Prevalence of and Risk Factors for Post-COVID-19 Condition during Omicron BA.5-Dominant Wave, Japan

Arisa Iba, Mariko Hosozawa, Miyuki Hori, Yoko Muto, Isao Muraki, Rie Masuda, Nanako Tamiya, Hiroyasu Iso

The increased risk for post-COVID-19 condition after the Omicron-dominant wave remains unclear. This population-based study included 25,911 persons in Japan 20-69 years of age with confirmed SARS-CoV-2 infection enrolled in the established registry system during July-August 2022 and 25,911 age- and sex-matched noninfected controls who used a self-reported questionnaire in January-February 2023. We compared prevalence and age- and sex-adjusted odds ratios of persistent COVID-19 symptoms (lasting ≥2 months). We evaluated factors associated with post-COVID-19 condition by comparing cases with and without post-COVID-19 condition. We analyzed 14,710 (8,392 cases and 6,318 controls) of 18,183 respondents. Post-COVID-19 condition proportion among cases was 11.8%, higher by 6.3% than 5.5% persistent symptoms among controls. Female sex, underlying medical conditions, mild to moderate acute COVID-19, and vaccination were associated with post-COVID-19 condition. Approximately 12% had post-COVID-19 condition during the Omicron-dominant wave, indicating the need for longer follow-up.

OVID-19 has caused a significant global disease burden since it was first identified in December 2019; as of May 2024, ≥750 million cases had been confirmed, and ≈7.5 million deaths had occurred worldwide (1). In addition to acute illnesses, the prolonged or recurrent symptoms occurring after an initial infection SARS-CoV-2, referred to as post-COVID-19 condition (2), have also raised concerns.

More than 65 million persons worldwide have post–COVID-19 condition (3). On the basis of Author affiliations: National Center for Global Health and Medicine, Tokyo, Japan (A. Iba, M. Hosozawa, M. Hori, Y. Muto, H. Iso); Osaka University, Osaka, Japan (I. Muraki); University of Tsukuba, Ibaraki, Japan (R. Masuda, N. Tamiya)

DOI: http://doi.org/10.3201/eid3007.231723

estimates of those infected during March 2020–November 2021, a total of 10%–30% of nonhospitalized case-patients and 50%–70% of hospitalized case-patients have had post–COVID-19 condition. Frequently reported symptoms included fatigue, dyspnea, neurocognitive impairment, and loss of smell in patients infected during January 2020–August 2021 (4–8). The risk of developing post–COVID-19 condition was higher in female patients, those with severe acute COVID-19, or those with a greater number of acute symptoms (4,7,9,10). We noted those results in patients infected with variants before the Omicron variant emerged.

The Omicron variant was identified in November 2021; the BA.5 lineage of that variant was detected in April 2022 and has since spread worldwide. The Omicron variant tends to cause less severe acute symptoms (11) and has a similar or lower risk for post-COVID-19 condition than the previous variants (12-16). However, most previous studies concerning post-COVID-19 condition in relation to the Omicron variant, except those that used electronic health record data (17), were hospital-based (13-15,18-21) or population-based without a control group (12,16,22,23). Longer sequelae and risks for post-COVID-19 condition in persons infected with the Omicron variant compared with noninfected populations remain unknown. As the number of COVID-19 cases has increased, with greater infectivity of the Omicron variant (24) in addition reductions in nonpharmaceutical interventions (e.g., lockdowns, social distancing, mask requirements), it is crucial to investigate the potential long-term consequences of infection with the Omicron variant. We conducted a population-based study of symptoms after acute COVID-19 using a self-reported questionnaire in a large city in Japan. Our objective was to examine the increased risk for persistent symptoms after SARS-CoV-2 infection

compared with a noninfected population, focusing specifically on the Omicron variant (especially the BA.5 lineage). We also investigated the factors associated with post–COVID-19 condition.

Methods

Study Design and Participants

We conducted a population-based study of community-dwelling adults 20–69 years of age who had confirmed SARS-CoV-2 infection during July-August 2022. We extracted data from the Japan Health Center Real-time Information-sharing System on COVID-19 (HER-SYS), the established registry system, and age- and sex-matched controls using a self-reported web-based questionnaire in Shinagawa City, a metropolitan area located in the Tokyo area of Japan. The population of Shinagawa City is ≈400,000 and its population density is 17,700 persons/km².

Japan experienced the 7th wave of COVID-19 in July 2022, caused by the Omicron subvariant BA.5 lineage. The prevalence of the BA.5 lineage increased from 67% in epidemiologic week 27 (July 7–10, 2022) to 92% in epidemiologic week 30 (July 25–31, 2022), becoming dominant (25). When COVID-19 was diagnosed by a positive reverse transcription PCR or a lateral flow antigen test for SARS-CoV-2 or a clinical diagnosis (for symptomatic close contacts), the attending physician was required to document every

case in HER-SYS until September 26, 2022. Patients needed to see a physician to undergo a test for SARS-CoV-2 until the Ministry of Health, Labour, and Welfare approved over-the-counter antigen test kits on August 24, 2022. However, most patients visited a physician even after the over-the-counter antigen test kits became available rather than testing themselves at home. Therefore, most of the infected persons were registered in HER-SYS during the study period.

We selected participants registered in the HER-SYS database who were 20–69 years of age and infected with SARS-CoV-2 during July 1-August 31, 2022. We excluded 3,365 of the 29,276 identified infected residents who had died or moved out of the area and selected the remaining 25,911 infected persons as study participants (infected group). We matched data from HER-SYS and the Basic Resident Registration system (the municipal residence record of the name, birthdate, sex, and address of all residents living in a municipality) to identify noninfected residents who had never been registered in the HER-SYS database during the participant selection. We selected 25,911 age- and sex-matched noninfected persons (noninfected group) from the matched dataset (Figure 1). The ethics committee of the National Center for Global Health and Medicine approved this study (NCGM-S-004571).

We sent research information and invitations to the online questionnaire to the selected participants

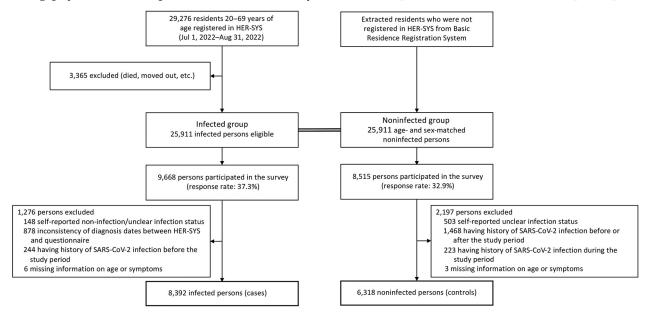


Figure 1. Flowchart of participant selection in study of prevalence and risk factors for post–COVID-19 condition during Omicron BA.5–dominant wave, Japan. Of 29,276 residents 20–69 years of age identified in the municipal HER-SYS database as infected with COVID-19, we selected a total of 25,911 participants; we extracted the same number of age- and sex-matched noninfected residents from the Basic Residence Registration System to serve as the control group. HER-SYS, Health Center Real-time Information-sharing System on COVID-19.

(25,911 each in the infected and noninfected group) by mail on January 11-13, 2023, approximately 6 months after infection for those who had COVID-19 (cases). Respondents were required to provide consent to participate in the study before accessing the website; those who agreed answered the questionnaire by February 13. At the beginning of the questionnaire, we asked participants if they had a diagnosis of COVID-19. If they answered "yes," they were directed to the questions for infected persons, which inquired about the number and date of infection episodes. If they answered "no," "I don't know," or "I prefer not to answer," they were directed to the questions for noninfected persons (Appendix, https://wwwnc. cdc.gov/EID/article/30/7/23-1723-App1.pdf). included persons whose answers on infection status were consistent with HER-SYS data and whose first infection was within the study period.

Post–COVID-19 Condition (Cases) and Persistent Symptoms (Controls)

We asked the participants about the presence of 26 symptoms that emerged during or after the first SARS-CoV-2 infection for cases and in July 2022 for controls. The symptoms were selected from the International Severe Acute Respiratory and Emerging Infection Consortium COVID-19 questionnaire. Symptoms were fever, cough, fatigue, sore throat, chest pain, anorexia, brain fog, difficulty concentrating, anosmia, ageusia, shortness of breath, hair loss, muscle weakness, palpitations, sleep disorder, rhinorrhea, headache, joint pain and swelling, muscle aches, nausea/vomiting, abdominal pain, skin rash, eye-related symptoms, dizziness, erectile dysfunction (male only), and menstrual change (female only) (26). If a symptom was present, we asked about its timing and duration: whether they had the symptom at illness onset or 3 months after infection (infected group only), whether they had it at the time of the survey, and whether the symptom persisted for ≥2 months. For those who affirmed they had any symptoms, we asked the extent to which the symptoms hindered daily life at the time of response using an 11-point scale from 0 (no effect) to 10 (extreme hindrance) and categorized those responses into 4 levels: 0, no effect; 1-3, mild hindrance; 4-6, moderate hindrance; and 7–10, serious hindrance.

For cases, we defined post-COVID-19 condition based on the World Health Organization (WHO) definition (27): a symptom that persisted for ≥2 months after the acute phase. For brain fog, difficulty concentrating, hair loss, and muscle weakness, we defined post-COVID-19 condition as symptoms

having lasted \geq 2 months during the observation period regardless of the timing because those symptoms develop in the subacute phase (17,28). For controls, we defined persistent symptoms as symptoms lasting \geq 2 months experienced between July 2022 and the date of the survey.

Variables

We asked infected persons about the severity of acute COVID-19 and categorized them into 4 groups according to the WHO clinical severity scale: asymptomatic, mild (symptomatic but not admitted to the hospital), moderate (admitted to the hospital, required supplemental oxygen, or both), and severe (received mechanical ventilation or intensive care admission) (29). We counted the number of infections because some participants had been infected >1 time during the observation period. We also asked participants about their demographics (i.e., age at the answering date, sex, height, and weight), underlying medical conditions before the infection (or before July 2022 in the noninfected group), lifestyle, and socioeconomic status (e.g., household income and educational level). We calculated equivalized household income by dividing household income by the square root of the household size. For vaccination status, we extracted the vaccination date, vaccination type, and number of vaccinations from the municipality's Vaccination Record System. We substituted the questionnaire responses for missing values for 1,589 (10%) respondents (e.g., those who had moved from the original municipality).

Statistical Analysis

We determined the participants' characteristics according to their infection status and compared using the *t*-test for continuous variables and χ^2 test for categorical variables. We calculated the proportions of overall and each post-COVID-19 condition (cases) and persistent symptoms (controls). Using multivariable logistic regression analysis, we calculated the age- and sex-adjusted odds ratios of each symptom in the cases compared with the persistent symptoms in the controls as a reference. We also investigated the risk factors associated with post-COVID-19 condition among cases using multivariate logistic regression models. Model 1 comprised age group and sex; model 2, underlying medical conditions, body mass index, severity, and vaccination status before infection; and model 3, household income and educational level. We conducted multiple imputations using chained equations to account for missing data in model 3; the proportion of missing values in household income was 13.1%. We included all explanatory and outcome variables in the imputation model to create 50 imputed datasets. We also calculated the proportion of influence of post-COVID-19 condition on daily life. We defined statistical significance as a 2-sided p value <0.05. We used Stata version 17 MP software (Stata-Corp LLC, https://www.stata.com) for all analyses.

Results

A total of 51,822 persons were invited to participate in the study, of whom 18,183 responded to the question-naire (response rate 35.1%). The response rate was higher in the infected group than in the noninfected group (37.3% vs. 32.9%, difference of 4.4% [95% CI 3.0%–5.8%]). The response rate was higher among female than male persons in all age groups of both infected and noninfected groups. Among male invitees, the difference in response rates between the infected and noninfected groups was large for age groups in their 50s (12.8% [95% CI 8.1%–17.5%]) and 60s (8.5% [95% CI 1.6%–15.4%]) (Table 1).

We excluded 3,473/18,183 respondents for responses of infectious status inconsistent with HER-SYS (answering different infection statuses or different diagnosis date) and reporting a prior infection and 9 because their records were missing data on age or symptoms. A total of 14,710 participants (8,392 cases and 6,318 controls) were eligible for the analysis (Figure 1). Mean age of all participants was 42.4 (SD 11.7) years; 8,502 (57.8%) participants were female and 6,087 (41.4%) male (Table 2). Mean age of case participants was 42.3 (SD 11.6) years; 4,802 (57.2%) case participants were female and 3,535 (42.1%) male. The mean follow-up period from SARS-CoV-2

infection to the response date was 167.9 (SD 14.5) days. Most cases (8,326 [99.2%] patients) demonstrated asymptomatic to mild disease, whereas 66 (0.8%) cases had moderate to severe disease.

The percentage of post-COVID-19 condition for cases was 11.8%, whereas the percentage of persistent symptoms among controls was 5.5% (Figure 2). The prevalence did not differ between cases under followup for <6 months (11.6%) and cases under followup for ≥ 6 months (12.6%). The most frequent post-COVID-19 condition was cough (3.7%), followed by difficulty concentrating (3.1%), hair loss (2.8%), fatigue (2.4%), and brain fog (2.2%). The most frequent persistent symptoms among the controls were sleep disorders (1.3%), followed by cough (0.9%), fatigue (0.7%), and rhinorrhea (0.7%). The age- and sex-adjusted odds ratio (OR) of any persistent symptoms for cases versus controls was 2.33 (95% CI 2.05-2.64). Symptoms with higher OR in cases than controls were ageusia (27.4 [95% CI 6.7-111.8]), muscle weakness (11.8 [95% CI 5.5-25.5]), anosmia (11.6 [95% CI 4.7-28.6]), hair loss (6.5 [95% CI 4.4-9.6]), and brain fog (5.9 [95% CI 3.8-9.0]).

We conducted multivariable logistic regression analysis to investigate the factors associated with post-COVID-19 condition among cases (Table 3, https://wwwnc.cdc.gov/EID/article/30/7/23-1723-T3.htm). In all 3 models, participants 40–49 years of age had higher odds of having post-COVID-19 condition than those 20–29 years (OR 1.26, 95% CI 1.01–1.57 for model 3); female participants had higher odds of having post-COVID-19 condition than male participants (OR 2.00, 95% CI 1.71–2.34). When models were further adjusted, 2 variables were

Table 1. Response rates of persons in study of prevalence and risk factors for post–COVID-19 condition during BA.5 Omicron-dominant wave, Japan*

_	Infected persons					Noninfect	Difference in		
Age	HER-	No.	No.	Response		No.	No.	Response	response rates
group, y	SYS†	participants	responses	rate, %	BRRS‡	participants	responses	rate, %	(95% CI)
Male patient	S								
20–29	3,404	2,979	611	20.5	3,404	2,979	574	19.3	1.2 (-3.3 to 5.7)
30–39	3,806	3,328	1,120	33.7	3,806	3,328	896	26.9	6.8 (2.8–10.8)
40-49	3,461	3,058	1,061	34.7	3,461	3,058	943	30.8	3.9 (-0.2 to 8.0)
50–59	2,586	2,243	923	41.2	2,586	2,243	636	28.4	12.8 (8.1–17.5)
60–69	1,152	1,024	413	40.3	1,152	1,024	326	31.8	8.5 (1.6-15.4)
Subtotal	14,409	12,632	4,129	32.7	14,409	12,632	3,375	26.7	6.0 (3.9–8.1)
Female pation	ents								
20–29	3,682	3,218	960	29.8	3,682	3,218	912	28.3	1.5 (-2.6 to 5.6)
30–39	4,028	3,582	1,565	43.7	4,028	3,582	1,491	41.6	2.1 (-1.4 to 5.6)
40–49	3,671	3,313	1,554	46.9	3,671	3,313	1,423	43.0	3.9 (3.2–7.5)
50–59	2,386	2,166	971	44.8	2,386	2,166	884	40.8	4.0 (-0.5 to 8.5)
60–69	1,100	1,000	402	40.2	1,100	1,000	333	33.3	6.9 (-0.1 to 13.9)
Subtotal	14,867	13,279	5,456	41.1	14,867	13,279	5,047	38.0	3.1 (1.2–5.0)
Total	29,276	25,911	9,668	37.3	29,276	25,911	8,515	32.9	4.4 (3.0-5.8)

*BRRS, Basic Resident Registration system; HER-SYS, Health Center Real-Time Information-Sharing System.

†Numbers of SARS-CoV-2-infected persons extracted from the HER-SYS database.

[‡]Numbers of age- and sex-adjusted noninfected persons extracted from the Basic Resident Registration system database.

Table 2. Characteristics of participants in study of prevalence and risk factors for post-COVID-19 condition during BA.5 Omicron-

dominant wave. Japan*

dominant wave, Japan* Characteristic	Cases, n = 8,392	Controls, n = 6,318	p value
Mean age, y (+SD)	42.3 (+11.6)	42.4 (+11.8)	0.63
Age group, y	.2.0 ()	.2 ()	0.29
20–29	1,316 (15.7)	1,036 (16.4)	0.20
30–39	2,340 (27.9)	1,674 (26.5)	
40–49	2,326 (27.7)	1,766 (28.0)	
50–59	1,695 (20.2)	1,270 (20.1)	
60–70†	715 (8.5)	572 (9.1)	
Patient sex	7 10 (0.0)	072 (0.1)	0.01
M	3,535 (42.1)	2,552 (40.4)	0.01
F	4,802 (57.2)	3,700 (58.6)	
Prefer not to answer	55 (0.7)	66 (1.0)	
Mean BMI, kg/m² (+SD)	22.1 (±3.5)	22.3 (<u>+</u> 3.8)	0.08
BMI, kg/m ²	22.1 (<u>1</u> 3.3)	22.3 (<u>1</u> 3.0)	0.001
<18.5	932 (11.1)	757 (12.0)	0.001
18.5–25.0	5,902 (70.3)	4,271 (67.6)	
16.5–25.0 ≥25.0	1,406 (16.8)	1,174 (18.6)	
Underlying medical conditions‡	1,400 (10.8)	1,174 (10.0)	0.01
, ,	C 445 (7C 0)	4.750 (75.0)	0.01
0	6,445 (76.8)	4,752 (75.2)	
1	1,382 (16.5)	1,057 (16.7)	
<u>>2</u>	565 (6.7)	509 (8.1)	0.44
Hypertension	557 (6.6)	441 (7.0)	0.41
Dyslipidemia	396 (4.7)	362 (5.7)	0.01
Respiratory diseases	394 (4.7)	317 (5.0)	0.37
Depression/anxiety	272 (3.2)	243 (3.8)	0.05
Heart diseases	197 (2.3)	180 (2.8)	0.06
Malignancy	169 (2.0)	131 (2.1)	0.80
Diabetes	152 (1.8)	167 (2.6)	0.001
No. COVID-19 vaccinations§	205 (2.2)	440 (0.5)	<0.001
0	685 (8.2)	412 (6.5)	
1	49 (0.6)	28 (0.4)	
2	1,675 (20.0)	1,145 (18.1)	
<u>></u> 3	5,983 (71.3)	4,733 (74.9)	
Household income, ¥			0.002
<4 million	2,520 (34.5)	2,022 (32.0)	
4–8 million	3,699 (50.7)	2,614 (41.4)	
≥8 million	1,077 (14.8)	858 (13.6)	
Education level			0.68
High school or lower	1,242 (14.8)	961 (15.2)	
Some college	1,710 (20.4)	1,259 (19.9)	
College or higher	5,299 (63.1)	4,004 (63.4)	
Mean follow-up, d (±SD)	167.9 (<u>+</u> 14.5)	NA	
No. SARS-CoV-2 infections			
1	8,284 (98.7)	NA	
2	108 (1.3)	NA	
Severity of infection	. ,		
Asymptomatic	228 (2.7)	NA	
Mild	8,098 (96.5)	NA	
Moderate/severe	66 (0.8)	NA	

^{*}Values are no. (%) except as indicated. Continuous variables were compared by using *t*-tests; categorical variables were compared by using χ² tests. BMI, body mass index; NA, not applicable.

associated with having post–COVID-19 condition: having any underlying medical conditions (OR 1.36, 95% CI 1.16–1.59, compared with no underlying medical conditions), and severity of acute COVID-19 (mild, OR 2.07, 95% CI 1.18–3.66; moderate, OR 4.49, 95% CI 1.97–10.23, compared with asymptomatic). Those participants vaccinated before infection had lower odds of developing post–COVID-19 condition

(OR 0.75, 95% CI 0.60–0.95, compared with unvaccinated). Socioeconomic status, including household income and educational level, was not associated with post–COVID-19 condition.

Among the 992 cases who had experienced any post-COVID-19 condition, 84 (8.5%) answered that the condition was a serious hindrance on their daily lives at the time of response. A total of 402 (40.5%)

[†]Includes patients who turned 70 years of age between the participant selection and survey periods.

[‡]Respiratory diseases included interstitial lung diseases, asthma, and chronic obstructive pulmonary diseases. Heart diseases included myocardial infarction, angina, heart failure, arrhythmia, myocarditis, and cardiomyopathy. Mental disorder included anxiety and depression. §Number of vaccinations administered until 14 d before infection (cases) or before June 2022 (controls).

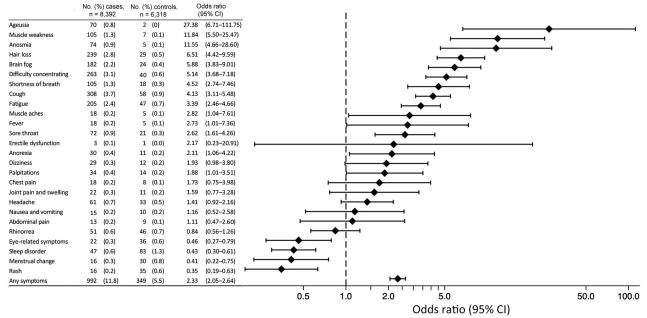


Figure 2. Prevalence and age- and sex-adjusted odds ratios of persistent symptoms in cases compared with controls in study of prevalence and risk factors for post–COVID-19 condition during Omicron BA.5–dominant wave, Japan. All cases and controls are included in the multivariable logistic regression analysis to estimate the odds ratio of developing post–COVID-19 condition among cases compared with controls adjusting for age (as a continuous variable) and sex.

noted that it was no hindrance, 362 (36.5%) mild hindrance, and 144 (14.5%) moderate hindrance.

Discussion

We conducted a population-based study using a self-reported questionnaire among adults in Japan who had confirmed SARS-CoV-2 infection during July-August 2022, when the Omicron BA.5 subvariant was dominant. We compared their post-COVID-19 condition with concordant persistent symptoms among noninfected controls. The percentage of post-COVID-19 condition was 11.8% for cases, which was 2.3 times higher than the 5.5% of persistent symptoms noted in controls. The cases had a 6.2% higher prevalence of post-COVID-19 condition than the controls, suggesting that their symptoms were likely associated with SARS-CoV-2 infection.

Population-based studies of infected persons in the United Kingdom (n = 56,003) and the United States (n = 1,480) using smartphone applications reported that the prevalence of post–COVID-19 condition associated with the Omicron variant, defined as symptoms lasting 4 weeks after the infection, was 4.5%–18.7% (12,23). Another population-based study of infected persons in the United States (n = 16,091) showed a prevalence of 11.2% (16) applying the WHO definition of the continuation or development of new symptoms 3 months after the initial SARS-CoV-2 infection, with those symptoms lasting for ≥ 2 months with no other explanation (27).

Although the definition of post-COVID-19 condition varies among previous studies (12,16,23,27), the proportion shown in our study is consistent with previous results. In those reports, post-COVID-19 condition was less prevalent among those infected during the Omicron variant-dominant wave than those infected during the previous waves with the ancestral strain predominance (16,23). However, although a multicenter prospective cohort study showed a higher proportion of prolonged severe fatigue and multiple symptoms at 3 months during the pre-Delta wave than that during the Delta and Omicron waves, the differences disappeared after accounting for sociodemographics and vaccination status (19). Systematic reviews suggested that vaccination before infection was associated with a lower risk of experiencing post-COVID-19 condition (30,31). Similarly, we found that vaccination before infection was associated with lesser post-COVID-19 condition. An in-depth study would clarify whether the reduced risk for post-COVID-19 condition during the Omicron wave was a result of the differences in strains, the effect of vaccination, or both.

Population-based large cohort studies in the United Kingdom (n = 606,434 and n = 486,149) and Germany (n = 11,710) reported that patients infected with previous-variant SARS-CoV-2 frequently experienced persistent symptoms such as fatigue, shortness of breath, concentration difficulties, memory disturbance, hair loss, and anosmia (5,7,32). Studies

on patients infected with the Omicron variant, including a population-based study in the United States (n = 16,091) and hospital-based studies from China (n = 1,829) and India (n = 524), revealed that fatigue, brain fog, cough, and shortness of breath were frequently observed as post–COVID-19 condition (13,16,33). Our findings were comparable with previous results; we observed that post–COVID-19 condition after the Omicron-dominant epidemic frequently included

neurologic symptoms such as difficulty concentrating, fatigue, and brain fog, in addition to cough and hair loss. In addition, those neurologic symptoms, as well as ageusia, anosmia, and muscle weakness, were distinctive symptoms among cases, who showed a higher OR than controls. Fatigue and neurocognitive impairment are reportedly related to impaired health recovery and reduced working capacity, even among young and middle-aged adults, after mild infection

Table 3. Factors as									
	No. at risk,	No. (%) cases,†			Model 2		Model 3		
Factor	n = 8,392	n = 992	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value	
Age group, y									
20–29	1,316	134 (10.2)	Referent	NA	Referent	NA	Referent	NA	
30–39	2,340	289 (12.4)	1.31	0.02	1.23	0.07	1.22	0.08	
		, ,	(1.05-1.63)		(0.98-1.54)		(0.97-1.52)		
40-49	2,326	307 (13.2)	1.40	0.003	1.32	0.01	1.26	0.05	
	•	,	(1.12 - 1.74)		(1.06-1.65)		(1.01-1.57)		
50-59	1,695	206 (12.2)	` 1.33 [′]	0.02	1.23	0.10	1.16	0.24	
	,	,	(1.05-1.69)		(0.96-1.56)		(0.91-1.48)		
60–70	715	56 (7.8)	0.83	0.28	0.75	0.10	0.70	0.04	
00 .0		00 (1.10)	(0.60–1.16)	0.20	(0.53–1.05)	00	(0.50-0.98)	0.0.	
Patient sex			(0.000)		(0.0000)		(0.00 0.00)		
M	3,535	280 (7.9)	Referent	NA	Referent	NA	Referent	NA	
F	4,802	703 (14.6)	1.98	<0.001	2.05	<0.001	2.00	<0.001	
•	1,002	100 (11.0)	(1.71–2.30)	0.001	(1.76–2.39)	0.001	(1.71–2.34)	0.001	
Underlying medica	l conditions		(1.7.1 2.00)		(1.70 2.00)		(1.7.1 2.01)		
Yes	1.947	263 (13.5)	NA	NA	1.36	< 0.001	1.36	< 0.001	
100	1,011	200 (10.0)			(1.15–1.60)	0.001	(1.16–1.59)	0.001	
No	6,445	729 (11.3)	NA	NA	Referent		Referent	NA	
BMI, kg/m ²	0,110	120 (11.0)	101	10.0	rtororont		rtororon	147	
<18.5	932	119 (12.8)	NA	NA	0.94	0.59	0.94	0.58	
10.0	002	110 (12.0)	14/1	147 ((0.76–1.17)	0.00	(0.76–1.16)	0.00	
18.5–25.0	5.902	686 (11.6)	NA	NA	Referent		Referent	NA	
>25.0	1,406	162 (11.5)	NA	NA	1.09	0.36	1.09	0.39	
<u>-</u> 20.0	1,400	102 (11.0)	14/1	147 ((0.90–1.32)	0.00	(0.90–1.31)	0.00	
Severity of acute C	:OVID-19				(0.00 1.02)		(0.00 1.01)		
Asymptomatic	228	13 (5.7)	NA	NA	Referent		Referent	NA	
Mild	8.098	965 (11.9)	NA	NA	2.00	0.02	2.07	0.01	
WIIIG	0,000	000 (11.0)	14/1	147 ((1.13–3.52)	0.02	(1.18–3.66)	0.01	
Moderate	64	14 (21.9)	NA	NA	4.00	0.001	4.49	<0.001	
Moderate	04	14 (21.0)	14/1	147 ((1.73–9.23)	0.001	(1.97–10.23)	-0.001	
Severe	2	0	NA	NA	NA	NA	(1.57–10.25) NA	NA	
Vaccination before		<u> </u>	14/1	147 (10/1	14/1	14/ (14/1	
Yes	7,707	890 (11.5)	NA	NA	0.74	0.01	0.75	0.02	
100	1,101	000 (11.0)	14/1	147 ((0.59–0.92)	0.01	(0.60–0.95)	0.02	
No	685	102 (14.9)	NA	NA	Referent	NA	Referent	NA	
Household income		102 (14.0)	14/1	147 (rtororont	14/1	TOTOTOTIC	14/ (
<4 million	2.520	295 (11.7)	NA	NA	NA	NA	Referent	NA	
4–8 million	3,699	433 (11.7)	NA NA	NA	NA	NA	1.05	0.54	
4-0 111111011	3,033	400 (11.7)	INA	INA	INA	INA	(0.89–1.25)	0.54	
>8 million	1,077	128 (11.9)	NA	NA	NA	NA	1.10	0.43	
<u>~</u> 0 1111111011	1,077	120 (11.9)	INA	INA	INA	INA	(0.87–1.40)	0.43	
Education level							(0.07-1.40)		
High school or	1,242	137 (11.0)	NA	NA	NA	NA	Referent	NA	
lower	1,242	137 (11.0)	INA	INA	INA	INA	I/CICICIII	INA	
Some college	1.710	252 (14.7)	NA	NA	NA	NA	1.20	0.12	
Some conege	1,7 10	232 (14.1)	INA	INA	INA	INA	(0.95–1.50)	0.12	
College or	5,299	583 (11.0)	NA	NA	NA	NA	(0.95–1.50)	0.92	
	3,233	303 (11.0)	INA	INA	INA	INA		0.52	
higher		ina multivariable legic					(0.82–1.25)		

^{*}Associations were determined by using multivariable logistic regression models for 8,392 infected persons (cases). Model 1 included age (as a categorical variable) and sex; model 2 added preexisting medical conditions (factor variable), BMI (categorical variable), severity of acute COVID-19 (categorical variable), and vaccination before infection (factor variable); model 3 added household income and education level (categorical variables). BMI, body mass index; NA, not applicable; OR, odds ratio. †Number of cases who had post—COVID-19 condition.

(7). Our results showed that ≈10% of those who had post-COVID-19 condition had persistent difficulties in daily living 4.5–7 months after the Omicron-dominant wave, which may have led to a deterioration in economic conditions or work productivity. Although background socioeconomic status was not associated with developing post-COVID-19 condition in this study, further investigation is required to evaluate the effect of post-COVID-19 condition on changes in economic conditions, schooling, and employment.

Large-scale population-based cohort studies on infection before the Omicron wave found that post-COVID-19 condition was more common in female persons, smokers, persons with obesity, those with more severe acute COVID-19 symptoms, and those who were deprived or had lower household income (5,7,32). Moreover, hospital-based studies in China (n = 21,799) and South Africa (n = 4,685) showed that the female sex, concurrent conditions, and severe acute illnesses were associated with post-COVID-19 condition in association with the Omicron variant (14,21), which was consistent with our findings. Although the results regarding age are unclear, some studies on the Omicron variant have suggested that the population 18-50 years of age has a higher risk for post-COVID-19 condition (21,34). Our study showed that post-COVID-19 condition for those infected during the Omicron-dominant epidemic was also more prevalent in middle-aged persons. A substantial proportion of the working-age population might have been affected; of 9 million persons infected during July-August 2022 in Japan, 31.2% were in their 30s and 40s (35).

The strengths of this study are the large number of participants including noninfected controls, the population-based approach, and the inclusion of all infected residents registered in the HER-SYS database within a municipality. We compared the infected persons with noninfected persons as a control and assessed the proportion of post-COVID-19 condition after the Omicron-dominant wave.

The first limitation of this study is that the response rate was higher among the infected group than the noninfected group overall. The infected participants may have been more interested in the survey on COVID-19 and post-COVID-19 condition. However, because we did not specify the purpose of the survey to investigate the post-COVID-19 condition but rather informed the participants that we aimed to investigate the effect of the pandemic on their health and daily lives, we believe that the influence of interest in post-COVID-19 condition on the responses to the questionnaire was small. Moreover, the response rate was higher for infected and noninfected female

participants and middle-aged infected male participants; this finding could have been because those persons were inherently willing to answer questionnaires more than other persons, or because patients with those attributes (such as female sex and middle age) suffered more from persistent symptoms and had a higher motivation to answer the questionnaire. The results could be biased in both ways; however, we believe the effect was small because the higher odds of having post-COVID-19 condition in our study were consistent with findings from previous studies. Second, although we excluded those who self-reported having SARS-CoV-2 infection, it is possible that some infected persons were included in the controls, causing an underestimation of the difference in persistent symptoms between the cases and controls. Third, because the study was retrospective, recall bias may have occurred. In addition, because we relied on self-reporting, we could not rule out the possibility that the participants' symptoms were caused by conditions other than COVID-19. However, we estimated the symptoms attributable to COVID-19 by comparing with a noninfected control group. Finally, although this study included all infected persons registered in the nationally established registry system, caution is needed to generalize the results of this single-city analysis to other populations in Japan.

In this population-based study, 11.8% of patients with COVID-19 had post-COVID-19 condition during the Omicron-dominant wave; this rate was 2.3 times higher than the persistent symptoms among noninfected controls. Among the cases, female sex, underlying medical conditions, and severity of acute COVID-19 were associated with having post-COVID-19 condition. We recommend a longer follow-up study of the effects on daily life and socioeconomic status after infection during the Omicron-dominant wave.

Acknowledgments

We thank Keiko Fukuuchi, Atsuko Abe, Shoji Sakano, and the staff of Shinagawa City Public Health Center for their cooperation in conducting this study.

This work was supported by MHLW Research on Emerging and Re-emerging Infectious Diseases and Immunization (program grant no. JPMH21HA2011).

About the Author

Dr. Iba is a senior research fellow at the Institute for Global Health Policy Research, Bureau of International Health Cooperation, National Center for Global Health and Medicine, Tokyo, Japan. Her research focuses on epidemiology and health services research.

References

- World Health Organization. WHO COVID-19 dashboard [cited 2023 Aug 29]. https://covid19.who.int
- Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV; WHO Clinical Case Definition Working Group on Post-COVID-19 Condition. A clinical case definition of post-COVID-19 condition by a Delphi consensus. Lancet Infect Dis. 2022; 22:e102-7. https://doi.org/10.1016/S1473-3099(21)00703-9
- Davis HE, McCorkell L, Vogel JM, Topol EJ. Long COVID: major findings, mechanisms and recommendations. Nat Rev Microbiol. 2023;21:133–46. https://doi.org/10.1038/ s41579-022-00846-2
- Huang L, Li X, Gu X, Zhang H, Ren L, Guo L, et al. Health outcomes in people 2 years after surviving hospitalisation with COVID-19: a longitudinal cohort study. Lancet Respir Med. 2022;10:863–76. https://doi.org/10.1016/ S2213-2600(22)00126-6
- Whitaker M, Elliott J, Chadeau-Hyam M, Riley S, Darzi A, Cooke G, et al. Persistent COVID-19 symptoms in a community study of 606,434 people in England. Nat Commun. 2022;13:1957. https://doi.org/10.1038/s41467-022-29521-z
- Ballering AV, van Zon SKR, Olde Hartman TC, Rosmalen JGM; Lifelines Corona Research Initiative. Persistence of somatic symptoms after COVID-19 in the Netherlands: an observational cohort study. Lancet. 2022;400:452-61. https://doi.org/10.1016/S0140-6736 (22)01214-4
- Peter RS, Nieters A, Kräusslich HG, Brockmann SO, Göpel S, Kindle G, et al.; EPILOC Phase 1 Study Group. Post-acute sequelae of covid-19 six to 12 months after infection: population based study. BMJ. 2022;379:e071050. https://doi.org/10.1136/bmj-2022-071050
- Sudre CH, Murray B, Varsavsky T, Graham MS, Penfold RS, Bowyer RC, et al. Attributes and predictors of long COVID. Nat Med. 2021;27:626–31. https://doi.org/10.1038/ s41591-021-01292-y
- Menges D, Ballouz T, Anagnostopoulos A, Aschmann HE, Domenghino A, Fehr JS, et al. Burden of post-COVID-19 syndrome and implications for healthcare service planning: a population-based cohort study. PLoS One. 2021;16:e0254523. https://doi.org/10.1371/journal.pone.0254523
- Sigfrid L, Drake TM, Pauley E, Jesudason EC, Olliaro P, Lim WS, et al.; ISARIC4C investigators. Long COVID in adults discharged from UK hospitals after COVID-19: a prospective, multicentre cohort study using the ISARIC WHO Clinical Characterisation Protocol. Lancet Reg Health Eur. 2021;8:100186. https://doi.org/10.1016/ j.lanepe. 2021.100186
- Menni C, Valdes AM, Polidori L, Antonelli M, Penamakuri S, Nogal A, et al. Symptom prevalence, duration, and risk of hospital admission in individuals infected with SARS-CoV-2 during periods of omicron and delta variant dominance: a prospective observational study from the ZOE COVID Study. Lancet. 2022;399:1618–24. https://doi.org/10.1016/ S0140-6736(22)00327-0
- Antonelli M, Pujol JC, Spector TD, Ourselin S, Steves CJ. Risk of long COVID associated with delta versus omicron variants of SARS-CoV-2. Lancet. 2022;399:2263-4. https://doi.org/10.1016/S0140-6736(22)00941-2
- Arjun MC, Singh AK, Roy P, Ravichandran M, Mandal S, Pal D, et al. Long COVID following Omicron wave in Eastern India – a retrospective cohort study. J Med Virol. 2023;95:e28214. https://doi.org/10.1002/jmv.28214
- 14. Jassat W, Mudara C, Vika C, Welch R, Arendse T, Dryden M, et al. A cohort study of post-COVID-19 condition

- across the Beta, Delta and Omicron waves in South Africa: 6-month follow-up of hospitalized and nonhospitalized participants. Int J Infect Dis. 2023;128:102–11. https://doi.org/10.1016/j.ijid.2022.12.036
- Morioka S, Tsuzuki S, Suzuki M, Terada M, Akashi M, Osanai Y, et al. Post–COVID-19 condition of the Omicron variant of SARS-CoV-2. J Infect Chemother. 2022;28:1546–51. https://doi.org/10.1016/j.jiac.2022.08.007
- Perlis RH, Santillana M, Ognyanova K, Safarpour A, Lunz Trujillo K, Simonson MD, et al. Prevalence and correlates of long COVID symptoms among US adults. JAMA Netw Open. 2022;5:e2238804. https://doi.org/ 10.1001/jamanetworkopen.2022.38804
- Taquet M, Sillett R, Zhu L, Mendel J, Camplisson I, Dercon Q, et al. Neurological and psychiatric risk trajectories after SARS-CoV-2 infection: an analysis of 2-year retrospective cohort studies including 1 284 437 patients. Lancet Psychiatry. 2022;9:815–27. https://doi.org/10.1016/ S2215-0366(22)00260-7
- Nehme M, Vetter P, Chappuis F, Kaiser L, Guessous I; CoviCare Study Team. Prevalence of post-COVID disease condition 12 weeks after Omicron infection compared with negative controls and association with vaccination status. Clin Infect Dis. 2023;76:1567–75. https://doi.org/ 10.1093/cid/ciac947
- Gottlieb M, Wang RC, Yu H, Spatz ES, Montoy JCC, Rodriguez RM, et al. Severe fatigue and persistent symptoms at 3 months following severe acute respiratory syndrome coronavirus 2 infections during the pre-Delta, Delta, and Omicron time periods: a multicenter prospective cohort study. Clin Infect Dis. 2023;76:1930–41. https://doi.org/10.1093/cid/ciad045
- Kahlert CR, Strahm C, Güsewell S, Cusini A, Brucher A, Goppel S, et al. Post-acute sequelae after severe acute respiratory syndrome coronavirus 2 infection by viral variant and vaccination status: a multicenter cross-sectional study. Clin Infect Dis. 2023;77:194–202. https://doi.org/10.1093/ cid/ciad143
- Cai J, Lin K, Zhang H, Xue Q, Zhu K, Yuan G, et al. A one-year follow-up study of systematic impact of long COVID symptoms among patients post SARS-CoV-2 Omicron variants infection in Shanghai, China. Emerg Microbes Infect. 2023;12:2220578. https://doi.org/10.1080/ 22221751.2023.2220578
- Diexer S, Klee B, Gottschick C, Xu C, Broda A, Purschke O, et al. Association between virus variants, vaccination, previous infections, and post–COVID-19 risk. Int J Infect Dis. 2023;136:14–21. https://doi.org/10.1016/j.ijid.2023.08.019
- 23. Durstenfeld MS, Peluso MJ, Peyser ND, Lin F, Knight SJ, Djibo A, et al. Factors associated with long COVID symptoms in an online cohort study. Open Forum Infect Dis. 2023;10:ofad047. https://doi.org/10.1093/ofid/ofad047
- Chen J, Wang R, Gilby NB, Wei GW. Omicron variant (B.1.1.529): infectivity, vaccine breakthrough, and antibody resistance. J Chem Inf Model. 2022;62:412–22. https://doi.org/ 10.1021/acs.jcim.1c01451
- CoV-Spectrum. Detect and analyze variants of SARS-CoV-2.
 2023 [cited 2023 Nov 24]. https://cov-spectrum.org
- International Severe Acute Respiratory and Emerging Infection Consortium. COVID-19 long-term protocol. 2023 [cited 2023 Nov 24]. https://isaric.org/research/ covid-19-clinical-research-resources/covid-19-long-term-follow-up-study
- World Health Organization. A clinical case definition of post-COVID-19 condition by a Delphi consensus, 6 October 2021 [cited 2023 Nov 24]. https://www.who.int/

- publications/i/item/WHO-2019-nCoV-Post_COVID-19_condition-Clinical_case_definition-2021.1
- Miyazato Y, Morioka S, Tsuzuki S, Akashi M, Osanai Y, Tanaka K, et al. Prolonged and late-onset symptoms of coronavirus disease 2019. Open Forum Infect Dis. 2020;7:ofaa507. https://doi.org/10.1093/ofid/ofaa507
- WHO Working Group on the Clinical Characterisation and Management of COVID-19 infection. A minimal common outcome measure set for COVID-19 clinical research. Lancet Infect Dis. 2020;20:e192-7. https://doi.org/10.1016/ S1473-3099(20)30483-7
- Watanabe A, Iwagami M, Yasuhara J, Takagi H, Kuno T. Protective effect of COVID-19 vaccination against long COVID syndrome: a systematic review and meta-analysis. Vaccine. 2023;41:1783–90. https://doi.org/10.1016/ j.vaccine.2023.02.008
- Byambasuren O, Stehlik P, Clark J, Alcorn K, Glasziou P. Effect of COVID-19 vaccination on long covid: systematic review. BMJ Med. 2023;2:e000385. https://doi.org/10.1136/ bmjmed-2022-000385
- 32. Subramanian A, Nirantharakumar K, Hughes S, Myles P, Williams T, Gokhale KM, et al. Symptoms and risk

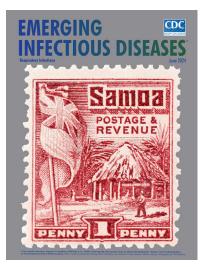
- factors for long COVID in non-hospitalized adults. Nat Med. 2022;28:1706–14. https://doi.org/10.1038/s41591-022-01909-w
- 33. Liao X, Guan Y, Liao Q, Ma Z, Zhang L, Dong J, et al. Long-term sequelae of different COVID-19 variants: the original strain versus the Omicron variant. Glob Health Med. 2022;4:322–6. https://doi.org/10.35772/ghm.2022.01069
- 34. Luo J, Zhang J, Tang HT, Wong HK, Lyu A, Cheung CH, et al. Prevalence and risk factors of long COVID 6-12 months after infection with the Omicron variant among nonhospitalized patients in Hong Kong. J Med Virol. 2023;95:e28862. https://doi.org/10.1002/jmv.28862
- 35. Japan Ministry of Health, Labour and Welfare. Visualizing the data: information on COVID-19 infections. 2023 [cited 2023 Sep 12]. https://covid19.mhlw.go.jp/en

Address for correspondence: Arisa Iba, Institute for Global Health Policy Research, Bureau of International Health Cooperation, National Center for Global Health and Medicine, 1-21-1 Toyama, Shinjuku, Tokyo, 162-8655, Japan; email: aiba@it.ncgm.go.jp

June 2024

Respiratory Infections

- Decolonization and Pathogen Reduction Approaches to Prevent Antimicrobial Resistance and Healthcare-Associated Infections
- Deciphering Unexpected Vascular Locations of Scedosporium spp. and Lomentospora prolificans Fungal Infections, France
- Severe Human Parainfluenza Virus Community- and Healthcare-Acquired Pneumonia in Adults at Tertiary Hospital, Seoul, South Korea, 2010–2019
- Electronic Health Record—Based Algorithm for Monitoring Respiratory Virus—Like Illness
- Carbapenem-Resistant and Extended-Spectrum β-Lactamase– Producing Enterobacterales in Children, United States, 2016–2020
- Chest Radiograph Screening for Detecting Subclinical Tuberculosis in Asymptomatic Household Contacts, Peru



- Yersinia ruckeri Infection and Enteric Redmouth Disease among Endangered Chinese Sturgeons, China, 2022
- Follow-Up Study of Effectiveness of 23-Valent Pneumococcal Polysaccharide Vaccine Against All-Type and Serotype-Specific Invasive Pneumococcal Disease, Denmark

- Outbreak of Highly Pathogenic Avian Influenza A(H5N1) Virus in Seals, St. Lawrence Estuary, Quebec, Canada
- Estimates of SARS-CoV-2 Hospitalization and Fatality Rates in the Prevaccination Period, United States
- Trends in Nationally Notifiable Infectious Diseases in Humans and Animals during COVID-19 Pandemic, South Korea
- Incubation Period and Serial Interval of Mpox in 2022 Global Outbreak Compared with Historical Estimates
- Evolution and Antigenic Differentiation of Avian Influenza A(H7N9) Virus, China
- SARS-CoV-2 Disease Severity and Cycle Threshold Values in Children Infected during Pre-Delta, Delta, and Omicron Periods, Colorado, USA, 2021–2022
- Lack of Transmission of Chronic Wasting Disease Prions to Human Cerebral Organoids

EMERGING INFECTIOUS DISEASES

To revisit the June 2024 issue, go to: https://wwwnc.cdc.gov/eid/articles/issue/30/6/table-of-contents

Article DOI: http://doi.org/10.3201/eid3007.231723

EID cannot ensure accessibility for supplementary materials supplied by authors. Readers who have difficulty accessing supplementary content should contact the authors for assistance.

Prevalence and Risk Factors of Post— COVID-19 Condition during Omicron BA.5— Dominant Wave, Japan

Appendix

Shown on the following pages is the questionnaire sent to residents in Shinagawa City, a metropolitan area located in the Tokyo area of Japan, who were 20–69 years of age and infected with SARS-CoV-2 during July 1–August 31, 2022, along with noninfected residents as controls (25,911 in each group).

Appendix

Questionnaire (written in green indicates directions)

_	3					
Su	rvey on the health of residents during COVID-19 pandemic					
	The purpose of this survey is to ask about your health and daily life during the	l agree.				
	Coronavirus Disease 2019 (COVID-19) pandemic and the recovery status of those					
	who have had COVID-19 in order to provide reference for future healthcare					
	systems.					
	Please read the enclosed "Regarding Cooperation with the 'Survey on the health of					
	residents during COVID-19 pandemic,'" and if you agree to cooperate with this					
	survey, please click the "I agree" button to proceed to the answer section.					
	This work was supported by MHLW Research on Emerging and Re-emerging					
	Infectious Diseases and Immunization (Program Grant Number JPMH21HA2011).					
Section 1 (questionnaire for all participants)						
Q	Respondent	1=the person himself/herself				
		2 = substitute				
Q	Sex (of the person himself/herself)	1 = m a le				
		2 = fe m a le				
		3=I prefer not to answer				
Q	Age (of the person himself/herself)	year				
Q	Have you ever been diagnosed to be a close contact with someone who had COVID-	1 = Y e s				
	19?	2 = N o				
		3=1 don't know				
		4=1 prefer not to answer				
Q	Has anyone living with you been diagnosed with COVID-19	1 = Y e s				
		2 = No				

		3=No roommate (living alone)
		4=I don't know
		5=1 prefer not to answer
Q	Have you ever been diagnosed to have COVID-19?	1 = Y e s
	Yes \rightarrow move to the questionnaire for infected persons; other answers \rightarrow move to	2 = N o
	the questionnaire for noninfected persons	3=I don't know
		4=I prefer not to answer

	Section 2-A (questionnaire fo				
Q	How many times have you be	Once			
					Twice
					Three times or more
	(Show only the number of tir	nes diagnosed) Whe	en was the date o	f diagnosis?	Choose from below
	If you do not know the exact	date, please provid	e an approximate	e date.	B: 2019, 2020, 2021, 2022, 2023
	First diagnosis date	B year	C mo	D day	C: January-December
			nth		D: 1-31, unknown
	Second diagnosis date	B year	C month	D day	
	Third diagnosis date	B year	C month	D	
				day	
Q	How was your medical condi	tion when you had C	OVID-19 for the	first time?	
	Did you have any symptoms?	1 = Yes 2 = No 3 = I don't know			
	Were you diagnosed with pn	eumonia?			1=Yes 2=No 3=I don't know
	Were you hospitalized?				1=Yes 2=No 3=I don't know

	<those being="" hospitalized="" reported="">Were you admitted to the intensive care unit (ICU)?</those>	1 = Yes 2 = No 3 = I don't know		
	Was oxygen administered?	1=Yes 2=No 3=I don't know		
	<those administration="" oxygen="" with="">Please select all methods of oxygen</those>	1 = Nasal cannula		
	administration received at that time.	2=oxygen mask		
		3=high-flow nasal cannula		
	1 2 3 3 4 5 5 6	4=noninvasive positive pressure		
		ventilation (NPPV)		
		5 = mechanical ventilation		
		6=extracorporeal membrane		
		oxygenation (ECMO)		
		7=Oxygen was administered, but I		
		don't know how.		
Q	How was your medical condition when you had COVID-19 for the second time?			
	Did you have any symptoms?	1=Yes 2=No 3=I don't know		
	Were you hospitalized?	1=Yes 2=No 3=I don't know		
	Was oxygen administered?	1=Yes 2=No 3=I don't know		
	Were you intubated (mechanical ventilation)?	1=Yes 2=No 3=I don't know		
Q	How was your medical condition when you had COVID-19 for the third time?			
	Did you have any symptoms?	1=Yes 2=No 3=I don't know		
	Were you hospitalized?	1=Yes 2=No 3=I don't know		
	Was oxygen administered?	1=Yes 2=No 3=I don't know		
	Were you intubated (mechanical ventilation)?	1=Yes 2=No 3=I don't know		
Q	<pre><female only="">Were you pregnant when you had COVID-19? (multiple choices)</female></pre>	1 = Yes 2 = No 3 = I don't know 4 = I		
		prefer not to answer		

_		·
	<those answered="" choice="" multiple="" who="" yes,="">During which infection episode were</those>	First infection, second infection, third
	you pregnant?	infection, other
	<those answered="" who="" yes="">What was the gestational age at the time of the first</those>	1=First trimester (≤15 weeks gestation)
	infection?	2=Second trimester (≥16weeks and ≤27
		weeks)
		3=Third trimester (≥28 weeks)
		4=1 don't know the gestational age at
		the time of infection
	<those answered="" who="" yes="">What was the gestational age at the time of the second</those>	1=First trimester (≤15 weeks gestation)
	infection?	2=Second trimester (≥16weeks and ≤27
		weeks)
		3=Third trimester (≥28 weeks)
		4=1 don't know the gestational age at
		the time of infection
	<those answered="" who="" yes="">What was the gestational age at the time of the third</those>	1=First trimester (≤15 weeks gestation)
	infection?	2=Second trimester (≥16weeks and ≤27
		weeks)
		3=Third trimester (≥28 weeks)
		4=1 don't know the gestational age at
		the time of infection
(We would like to ask you about the symptoms that appeared after the COVID-19	Selecting symptoms will display "Was
	diagnosis.	present from the time of infection
	Please select the symptoms that existed between the COVID-19 diagnosis in the	through the recovery period", "Was
	summer of 2022 to date.	present at 3 months after the
	Please check all that apply regarding the duration of the symptoms.	

- If the symptoms were present from the time of infection through the recovery period, check "Was present from the time of infection through the recovery period"
- If the symptoms were present at 3 months after the infection, check "Was present after three months of infection"
- If the symptom lasted 2 months or more, check "lasted 2 months or more"
- If the symptom is present, check "Still present"

If none of the symptoms were present, please select "No symptoms of any of the above" at the bottom.

*For those who had COVID-19 more than once, please answer the following questions regarding the infection in the summer of 2022.

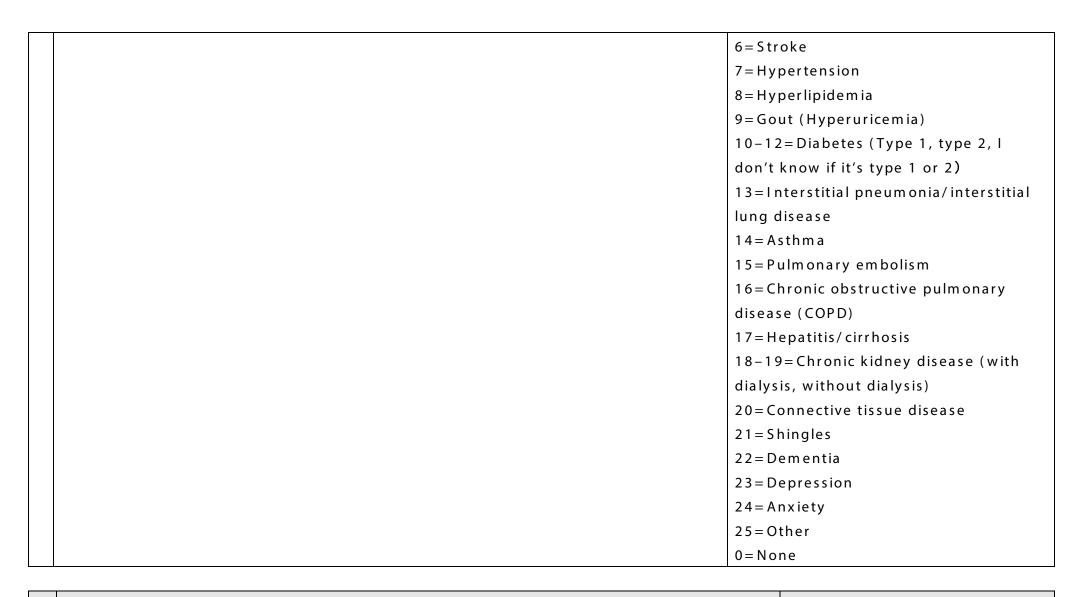
Symptom	Symptom	Was	Was	Lasted 2	Still
s that		present	present	months	present
have		from the	at 3	or more	
existed		time of	months		
between		infection	after the		
the		through	infection		
COVID-		the			
19		recovery			
diagnosis		period			
in the					
s u m m e r					
of 2022					
to date					
	Fever (≥37.5 °C)				

infection", "Lasted 2 months or more", and "Still present".>

Т	Т	I	T	
	Cough			
	Fatigue			
	Sore throat			
	Chest pain			
	Lack of appetite (anorexia)			
	Brain fog (Brain fog is a state such as being "foggy," "confused," "having difficulty learning new things," "indecisive," or "unable to think clearly.")			
	Difficulty in concentrating			
	Loss of smells (smelling disorder)			
	Loss of tastes (tasting disorder)			
	Shortness of breath			
	Hair loss			
	Muscle weakness			
	Palpitations			

Difficulty sleeping,			
waking up at night or			
early in the morning			
 (sleep disorder)			
Runny nose			
Headache			
Joint pain or swelling			
Muscle pain			
Nausea and vomiting			
Abdominal pain			
Skin rash			
Eye symptoms (eye pain,			
itching, foreign body			
sensation, redness,			
watery eyes, blurred			
vision, difficulty seeing)			
Dizziness			
Erectile disfunction (male			
only)			
Menstrual change			
 (female only)			
Other 1 (in detail			
)			

		Other 2 (in detail					
		No symptoms of any of the above					
Q	question cu Please choo	rent are the symptoms after rrently interfering with your se a number from 0 to 10, we me hindrance."	0 to 10				
Q	Are you cur	rently receiving treatment fo	or any of th	ie symptom	s selected in	the	1 = Y e s
	previous qu	estion?					2 = N o
	<those td="" who<=""><td>o answered yes> Please sele</td><td>ct all treat</td><td>ments you a</td><td>re currently</td><td>receiving.</td><td>1=in-patient care</td></those>	o answered yes> Please sele	ct all treat	ments you a	re currently	receiving.	1=in-patient care
							2=out-patient care
							3=prescription drugs (other than
							herbal medicines)
							4=prescription drugs (herbal
							medicines)
							5=over-the-counter drug
							6=rehabilitation
							7 = psychological counseling
							8 = other ()
Q	Please selec	ct all new diseases diagnosed	d at medica	al facilities a	fter COVID-	19	1 = Malignancy
	diagnosis in	the summer of 2022.					2 = Myocardial infarction, angina
							3=Heart failure
							4 = Arrhythmia
							5 = Myocarditis / cardiomyopathy



Q We would like to ask you about the symptoms that appeared after July 2022.

Please select the symptoms that existed between July 2022 to date.

- If the symptom lasted 2 months or more, check "lasted 2 months or more"
- If the symptom is present, check "Still present"

If none of the symptoms were present, please select "No symptoms of any of the above" at the bottom.

Symptoms that have existed from July 2022 to date	5 y m p t o m	Lasted 2 months or more	Still present
	Fever (≥37.5 °C)		
	Cough		
	Fatigue		
	Sore throat		
	Chest pain		
	Lack of appetite (anorexia)		
	Brain fog (Brain fog is a state such as being "foggy," "confused," "having difficulty learning new things," "indecisive," or "unable to think clearly.")		
	Difficulty in concentrating		

Loss of smells (smelling disorder)	
Loss of tastes (tasting disorder)	
Shortness of breath	
Hair loss	
Muscle weakness	
Palpitations	
Difficulty sleeping, waking up at night	
or early in the morning (sleep	
disorder)	
Runny nose	
Headache	
Joint pain or swelling	
Muscle pain	
Nausea and vomiting	
Abdominal pain	
Skin rash	
Eye symptoms (eye pain, itching,	
foreign body sensation, redness,	
watery eyes, blurred vision, difficulty	
seeing)	
Dizziness	
Erectile disfunction (male only)	
Menstrual change (female only)	

					1
		Other 1 (in detail)			4
		Other 2 (in detail)			_
		No symptoms of any of the above			
Q	Please select all r	new diseases diagnosed at medical facilition	es after July 2022	2.	1 = Malignancy
					2= Myocardial infarction, angina
					3=Heart failure
					4 = Arrhythmia
					5 = Myocarditis/cardiomyopathy
					6 = Stroke
					7 = Hypertension
					8 = Hyperlipidemia
					9=Gout (Hyperuricemia)
					10-12=Diabetes (Type 1, type 2,
					I don't know if it's type 1 or 2)
					13=Interstitial
					pneumonia/interstitial lung
					disease
					14 = Asthma
					15=Pulmonary embolism
					16=Chronic obstructive
					pulmonary disease (COPD)
					17 = Hepatitis/cirrhosis
					18-19=Chronic kidney disease
					(with dialysis, without dialysis)
					20 = Connective tissue disease

	21 = Shingles
	22 = Dementia
	23 = Depression
	24 = Anxiety
	25 = Other
	0 = None
<pre><female only="">Have you been pregnant between July 2022 to date?</female></pre>	1 = Yes 2 = No 3 = I don't know
	4=I prefer not to answer

Section 3 (questionnaire for all participants)

	We would like to ask about COVID-19 vaccines.	
Q	How many doses of COVID-19 vaccine have you received so	0 (unvaccinated), once, twice, three times, four times or
	far?	more
Q	Please indicate the date of vaccination.	Choose from below
	If you do not know the exact date, please provide an	A: 2020, 2021, 2022, 2023
	approximate date.	B : January-December
	(Displayed according to the number of vaccinations	
	selected)	
	First dose : A year B month	
	Second dose : A year B month	
	Third dose : A year B month	
	Fourth dose : A year B month	

	We would like to ask about your health and daily life.	
Q	Current height	cm

Q	Current weight	kg
Q	Weight about 6 months ago	kg
	For infected persons: Weight about 6 months ago (before COVID-19	
	diagnosis in summer 2022)	
Q	Do you currently have "breathlessness"? Please choose one that	1 = No breathlessness
	comes closest.	2=1 only get breathless with strenuous exercise
		3=1 get short of breath when hurrying on level ground
		or walking up a slight hill
		4=On level ground, I walk slow than people of my age
		because of breathlessness, or I have to stop for
		breath when walking at my own pace on the level
		5=1 stop for breath after walking about 100 m or after
		a few minutes on level ground
		6=1 am too breathless to leave the house or 1 am
		breathless when dressing/undressing
Q	Do you currently have "fatigue"? Please choose one that comes	1=Fully active, able to carry on all (infected persons:
	closest. If you do not have "fatigue," please choose "Fully active."	pre-disease) performance without restriction
		2=Restricted in physically strenuous activity but
		ambulatory and able to carry out work of a light or
		sedentary nature, e.g., light house work, office work
		3 = Ambulatory and capable of all selfcare but unable
		to carry out any work activities. Up and about more
		than 50% of waking hours
		4=Capable of only limited selfcare, confined to bed or
		chair more than 50% of waking hours

		5 = Completely disabled. Cannot carry on any selfcare.
		Totally confined to bed or chair
Q	Please select all diseases diagnosed at medical institutions before	1 = Malignancy
	July 2022.	2= Myocardial infarction, angina
	For infected persons: Please select all diseases diagnosed at medical	3=Heart failure
	facilities prior to the COVID-19 infection in the summer of 2022.	4 = Arrhythmia
		5 = Myocarditis/cardiomyopathy
		6=Stroke
		7 = Hypertension
		8 = Hyperlipidemia
		9=Gout (Hyperuricemia)
		10-12=Diabetes (Type 1, type 2, I don't know if it's
		type 1 or 2)
		13=Interstitial pneumonia/interstitial lung disease
		14 = Asthma
		15=Pulmonary embolism
		16=Chronic obstructive pulmonary disease (COPD)
		17 = Hepatitis/cirrhosis
		18-19=Chronic kidney disease (with dialysis, without
		dialysis)
		20=Connective tissue disease
		21 = Shingles
		22=Dementia
		23 = Depression
		24= Anxiety

		25 = Other
		0 = None
Q	On or about July 2022 (infected persons: at the time of COVID-19	1 = Y e s
	diagnosis in summer 2022), were you treated with steroids	2 = No
	, , , , , , , , , , , , , , , , , , ,	
	(excluding ointments), anticancer drugs, immunosuppressive drugs	3=I don't know
	or biologics (such as Remicade)?	
Q	Do you smoke cigarettes (cigarettes, heated tobacco products, e-	1 = Never smoked cigarettes habitually before
	cigarettes including nicotine)?	2=Smoked cigarettes in the past but have quit
		3 = Currently still smoking cigarettes
	<those answered="" have="" quit="" to="" who=""></those>	1 = Before COVID-19 diagnosis (noninfected persons:
	When did you quit smoking cigarettes?	before July 2022)
		2 = After COVID-19 diagnosis (noninfected persons:
		after July 2022)
	<those answered="" currently="" smoking="" who=""></those>	1 = Decreased
	Has the amount of cigarettes you smoke changed compared with	2 = Unchanged
	that 6 months ago (infected persons: 6 months ago (before COVID-	3=Increased
	19 infection in summer 2022))?	
Q	How often do you currently drink alcohol (alcohol-containing	1=I don't drink at all (can't drink)
	beverages)?	2=Hardly drink (about once a month)
		3=1-3 times a month
		4=1-2 times a week
		5=3-4 times a week
		6=5-6 times a week
		7=every day

	<those "don't="" above="" all"="" at="" chose="" drink="" other="" than="" who=""></those>	1=Less than 1 cup (180ml) of sake
	What is the average amount of alcohol you drink per day? Please	2=1 cup of sake
	choose one that applies to you in terms of sake.	3=2 cups of sake
		4=3-4 cups of sake
		5=5 cups of sake
	Compared with that 6 months ago (infected person: 6 months ago	1=I quit
	(before COVID-19 infection in summer 2022)), has the amount of	2 = Decreased
	alcohol you drink changed?	3 = Unchanged
		4=Increased (started drinking)
Q	Please select your current average daily sleep duration.	1=less than 5 hours
		2=5 hours
		3=6 hours
		4=7 hours
		5=8 hours
		6=9 hours
		7=10 hours or more
Q	Compared with that 6 months ago (infected persons: 6 months ago	1 = Decreased
	(before COVID-19 infection in summer 2022)), has your sleeping	2 = Unchanged
	duration changed?	3 = Increased
Q	How much sports or exercise do you currently do on average per	5=7 hours or more
	week in total?	4=5-6 hours
		3=3-4 hours
		2=1-2 hours
		1 = seldom or never

Q	How much time do you currently spend v	walkin	g indo	oors o	r outdoors	4=3 hours or more
	on average per day?					3=about 2 hours
						2=about 1 hour
						1 = about 30 minutes
						0=seldom or never
Q	Compared with that 6 months ago (infec	ted pe	ersons	: 6 m	onths ago	
	(before COVID-19 infection in summer 2	022))	, have	you	changed	
	the way you move your body or how long	gyou	sit?		-	
		De	∪ _r	_		
		crea	Uncha	ncre		
		s e	a n g e	ease		
		ď	e d	bg		
	Frequency and duration of sports and					
	exercise					
	Time spent walking indoors and					
	outdoors					
	Sitting time					
Q	< For those aged 50 years or older only>				_	
	Please select "Yes" or "No" for the follow	ing fi	ve ite	ms.		

-	7				
				Yes	No
	Have you lost 2 kg or more in the	e past 6	months?		
	Do you think you walk slower tha	an befor	e?		
	Do you go for a walk for your hea	alth at le	east once a	a 🗆	
	Can you recall what happened 5	minutes	ago?		
	In the past 2 weeks, have you fe reason?	lt tired v	vithout a		
Q	For each item, please indicate how often you feel.		.	-	
		None of the time	Seldom of the time	Often	All of the time
	How often do you feel that you lack companionship?				
	How often do you feel left out?				
	How often do you feel isolated from others?				

Q	During the past 30 days,	, about h	now ofter	n did yo	u feel	•	
		None of the time	A little of the time	Some of the time	Most of the time	All of the time	
	nervous?						
	hopeless?						
	restless or fidgety?						
	so depressed that nothing could cheer you up?						
	that everything was an effort?						
	worthless?						
Q	Over the last 2 weeks, h	ow ofter	have vo	ou been	bother	ed by	
,	thoughts that you would						elf in
	some way?						

Q	What is your current marital status?	1 = Unmarried
		2 = Married
		3 = Widowed
		4= Divorced
		5 = Prefer not to answer
Q	Who do you currently live with? Please check all persons living with	1 = S pouse
	you.	2 = Child
		3 = Parent
		4=Other ()
Q	<those above="" check="" question="" the="" who=""></those>	persons
	How many people are currently living with you (not including you)?	
	Of the number of people living with you above, how many are under	persons
	the age of 18 (not including you)?	
Q	What was the last school you graduated from?	1=Junior high school
		2=High school
		3 = Vocational school
		4=Some college
		5 = University
		6=Graduate school
		7=Prefer not to answer
Q	What is your household income (including taxes and income from	1 = No household income
	pensions and dividends) in 2021?	2 = < 500,000 yen
		3 =≥500,000 yen and <1,000,000 yen
		4 =≥1,000,000 yen and <2,000,000 yen
		5 =≥2,000,000 yen and <4,000,000 yen

		6 =≥4,000,000 yen and <6,000,000 yen
		7 =≥6,000,000 yen and <8,000,000 yen
		8 =≥8,000,000 yen and <10,000,000 yen
		9=≥10,000,000 yen and <12,000,000 yen
		10=≥12,000,000 yen and <14,000,000 yen
		11 =≥14,000,000 yen
		12=Prefer not to answer/don't know
Q	Has your financial situation changed compared with that 6 months	1 = Very worse
	ago (infected persons: 6 months ago (before COVID-19 infection in	2 = W or s e
	summer 2022))?	3 = Unchanged
		4 = Better
		5=Very better
Q	Please select one of your main occupations at present. If you have	1= Administrative and managerial
	more than one occupation, please select one main job.	2=Professional and engineering (healthcare)
		3 = Professional and engineering (nursing
		care/welfare)
		4=Professional and engineering (childcare/education)
		5 = Professional and engineering (other)
		6=Clerical
		7 = Service (accommodation industry)
		8=Service (restaurant business serving alcohol
		beverage)
		9=Service (restaurant business without serving
		alcohol beverage)

		10=Service (entertainment)
		11=Service (other)
		12=Sales (retail store owners, sales clerks, etc.)
		13=Security
		14=Manufacturing process
		15 = Agricultural, forestry and fishery
		16=Transport and machine operation
		17=Construction and mining
		18=Carrying, cleaning, packaging, and related
		19=Student
		20 = Housewife/househusband
		21=Not apply to the above
		22=Unem ployed
Q	Please select one of your current employment statuses (including	1=Regular employee (manager)
	student). If you have more than one type of employment, please	2=Regular employee (other than managers)
	choose one main status.	3=Executive of company or corporation
		4=Self-employed worker
		5 = Assistance in private business
		6=Dispatched worker from temporary labor agency
		7=Contract employee
		8=Part-time worker
		9=Doing piecework at home
		10=Students
		11 = Housewife / househusband

		12=Unemployed
		13 = Other ()
Q	< Display selected occupations > Is the occupation here the same as	1=Yes
	the occupation as of July 1, 2022?	2 = No
	<those answered="" no="" who=""></those>	1 = Administrative and managerial
	Please select your occupation as of July 1, 2022. If you have more	2=Professional and engineering (healthcare)
	than one occupation, please select one main occupation.	3 = Professional and engineering (nursing
		care/welfare)
		4=Professional and engineering (childcare/education)
		5 = Professional and engineering (other)
		6 = Clerical
		7=Service (accommodation industry)
		8=Service (restaurant business serving alcohol
		beverage)
		9=Service (restaurant business without serving
		alcohol beverage)
		10=Service (entertainment)
		11=Service (other)
		12=Sales (retail store owners, sales clerks, etc.)
		13 = Security
		14 = Manufacturing process
		15 = Agricultural, forestry and fishery
		16=Transport and machine operation
		17 = Construction and mining

		18=Carrying, cleaning, packaging, and related
		19=Student
		20 = Housewife/househusband
		21 = Not apply to the above
		22 = Unemployed
Q	<< Display selected employment status>	1=Yes
	Is the employment status here the same as of July 1, 2022?	2 = N o
	<those answered="" no="" who=""></those>	1 = Regular employee (manager)
	Please select your employment status as of July 1, 2022. If you have	2=Regular employee (other than managers)
	more than one employment status, please select one main status.	3=Executive of company or corporation
		4=Self-employed worker
		5 = Assistance in private business
		6=Dispatched worker from temporary labor agency
		7 = Contract employee
		8=Part-time worker
		9=Doing piecework at home
		10 = Students
		11 = Housewife/househusband
		12=Unemployed
		13 = Other ()
Q	In the past 6 months, have you experienced any of the following?	1 = Working (schooling) hours increased
	Please select all that apply.	2 = Working (schooling) hours decreased
		3 = Telecommuting (online classes) has increased
		4=Telecommuting (online classes) has decreased
		5 = I have found a job (entered to school)

	6=1 took a leave of absence
	7 = Changed jobs (schools)
	8=Retired (withdrew from school)
	9=1've been frequently absent
	10=Other ()
	11 = None of the above
<those above="" no.1-10="" selected="" who=""></those>	1 = Because I was instructed by my employer or school
Please select all applicable reasons.	2=Due to deteriorating health conditions caused by
	COVID-19
	3 = Due to deteriorating health conditions caused by
	conditions other than COVID-19
	4= Due to a new need for childcare or nursing care for
	a family member, etc.
	5=For financial reasons
	6=Because I could no longer pay my tuition fees
	7 = Other ()