# **Original Article**

# Prevalence of Immunity Presumed Using Rabies Vaccination History and Household Factors Associated with Vaccination Status among Domestic Dogs in Japan

Arata Hidano<sup>1,2</sup>, Yoko Hayama<sup>1</sup>, and Toshiyuki Tsutsui<sup>1\*</sup>

<sup>1</sup>Viral Disease and Epidemiology Research Division, National Institute of Animal Health, Ibaraki 305-0856, Japan; and <sup>2</sup>EpiCentre, Institute of Veterinary, Animal and Biomedical Science, Massey University, Palmerston North, New Zealand

(Received February 8, 2012. Accepted June 8, 2012)

**SUMMARY:** Rabies was eliminated in Japan over 50 years ago; however, the recent increase in the movement of humans and animals across the world highlights the potential threat of disease reentry into the country. The immune status against rabies among the dog population in Japan is not well known; thus, the purpose of this study was to estimate the prevalence of dogs with effective immunity from the vaccination history using a web-based survey. We found that 76.9% (95% confidence interval, 75.8–78.1) of dogs in this study population belonged to the population in which 90% were assumed to have the internationally accepted antibody titer. We showed that dogs taken less frequently for walks were less likely to be vaccinated. Additionally, the frequency of encounters with other dogs during walks and the number of individuals in households were associated with vaccination history. To our knowledge, this study is the first report estimating the prevalence of dogs in Japan with effective immunity against rabies. Further, we identified the population with low vaccination coverage as well as the heterogeneous characteristics of vaccination history among the dog population. These findings contribute to the implementation of an efficient strategy for improving the overall vaccination coverage in Japan and the development of a quantitative risk assessment of rabies.

## **INTRODUCTION**

Japan has been free from rabies since 1957 with systematic control measures such as strict quarantine of imported animals and mandatory vaccination for dogs; moreover, it has the geographic advantage of being surrounded by water. Under the current import quarantine regimen, it is estimated that rabies would enter Japan once every 4,932 years (90% confidence interval [CI] 1,812–13,412) through the importation of dogs and cats from the United States (1). This suggests a very low risk of rabies entry through the importation of animals. However, rabies introduction through illegal entry of animals from surrounding countries is of great concern as international transportation of humans and animals has been increasing (2). In addition, there are fears of a decline in compliance with compulsory vaccination of dogs against rabies because the absence of rabies in Japan, which has probably reduced the perceived threat of the disease. The officially reported rabies vaccination coverage rate in Japan, obtained from the number of dogs registered and those vaccinated, has been kept at more than 70% (3), a rate recommended by the World Health Organization for dog populations in order to

stop virus circulation in rabies endemic countries (4). There has been, however, a concern that the reported rates may be overestimated because it is reasonable to assume that not all dogs in Japan are registered (5). Moreover, the rates cited in annual reports only present a cross-sectional vaccination status of dogs and do not provide information regarding vaccination history, which is the actual determinant of the antibody titer in individual animals. It has been reported that a single dose vaccination without boosters would result in only 75% of animals retaining the internationally accepted threshold of antibody titer (>0.5 IU/mL) 1 year after vaccination; however, 90% of animals would have antibody titers above the threshold if administered a booster vaccination every year or vaccinated more than once within a year (6).

Therefore, it is essential to obtain information on past vaccination history to estimate the immune status among dogs. Identification of the characteristics of households with low rabies vaccination coverage should also be required in order to recognize the target population that requires improvement in overall vaccination coverage in Japan.

The aim of this study was to estimate the prevalence of dogs with the required rabies immune status from the vaccination history of dogs in Japan. In addition, factors associated with the vaccination history of dogs were analyzed to characterize the dog population with low rabies vaccination coverage.

<sup>\*</sup>Corresponding author: Mailing address: Viral Disease and Epidemiology Research Division, National Institute of Animal Health, 3-1-5 Kannondai, Tsukuba, Ibaraki 305-0856, Japan. Tel & Fax: +81-29-838-7793, E-mail: tsutsui@affrc.go.jp

Question 1: Numbe of dogs Large/Medium/Small

Question 2: Number of cats

Question 3: Type of surroundings Urban/Suburb/Countryside/Other (please specify)

Question 4: Type of accommodation Detached/Apartment/Other (please specify)

Question 5: Keeping style of dogs Only inside house/Mainly inside house/ Mainly outside house/Only outside house/Untied/Other

Question 6: Rabies vaccination history

Every year/

Not every year but administered before
(please specify: once within this year/
more than once within this year/once within these 2 years/
more than once within these 2 years/
once prior to the past 2 years/
more than once prior to the past 2 years/
Never/
Unknown

Question 7: Registration of dogs Yes/No/Unknown

Question 8: Frequency of walks per week (applicable if only answered other than "Untied" in question 5)

Question 9: Frequency of encounters with other dogs per 10 times walk (only applicable for those answered more than 0 times walk per week

(only applicable for those answered more than 0 times walk per week in question 8)

Question 10: Ever took dogs to shopping or trips (only applicable for those keep dogs only inside house and do not take dogs for a walk)

Yes/No

Question 11: Presence of animals around the house and the daily walking area

Stray dogs/Stray cats/Racoon dogs/Foxes/Racoons

Question 12: Marital status Married/Single

Question 13: Number of people in the household

## MATERIALS AND METHODS

Study population and questionnaire survey: We collected information regarding rabies vaccination history and other factors from areas all over Japan with a webbased survey using a structured questionnaire as shown in Table 1. Data were collected between March 6 and 10, 2010. All 47 prefectures in Japan were divided into 6 regions as shown in Fig. 1. One region, "Kanto," which has the largest population, was further split into 7 areas based on prefectures, resulting in a total of 12 sampling areas. Dog owners who had voluntarily registered with commercial access panels (Yahoo Japan Value Insight Corporation [currently Macromill Inc.], Tokyo, Japan) were identified by a preliminary survey and were asked to attend the questionnaire study. Out of 4,368 households that used the questionnaire survey, 333 or 334 households were randomly selected in each sampling area, resulting in a selection of 4,000 households across Japan. The sample size of our study was determined to maximize the sample size in each area within budget limitations. Any person with internet access could voluntarily register as a member of the access panels. Data from the 4,000 completed questionnaires were



Fig. 1. Geographic locations of the 6 study regions covering all of Japan.

stored and handled with commercially available spreadsheet software (Excel 2007; Microsoft Corp., Redmond, Wash., USA).

Statistical analysis: (i) Descriptive analysis of the rabies immune status presumed using vaccination history: Information regarding vaccination history was obtained separately for dogs in each size category (large, weight  $[W] \ge 20 \text{ kg}$  and withers height  $[WH] \ge 50 \text{ cm}$ ; medium, W 10 kg < 20 kg and WH 40 cm < 50 cm; small, W < 10 kg and WH < 40 cm) in each household. Households with more than 1 dog of the same size were asked to provide information for only 1 dog, which was assumed as consistent among other same-sized dogs in the household. Animals in the household that were reported to have a rabies vaccination every year or to have been vaccinated twice or more within the past year were defined as  $P_{90}$ , the population where 90% of dogs were assumed to have the threshold titer (6). Similarly, dogs reported to have had a vaccination only once within the past year, or twice or more within the past 2 years were defined as  $P_{75}$ , the population where 75% of dogs were assumed to have the threshold titer (6). The dogs that were reported to have been vaccinated only once or not at all within the past 2 years were defined as P<sub>RISK</sub>, i.e., the population at risk of rabies infection. The dogs with unknown vaccination status were also classified as P<sub>RISK</sub>. The total number of dogs belonging to P<sub>90</sub>, P<sub>75</sub>, and P<sub>RISK</sub> were obtained for each defined region and area.

(ii) Analysis of factors associated with the vaccination status of dogs: The factors associated with the vaccination status of dogs (i.e., maintenance of favorable immune status against rabies) were analyzed based on the herd level. The herd level was defined as an aggregation of the same-sized dogs within each household. Each herd was considered to have preferable rabies vaccination status if all of the animals in the herd were in  $P_{90}$ . Households that answered "other" to questions regarding either "Keeping style of dog," "Type of accommodation," or "Type of surroundings" were excluded from the analysis. Frequency of walks per week was

converted into a categorical variable with 4 levels as "None," "1-6 times" (at most 1 walk per day), "7-13 times" (1 to 2 walks per day), and "More than 13 times" (at least 2 walks per day). Frequency of encounters with other dogs per 10 walks was categorized into 3 levels to have an approximately equal number of households in each level for each dog size as "Less than 5 times," "5-9 times," and "10 times" per 10 walks. All explanatory variables were subjected to univariable analysis by fitting into logistic regression. The variable representing "Keeping style of dogs" was forced into the final model as an a priori confounder. Only variables with P < 0.20 (in  $\chi^2$  tests) in the univariable analysis were preceded to the multivariable analysis. Multicollinearity was examined for each variable by comparing the sign of the crude coefficient in the univariable model with that of the adjusted coefficient in the multivariable model. A switch in the sign of the coefficient was considered evidence of multicollinearity. The final model was constructed by the manual forward variable selection approach by adding variables one by one in the descending order of the strength of the statistics and retaining only significant variables (P < 0.05 in Wald tests). The log-likelihood ratio test was conducted to obtain overall P values for variables with more than one category. Two-way interaction terms (i.e., the phenomenon that the effect of one variable depends on the level of another variable) were not examined in this study because our objective was to identify factors affecting vaccination status. The series of statistical

analyses were conducted using Stata Version 12.0 (Stata Press, College Station, Texas, USA).

### **RESULTS**

Description of immune status among dogs presumed using vaccination history: The geographic locations of the 6 regions are displayed in Fig. 1. Rabies immune status was estimated from the vaccination history of dogs for each region and the results are shown in Table 2. The overall proportion of  $P_{90}$  dogs was 76.9% (95%) CI, 75.8-78.1) and it varied from 72.7% (95% CI, 68.4-76.9) to 82.2% (95% CI, 78.6-85.8) across all regions. The overall proportion of  $P_{75}$  was found to be very small (3.2%; 95% CI, 2.7-3.6), whereas that of  $P_{RISK}$  accounted for 19.9% (95% CI, 18.8-21.0) of the total study population. The average number of dogs in one household varied from 1.27 to 1.44 across the regions studied. Details of the prevalence of the immune status presumed using vaccination history across the Kanto region are shown in Table 3. The proportion of P<sub>90</sub> showed a wide variation, ranging from 66.1% (95% CI, 61.8-70.4) to 87.1% (95% CI, 84.0-90.3) across the areas in the Kanto region.

Analysis of factors associated with the vaccination status of dogs: Tables 4–6 show the results of descriptive statistics and univariable analyses of the factors associated with vaccination status for each dog-size category. The odds ratio (OR) was described in each variable level. "Frequency of walking dog per week" and

Table 2. Number of dogs in each population of rabies immune status presumed using vaccination history and average number of dogs per household across 6 regions covering 47 prefectures in Japan

Region	No. of dogs in $P_{90}^{1)}$	% (95% CI)	No. of dogs in P <sub>75</sub> <sup>2)</sup>	% (95% CI)	No. of dogs in $P_{RISK}^{3)}$	% (95% CI)	Total no. of dogs	Averegae no. of dogs per houshold
Hokkaido/Tohoku	358	74.7 (70.8–78.6)	22	4.6 (2.7-6.5)	99	20.7 (17.0-24.3)	479	1.44
Chubu	360	82.2 (78.6-85.8)	27	6.2 (3.9-8.4)	51	11.6 (8.6-14.6)	438	1.32
Kanto	2,417	77.3 (75.8-78.7)	71	2.3 (1.8-2.8)	639	20.4 (19.0-21.8)	3,127	1.34
Kinki	311	72.7 (68.4–76.9)	20	4.7 (2.7-6.7)	97	22.7 (18.7-26.6)	428	1.29
Chugoku/Shikoku	335	76.0 (72.0-80.0)	9	2.0 (0.7-3.4)	97	22.0 (18.1-25.9)	441	1.32
Kyushu/Okinawa	323	76.5 (72.5-80.6)	20	4.7 (2.7-6.8)	79	18.7 (15.0-22.4)	422	1.27
Total	4,104	76.9 (75.8–78.1)	169	3.2 (2.7-3.6)	1,062	19.9 (18.8–21.0)	5,335	1.33

<sup>1):</sup> P90, Dogs which have vaccination every year or have had vaccination twice or more within the past year.

Table 3. Number of dogs in each population of rabies immune status presumed using vaccination history and average number of dogs per household across 7 areas in Kanto region in Japan

Region	No. of dogs in $P_{90}^{1)}$	% (95% CI)	No. of dogs in $P_{75}^{(2)}$	% (95% CI)	No. of dogs in $P_{RISK}^{3)}$	% (95% CI)	Total no. of dogs	Averegae no. of dogs per houshold
Ibaraki	360	75.5 (71.6–79.3)	15	3.1 (1.6-4.7)	102	21.4 (17.7-25.1)	477	1.43
Tochigi	341	78.0 (74.2-81.9)	7	1.6 (0.4-2.8)	89	20.4 (16.6-24.1)	437	1.31
Gunma	344	79.4 (75.6-83.3)	13	3.0 (1.4-4.6)	76	17.6 (14.0-21.1)	433	1.30
Saitama	340	75.7 (71.8-79.7)	11	2.4 (1.0-3.9)	98	21.8 (18.0-25.6)	449	1.34
Chiba	314	66.1 (61.8-70.4)	8	1.7 (0.5-2.8)	153	32.2 (28.0-36.4)	475	1.42
Tokyo	345	80.6 (76.9-84.4)	12	2.8 (1.2-4.4)	71	16.6 (13.1-20.1)	428	1.28
Kanagawa	373	87.1 (84.0–90.3)	5	1.2 (0.2-2.2)	50	11.7 (8.6–14.7)	428	1.28

Footnotes are in Table 2.

<sup>2):</sup> P<sub>75</sub>, Dogs which have had vaccination once within the past year or twice or more within the past 2 years.

<sup>3):</sup> PRISK, Dogs which have had vaccination only once or not at all within the past 2 years and those whose vaccination histories were unknown.

Table 4. Description of household characteristics and summary of univariable analysis for their association with rabies vaccination status (large dogs)

Variable	Level	No. (%) household with preferable vaccine status	Total no. of household	OR	95% CI	$P^{(1)}$
No. of dogs kept	Only one	260 (87.5)	296	ref.		0.06
	More than one	100 (80.6)	124	0.58	0.33-1.02	
Keeping style of dogs	Only inside house	116 (85.3)	136	ref.		0.41
	Mainly inside house	85 (87.6)	97	1.22	0.57 - 2.63	
	Mainly outside house	62 (89.9)	69	1.53	0.61 - 3.81	
	Only outside house	93 (81.6)	114	0.76	0.39 - 1.49	
	Untied	4 (100.0)	4	NA	NA	
Type of surroundings	Urban	144 (86.7)	166	ref.		0.77
	Suburb	173 (85.6)	202	0.91	0.50-1.66	
	Countryside	43 (82.7)	52	0.73	0.31 - 1.70	
Type of accommodation	Detached	335 (86.1)	389	ref.		0.41
	Apartment	25 (80.6)	31	0.67	0.26 - 1.71	
Frequency of walking dog per week	More than 13 times	146 (91.3)	160	ref.		0.005
	7–13 times	114 (85.7)	133	0.58	0.28 - 1.20	
	1-6 times	77 (81.1)	95	0.41	0.19-0.87	
	None	19 (67.9)	28	0.20	0.08-0.53	
Frequency of encounters with other	10 times	123 (87.9)	140	ref.		0.04
dogs per 10 walks	5-9 times	110 (90.2)	122	1.27	0.58 - 2.77	
	Less than 5 times	123 (79.9)	154	0.55	0.29-1.04	
Presence of cat in the houshold	No	280 (87.2)	321	ref.		0.11
	Yes	80 (80.8)	99	0.62	0.34-1.12	
No. of people in the household	More than one	340 (85.6)	397	ref.		0.86
	only one	20 (87.0)	23	1.12	0.32-3.88	

<sup>1):</sup> P value for  $\chi^2$  test.

Table 5. Description of household characteristics and summary of univariable analysis for their association with rabies vaccination status (medium dogs)

Variable	Level	No. (%) household with preferable vaccine status	Total no. of household	OR	95% CI	$P^{(1)}$
No. of dogs kept	Only one	1,064 (83.6)	1,272	ref.		0.96
	More than one	279 (83.5)	334	0.99	0.72 - 1.37	
Keeping style of dogs	Only inside house	340 (85.4)	398	ref.		0.01
	Mainly inside house	275 (86.2)	319	1.07	0.70 - 1.63	
	Mainly outside house	203 (87.9)	231	1.24	0.76 - 2.01	
	Only outside house	517 (79.8)	648	0.67	0.48 - 0.94	
	Untied	8 (80.0)	10	0.68	0.14-3.30	
Type of surroundings	Urban	498 (84.6)	589	ref.		0.32
	Suburb	662 (83.9)	789	0.95	0.71-1.28	
	Countryside	183 (80.3)	228	0.74	0.50-1.1	
Type of accommodation	Detached	1,220 (83.8)	1,456	ref.		0.57
	Apartment	123 (82.0)	150	0.88	0.57-1.37	
Frequency of walking dog per week	More than 13 times	521 (90.0)	579	ref.		< 0.001
	7–13 times	414 (84.0)	493	0.58	0.41 - 0.84	
	1-6 times	345 (80.8)	427	0.47	0.33 - 0.67	
	None	55 (56.7)	97	0.15	0.09 - 0.24	
Frequency of encounters with other	10 times	400 (91.1)	439	ref.		< 0.001
dogs per 10 walks	5-9 times	480 (86.5)	555	0.62	0.41-0.94	
	Less than 5 times	455 (75.6)	602	0.30	0.21 - 0.44	
Presence of cat in the houshold	No	1,037 (84.5)	1,227	ref.		0.08
	Yes	306 (80.7)	379	0.77	0.57 - 1.03	
No. of people in the household	More than one	1,295 (84.1)	1,539	ref.		0.008
	only one	48 (71.6)	67	0.48	0.28 - 0.82	

Footnotes are in Table 4.

Table 6. Description of household characteristics and summary of univariable analysis for their association with rabies vaccination status (small dogs)

Variable	Level	No. (%) household with preferable vaccine status	Total no. of household	OR	95% CI	$P^{(1)}$
No. of dogs kept	Only one	1,300 (78.2)	1,662	ref.		0.05
	More than one	412 (74.1)	556	0.8	0.64-1.00	
Keeping style of dogs	Only inside house	1,126 (76.1)	1,480	ref.		0.02
	Mainly inside house	440 (78.0)	564	1.12	0.88 - 1.41	
	Mainly outside house	58 (89.2)	65	2.60	1.18-5.76	
	Only outside house	87 (82.1)	106	1.44	0.86 - 2.40	
	Untied	1 (33.3)	3	0.16	0.01-1.74	
Type of surroundings	Urban	902 (77.6)	1,163	ref.		0.86
	Suburb	704 (76.6)	919	0.95	0.77 - 1.16	
	Countryside	106 (77.9)	136	1.02	0.67 - 1.57	
Type of accommodation	Detached	1,285 (78.5)	1,637	ref.		0.01
	Apartment	427 (73.5)	581	0.76	0.61 - 0.95	
Frequency of walking dog per week	More than 13 times	407 (83.9)	485	ref.		< 0.001
	7–13 times	482 (81.7)	590	0.86	0.62 - 1.18	
	1-6 times	633 (74.4)	851	0.57	0.42 - 0.74	
	None	189 (65.4)	289	0.36	0.26-0.51	
Frequency of encounters with other	10 times	433 (83.4)	519	ref.		< 0.001
dogs per 10 walks	5-9 times	604 (80.5)	750	0.82	0.61-1.10	
	Less than 5 times	674 (71.2)	946	0.49	0.38 - 0.65	
Presence of cat in the houshold	No	1,469 (77.6)	1,892	ref.		0.22
	Yes	243 (74.5)	326	0.84	0.64-1.10	
No. of people in the household	More than one	1,636 (77.9)	2,099	ref.		< 0.001
	only one	76 (63.9)	119	0.50	0.34-0.74	

Footnotes are in Table 4.

Table 7. Multivariable analysis for factors associated with rabies vaccination status by dog size

37 1.11	T 1	Large size		Medium size		Small size	
Variable	Level	OR (95% CI)	$P^{1)}$	OR (95% CI)	$P^{(1)}$	ref. 1.04 (0.82-1.32) 2.30 (1.03-5.14) 1.22 (0.73-2.06) ref. 0.88 (0.63-1.14) 0.62 (0.46-0.83) 0.50 (0.34-0.73) ref. 0.85 (0.63-1.14)	$P^{1)}$
Keeping style of dogs	Only inside	ref.	0.512)	ref.	0.242)	ref.	0.142)
	Mainly inside	1.32 (0.60-2.90)	0.48	0.95 (0.61-1.47)	0.81	1.04 (0.82-1.32)	0.76
	Mainly outside	1.66 (0.65-4.23)	0.28	1.09 (0.66-1.79)	0.74	2.30 (1.03-5.14)	0.04
	Only outside	0.92 (0.45-1.85)	0.81	0.75 (0.53-1.08)	0.12	1.22 (0.73-2.06)	0.44
Frequency of walking dog per	More than 13 times	ref.	$0.01^{2)}$	ref.	$< 0.001^{2)}$	ref.	$< 0.001^{2)}$
week	7–13 times	0.55 (0.26-1.17)	0.12	0.68 (0.47-0.99)	0.04	0.88 (0.63-1.14)	0.42
	1-6 times	0.40 (0.19-0.87)	0.02	0.59 (0.41-0.87)	0.007	0.62 (0.46-0.83)	0.001
	None	0.21 (0.08-0.58)	0.002	0.24 (0.14-0.40)	< 0.001	0.50 (0.34-0.73)	< 0.001
Frequency of encounters with	10 times			ref.	$< 0.001^{2)}$	ref.	$0.002^{2)}$
other dogs per 10 walks	5-9 times			0.63 (0.42-0.95)	0.03	0.85 (0.63-1.14)	0.27
	Less than 5 times			0.43 (0.29-0.65)	< 0.001	0.61 (0.46-0.82)	0.001
No. of people in the	More than one			ref.		ref.	
household	Only one			0.44 (0.25-0.78)	0.005	0.52 (0.35-0.77)	0.001

<sup>1):</sup> P value of Wald tests.

"Frequency of encounters with other dogs per 10 walks" were found to be associated with vaccination status in all dog sizes. "Number of dogs kept" for large- and small-sized dogs, "Keeping style of dogs" and "Number of people in the household" for medium- and small-sized dogs, "Presence of cat" for large- and medium-sized dogs, and "Type of accommodation" for small-sized dogs were found to be significant at P < 0.20 and were used as candidate variables for the multivariable model.

Table 7 shows the results of the final multivariable model for each dog size. Only "Frequency of walking

dog per week" was found to be a common significant factor associated with favorable vaccination status among all sizes. The herds categorized as "Untied" in the variable representing "Keeping style of dogs" were excluded from the final model because they were not asked the question "Frequency of walking dog per week." "Frequency of encounters with other dogs per 10 walks" and "Number of people in the household" were significant in the models for medium- and small-sized dogs. Multicollinearity was not observed for significant variables.

<sup>2):</sup> P value of the log-likelihood ratio (LR) test.

#### DISCUSSION

Because Japan has been free from rabies for more than half a century, the perception of disease risk may have declined among pet owners, health care providers, and society. There has been concern that rabies vaccination coverage has been decreasing; however, few studies have been conducted to estimate the coverage rate across Japan. To our knowledge, this is the first study estimating the overall prevalence of effective immunity against rabies among the dog population in Japan. Dogs were classified into three populations, i.e., P<sub>90</sub>, P<sub>75</sub>, and P<sub>RISK</sub>, based on their vaccination history. Our results showed that 76.9% (95% CI, 75.8-78.1) of dogs in the study population belonged to P<sub>90</sub>, which has a preferable vaccination history, and 90% of these could be assumed to have valid antibody levels. Although the actual antibody titer levels were not examined in our study, vaccination history is a very useful alternative to immune status. Therefore, the relatively high proportion of P<sub>90</sub> identified in the overall study area may suggest that the vaccination coverage rate is not as low as expected in Japan. However, our study results covered only owned dogs and not stray dogs. A previous study reports that less than 30% of examined stray dogs were found to possess a protective immune status (7). Although the number of stray dogs in Japan is very small, the existence of these stray dogs may lessen the actual number of dogs with effective immunity. Thus, the population size of stray dogs and their immune status against rabies should be further investigated to obtain the true picture of immune status among the dog population in Japan.

The factors associated with vaccination history were analyzed to identify the population with low vaccination coverage. The frequency of dog walking was found to be strongly associated with rabies immune status presumed using the vaccination history for dogs of all sizes. Although not all of the point estimates of OR were statistically significant, there was a general decreasing trend as the frequency of walking decreased. The odds of having a preferable vaccination history among herds that did not go for walks at all were 0.21, 0.24, and 0.50 times than that of those who walked more than 13 times a week in herds of large-, medium-, and small-sized dogs, respectively. This result suggests that dogs not taken for a walk would have a markedly lower level of presumed antibody status than others, regardless of their size. Although it is difficult to define causal relationships between the explanatory variable and rabies vaccination status because of the limitations of cross-sectional studies, one possible explanation is that dog owners would consider taking dogs for walks as increasing their risk of rabies infection. Thus, dog owners who tend to take dogs for walks might be more likely to have their dogs vaccinated. Interestingly, fewer encounters with other dogs was found to be associated with less preferable vaccination status for medium- and smallsized dogs. The frequency of encounters might positively correlate with the distance of walking and could be closely related to the owners' concern for the health of their pets. Dog owners with more concern about the health of their pets might be more likely to have their dogs vaccinated against rabies. Further, owners of dogs

who are more likely to be exposed to other dogs during dog walks would tend to have better recognition of the risk of rabies.

Being a single-person household was found to decrease the odds of vaccination significantly by a factor of 0.44 (95% CI, 0.25–0.78) and 0.52 (95% CI, 0.35–0.77) compared with households with more than one person for medium- and small-sized dogs, respectively. This may be related to easier access to a vaccination service among households with more than one person compared with single-person households. Thus, developing campaigns that provide easier access to vaccination services should be considered for achieving higher overall vaccination coverage.

A low risk of rabies introduction through the animal quarantine service has been demonstrated by a release of a recent assessment (1). However, the increased ease of international travel has increased the risk of rabies entry via illegal means; this should not be neglected. Preparation for such scenarios is necessary to minimize the adverse outcomes of rabies entry. Therefore, it is essential to simulate the transmission behavior of rabies under hypothetical scenarios and to arrange control measures against disease spread. Many studies have been conducted to predict the transmission dynamics of rabies and assess the effects of control measures against rabies using mathematical models (8-12). However, data on quantitative information that is essential for model building, such as vaccination coverage and behavior of dogs and their owners in Japan, is lacking. Our study estimated the proportion of dogs with effective immunity against rabies using their vaccination history. In addition, we quantitatively described the daily walking activity and contact pattern between dogs during their walks. These factors were further identified to be associated with preferable vaccination status, suggesting the critical characteristics of heterogeneity among the dog population. These results will be indispensable for further simulation of rabies disease transmission.

In the United States, it has been reported that approximately 92% of 6,154 rabid animals were in the wild in 2010 (13), suggesting the important role of wildlife in the epidemiology of disease in rabies endemic countries. Our study revealed that 71.3% of households had witnessed stray and wild animals including dogs, cats, foxes, raccoons, and raccoon dogs roaming around their houses or during dog walks (data not shown), which implies that contact between wildlife and domestic dogs could easily occur, even in Japan. Therefore, further studies should also quantitatively assess the risk of rabies transmission between domestic dogs and wild animals to prepare a rabies introduction scenario.

It should be noted that our study might be subject to some miscellaneous biases. We used a web-based survey using voluntary registered panels. Although this method has been reported to be used in only 1% of recent epidemiological research (14), many studies have already been conducted in other disciplines to characterize its validity and issues, especially selection bias such as under coverage and non-response error (15–17), and to develop methods of reducing its bias (18–22). One of the sources of selection bias in web-based surveys is under coverage. The population selected by web-based surveys

has been known not to cover the target population well because some of the population might not have internet access (15). In addition, those who register to access panels might be skewed from the general population in terms of age, gender, and life style (16). Another source of selection bias is non-response error. The response to the study questionnaire depends thoroughly on the willingness of individuals; thus, a difference in population make-up could exist between those responding to the questionnaire and those that do not. However, the traditional mode of data collection also has this limitation. Internet access has improved through the recent dramatic development of technology. The non-response error can be reduced by introducing a monetary incentive and providing a PDF questionnaire (21,22). In our study, a monetary incentive was provided to reduce non-response bias. The biased results from web-based surveys can be adjusted by several methods such as propensity weighting (18-20). This adjustment method compares the difference between groups that participate in the web-based survey and those that do not; thus, information from both populations is required. However, in our study, there is no information regarding potential differences in population characteristics between registered participants who own dogs and the general dog owner population in the country; hence, it is impossible to evaluate how these potential biases affected the results. We designed our study to employ a well-known and common access panel that could be assumed to cover various populations and reduce bias as much as possible. On the other hand, our study objective would have hardly been achieved if we had used traditional methods such as paper-based questionnaires because they are expensive and time consuming. In addition, it is very likely that not all dogs are registered in Japan; thus, households with dogs would need to be identified in advance by a preliminary survey with a large enough coverage to collect enough data from households with dogs. In contrast, our study using a web-based survey could employ 4,000 households encompassing the whole area of Japan. In addition, web-based surveys have a strong advantage as they enable respondents to avoid face-to-face questions. This is especially useful for increasing the accuracy of responses to sensitive questions because respondents would be less hesitant to tell the truth (14,23). As annual rabies vaccination for dogs is mandatory under the current laws in Japan, our study objective of obtaining information on vaccination history should be sensitive enough to take advantage of a web-based survey. Further examination of the validity and generalizability of our results is needed; however, we believe a web-based survey was a practical method for our study objective.

The present study provides significant information that fills the gap between current knowledge and that required for quantitative assessment. This will enable us to establish a mathematical model to simulate rabies transmission dynamics, which will in turn deliver critical information regarding rabies risk for domestic dogs and public health in the case of rabies reentry into Japan. Further, our study contributes to the development of an efficient strategy to improve overall rabies vaccination coverage by focusing on those identified as being a low coverage population.

Conflict of interest None to declare.

#### REFERENCES

- 1. Kamakawa, H., Koiwai, M., Satomura, S., et al. (2009): Quantitative assessment of the risk of rabies entering Japan through the importation of dogs and cats from the USA. Epidemiol. Infect., 137, 1149-1154.
- 2. Tamashiro, H., Matibag, G., Ditangco, R., et al. (2007): Revisiting rabies in Japan: is there cause for alarm? Travel Med. Infect. Dis., 5, 263-275.
- 3. Ministry of Health, Labour and Welfare (2011): "Number of Registered Dogs and Number of Dogs Vaccinated against Rabies by Prefecture in Japan, 2004–2009." Online at <a href="http://www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou10/01.html">http://www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou10/01.html</a> (in Japanese).
- 4. World Health Organization (2004): Expert Consultation on Rabies: First Report. World Health Organization, Geneva.
- 5. Japan Veterinary Medical Association (2008): Online at <a href="http://www.scj.go.jp/ja/info/kohyo/pdf/kohyo-22-t62-3.pdf">http://www.scj.go.jp/ja/info/kohyo/pdf/kohyo-22-t62-3.pdf</a> (in Japanese).
- Ezoe, S., Ohmori, T., Kusanagi., K., et al. (2007): Efficacy and safety of Japanese rabies vaccine (inactivated) in dogs according to the injection method mandated the Import-Export Quarantine Regulation for Dogs and Other Animals. J. Jpn. Vet. Med. Assoc., 60, 873–878 (in Japanese).
- Ogawa, T., Gamoh, K., Kanda, K., et al. (2009): Rabies immune status of dogs brought into the Hyogo Prefecture Animal Wellbeing Center, Japan. J. Vet. Med. Sci., 71, 825–826.
- Coleman, P. and Dye, C. (1996): Immunization coverage required to prevent outbreaks of dog rabies. Vaccine, 14, 185–186.
- 9. Kitala, P., McDermott. J., Coleman. P., et al. (2002): Comparison of vaccination strategies for the control of dog rabies in Machakos District, Kenya. Epidemiol. Infect., 129, 215-222.
- Haydon, D., Randall, D., Mattews, L., et al. (2006): Lowcoverage vaccination strategies for the conservation of endangered species. Nature, 443, 692-695.
- 11. Hampson, K., Dushoff, J., Cleaveland, S., et al. (2009): Transmission dynamics and prospects for the elimination of canine rabies. PLoS Biol., 7, 462–471.
- Zinsstag, J., Dürr, S., Penny, M., et al. (2009): Transmission dynamics and economics of rabies control in dogs and humans in an African city. Proc. Natl. Acad. Sci. USA, 106, 14996-15001.
- Blanton, J., Palmer, D., Dyer, J., et al. (2011): Rabies surveillance in the United States during 2010. J. Am. Vet. Med. Assoc., 239, 773-783.
- van Gelder, M.M.H.J., Bretveld, R.W., Roeleverd, N., (2010): Web-based questionnaires: the future in epidemiology? Am. J. Epidemiol., 172, 1292-1298.
- 15. Couper, M. (2000): Web surveys: a review of issues and approaches. Public Opin. Q., 64, 464-494.
- Ohsumi, N. (2002): Internet surveys: a review of several experimental results—applying data science approach to the exploration of internet surveys—. Jpn. J. Behaviormetrics, 29, 20-44 (in Japanese).
- Bethlehem, J. (2010): Selection bias in web surveys. Int. Stat. Rev., 78, 161-188.
- Rosenbaum, R. and Rubin, B. (1984): Reducing bias in observational studies using subclassification on the propensity score. J. Am. Statist. Assoc., 79, 516-524.
- Duffy, B., Smith, K., Terhanian, G., et al. (2005): Comparing data from online and face-to-face surveys. Int. J. Market Res., 47, 615-639.
- Hoshino, T. (2007): An experimental research of reproducibility of bias reduction using propensity score adjustment for internet marketing surveys. Jpn. J. Behaviormetrics, 34, 33-48 (in Japanese).
- Edwards, P.J., Roberts, I., Clarke, M.J., et al. (2009): Methods to increase response to postal and electronic questionnaires. Cochrane Database Syst. Rev., 8, MR0000008.
- 22. Ekman, A., Dickman, P.W., Klint, A., et al. (2006): Feasibility of using web-based questionnaires in large population-based epidemiological studies. Eur. J. Epidemiol., 21, 103-111.
- 23. Wright, K. (2005): Researching internet-based populations: advantages and disadvantages of online survey research, online questionnaire authoring software packages, and web survey services. J. Comput. Mediat. Commun., 10, 00.