# **BMJ Open** Factors associated with PPSV23 coverage among older adults in Japan: a nationwide community-based survey

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#### ABSTRACT

**To cite:** Murakami Y, Kanazu S, Petigara T, *et al.* Factors associated with PPSV23 coverage among older adults in Japan: a nationwide communitybased survey. *BMJ Open* 2019;**9**:e030197. doi:10.1136/ bmjopen-2019-030197

Prepublication history and additional material for this paper are available online. To view these files, please visit the journal online (http://dx.doi. org/10.1136/bmjopen-2019-030197).

Received 4 March 2019 Revised 20 June 2019 Accepted 20 June 2019



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#### **Correspondence to**

Professor Yoshitaka Murakami; yoshitaka.murakami@med. toho-u.ac.jp **Objectives** The 23-valent pneumococcal polysaccharide vaccine (PPSV23) was included in Japan's national immunisation programme for older adults in 2014. While vaccination coverage has increased following the implementation of the national immunisation programme, little is known about the factors that have influenced changes in PPSV23 uptake in Japan. This study aimed to investigate the effects of municipality-level activities implemented to improve vaccine uptake during the fiscal year 2015 (April 2015–March 2016).

**Design** Community-based national survey. A postal and web-based nationwide survey was sent to all municipalities in Japan in June 2016 (n=1741). The survey included questions regarding PPSV23 coverage, out-of-pocket costs by individuals for vaccination and community-level activities implemented to improve and promote PPSV23 uptake. Municipality-level and prefecture-level variables (eg, unemployment rates, average per capita income) retrieved from published sources were also incorporated to explore the impact of social determinants on vaccine uptake.

## Setting Japan.

**Participants** Municipal vaccination officers. **Primary and secondary outcome measures** The primary study outcome was PPSV23 coverage among adults aged 65 years in Japanese municipalities. **Results** A total of 1010 municipalities (58.0%) responded to the survey. The median PPSV23 coverage among responding municipalities was 41.8%. Vaccine coverage increased by 18.7% (16.7%–20.7%)%) in municipalities that sent a direct mail notification to the target population of adults compared with municipalities that did not send any notification. Vaccine coverage decreased by 3.02% (2.4%–3.6%)%) for every 1000 JPY increase in out-of-pocket costs. Municipality-level unemployment rates and average per capita income were negatively associated with PPSV23 coverage.

**Conclusions** This nationwide survey provides insight into factors that may influence PPSV23 coverage in Japanese municipalities. Reduced out-of-pocket costs and direct mail notifications to the target population were associated with higher PPSV23 coverage in Japanese municipalities.

## INTRODUCTION

Pneumococcal disease is a major public health problem worldwide. Although it affects all age

## Strengths and limitations of this study

- This is the first nationwide survey conducted of 23-valent pneumococcal polysaccharide vaccine (PPSV23) uptake in municipalities of Japan.
- Comprehensive questionnaire were used for examining the factors associated with PPSV23 coverage among older adults.
- High response rates were given from all municipalities of Japan.
- This was an ecological study conducted at the municipality level; therefore, our conclusions are limited to a population level.

groups, incidence is highest in young children and the elderly. In Japan, pneumonia is the fifth leading cause of deaths (77.7 per 100000 population in 2017). According to the National Epidemiological Surveillance of Infectious Diseases in Japan, 11104 cases of invasive pneumococcal disease (IPD) were reported between April 2013 and December 2017. The incidence of IPD in adults aged ≥65 years was 4.56 per 100000 personyears in 2016<sup>1</sup> and that of pneumococcal pneumonia in adults aged 65-74 years, 75-84 years and  $\geq 85$  years was 8.7, 16.9 and 15.7 per 1000 person-years, respectively, between 2011 and 2013.<sup>23</sup> The direct cost per episode of bacteraemic pneumococcal pneumonia and pneumococcal bacteraemia without focus is 869 242 JPY and 906 307 JPY, respectively.<sup>4</sup> The 23-valent pneumococcal polysaccharide vaccine (PPSV23) was approved in Japan in 1988, but a national immunisation programme (NIP) for older adults, the details of which is shown in the online supplementary appendix S1, was not established until 2014. In the interim, programmes were developed by municipal governments, starting in 2001 with Setana-town in Hokkaido where the vaccine cost was partially subsidised to reduce out-of-pocket expenditures for older adults.<sup>5</sup> Subsequently, other municipalities

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introduced similar programmes, and by June 2013, 880 municipalities (50.5%) provided subsidies for pneumococcal vaccination.<sup>6</sup> To meet the growing demand for pneumococcal vaccination in an ageing population, in October 2014, the PPSV23 was added to the list of voluntary vaccinations covered by Japan's NIP for adults age 65 years and older.<sup>7</sup> This action directed the national government to subsidise up to 30% of the total vaccine cost to local governments. However, this subsidy depended on their municipal per capita income, and thus not all local governments are eligible to receive it.

According to recent national government estimates, calculated from the mandatory reports from municipalities in Japan, the pneumococcal vaccination coverage rate among older adults was 42.6%, 38.3% and 40.4% in the fiscal year of 2014, 2015 and 2016, respectively, following its inclusion in the NIP.<sup>8</sup> Estimates of pneumococcal vaccine coverage under municipal government programmes have been previously derived from doses shipped by MSD K.K. Using this method, vaccine coverage following NIP implementation was estimated to be 40.6% by December 2015, with substantial variation in coverage between municipalities (28%–71%).<sup>9</sup>

Several factors may explain the observed variation in vaccine coverage between the municipalities. First, variations in out-of-pocket costs between communities owing to the structure of the national subsidy may continue to influence PPSV23 uptake even after its inclusion in the NIP. Particularly, the implementation of pneumococcal and other routine immunisation programmes is not under the jurisdiction of the national government, but under municipal control. Municipalities that are eligible to receive the national subsidy may elect to further subsidise the vaccine cost to patients, while those that are ineligible for the subsidy may elect to subsidise only a portion of the vaccine cost. Prior to NIP implementation, Naito et al demonstrated that vaccine uptake was higher in municipalities that subsidised the vaccine cost for older adults through local programmes.<sup>6</sup>

In addition to financial subsidies, municipalities may implement various community-based activities to promote vaccine uptake. For example, information regarding pneumococcal disease, pneumococcal vaccination, NIP eligibility and vaccine locations may be provided through municipal government websites, community newsletters, hospital and clinic brochures and local cable television networks. Kondo et al studied the impact of financial subsidies and these community-based activities on pneumococcal vaccine uptake in 63 municipalities prior to NIP implementation. Only vaccine price, after accounting for municipal subsidies, was found to be significantly associated with vaccine uptake.<sup>10</sup> Following NIP implementation, the extent to which each municipality implements these community-based activities and their impact on pneumococcal vaccine coverage is unknown.

To explore the impact of community-based activities on pneumococcal vaccination rates, a community-based survey was conducted to document municipality-level activities focused on raising awareness around PPSV23 inclusion in the NIP, and out-of-pocket costs for PPSV23 vaccination among adults aged 65 years in Japan.<sup>11</sup> This study aimed to investigate the effects of out-of-pocket costs and municipality-level activities on vaccine coverage during the fiscal year 2015 (April 2015–March 2016).

## MATERIALS AND METHODS Study design

We conducted a community-based study of all municipalities in Japan to determine PPSV23 coverage in adults aged 65 years who were born between 2 April 1950 and 1 April 1951.<sup>11</sup> A postal and web-based nationwide survey was sent in June 2016 to municipal vaccination officers responsible for the implementation of the national immunisation programme. Vaccine officers representing each municipality were asked to estimate vaccine coverage among adults aged 65 years who were residing in their municipality from municipal records and describe activities implemented during the fiscal year 2015 to improve vaccine uptake. We sent our questionnaire to all municipalities in Japan (1741 municipalities comprising 1718 cities and district municipalities and 23 Tokyo metropolitan wards).<sup>12</sup>

The survey also included questions regarding individual out-of-pocket costs for the PPSV23 vaccination during the fiscal year and community-level activities to improve PPSV23 uptake. Activities to improve PPSV23 uptake included direct mail notifications to inform adults of the inclusion of the pneumococcal vaccine in the NIP, announcements and messages disseminated through television, radio and disaster prevention broadcasting systems, webpages of municipal government, newspapers, public health lecture meetings and brochures or posters placed in hospitals or clinics. Information regarding the number of notifications sent during the fiscal year, type of mail notification and enclosed contents (ie, vaccine eligibility, co-payment, designated hospitals, information on disease and vaccination) were also obtained through the survey.

We also included municipality-level demographic, socioeconomic and healthcare supply variables (ie, proportion of adults aged  $\geq 65$  years, proportion of men aged  $\geq 65$  years, unemployment rate, average per capita income, population density, density of medical doctors and density of medical institutions) and prefecture-level socioeconomic and healthcare supply variables (ie, education level, average savings per household as a proxy for wealth, death rates and density of nurses). All variables were collected from the publicly available webpage of the Japanese government statistics archive.<sup>13</sup>

The primary study outcome was PPSV23 coverage among adults aged 65 years in Japanese municipalities, which was defined as the number of adults aged 65 years who received PPSV23 during the fiscal year of 2015 (1 April 2015–31 March 2016) divided by the number of adults aged 65 years who resided in the municipality during that period. Written informed consent from 
 Table 1
 Baseline characteristics of the municipalities in this study (self-reported questionnaires)\*

	Numbers	%					
Number of direct mail notifications sent							
0	154	15.3					
1	743	73.6					
2	94	9.3					
3 or more	19	1.9					
Seasons							
Spring	777	76.93					
Summer	56	5.54					
Autumn	55	5.45					
Winter	90	8.91					
Type of mail notification (first wave)							
Letters	652	64.6					
Pamphlet	30	3.0					
Postcards	78	7.7					
Others	15	1.5					
Enclosed contents (first wave)							
Eligibility for vaccination programme	743	73.6					
Coverage period of national immunisation programme	751	74.4					
Co-payment	698	69.1					
Subsidy voucher	227	22.5					
Designated hospitals	584	57.8					
Application forms for subsidy voucher	482	47.7					
Forms to bring on vaccination days	624	61.8					
Information on disease and vaccination	640	63.4					
Others	167	16.5					
Dissemination							
TV networks	2	0.2					
Cable TV networks	42	4.2					
Radio spots	16	1.6					
Cable broadcasting	27	2.7					
Disaster prevention broadcasting systems	24	2.4					
Local government webpage	744	73.7					
Newspapers	9	0.9					
Public health lecture meetings	38	3.8					
Posters placed on clinics	308	30.5					
Request for vaccination to medical institutions	249	24.7					
Municipality newspapers	877	86.8					
Notice for circulation in the local area	99	9.8					
		Continued					

Table 1	Continued				
		Numbers	%		
Others	;	120	11.9		
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\*These questionnaire items allowed multiple answers.

vaccine officers was waived for this study because personal health information was not collected in the surveys.

# Patient and public involvement

We interviewed several public officers for asking questionnaire items. No patients were involved in the study protocol design, the specific aims or the research questions, and the plans for the design or implementation of the current study. No patients or the public were involved in the interpretation of the results of the study or preparation of the manuscript. We made a booklet to disseminate the results of the research to the municipalities.

## **Statistical analyses**

Descriptive statistics were used to summarise PPSV23 coverage, out-of-pocket costs and the promotional activities implemented by municipalities to improve vaccine uptake. To explore factors associated with PPSV23 coverage, likelihood ratio tests were used to compare the fit of a parsimonious model that included only the number of direct mail notifications sent to individuals to expanded models that included predictor variables for out-of-pocket costs, the content of direct mail notifications and other dissemination activities (eg, radio spots, cable television broadcasting and publication in municipal newspapers). After selecting factors significantly associated with PPSV23 coverage (p<0.05), a linear mixed model was applied to account for municipality-level and prefecture-level demographic, socioeconomic and healthcare supply variables.<sup>14</sup> All analyses were conducted using SAS 9.40.

## RESULTS

In total, 1010 municipalities responded to the survey (response rate, 58.0%) and the coverage rates markedly differed between the municipalities (median, 41.8%; fifth percentile, 13.6%; 95th percentile, 62.6%). However, municipalities with the highest and lowest coverage rates were equally distributed by region. Thirty-eight municipalities (7.7%) in the east and 31 municipalities (6.0%)in the west of Japan had high coverage rates of >60%. Meanwhile, approximately 10.5% and 8.5% of municipalities in the east and west of Japan, respectively, had low coverage rates (<20%). We found regional differences in response rates ranging from 51.1% (Kyushu-Okinawa region) to 64.4% (Chuugoku-Shikoku region). The low response rate in the Kyushu-Okinawa region was due to an earthquake that occurred in the region during the survey. Official records were used as the source of vaccine coverage rates in 949 (94.0%) municipalities.

Table 2         Baseline characteristics of the municipalities in this study								
Characteristics	Unit	Number of municipalities	Mean	SD	Minimum	Maximum		
Out-of-pocket costs	1000 JPY	1003	3.1	1.3	0.0	6.5		
Population aged ≥65 years	%	1010	27.5	6.8	13.6	55.1		
Unemployment rates	%	1010	3.2	1.0	0.5	9.1		
Population density	Units: 10000 person/km <sup>2</sup>	1010	0.1	0.2	0.0	1.9		
Male sex (aged ≥65 years)	%	983	49.7	4.4	33.3	74.1		
Density of medical doctors	Per 100 people	1010	0.2	0.2	0.0	3.6		
Density of medical institutions	Per 10000 people	1010	7.3	4.4	0.0	97.6		
Income	1 000 000 JPY	1010	2.8	0.6	2.0	12.7		

The out-of-pocket costs and community-level activities undertaken by municipalities to improve vaccine uptake are summarised in table 1. The mean out-of-pocket costs for vaccination was 3100 JPY (range 0-6500 JPY). This indicates that in certain municipalities, the vaccine cost was completely subsidised by the national and municipal governments, whereas in other municipalities, adults paid up to 70% of the vaccine cost out of pocket. Most municipalities (84.8%) sent at least one direct mail notification to the target population during the 2015 fiscal year. Notifications were mainly sent during the spring season (76.9%) via letters (64.6%) that informed adults about the NIP period (74.4%) and eligibility criteria for vaccination (73.6%). Municipal newspapers (86.8%) and webpages of municipal governments (73.7%) were also commonly used to inform adults about the availability of pneumococcal vaccination through the NIP.

The municipality-level and prefecture-level sociodemographic, economic and healthcare supply characteristics are presented in table 2. The proportion of adults aged  $\geq 65$  years ranged from 14% to as high as 55% in some municipalities. Across municipalities, approximately 50% of the population aged  $\geq 65$  years were men. The mean unemployment rate was low at 3.2%. There was a wide variation in the population density (0–1.9 persons per 10000 km<sup>2</sup>), density of medical institutions (0–97.6 institutions per 10000 persons) and average per capita income (2 000 000–12 700 000 JPY).

The likelihood ratio tests used to compare parsimonious and expanded models are provided in tables 3 and 4. Models including out-of-pocket costs, unemployment rates, population density and average per capita income as predictor variables fit the data significantly better than the more restrictive model that included only the number of direct mail notifications (p<0.05). The final model including these variables is presented in table 5. The number of direct mail notifications was positively associated with PPSV23 vaccination. The vaccination rate increased by 18.7% (16.7%–20.7%)%) in municipalities that sent a notification to the target population of adults compared with municipalities that did not send any notification. High out-of-pocket costs, high unemployment rates and high average per capita income decreased PPSV23 coverage in municipalities. The vaccination rate decreased by 3.02% (2.4%–3.6%)%) for every 1000 JPY increase in out-of-pocket costs, by 1.02% (0.2%–1.9%) for every 1% increase in the unemployment rate and by 1.91% (0.4%–3.4%) for every 1 000 000 JPY increase in per capita income. The population density was not significantly associated with PPSV23 vaccination in the final model.

Prefecture-level variables (average savings, education rates, number of nurses, death rate and prefecture) were included as random effects in the model. The least-square mean methods were used to estimate the adjusted means of vaccine coverage rate based on the number of direct mail notifications sent.

The adjusted mean PPSV23 vaccination rate among adults aged 65 years according to the number of direct mail notifications is shown in figure 1. The rate of vaccine coverage was 27.3% (22.7%-31.9%)%) in municipalities that sent out no notifications to the target population. The coverage rate improved as the number of direct mail notifications increased. The coverage rate reached 54.2% (49.4%-58.9%)%) in municipalities that sent out 2 notifications and 48.5% (42.1%-54.9%)%) in those that sent out  $\ge 3$  notifications to the target population.

## DISCUSSION

The nationwide survey showed that the vaccine coverage increased in municipalities that sent a direct mail notification and decreased with increasing in out-of-pocket costs. This study also showed that municipality-level unemployment rates and average per capita income were negatively associated with vaccine coverage rate.

A total of 1010 municipalities (58%) responded to the survey. Among these municipalities, the median vaccination rate among adults aged 65 years during the 2015–2016 fiscal year was 41.8% (range 13.6%-62.6%). This is similar to the vaccination rate estimated by Naito *et al* (40.6% by the end of the year 2015) and the 2015 estimate published by the national government (38.3%).<sup>78</sup>

We focused on adults aged 65 only as the target population for this survey. Several municipalities had already introduced subsidies for pneumococcal vaccination prior to the start of the NIP in 2014. By including this specific age group only, we can compare municipalities that

Table 3	Relationship between the number of	direct mail notification,	questionnaire item	is and the coverage ra	ites of 23-valent
pneumo	coccal polysaccharide vaccine among	Japan municipalities			

lets         Base model         Expanded municipalities         1010'         1010'         1010'         1010'         1010'         1003'         1010'           Intercept         23.69'		Likelihood ratio	elihood ratio Regression coefficients*						
Number of municipalities         1010* <th100*< th="">         100*         100*<!--</td--><td></td><td>tests</td><td>Base model</td><td></td><td></td></th100*<>		tests	Base model						
Intercopt       23.69°       23.69°       23.69°       23.69°       23.69°       23.69°       23.69°       23.69°       23.69°       23.69°       23.69°       23.69°       23.69°       23.69°       23.69°       30.69°       30.44°       23.59°       10.71°         1       19.16°       24.03°       21.34°       21.34°       21.38°       16.79°       19.71°         2       27.75°       35.77°       30.27°       30.45°       26.76°       28.51°         3 or more       22.95       35.67°       30.27°       30.45°       26.76°       28.51°         Summer       -7.47       -4.87°       - </td <td>Number of municipalities</td> <td></td> <td>1010*</td> <td>1010*</td> <td>1010*</td> <td>1010*</td> <td>1003*</td> <td>1010*</td>	Number of municipalities		1010*	1010*	1010*	1010*	1003*	1010*	
Number of direct mail notifications sent (reference: 0)         1         19.16*         24.03*         21.34*         21.36*         18.79*         19.71*           2         27.75*         35.77*         30.45*         26.76*         28.51*           3 or more         22.95         36.25         25.60         25.49         21.40         23.32           Seasons	Intercept		23.69*	23.69*	23.69*	23.69*	32.44*	23.59*	
1       19.16'       24.03'       21.34'       21.36'       18.79'       19.71'         2       27.75'       35.77'       30.27'       30.45'       28.76'       28.11'         3 or more       22.95       38.25       25.60       25.49       21.40'       23.51'         Sammer       -7.47'       -	Number of direct mail notificat	ions sent (referend	ce: 0)						
2         27.75°         35.77°         30.27°         30.45°         28.76°         28.51°           3 or more         22.95         36.25         25.60         25.49         21.40         23.32           Seasons	1		19.16*	24.03*	21.34*	21.38*	18.79*	19.71*	
3 or more       22.95       36.25       25.60       25.49       21.40       23.32         Seesons       Spring       0.118       -4.87'       Image: Spring       Image: Spring <td>2</td> <td></td> <td>27.75*</td> <td>35.77*</td> <td>30.27*</td> <td>30.45*</td> <td>26.76*</td> <td>28.51*</td>	2		27.75*	35.77*	30.27*	30.45*	26.76*	28.51*	
Seasons         -4.87°           Summer         -7.47           Autum         -3.94           Winer         -2.35           Type of mail notification (first wave)         -           Letters         0.199         -2.76°           Attached postcards         -0.43           Postcards         -0.28           Others         -1.60           Enclosed contents (first wave)         -           Eligibility of vaccination         0.053         -3.15           programme         0.65         -           Co-payment         0.48         -           Voucher         -0.14         -           Designated hospitals         -0.28         -           Voucher with application form         0.13         -           form         -0.28         -         -           Voucher with application days         -0.28         -         -           Information on disease and vaccination days         -         -         -         -           Others         -2.02°         -         -         -         -           Units: 1000 JPY)         <0.01	3 or more		22.95	36.25	25.60	25.49	21.40	23.32	
Spring       0.118       -4.87°         Summer       -7.47         Autumn       -3.394         Winter       -2.35         Type of mail notification (first wave)       -2.76°         Latters       0.199       -2.76°         Attached postcards       -0.43         Postcards       -0.28         Others       -1.60         Enclosed contents (first wave)       -1.60         Eligibility vaccination       0.053       -3.15         programme       0.65       -0.28         Coverage period       0.65       -0.14         Designated hospitals       -0.29       -0.14         Voucher with application       0.13       -0.28         Voucher with application       0.13       -0.28         vaccination days       0.18       -0.28         Information on disease and vaccination days       -0.28       -0.28         Out-of-pocket costs       -2.02*       -0.14         Out-of-pocket costs       -9.31       -0.28         (Units: 1000 JPY)       <0.001	Seasons								
Summer         -7.47           Autumn         -3.94           Winter         -2.35           Type of mall notification (first wave)         -2.76*           Letters         0.199         -2.76*           Attached postcards         -0.043           Postcards         -0.28           Others         -1.60           Enclosed contents (first wave)         -3.15           Eligibility of vaccination         0.053         -3.15           Coverage period         0.65           Co-payment         0.48           Voucher         -0.14           Designated hospitals         -0.29           Voucher with application form         0.18           Information on disease and vaccination days         -0.20           Information on disease and vaccination         -2.02*           Out-of-pocket costs         -2.01*           Untis': 1000 JPV)         <0.01	Spring	0.118		-4.87*					
Autumn       -3.94         Winter       -2.35         Type of mail notification (first wave)	Summer			-7.47					
Winter         -2.35           Type of mail notification (first wave)         -           Letters         0.199         -2.76*           Attached postcards         -0.43           Postcards         -0.28           Others         -1.60           Enclosed contents (first wave)         -           Eligibility of vaccination         0.053         -3.15           programme         0.65         -           Coverage period         0.65         -           Coverage period         0.48         -           Voucher         -0.14         -           Designated hospitals         -0.29         -           Voucher with application         0.13         -           form         0.13         -         -           Forms to bring on vaccination days         -0.28         -         -           Information on disease and vaccination days         -0.28         -         -           Others         -2.02*         -         -         -           Out-of-pocket costs	Autumn			-3.94					
Type of mail notification (first wave) <ul> <li>Letters</li> <li>0.199</li> <li>-2.76°</li> <li>Attached postcards</li> <li>-0.43</li> </ul> Postcards         -0.28           Others         -1.60           Enclosed contents (first wave) <ul> <li>Scard and and a contents (first wave)</li> <li>Coverage period</li> <li>0.053</li> <li>-3.15</li> <li>Coverage period</li> <li>0.65</li> <li>Co-payment</li> <li>0.48</li> <li>Voucher</li> <li>-0.29</li> <li>Voucher</li> <li>-0.14</li> <li>Designated hospitals</li> <li>-0.29</li> <li>Voucher with application and ass</li> <li>-0.29</li> <li>Voucher with application and sease and vaccination adys</li> <li>-0.28</li> <li>-0.28</li> <li>-0.29</li> <li>Voucher with application and sease and vaccination adys</li> <li>-2.02*</li> <li>Outhors</li> <li>-2.02*</li> <li>Outhors</li> <li>-2.02*</li> <li>Outhor -pocket costs</li> <li>-2.01*</li> <li>-2.01*</li> <li>-2.01*</li> <li>-2.01*</li></ul>	Winter			-2.35					
Letters         0.199         -2.76*           Attached postcards         -0.43           Postcards         -0.28           Others         -1.60           Enclosed contents (first wave)         -3.15           Eligibility of vaccination         0.053           programme         0.665           Coverage period         0.665           Coverage period         0.614           Voucher         -0.14           Designated hospitals         -0.29           Voucher with application form         0.18           Forms to bring on vaccination days         -0.28           Information on disease and vaccination days         -0.28           Others         -2.02*           Out-of-pocket costs         -2.02*           Out-of-pocket costs         -2.02*           Out-of-pocket costs         -0.43           Cable TV networks         0.573         -8.61           Cable TV networks         0.573         -0.47           Dissemination         -0.02         -0.02           TV networks         0.573         -0.61           Cable TV networks         0.573         -0.61           Cable TV networks         0.573         -0.02	Type of mail notification (first v	vave)							
Attached postcards       -0.43         Postcards       -0.28         Others       -1.60         Enclosed contents (first wave)       -3.15         Eligibility of vaccination       0.053       -3.15         programme       0.65       -0.29         Coverage period       0.61       -0.29         Voucher       -0.14       -0.29         Voucher with application form       0.13       -0.29         Voucher with application days       -0.28       -0.29         Information on disease and vaccination       -0.28       -0.28         Vaccination       -0.28       -0.29         Others       -0.28       -0.29         Others       -0.28       -0.28         Vaccination days       -0.28       -0.28         Others       -2.02*       -0.28         Others       -2.02*       -0.28         Others       -2.71*       -0.51         Dissemination       -2.71*       -0.43         Cable TV networks       0.573       -8.61         Cable TV networks       0.573       -0.61         Disaster prevention       -0.02       -0.02         broadcasting systems       -0.02       -0.02 <td>Letters</td> <td>0.199</td> <td></td> <td></td> <td>-2.76*</td> <td></td> <td></td> <td></td>	Letters	0.199			-2.76*				
Postcards       -0.28         Others       -1.60         Enclosed contents (first wave)       -3.15         Eligibility of vaccination programme       0.65         Coverage period       0.65         Vaccination form       0.13         form       0.13         form       0.13         form       0.13         form       0.13         vaccination days       -0.28         Others       -2.02*         Out-of-pocket costs       -2.02*         Cut-of-pocket costs       -9.03         TV networks       0.573       -8.61         Gable TV networks       0.573       -0.47         Cable broadcasting systems       -0.02       -0.02         broadcasting systems       -0.02       -0.02<	Attached postcards				-0.43				
Others       -1.60         Enclosed contents (first wave)       -3.15         Eligibility of vaccination       0.053       -3.15         programme       0.65       -0.24         Coverage period       0.65       -0.14         Designated hospitals       -0.29       -0.29         Voucher with application form       0.13       -0.29         Voucher with application days       0.13       -0.28         Information on disease and vaccination       -0.28       -0.28         Vaccination on disease and vaccination       -0.28       -0.29         Others       -2.02*       -0.28         Others       -2.02*       -0.29         Out-of-pocket costs       -2.02*       -0.29         (Units: 1000 JPY)       <0.001	Postcards				-0.28				
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Eligibility of vaccination         0.053         -3.15           programme         0.65         -           Coverage period         0.48         -           Voucher         -0.14         -           Designated hospitals         -0.29         -           Voucher with application form         0.13         -           Forms to bring on vaccination days         0.13         -           Information on disease and vaccination         -0.28         -           Others         -2.02*         -         -           Out-of-pocket costs         -2.24*         -         -           Units: 1000 JPY)         <0.001	Enclosed contents (first wave)								
Coverage period         0.65           Co-payment         0.48           Voucher         -0.14           Designated hospitals         -0.29           Voucher with application form         0.13           Forms to bring on vaccination days         0.18           Information on disease and vaccination         -2.02*           Out-of-pocket costs         -2.02*           Out-of-pocket costs         -2.71*           Out-of-pocket costs         -8.61           Cable TV networks         0.573         -8.61           Cable TV networks         0.93           Radio spots         -0.47           Cable broadcasting         -1.17*           Disaster prevention broadcasting systems         -0.02           Local government webpage         -0.01           webpage         -0.01           Public health lecture neetings         -0.15           Posters placed in clinics         -0.05	Eligibility of vaccination programme	0.053				-3.15			
Co-payment         0.48           Voucher         -0.14           Designated hospitals         -0.29           Voucher with application form         0.13           Forms to bring on vaccination days         0.18           Information on disease and vaccination         -0.28           Others         -2.02*           Out-of-pocket costs         -2.02*           (Units: 1000 JPY)         <0.001	Coverage period					0.65			
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Designated hospitals       -0.29         Voucher with application form       0.13         Forms to bring on vaccination days       0.18         Information on disease and vaccination       -0.28         Others       -0.20°         Out-of-pocket costs       -2.02°         (Units: 1000 JPY)       <0.001	Voucher					-0.14			
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Forms to bring on vaccination days       0.18         Information on disease and vaccination       -0.28         Others       -2.02*         Out-of-pocket costs       -2.02*         (Units: 1000 JPY)       <0.001	Voucher with application form					0.13			
Information on disease and vaccination       -0.28         Others       -2.02*         Out-of-pocket costs       -2.02*         (Units: 1000 JPY)       <0.001	Forms to bring on vaccination days					0.18			
Others      2.02*         Out-of-pocket costs       (Units: 1000 JPY)       <0.001	Information on disease and vaccination					-0.28			
Out-of-pocket costs         -2.71*           (Units: 1000 JPY)         <0.001	Others					-2.02*			
(Units: 1000 JPY)       <0.001	Out-of-pocket costs								
Dissemination       TV networks       0.573       -8.61         Cable TV networks       0.93       -0.47         Radio spots       -0.47       1.17*         Cable broadcasting       -0.02       -0.02         Disaster prevention broadcasting systems       -0.01       -0.01         Local government webpage       0.24       -0.15         Newspapers       0.24       -0.15         Public health lecture meetings       -0.05       -0.05	(Units: 1000 JPY)	<0.001					-2.71*		
TV networks0.573-8.61Cable TV networks0.93Radio spots-0.47Cable broadcasting1.17*Disaster prevention broadcasting systems-0.02Local government webpage-0.01Newspapers0.24Public health lecture meetings-0.15Posters placed in clinics-0.05	Dissemination								
Cable TV networks0.93Radio spots-0.47Cable broadcasting1.17*Disaster prevention broadcasting systems-0.02Local government webpage-0.01Newspapers0.24Public health lecture meetings-0.15Posters placed in clinics-0.05	TV networks	0.573						-8.61	
Radio spots-0.47Cable broadcasting1.17*Disaster prevention broadcasting systems-0.02Local government webpage-0.01Newspapers0.24Public health lecture meetings-0.15Posters placed in clinics-0.05	Cable TV networks							0.93	
Cable broadcasting1.17*Disaster prevention broadcasting systems-0.02Local government webpage-0.01Newspapers0.24Public health lecture meetings-0.15Posters placed in clinics-0.05	Radio spots							-0.47	
Disaster prevention broadcasting systems-0.02Local government webpage-0.01Newspapers0.24Public health lecture meetings-0.15Posters placed in clinics-0.05	Cable broadcasting							1.17*	
Local government webpage-0.01Newspapers0.24Public health lecture meetings-0.15Posters placed in clinics-0.05	Disaster prevention broadcasting systems							-0.02	
Newspapers0.24Public health lecture meetings-0.15Posters placed in clinics-0.05	Local government webpage							-0.01	
Public health lecture meetings-0.15Posters placed in clinics-0.05	Newspapers							0.24	
Posters placed in clinics -0.05	Public health lecture meetings							-0.15	
	Posters placed in clinics							-0.05	

Table 3   Continued	_		
	Likelihood ratio	Regression coefficients*	
	tests	Base model Expanded models	
Request for vaccination to medical institutions			0.03
Municipality newspapers			-0.07
Notice for circulation in the local area			0.18
Others			0.78*

\*Statistically significant regression coefficient (p<0.05). Likelihood ratio tests (LR tests) were used to determine whether each questionnaire item was included in the base model (model with the number of mail notifications as the only variable) or not.

introduced subsidies for PPSV23 only at the beginning of the NIP (October 2014) to municipalities who had previously introduced programmes on their own. This age group would not have been the target of previous PPSV23 immunisation campaigns, except in the case of belonging to a pneumococcal infection high-risk group between 60-64 years or in the case of immunocompromised patients having splenectomy or cancer.

Official records were used as the source of vaccine coverage rates in 949 (94.0%) municipalities. All vaccinations in Japan are provided only through physicians

or public health centres. Under the Immunisation Law, the Ministry of Health and Labour Welfare provides a patient questionnaire for each vaccine included in the NIP. Patients must fill in this questionnaire prior to being vaccinated (https://www.mhlw.go.jp/file/06-Seisakujouhou-10900000-Kenkoukyoku/0000144221.pdf). Physicians and public health centres must submit these questionnaires to the municipal government in order to receive reimbursement for the vaccinations provided. Therefore, the submission rate of this form is almost perfect. The official records of vaccination are compiled

Table 4Relationship between the number of direct mail notification, statistical information and the coverage rates of23-valent pneumococcal polysaccharide vaccine among Japan municipalities

	Likelihood	Regression coefficients**							
	tests	Base model	Expande	d models					
Intercept		23.69*	24.12*	26.01*	21.71*	27.30*	20.26*	24.06*	24.44*
Number of direct mail noti	fications sent	(reference: 0)							
1		19.16*	19.25*	19.32*	19.55*	19.41*	19.46*	19.38*	19.32*
2		27.75*	27.83*	27.91*	28.09*	28.00*	27.91*	27.95*	27.86*
3 or more		22.95*	23.03*	23.36*	23.32*	23.12*	23.36*	23.27*	23.04*
Population aged ≥65 years	6								
(%)	0.720		-0.02						
Unemployment rates									
(%)	0.046			-0.78*					
Ln (population density)*									
(Units: 10 000 person/ km²)	0.033				-0.45*				
Income									
(Units: 1 000 000 JPY)	0.021					-1.37*			
Sex ratio in the elderly pop	oulation (age	≥65 years)							
(%)	0.419						0.06		
Density of medical doctors									
(per 100 people)	0.056							-3.43	
Density of medical institut	ions								
(per 10000 people)	0.136								-0.12

\*Statistically significant regression coefficient (p<0.05). Likelihood ratio tests were used to determine whether each variable was included in the base model (model with the number of mail notifications as the only variable) or not.

 
 Table 5
 Multivariate regression analysis of the coverage rates of 23-valent pneumococcal polysaccharide vaccine among the municipalities

	Estimates	95% CI	
Intercept	46.30	37.09	55.50
Direct mail notifications sent	(reference:	0)	
1	18.70	16.72	20.68
2	26.85	23.98	29.73
3	21.21	15.94	26.49
Out-of-pocket costs			
(Units: 1000 JPY)	-3.02	-3.62	-2.42
Unemployment rates			
(%)	-1.02	-1.89	-0.16
Log (population density)			
(Units: 10000 person/km <sup>2</sup> )	0.29	-0.29	0.88
Incomes			
(Units: 1 000 000 JPY)	-1.91	-3.40	-0.42

Prefecture-level variables (average savings, education rates, number of nurses, death rate and prefecture) were included as random effects in the model.

based on these questionnaires and are well managed by the municipal government.

The mean out-of-pocket cost was 3100 JPY, but ranged from 0 to 6500 JPY, indicating that PPSV23 vaccination was not subsidised at all in some municipalities, while it was fully subsidised in other municipalities. Most municipalities also engaged in promotional activities at the community level to encourage vaccine uptake. Direct mail notifications to the target population and announcements through municipal newspapers and webpages were the most commonly used means to inform about the NIP opportunity. The associations of these activities and municipality-level and prefecture-level sociodemographic, economic and health supply variables on vaccine coverage were explored through regression analysis.



**Figure 1** Number of direct mail notifications sent and the adjusted mean coverage rates of the 23-valent pneumococcal polysaccharide vaccine among adults aged 65 years in Japan, 2015.

Out-of-pocket costs, direct mail notifications, municipal unemployment rates and municipal per capita income were significantly associated with vaccine coverage in the final model.

Similar to the previous studies prior to NIP implementation in Japan by Kondo and Naito, out-of-pocket costs were negatively associated with vaccine coverage.<sup>9 10</sup> Not all municipalities are eligible for the national subsidy and eligible municipal governments can choose whether to further subsidise the vaccine cost for their residents. Along with direct mail notifications, subsidies to reduce out-of-pocket costs can also influence vaccine uptake among older adults.

Previous research have shown that reminding individuals of due vaccinations through telephone calls, letters or postcards can increase vaccine coverage rates by 6% when used alone or by 12% when used in conjunction with other interventions.<sup>15</sup> Recently, Shono *et al* conducted a cross-sectional web-based survey of adults aged 65–74 years in Japan and demonstrated that postal notifications from municipal governments were the main reason for availing pneumococcal vaccinations after the introduction of NIP.<sup>16</sup> Similarly, our results demonstrate that sending mail notifications to the target population was an effective measure for increasing PPSV23 vaccination coverage among the elderly. Repeat mail notifications increased PPSV23 vaccine coverage even further.

In our study, dissemination activities such as TV broadcasting or brochures, showed little effect on vaccine uptake. This finding is similar to Kondo *et al* who showed that activities such as the distribution of brochures or provision of information on websites also had little effect on vaccine uptake.<sup>10</sup> Both studies indicated that the effect of subsidies on vaccine uptake was strong, compared with the effect on these dissemination activities.

Municipality-level unemployment rates were negatively associated with PPSV23 uptake, which may reflect the impact of social determinants on preventive care. Previous studies have shown that neighbourhood or county-level education, income, housing, employment and population density are indicative of the level of socioeconomic deprivation in a geographic area and can influence the use of preventive care.<sup>17-19</sup> However, we also found that municipality-level per capita income was negatively associated with PPSV23 uptake. While this finding was unexpected, higher income municipalities may not be eligible for the national subsidy, or if eligible, their governments may not further subsidise the vaccine cost.

This study had several limitations. First, this was an ecological study conducted at the municipality level; therefore, adults were not surveyed and our conclusions are limited to a population level. Because a nationwide person-level survey was deemed impossible, confounding factors at the individual level that may influence vaccination were not controlled for in this analysis. Second, while we incorporated several sociodemographic, economic and healthcare supply variables at the municipality and prefecture level in the analysis, we did not attempt to

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construct a deprivation index for each municipality. Third, we cannot confirm the completeness of the officers' responses on communication activities conducted to increase pneumococcal vaccination uptake as other official sources are not available. However, our estimates of vaccine coverage from this survey are similar to those published by the national government.

Despite these limitations, this study was the first nationwide survey to estimate PPSV23 coverage rates in adults aged 65 years in Japan. This survey was sent to all municipalities in Japan with nearly 60% response rate. Most municipalities relied on official records for reporting vaccine coverage; 943 municipalities (93.4%) used official municipal records of vaccination and 949 municipalities (94.0%) used a basic resident registration system for population numbers. These factors along with the high response rate suggest that study results are likely valid and generalizable to all Japanese municipalities.

### **CONCLUSION**

This nationwide survey provides insight into the factors that may influence PPSV23 coverage in Japanese municipalities. Low out-of-pocket costs and providing mail notifications to the target population were associated with higher municipal PPSV23 coverage rates in Japan.

Acknowledgements The authors thank all the municipal officers who answered the survey. The authors thank Aya Yano, Mio Komura, Megumi Yoshinaga and Kenichi Takahashi from MSD K.K., Tokyo, Japan, for supporting the development of the study concept and protocol.

**Contributors** YM, SK, TP and AW contributed to the conception and design of the study and interpretation of data. YM and SK contributed to the drafting of the manuscript. YM, YN and MSO contributed to the acquisition and analysis of data. TP contributed to the critical review of the manuscript. YN and MSO contributed to the interpretation of the paper. AW provided comments from infectious disease and vaccine specialist's point of view. All authors gave final approval of the version to be published.

Funding This study was funded by MSD K.K., Tokyo, Japan.

**Competing interests** YM received research grants from grants from MSD K.K., Tokyo, Japan. SK is an employee of MSD K.K., Tokyo, Japan, and may hold stock and/or stock options in the company. TP is an employee of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co, Kenilworth, New Jersey, USA, and may hold stock and/or stock options in the company. AW received lecture fees from MSD K.K., Tokyo, Japan. The study sponsor, MSD K.K., Tokyo, Japan, developed the study design; reviewed in the collection, analysis and interpretation of the data; critically reviewed the report and decided to submit the paper for publication.

Patient consent for publication Not required.

Ethics approval This study was approved by the Toho University Ethics Committee (approval number: A16008) and registered in the University Hospital Medical Information Network, Japan (ID: UMIN000024860).

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

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