates in fiscal year 2012 divided into two groups based on the median rate as the objective variables and municipality characteristics as the explanatory variables to examine effective explanatory variables.

**Table 2** shows 15 of 29 explanatory variables with low AIC values in the univariate regression analysis. **Table 3** shows a two-dimensional cross table for the six explanatory variables included in the multivariate analysis. We found that the AIC scores were the lowest for “num-



**Figure 2** A histogram of the number of municipalities according to the HPV vaccination rates. HPV, human papilloma virus.



**Figure 3** Percentages of high and low HPV vaccination rate groups in five population-based groups of municipalities. HPV, human papilloma virus.

□ Low vaccination rate group (n)  
 ■ High vaccination rate group (n)  
 ◆◆◆ Rate of high vaccination rate group (%)

ber of kindergartens” (AIC: -22.35), followed by “population” (AIC: -11.32) and “household”(AIC: -8.66). Furthermore, lower values of these explanatory variables could effectively predict a high HPV vaccination rate. Higher values for explanatory variables, such as “national treasury disbursements” (AIC: -6.71), “percentage of the elderly population” (AIC: -5.78) were found to be

effective for predicting a high HPV vaccination rate.

**Table 4** presents the top five combinations of variables in the multivariate analysis. In the multivariate analysis, we found that the combination of “number of kindergartens” and “number of households” (AIC: -30.29) exhibited the lowest AIC score and was the optimal model for HPV vaccination rates in local municipalities. And

**Table 2** Univariate analysis of HPV vaccination rate for characteristics of local governments.

Rank	Explanatory Variables	AIC
1	Kindergarten	-22.35
2	Population	-11.32
3	Number of council members	-8.94
4	Household	-8.66
5	Number of elementary schools	-7.4
6	National treasury disbursements	-6.71
7	Property income	-5.95
8	Fixed property tax	-5.94
9	Percentage of elderly population	-5.78
10	Prefectural endorsement	-5.02
11	Municipal inhabitant tax	-4.2
12	Local tax	-3.12
13	Municipal medical examinee	-2.67
14	Number of staff of the local government	-1.76
15	Local bond	-1.76

HPV, human papilloma virus.

these were considered statistically significant ( $p = 0.0388$ ).

AIC is a combination of variables when analyzing using CATDAP-02, and the p value is a combination of those predictor variables. There is no correlation between the AIC and p values, but from the results of multivariate analysis, these can be said to demonstrate significance.

## Discussion

Using CATDAP-02, we analyzed a program designed to assess the optimal explanatory variables for a categorical objective variable. The use of HPV vaccination rates categorized into two groups based on the median as objective variables implied that factors, such as population, number of kindergartens, and financial condition, were

**Table 3** Cross table of univariate analysis of HPV vaccination rate for characteristics of local governments.

Explanatory Variables (median $\pm$ SD)	n (range)	HPV Vaccination Rate		Total
		Low vaccination rate group <sup>a</sup>	High vaccination rate group <sup>b</sup>	
Kindergarten (9 $\pm$ 21.2)	1-6	16 (25.4%)	47 (74.6%)	63
	7-128	57 (65.5%)	30 (34.5%)	87
Population (79,576.5 $\pm$ 237,905.3)	2,404-365,673	58 (43.6%)	75 (56.4%)	133
	366,255-1409,297	15 (88.2%)	2 (11.8%)	17
Household (932 $\pm$ 767,600)	932-138,010	57 (44.2%)	72 (55.8%)	129
	138,010-767,600	16 (76.2%)	5 (23.8%)	21
Elementary school (15.5 $\pm$ 27.2)	1-37	51 (42.5%)	69 (57.5%)	120
	37-150	22 (73.3%)	8 (26.7%)	30
National treasury disbursements (4,200,464.5 $\pm$ 18,832,144.2)	73,009-9,738,973	61 (56.0%)	48 (44.0%)	109
	9,748,059-126,172,073	12 (29.3%)	29 (70.7%)	41
Percentage of the elderly population (24.8 $\pm$ 5.0)	14.7-24.2	45 (60.0%)	30 (40.0%)	75
	24.2-62.0	28 (37.3%)	47 (62.7%)	75

<sup>a</sup>Low vaccination rate group: HPV vaccination rate  $<76.5\%$ .

<sup>b</sup>High vaccination rate group: HPV vaccination rate  $\geq 76.5\%$ .

HPV, human papilloma virus.

**Table 4** Multivariate analysis of HPV vaccination rate for characteristics of local governments.

Rank	Explanatory variables	AIC	p-value
1	Kindergarten, household	-30.29	0.0388
2	Kindergarten, population	-27.52	0.0469
3	Kindergarten, household, percentage of the elderly population	-26.78	0.0084
4	Kindergarten, elementary school	-26.6	0.0528
5	Kindergarten, household, elementary school	-24.29	0.0312

HPV, human papilloma virus.

associated with HPV vaccination rates.

Thus, we used CATDAP-02 to investigate the optimal explanatory variables and their combinations using a two-dimensional cross table analysis. The advantage of this method was that the number of explanatory variables and the sample size could be applied irrespective of collinearity, and explanatory variables and their combinations could be compared and evaluated using the AIC scoring system. Hence, we considered this method suitable for this study.

Cost-benefit analyses of HPV vaccination in Japanese females have demonstrated the relevance of public-funded vaccination.<sup>2,17</sup> Using this economic evaluation simulation model, the present study estimated an approximately 73% decrease in the future incidence and mortality of cervical cancer by HPV vaccination of the entire population of 12-year-old girls and a 19-43 billion yen reduction in the social disease burden by public-funded HPV vaccination of 10-45-year-old females. As the relevance of public-funded HPV vaccination has already been established in developed countries, such systems have been established in many countries, and HPV vaccination is available entirely or nearly without out-of-pocket expense through health insurance, particularly for adolescent girls, the primary target population for vaccination.<sup>4</sup>

While almost no reports exist for examining municipality characteristics associated with HPV vaccination rates in regions in Europe and the United States, a recent study conducted in England found that local authorities with more number of high-income families had lower vaccination rate than that of local authorities with more low-income families.

Local authorities with a higher percentage of whites had higher HPV vaccination rates than those with a higher percentage of nonwhites. Furthermore, local authorities with more education deprivation had higher vaccination rates. Local authorities with higher proportions of high-status occupations had worse vaccination coverage.<sup>18</sup>

In Japan also, there are few studies comparing characteristics of municipalities as factors related to improving the rate of cervical cancer vaccination, but it has been indicated that vaccination education and information provision to target persons and parents, and public awareness

programs using the internet, are particularly important.<sup>19,20</sup>

In the case of measles and voluntary vaccination, contrary to the results of the present study, it was reported that few infants, a high percentage of elderly persons, low income and low educational background of parents, young age of mothers, etc., were correlated with a low vaccination rate.<sup>21-24</sup>

Furthermore, the fact that the number of households is smaller than that of **Table 3 and 4** appears to be a factor that increases the vaccination rate, and on the basis of such findings, there is a possibility that the vaccination rate is higher in municipalities with more households, such as those with three generations living together, rather than nuclear families. This suggests the possibility of increasing the vaccination rate by increasing the information from parents and legal guardians such as grandparents.

However, regarding the correlation between the proportion of elderly population and influenza vaccination coverage rate, concerning the influenza vaccination rate of the elderly, a positive correlation with proportion of the elderly population and the cancer screening examination rate showed a negative correlation with population density<sup>25</sup>.

The fact that the vaccination cost is free has been mentioned as an important factor affecting vaccination behaviors for all vaccinations.<sup>26</sup> Thus, it could be inferred that the public expenditure burden ratio and other vaccination recommendation methods may be influenced by the financial situation of the municipality.

Municipalities with high vaccination rates accounted for 57%-63% of municipalities with a population of < 100,000, with vaccination rates being 1.5-1.8-fold greater than those in municipalities with larger populations. These data suggested that more detailed government services, such as personalized services, are possible and could thus affect the vaccination rate in low-population municipalities.

And it is also suggested that in municipalities with a large population, there tends to be a low rate of known inoculation history. In addition, it is difficult to respond to/notify persons who have not been vaccinated, which may have an influence on the vaccination rate.

Unlike municipal services, municipality characteristics are not factors that can be readily changed to increase the



HPV vaccination rate. However, while the recommendation for periodic vaccination continues to remain suspended in Japan, HPV vaccination measures and policies by local governments are crucial. The results of this study offers useful information to predict the characteristics of municipalities that determined the effectiveness of measures and policies implemented to improve the HPV vaccination rates.

The higher the number of residents, the more insufficient government consideration of individuals tends to be. Conversely, it is easier for the government to communicate its intentions and to receive demands from residents in smaller populations. Therefore, it is not always true that cities with a larger budget have improved vaccination rates.

## Conclusions

In the present study, a small number of kindergartens and a high ratio of national treasury disbursements and elderly persons were correlated as predictors in improving the HPV vaccination rate, and a high population and number of households were correlated as risk factors for a low vaccination rate.

Based on these findings, it is predicted that the population aging rate is predicted to display an increasing trend in the future, and information provision and awareness programs aimed at the parents of targets of vaccination and the local community appear to contribute to improving the vaccination rate.

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**Conflicts of Interest:** The authors indicated no conflicts of interest.

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