



Title	Associations of COVID-19 symptoms with omicron subvariants BA.2 and BA.5, host status, and clinical outcomes in Japan: a registry-based observational study
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Citation	Lancet Infectious Diseases, 23(11), 1244-1256 https://doi.org/10.1016/S1473-3099(23)00271-2
Issue Date	2023-11
Doc URL	http://hdl.handle.net/2115/91341
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Supplementary Appendix

Associations of COVID-19 Symptoms with Omicron Subvariants BA.2 and BA.5, Host Status, and Clinical Outcomes:

A Registry-Based Observational Study in Sapporo, Japan

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Supplementary Methods

Registry systems

Data from treatment decision sites (TDS) and registration centres for test-positive patients (RCPP) were utilized for analyses. The TDS is a system launched by the City of Sapporo to notify individuals with a COVID-19 diagnosis of the need for hospitalization and clinical advice. Individuals diagnosed with COVID-19 (see **Inclusion criteria** below for diagnostic methods for COVID-19) were requested to immediately register clinical information with the TDS through a web device, including the presence/absence of 12 preselected specific symptoms at the time of registration and the date of symptom onset. The RCPP is a registration system operated by the City of Sapporo for symptomatic individuals who cannot visit a healthcare provider. The RCPP sends SARS-CoV-2 antigen test kits to symptomatic individuals at home upon request. A self-test is conducted, and information identical to that for the TDS is entered into the RCPP system by test-positive individuals. Based on the registered information, a medical care policy was automatically developed and individuals notified. Individuals with a diagnosis of COVID-19 were provided with food delivery services and medical advice when the decision was made for home isolation. For those who were unable to provide care at home or at high risk, hospitalisation was arranged. The costs of diagnosis and treatment of COVID-19 were covered by public funds. Details of the two systems are also shown in **Fig. S1**.

Inclusion criteria

Individuals with COVID-19 who registered for the TDS or the RCPP website during the study periods were included in the study. Individuals residing in Sapporo were eligible to register for TDS if they met the following criteria: 1) symptomatic individuals who visited a medical institution and tested positive for SARS-CoV-2 (polymerase chain reaction or antigen test); and 2) individuals who were not tested for SARS-CoV-2 but developed new symptoms after a household member tested positive for SARS-CoV-2.

Exclusion criteria

- 1) Incorrect input value for the date of onset (later than the registration date).
- 2) Registration date is more than five days after the onset date.
- 3) Under the term "Symptoms to date", "Nothing" was selected. Applicable cases were treated as asymptomatic individuals and excluded.

We defined an acute phase of COVID-19 infection as a period of five days following symptom onset as previously reported¹, and included individuals who developed COVID-19 symptoms during the defined period. Individuals who registered in our registry system six or more days after symptom onset were excluded from the analysis.

Our registry system included some individuals who reported no symptoms. However, the TDS and RCPP were designed to provide clinical instructions for symptomatic individuals with COVID-19 infection and asymptomatic individuals with COVID-19 infection were not considered as a main target of the system. Thus, we excluded asymptomatic individuals with COVID-19 infection registered in the system from the study.

Definition of symptoms

Fever was defined as body temperature ≥ 38 °C. Decreased food intake was defined as less than 30% of baseline food intake.

Definition of missing values and treatment

The missing values were applicable for age, sex, and body mass index (BMI). For age, values above 120 were determined to be erroneously entered and were considered missing values. Missing values were assigned to cases in which sex was unknown. A BMI of < 8 and > 70 were determined to be inappropriate values and considered as missing values. The number and percentage of cases in each category were calculated, excluding cases with missing values. Multivariable analysis was performed for cases without missing values.

Statistical analysis

We used the following formula to estimate the appropriate sample size:

$$n = Z^2 \times P \times (1 - P) / d^2.$$

- Z = value from standard normal distribution corresponding to desired confidence level (Z=1.96 for 95% confidence interval [CI])

- P = expected true proportion

- d = desired precision (half desired CI width)

In previous reports, the prevalence of COVID-19 symptoms ranged from 1-80%¹. In the present study, the 50% with the largest calculated estimated sample size was set as the prevalence, and a precision of 0.01 was used to calculate the optimal sample size with a confidence interval width of 1% for the 50% proportion, which was 9604. The sample size of our study exceeded the figure.

Continuous data were presented as medians (interquartile range) and categorical data were presented as numbers and percentages. A 95% CI for symptom prevalence, odds ratio (OR) and hazard ratio (HR) was calculated by the score method and Wald test, respectively.

Multivariable logistic regression analyses were performed, using days from symptom onset, age, sex, BMI, underlying diseases, SARS-CoV-2 omicron subvariant, vaccination status, and previous SARS-CoV-2 infection as explanatory variables, with the development of each symptom as the outcome. Considering that times for development of each symptom could vary after the first symptom onset, the number of days that passed since first symptom onset was treated as a categorical variable. Other variables have been reported as predictors of COVID-19 outcomes, and all variables that were available from the registry system were incorporated. Vaccination status was divided into two groups with more vs. less than three vaccinations as the boundary, a number clinically relevant to omicron variants. For two- and three-dose vaccinees, categories were created to account for the passage of time by dividing the number of days since last vaccination into 60-day intervals and incorporated into specific models. The number of individuals who received the single and four doses was small and they were excluded from the models. To test whether specific symptoms increased the odds of severe disease, a multivariable logistic regression analysis was performed. The objective variable was progression to severe disease, and 12 symptoms were used as explanatory variables along with the above variables.

Propensity score matching was performed using a 1:1 nearest available matching algorithm without replacement and a caliper of 0.05. The propensity score for

each variable was calculated by logistic regression analysis with the variables, including omicron subvariants, age, sex, obesity, underlying disease, vaccine status, including time since last vaccination, and previous SARS-CoV-2 infection. Absolute value of standardized difference greater than 0.1 was considered as a sign of imbalance.

To estimate symptom time courses, proportion of the 12 predefined symptoms were calculated from individuals aligned by days from first symptom onset and plotted on a day 0-5 scale (Table S7).

The estimation of HR of symptom accumulation was analysed using a multivariable Cox regression model, starting from day 0 as the symptom onset to day 5 as the end time. Built-in selection bias should be taken into account when estimating HR in observational study. However, it seems to have less influence in this study because the time period was not delimited, and the follow-up period was short (Table S8). We performed a proportional hazards assumption check using the graph of the log of the negative log of the estimated survivor functions against the log of time.

Spearman's correlation coefficient was calculated to test the strength of the correlation between the two symptoms (Figure S2).

We conducted a multivariable logistic regression analysis to investigate the changes in OR for progression to severe disease based on the number of systemic symptoms and upper respiratory symptoms. Ordinal variables were set for the number of systemic symptoms (fever, decreased food intake, severe fatigue, and dyspnea, 0-4) and the number of upper respiratory symptoms (sore throat and nasal discharge, 0-2), and they were incorporated along with the remaining six symptoms as explanatory variables (Table S12).

All statistical analyses were performed using JMP[®] Pro Version 16.2.0 and SAS[®] Version 9.4 (SAS Institute Inc., Cary, NC, USA).

Reference:

1. Menni C, Valdes AM, Polidori L, 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(10335): 1618-24.

Table S1. SARS-CoV-2 vaccine types in individuals with vaccination history

	First			Second			Third			Fourth			Total
	Total N=97828	BA.2 n=18997	BA.5 n=78471	Total N=96776	BA.2 n=18656	BA.5 n=78120	Total N=58472	BA.2 n=7424	BA.5 n=51048	Total N=5083	BA.2 n=0	BA.5 n=5083	N=258159
	Number (%)												
BNT162b2	60909 (62.3)	12334 (64.9)	48575 (61.9)	60,221 (62.2)	12085 (64.8)	48126 (61.6)	35977 (61.5)	4846 (65.3)	31131 (61.0)	4043 (79.5)	0	4043 (79.5)	161150 (62.4)
mRNA-1273	35903 (36.7)	6564 (34.6)	29339 (37.4)	35,641 (36.8)	6489 (34.8)	29152 (37.3)	22449 (38.4)	2578 (34.7)	19871 (38.9)	1040 (20.5)	0	1040 (20.5)	95033 (36.9)
ChAdOx1	17 (0.0)	3 (0.0)	14 (0.0)	21 (0.0)	4 (0.0)	17 (0.0)	0	0	0	0	0	0	28 (0.0)
NVX-CoV2373	11 (0.0)	0	23 (0.0)	13 (0.0)	0	13 (0.0)	31 (0.1)	0	31 (0.1)	0	0	0	55 (0.0)
Data missing	976 (1.0)	96 (0.5)	880 (0.7)	890 (0.9)	78 (0.4)	812 (1.0)	15 (0.0)	0	15 (0.0)	0	0	0	1881 (0.7)

Table S2. Prevalence of COVID-19 symptoms in total and subgroups

	Total	Subvariants		Vaccination doses		Previous SARS-CoV-2 infection	
	(N=157 861)	BA.2 (n=34 336)	BA.5 (n=123 525)	2 or less (n=99 389)	3 or more (n=58 472)	No previous infection (n=152 094)	Previous infection (n=5 797)
	Number (%)						
Fever	61 218 (38.8)	10 131 (29.5)	51 087 (41.4)	45 304 (45.6)	15 914 (27.2)	59 527 (39.1)	1691 (29.3)
Cough	99 032 (62.7)	20 967 (61.1)	78 065 (63.2)	57 913 (58.3)	41 119 (70.3)	95 436 (62.7)	3596 (62.4)
Sore throat	95 838 (60.7)	19 681 (57.3)	76 157 (61.7)	55 357 (55.7)	40 481 (69.2)	92 455 (60.8)	3383 (58.7)
Nasal discharge	69 968 (44.3)	16 043 (46.7)	53 925 (43.7)	39 884 (40.1)	30 084 (51.5)	67 004 (44.1)	2964 (51.4)
Phlegm	56 915 (36.1)	12 513 (36.4)	44 402 (35.9)	33 961 (34.2)	22 954 (39.3)	55 065 (36.2)	1850 (32.1)
Headache	66 425 (42.1)	12 215 (35.6)	54 210 (43.9)	43 129 (43.4)	23 296 (39.8)	64 250 (42.2)	2175 (37.7)
Joint or muscle pain	45 955 (29.1)	7829 (22.8)	38 126 (30.9)	29 980 (30.2)	15 975 (27.3)	44 730 (29.4)	1225 (21.2)
Decreased food intake	44 359 (28.1)	7687 (22.4)	36 672 (29.7)	34 071 (34.3)	10 288 (17.6)	43 231 (28.4)	1128 (19.6)
Severe fatigue	42 242 (26.8)	7057 (20.6)	35 185 (28.5)	28 524 (28.7)	13 718 (23.5)	41 020 (27.0)	1222 (21.2)
Dyspnea	23 914 (15.1)	4153 (12.1)	19 761 (16.0)	14 403 (14.5)	9511 (16.3)	23 007 (15.1)	907 (15.7)
Diarrhea	12 392 (7.9)	2587 (7.5)	9805 (7.9)	9272 (9.3)	3120 (5.3)	11921 (7.8)	471 (8.2)
Smell or taste disorder	5908 (3.7)	967 (2.8)	4941 (4.0)	3853 (3.9)	2055 (3.5)	5716 (3.8)	192 (3.3)

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table S3. COVID-19 symptoms prevalence in unvaccinated individuals and subgroups

	Total	Subvariants	
	(N=60 033)	BA.2 (n=15 339)	BA.5 (n=44 694)
		Number (%)	
Fever	29 326 (48.9)	5854 (38.2)	23 472 (52.5)
Cough	31 781 (52.9)	7971 (52.0)	23 810 (53.3)
Sore throat	28 372 (47.3)	6625 (43.2)	21 747 (48.7)
Nasal discharge	21 401 (35.6)	5880 (38.3)	15 521 (34.7)
Phlegm	17 600 (29.3)	4484 (29.2)	13 116 (29.3)
Headache	23749 (39.6)	5035 (32.8)	18 714 (41.9)
Joint or muscle pain	15 835 (26.4)	3126 (20.4)	12 709 (28.4)
Decreased food intake	22 471 (37.4)	4490 (29.3)	17 981 (40.2)
Severe fatigue	16 188 (27.0)	3102 (20.2)	13 086 (29.3)
Dyspnea	7191 (12.0)	1397 (9.1)	5794 (13.0)
Diarrhea	5946 (9.9)	1412 (9.2)	4534 (10.1)
Smell or taste disorder	2199 (3.7)	383 (2.5)	1816 (4.1)

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table S4. Logistic regression analysis of factors for COVID-19 symptoms

A. Fever, cough, sore throat, nasal discharge, phlegm, headache

	Fever	Cough	Sore throat	Nasal discharge	Phlegm	Headache
	Adjusted OR (95% CI)					
Days from onset						
0	(reference)	(reference)	(reference)	(reference)	(reference)	(reference)
1	0.85 (0.82 - 0.88)	1.40 (1.36 - 1.45)	1.19 (1.15 - 1.23)	1.21 (1.17 - 1.25)	1.34 (1.29 - 1.39)	1.00 (0.96 - 1.03)
2	0.39 (0.38 - 0.41)	2.00 (1.93 - 2.06)	1.33 (1.29 - 1.38)	1.63 (1.58 - 1.69)	1.92 (1.85 - 1.99)	0.79 (0.77 - 0.82)
3	0.17 (0.16 - 0.18)	2.29 (2.20 - 2.38)	1.28 (1.23 - 1.33)	1.95 (1.88 - 2.03)	2.16 (2.07 - 2.25)	0.57 (0.55 - 0.59)
4	0.10 (0.09 - 0.10)	2.20 (2.10 - 2.32)	0.96 (0.91 - 1.01)	2.04 (1.94 - 2.13)	2.13 (2.02 - 2.23)	0.43 (0.41 - 0.45)
5	0.07 (0.06 - 0.08)	2.07 (1.94 - 2.22)	0.73 (0.69 - 0.78)	1.88 (1.76 - 2.00)	2.11 (1.98 - 2.26)	0.35 (0.33 - 0.38)
BA.5 group (compared with BA.2)	2.18 (2.12 - 2.25)	1.00 (0.98 - 1.03)	1.08 (1.05 - 1.11)	0.81 (0.79 - 0.83)	0.95 (0.93 - 0.98)	1.51 (1.47 - 1.55)
Age						
<10	1.22 (1.18 - 1.27)	0.47 (0.46 - 0.49)	0.11 (0.11 - 0.12)	0.74 (0.71 - 0.77)	0.23 (0.22 - 0.24)	0.22 (0.21 - 0.23)
10s	1.15 (1.10 - 1.20)	0.72 (0.69 - 0.75)	0.73 (0.70 - 0.76)	0.84 (0.81 - 0.87)	0.59 (0.57 - 0.62)	0.73 (0.70 - 0.75)
20s	(reference)	(reference)	(reference)	(reference)	(reference)	(reference)
30s	0.91 (0.88 - 0.95)	0.77 (0.75 - 0.80)	0.79 (0.76 - 0.82)	0.85 (0.82 - 0.88)	0.82 (0.79 - 0.84)	1.10 (1.06 - 1.13)
40s	0.78 (0.75 - 0.81)	0.70 (0.67 - 0.72)	0.72 (0.70 - 0.75)	0.69 (0.66 - 0.71)	0.68 (0.66 - 0.71)	1.00 (0.96 - 1.03)
50s	0.64 (0.62 - 0.67)	0.77 (0.73 - 0.80)	0.69 (0.66 - 0.72)	0.63 (0.61 - 0.66)	0.58 (0.56 - 0.61)	0.89 (0.85 - 0.92)
60s	0.45 (0.42 - 0.48)	0.76 (0.72 - 0.80)	0.56 (0.53 - 0.59)	0.54 (0.51 - 0.57)	0.49 (0.47 - 0.52)	0.57 (0.54 - 0.61)
70s	0.32 (0.29 - 0.35)	0.71 (0.66 - 0.76)	0.38 (0.35 - 0.41)	0.39 (0.37 - 0.42)	0.42 (0.39 - 0.45)	0.34 (0.31 - 0.36)
≥80	0.30 (0.27 - 0.34)	0.52 (0.48 - 0.58)	0.17 (0.15 - 0.18)	0.30 (0.27 - 0.33)	0.39 (0.35 - 0.43)	0.13 (0.11 - 0.15)
Male	1.14 (1.11 - 1.16)	0.85 (0.83 - 0.87)	0.84 (0.82 - 0.86)	0.90 (0.88 - 0.92)	0.96 (0.94 - 0.98)	0.72 (0.70 - 0.73)
Obesity (BMI≥30)	1.00 (0.95 - 1.06)	1.38 (1.31 - 1.46)	0.90 (0.85 - 0.95)	1.50 (1.43 - 1.58)	1.37 (1.30 - 1.44)	1.02 (0.97 - 1.07)
Malignancy	1.47 (1.27 - 1.70)	1.11 (0.97 - 1.27)	0.99 (0.87 - 1.13)	0.99 (0.87 - 1.13)	1.10 (0.97 - 1.25)	0.99 (0.86 - 1.13)
Immuno-compromised	1.00 (0.74 - 1.34)	0.87 (0.66 - 1.14)	0.95 (0.73 - 1.24)	1.05 (0.81 - 1.36)	1.21 (0.93 - 1.57)	1.18 (0.89 - 1.55)
Chronic respiratory diseases	1.04 (0.98 - 1.10)	1.47 (1.39 - 1.56)	0.95 (0.90 - 1.01)	1.41 (1.33 - 1.48)	1.60 (1.52 - 1.69)	1.36 (1.28 - 1.43)
Chronic kidney diseases	0.82 (0.48 - 1.39)	0.81 (0.52 - 1.24)	0.80 (0.52 - 1.24)	1.22 (0.79 - 1.88)	0.79 (0.48 - 1.29)	0.56 (0.32 - 1.00)
Cardiovascular diseases	1.19 (1.05 - 1.35)	1.22 (1.09 - 1.36)	1.14 (1.03 - 1.27)	1.17 (1.05 - 1.30)	1.16 (1.04 - 1.29)	0.94 (0.83 - 1.06)
Cerebrovascular diseases	1.18 (0.71 - 1.96)	0.92 (0.61 - 1.40)	0.92 (0.62 - 1.39)	1.03 (0.69 - 1.55)	0.87 (0.57 - 1.34)	0.63 (0.37 - 1.08)
Hypertension	1.04 (0.98 - 1.10)	1.12 (1.07 - 1.19)	1.00 (0.95 - 1.06)	1.09 (1.03 - 1.14)	1.08 (1.03 - 1.14)	0.88 (0.83 - 0.93)
Diabetes	0.88 (0.81 - 0.96)	1.12 (1.04 - 1.21)	1.00 (0.93 - 1.07)	1.14 (1.06 - 1.22)	1.04 (0.96 - 1.11)	0.91 (0.84 - 0.99)

Vaccination ≥ 3 doses	0.50 (0.49 - 0.51)	1.49 (1.45 - 1.52)	1.33 (1.29 - 1.36)	1.84 (1.80 - 1.89)	1.06 (1.04 - 1.09)	0.65 (0.64 - 0.67)
Previous SARS-CoV-2 infection	0.41 (0.39 - 0.44)	1.13 (1.07 - 1.20)	1.10 (1.03 - 1.16)	1.50 (1.42 - 1.59)	0.87 (0.82 - 0.92)	0.75 (0.71 - 0.80)

BMI, body mass index; CI, confidence interval; OR, odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

B. Joint or muscle pain, decreased food intake, severe fatigue, dyspnea, diarrhea, smell or taste disorder

	Joint or muscle pain	Decreased food intake	Severe fatigue	Dyspnea	Diarrhea	Smell or taste disorder
Adjusted OR (95% CI)						
Days from onset						
0	(reference)	(reference)	(reference)	(reference)	(reference)	(reference)
1	1.08 (1.05 - 1.12)	1.03 (0.99 - 1.06)	0.94 (0.90 - 0.97)	1.09 (1.04 - 1.14)	1.28 (1.20 - 1.37)	1.03 (0.93 - 1.14)
2	0.83 (0.80 - 0.86)	0.82 (0.79 - 0.85)	0.69 (0.66 - 0.71)	1.28 (1.22 - 1.34)	1.60 (1.50 - 1.71)	1.48 (1.34 - 1.63)
3	0.57 (0.55 - 0.60)	0.59 (0.57 - 0.62)	0.50 (0.48 - 0.52)	1.31 (1.24 - 1.38)	1.64 (1.52 - 1.76)	2.04 (1.84 - 2.27)
4	0.39 (0.37 - 0.42)	0.45 (0.42 - 0.48)	0.40 (0.37 - 0.42)	1.27 (1.19 - 1.36)	1.59 (1.46 - 1.74)	2.49 (2.21 - 2.80)
5	0.30 (0.28 - 0.33)	0.37 (0.34 - 0.40)	0.35 (0.32 - 0.38)	1.19 (1.09 - 1.30)	1.58 (1.41 - 1.78)	4.02 (3.53 - 4.57)
BA.5 group (compared with BA.2)	1.59 (1.54 - 1.63)	1.80 (1.75 - 1.86)	1.64 (1.59 - 1.69)	1.37 (1.32 - 1.42)	1.20 (1.14 - 1.25)	1.52 (1.42 - 1.63)
Age						
<10	0.12 (0.11 - 0.13)	0.91 (0.87 - 0.94)	0.27 (0.26 - 0.29)	0.18 (0.17 - 0.19)	0.86 (0.80 - 0.91)	0.21 (0.19 - 0.25)
10s	0.40 (0.39 - 0.42)	1.07 (1.02 - 1.11)	0.60 (0.58 - 0.63)	0.52 (0.49 - 0.55)	0.80 (0.75 - 0.86)	0.64 (0.58 - 0.70)
20s	(reference)	(reference)	(reference)	(reference)	(reference)	(reference)
30s	1.25 (1.20 - 1.29)	0.87 (0.84 - 0.90)	1.08 (1.04 - 1.12)	0.77 (0.74 - 0.81)	1.05 (0.99 - 1.12)	0.97 (0.90 - 1.05)
40s	1.18 (1.13 - 1.22)	0.87 (0.84 - 0.91)	0.89 (0.86 - 0.93)	0.66 (0.63 - 0.69)	0.99 (0.93 - 1.05)	0.80 (0.74 - 0.87)
50s	1.03 (0.99 - 1.08)	0.94 (0.89 - 0.98)	0.76 (0.73 - 0.79)	0.65 (0.62 - 0.69)	0.88 (0.81 - 0.95)	0.88 (0.80 - 0.97)
60s	0.72 (0.68 - 0.76)	0.70 (0.66 - 0.75)	0.54 (0.50 - 0.57)	0.50 (0.46 - 0.53)	0.65 (0.58 - 0.72)	0.76 (0.67 - 0.87)
70s	0.46 (0.42 - 0.50)	0.67 (0.61 - 0.73)	0.47 (0.43 - 0.51)	0.39 (0.35 - 0.43)	0.46 (0.39 - 0.54)	0.57 (0.48 - 0.69)
≥80	0.20 (0.17 - 0.23)	0.76 (0.68 - 0.86)	0.48 (0.43 - 0.54)	0.48 (0.43 - 0.55)	0.44 (0.35 - 0.56)	0.40 (0.30 - 0.55)
Male	0.88 (0.86 - 0.90)	0.68 (0.66 - 0.69)	1.07 (1.05 - 1.09)	0.89 (0.86 - 0.92)	1.27 (1.23 - 1.32)	1.11 (1.05 - 1.17)
Obesity (BMI≥30)	1.01 (0.96 - 1.07)	0.83 (0.78 - 0.89)	1.12 (1.06 - 1.18)	1.53 (1.44 - 1.62)	1.53 (1.41 - 1.65)	1.33 (1.19 - 1.48)
Malignancy	0.96 (0.83 - 1.11)	1.28 (1.10 - 1.48)	1.17 (1.01 - 1.35)	1.31 (1.11 - 1.53)	0.72 (0.54 - 0.97)	1.42 (1.07 - 1.88)
Immunocompromised	1.27 (0.96 - 1.70)	1.48 (1.11 - 1.97)	1.23 (0.92 - 1.63)	1.27 (0.93 - 1.73)	1.50 (0.89 - 2.52)	0.99 (0.55 - 1.79)
Chronic respiratory diseases	1.43 (1.35 - 1.52)	1.26 (1.19 - 1.34)	1.50 (1.41 - 1.59)	2.39 (2.25 - 2.54)	1.41 (1.29 - 1.54)	1.53 (1.36 - 1.72)
Chronic kidney diseases	0.26 (0.11 - 0.61)	1.05 (0.59 - 1.87)	0.69 (0.39 - 1.23)	1.15 (0.63 - 2.09)	2.24 (1.07 - 4.69)	0.44 (0.06 - 3.20)
Cardiovascular diseases	1.21 (1.07 - 1.37)	1.12 (0.99 - 1.28)	1.36 (1.21 - 1.53)	1.54 (1.35 - 1.75)	1.15 (0.93 - 1.40)	1.00 (0.76 - 1.32)
Cerebrovascular diseases	1.03 (0.61 - 1.73)	1.44 (0.88 - 2.36)	1.08 (0.65 - 1.78)	0.88 (0.48 - 1.62)	2.42 (1.28 - 4.60)	0.58 (0.14 - 2.36)
Hypertension	0.99 (0.94 - 1.05)	0.85 (0.80 - 0.91)	0.94 (0.89 - 1.00)	1.09 (1.02 - 1.17)	1.17 (1.06 - 1.29)	1.03 (0.91 - 1.17)
Diabetes	1.01 (0.93 - 1.10)	0.82 (0.74 - 0.90)	1.05 (0.97 - 1.15)	1.17 (1.07 - 1.29)	1.14 (1.00 - 1.30)	1.03 (0.86 - 1.22)

Vaccination ≥ 3 doses	0.54 (0.52 - 0.55)	0.39 (0.37 - 0.40)	0.59 (0.58 - 0.61)	0.90 (0.87 - 0.93)	0.55 (0.52 - 0.57)	0.70 (0.66 - 0.74)
Previous SARS-CoV-2 infection	0.58 (0.54 - 0.62)	0.46 (0.43 - 0.49)	0.63 (0.59 - 0.67)	1.04 (0.97 - 1.12)	0.89 (0.81 - 0.98)	0.83 (0.71 - 0.96)

BMI, body mass index; CI, confidence interval; OR, odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

Table S5. Logistic regression analysis of factors for severe disease progression

	Age < 65		Adjusted OR (95% CI)	Age ≥ 65		Adjusted OR (95% CI)
	Progression to severe disease -n, %			Progression to severe disease- n, %		
	No (n=146 462)	Yes (n=31)		No (n=10 757)	Yes (n=110*)	
Days from onset						
0	21 129 (14.4)	7 (22.6)	(reference)	1409 (13.1)	31 (28.2)	(reference)
1	49 435 (33.8)	12 (38.7)	0.81 (0.31 - 2.12)	2739 (25.5)	31 (28.2)	0.73 (0.43 - 1.26)
2	41 307 (28.2)	3 (9.7)	0.21 (0.05 - 0.84)	2840 (26.4)	24 (21.8)	0.79 (0.44 - 1.41)
3	20 900 (14.3)	3 (9.7)	0.37 (0.09 - 1.53)	1936 (18.0)	12 (10.9)	0.65 (0.31 - 1.33)
4	9435 (6.4)	2 (6.5)	0.54 (0.10 - 2.80)	1174 (10.9)	3 (2.7)	0.23 (0.07 - 0.78)
5	4256 (2.9)	4 (12.9)	2.19 (0.56 - 8.48)	659 (6.1)	9 (8.2)	1.21 (0.51 - 2.85)
BA.5 (compared with BA.2)	113 758 (77.7)	24 (77.4)	0.92 (0.38 - 2.23)	9331 (86.7)	98 (89.1)	1.21 (0.64 - 2.29)
Age group						
<10	23 177 (15.8)	4 (12.9)	3.38 (0.35 - 32.56)	N/A	N/A	N/A
10s	21 134 (14.4)	2 (6.5)	2.42 (0.22 - 27.14)	N/A	N/A	N/A
20s	26 208 (17.9)	1 (3.2)	(reference)	N/A	N/A	N/A
30s	27 636 (18.9)	2 (6.5)	1.85 (0.17 - 20.46)	N/A	N/A	N/A
40s	26 506 (18.1)	7 (22.6)	6.18 (0.74 - 51.28)	N/A	N/A	N/A
50s	16 607 (11.3)	8 (25.8)	9.89 (1.17 - 83.61)	N/A	N/A	N/A
60s	5194 (3.5)	7 (22.6)	26.07 (2.91 - 233.84)	3664 (34.1)	8 (7.3)	(reference)
70s	N/A	N/A	N/A	4812 (44.7)	25 (22.7)	2.14 (0.95 - 4.82)
≥80	N/A	N/A	N/A	2281 (21.2)	77 (70.0)	10.17 (4.72 - 21.93)
Male	70 089 (47.9)	15 (48.4)	0.91 (0.44 - 1.92)	4929 (45.8)	59 (53.6)	1.62 (1.07 - 2.46)
Obesity (BMI≥30)	6298 (4.3)	7 (22.6)	3.55 (1.33 - 9.49)	401 (3.7)	3 (2.7)	0.80 (0.21 - 2.99)
Malignancy	714 (0.5)	6 (19.4)	14.46 (4.55 - 45.93)	543 (5.0)	19 (17.3)	2.56 (1.40 - 4.66)
Immunocompromised	198 (0.1)	2 (6.5)	2.39 (0.38 - 14.86)	88 (0.8)	2 (1.8)	0.39 (0.07 - 2.04)
Chronic respiratory diseases	5029 (3.4)	3 (9.7)	1.29 (0.35 - 4.72)	590 (5.5)	17 (15.5)	2.89 (1.61 - 5.20)
Chronic kidney diseases	36 (0.0)	1 (3.2)	30.16 (3.01 - 302.44)	48 (0.4)	3 (2.7)	5.62 (1.55 - 20.36)
Cardiovascular diseases	756 (0.5)	0 (0.0)	N/A**	840 (7.8)	18 (16.4)	1.04 (0.59 - 1.82)
Cerebrovascular diseases	34 (0.0)	0 (0.0)	N/A**	65 (0.6)	3 (2.7)	4.22 (1.07 - 16.61)

Hypertension	5116 (3.5)	5 (16.1)	1.06 (0.34 - 3.34)	3608 (33.5)	29 (26.4)	0.57 (0.36 - 0.91)
Diabetes	2139 (1.5)	5 (16.1)	2.93 (0.90 - 9.52)	1567 (14.6)	19 (17.3)	1.40 (0.82 - 2.39)
Vaccination ≥ 3 doses	49 411 (33.7)	9 (29.0)	0.36 (0.14 - 0.90)	8933 (83.0)	69 (62.7)	0.37 (0.24 - 0.56)
Previous SARS-CoV-2 infection	5690 (3.9)	1 (3.2)	0.78 (0.09 - 6.80)	64 (0.6)	2 (1.8)	1.78 (0.37 - 8.55)
Vaccination ≥ 3 doses + Previous SARS-CoV-2 infection	848 (0.6)	0 (0.0)	N/A***	46 (0.4)	1 (0.9)	N/A***
Fever	59 257 (40.5)	12 (38.7)	0.78 (0.32 - 1.90)	1718 (16.0)	46 (41.8)	2.93 (1.89 - 4.52)
Cough	91 343 (62.4)	24 (77.4)	1.84 (0.72 - 4.73)	7288 (67.8)	70 (63.6)	1.08 (0.68 - 1.70)
Sore throat	89 806 (61.3)	13 (41.9)	0.40 (0.18 - 0.87)	5679 (52.8)	26 (23.6)	0.38 (0.24 - 0.63)
Nasal discharge	65 628 (44.8)	14 (45.2)	0.90 (0.42 - 1.96)	4096 (38.1)	20 (18.2)	0.48 (0.28 - 0.81)
Phlegm	53 366 (36.4)	14 (45.2)	1.16 (0.52 - 2.61)	3324 (30.9)	34 (30.9)	1.00 (0.62 - 1.62)
Headache	64 002 (43.7)	12 (38.7)	0.66 (0.29 - 1.53)	2187 (20.3)	12 (10.9)	0.62 (0.32 - 1.23)
Joint or muscle pain	44 094 (30.1)	9 (29.0)	0.69 (0.28 - 1.71)	1704 (15.8)	11 (10.0)	0.53 (0.27 - 1.08)
Decreased food intake	42 469 (29.0)	13 (41.9)	1.81 (0.79 - 4.14)	1684 (15.7)	47 (42.7)	2.38 (1.54 - 3.69)
Severe fatigue	40 345 (27.5)	13 (41.9)	1.91 (0.83 - 4.40)	1717 (16.0)	40 (36.4)	1.90 (1.20 - 3.01)
Dyspnea	22 498 (15.4)	12 (38.7)	2.78 (1.20 - 6.46)	1294 (12.0)	36 (32.7)	3.01 (1.84 - 4.91)
Diarrhea	11 927 (8.1)	3 (9.7)	0.74 (0.20 - 2.75)	413 (3.8)	4 (3.6)	0.88 (0.31 - 2.51)
Smell or taste disorder	5564 (3.8)	2 (6.5)	1.12 (0.25 - 5.07)	327 (3.0)	0 (0.0)	N/A**

* One was excluded due to missing data out of 111 individuals.

** Excluded from analysis due to small number of symptomatic individuals for which confidence intervals could not be determined.

*** Not included in multivariable analysis.

BMI, body mass index; CI, confidence interval; OR, odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table S6. Propensity score matching analysis of day-of-onset symptoms (grouped with subvariants)

A. Unvaccinated individuals.

	Before match			1:1 matched		
	BA.2	BA.5	Std diff	BA.2	BA.5	Std diff
Total	2402	7393		2401	2401	
Age, mean (SD)	16.3 (15.7)	18.1 (17.9)	-0.111	16.2 (15.7)	16.1 (15.8)	0.011
Age group						
<10	1169 (48.7)	3492 (47.2)	0.029	1169 (48.7)	1168 (48.6)	0.001
10s	503 (20.9)	1288 (17.4)	0.089	503 (21.0)	501 (20.9)	0.002
20s	268 (11.2)	862 (11.7)	-0.016	268 (11.2)	269 (11.2)	-0.001
30s	187 (7.8)	714 (9.7)	-0.066	187 (7.8)	189 (7.9)	-0.003
40s	167 (7.0)	505 (6.8)	0.005	166 (6.9)	174 (7.2)	-0.013
50s	70 (2.9)	306 (4.1)	-0.066	70 (2.9)	67 (2.8)	0.008
60s	22 (0.9)	105 (1.4)	-0.047	22 (0.9)	17 (0.7)	0.023
70s	10 (0.4)	60 (0.8)	-0.051	10 (0.4)	11 (0.5)	-0.006
≥ 80	6 (0.3)	61 (0.8)	-0.079	6 (0.3)	5 (0.2)	0.009
Male	1284 (53.5)	4052 (54.8)	-0.027	1284 (53.5)	1285 (53.5)	-0.001
Obesity (BMI ≥ 30)	61 (2.5)	185 (2.5)	0.002	60 (2.5)	54 (2.2)	0.016
Comorbidities						
Malignancy	8 (0.3)	29 (0.4)	-0.010	7 (0.3)	4 (0.2)	0.026
Immunocompromised	1 (0.0)	7 (0.1)	-0.020	1 (0.0)	1 (0.0)	0.000
Chronic respiratory diseases	77 (3.2)	251 (3.4)	-0.011	77 (3.2)	74 (3.1)	0.007
Chronic kidney diseases	0 (0.0)	1 (0.0)	-0.016	0 (0.0)	0 (0.0)	0.000
Cardiovascular diseases	9 (0.4)	36 (0.5)	-0.017	9 (0.4)	8 (0.3)	0.007
Cerebrovascular diseases	0 (0.0)	1 (0.0)	-0.016	0 (0.0)	0 (0.0)	0.000
Hypertension	26 (1.1)	135 (1.8)	-0.062	26 (1.1)	25 (1.0)	0.004
Diabetes	20 (0.8)	63 (0.9)	-0.002	19 (0.8)	18 (0.8)	0.005
Previous SARS-CoV-2 infection	76 (3.2)	540 (7.3)	-0.187	76 (3.2)	77 (3.2)	-0.002
Prevalence of symptoms						
Fever				1539 (64.1)	1827 (76.1)	
Cough				997 (41.5)	995 (41.4)	
Sore throat				925 (38.5)	915 (38.1)	
Nasal discharge				799 (33.3)	708 (29.5)	
Phlegm				524 (21.8)	444 (18.5)	

Headache	995 (41.4)	1074 (44.7)
Joint or muscle pain	541 (22.5)	654 (27.2)
Decreased food intake	919 (38.3)	1072 (44.6)
Severe fatigue	663 (27.6)	785 (32.7)
Dyspnea	197 (8.2)	233 (9.7)
Diarrhea	145 (6.0)	145 (6.0)
Smell or taste disorder	37 (1.5)	57 (2.4)
Number of symptoms, median (IQR)	3 (2-5)	3 (2-5)

Data are n (%) unless otherwise specified.

Absolute value of standardized difference (Std diff) greater than 0.1 is considered as a sign of imbalance.

BMI, body mass index; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation.

B. Two doses vaccinees

	Before match			1:1 matched		
	BA.2	BA.5	Std diff	BA.2	BA.5	Std diff
Total	1252	3427		644	644	
Age, mean (SD)	31.8 (14.1)	31.9 (14.9)	-0.009	28.7 (14.4)	27.3 (14.9)	0.093
Age group						
>10	22 (1.8)	151 (4.4)	-0.154	20 (3.1)	20 (3.1)	0.000
10s	308 (24.6)	722 (21.1)	0.084	223 (34.6)	231 (35.9)	-0.026
20s	254 (20.3)	632 (18.4)	0.047	121 (18.8)	125 (19.4)	-0.016
30s	278 (22.2)	840 (24.5)	-0.055	127 (19.7)	123 (19.1)	0.016
40s	247 (19.7)	697 (20.3)	-0.015	97 (15.1)	89 (13.8)	0.035
50s	109 (8.7)	277 (8.1)	0.022	40 (6.2)	40 (6.2)	0.000
60s	28 (2.2)	73 (2.1)	0.007	12 (1.9)	11 (1.7)	0.012
70s	5 (0.4)	15 (0.4)	-0.006	4 (0.6)	5 (0.8)	-0.019
80s	1 (0.1)	20 (0.6)	-0.088	0 (0.0)	0 (0.0)	0.000
Male	642 (51.3)	1863 (54.4)	-0.062	339 (52.6)	328 (50.9)	0.034
Obesity (BMI \geq 30)	62 (5.0)	189 (5.5)	-0.025	29 (4.5)	28 (4.3)	0.008
Comorbidities						
Malignancy	6 (0.5)	15 (0.4)	0.006	2 (0.3)	0 (0.0)	0.079
Immunocompromised	1 (0.1)	1 (0.0)	0.022	0 (0.0)	0 (0.0)	0.000
Chronic respiratory diseases	48 (3.8)	121 (3.5)	0.016	17 (2.6)	17 (2.6)	0.000
Chronic kidney diseases	0 (0.0)	(0.0)	0.000	0 (0.0)	0 (0.0)	0.000
Cardiovascular diseases	5 (0.4)	22 (0.6)	-0.034	2 (0.3)	2 (0.3)	0.000
Cerebrovascular diseases	1 (0.1)	1 (0.0)	0.022	0 (0.0)	0 (0.0)	0.000
Hypertension	42 (3.4)	118 (3.4)	-0.005	21 (3.3)	19 (3.0)	0.018
Diabetes	18 (1.4)	53 (1.5)	-0.009	8 (1.2)	6 (0.9)	0.030
Days since vaccination						
-60	42 (3.4)	47 (1.4)	0.131	40 (6.2)	43 (6.7)	-0.019
61-120	41 (3.3)	190 (5.5)	-0.111	35 (5.4)	35 (5.4)	0.000
121-180	210 (16.8)	195 (5.7)	0.357	152 (23.6)	142 (22.1)	0.037
181-240	759 (60.6)	225 (6.6)	1.396	217 (33.7)	224 (34.8)	-0.023
241-	200 (16.0)	2770 (80.8)	-1.706	200 (31.1)	200 (31.1)	0.000
Previous SARS-CoV-2 infection	27 (2.2)	155 (4.5)	-0.132	18 (2.8)	20 (3.1)	-0.018
Prevalence of symptoms						

Fever	296 (46.0)	381 (59.2)
Cough	380 (59.0)	349 (54.2)
Sore throat	450 (69.9)	393 (61.0)
Nasal discharge	293 (45.5)	240 (37.3)
Phlegm	235 (36.5)	171 (26.6)
Headache	326 (50.6)	340 (52.8)
Joint or muscle pain	221 (34.3)	224 (34.8)
Decreased food intake	173 (26.9)	220 (34.2)
Severe fatigue	193 (30.0)	215 (33.4)
Dyspnea	107 (16.6)	96 (14.9)
Diarrhea	43 (6.7)	38 (5.9)
Smell or taste disorder	21 (3.3)	14 (2.2)
Number of symptoms, median (IQR)	4 (2-6)	4 (2-6)

Data are n (%) unless otherwise specified.

Absolute value of standardized difference (Std diff) greater than 0.1 is considered as a sign of imbalance.

BMI, body mass index; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation.

C. Three doses vaccinees

	Before match			1:1 matched		
	BA.2	BA.5	Std diff	BA.2	BA.5	Std diff
Total	1038	6175		902	902	
Age, mean (SD)	44.8 (16.4)	43.6 (16.4)	0.077	43.6 (15.9)	42.0 (14.9)	0.107
Age group						
10s	17 (1.6)	317 (5.1)	-0.194	17 (1.9)	17 (1.9)	0.000
20s	181 (17.4)	1050 (17.0)	0.011	166 (18.4)	177 (19.6)	-0.031
30s	255 (24.6)	1279 (20.7)	0.092	235 (26.1)	252 (27.9)	-0.042
40s	225 (21.7)	1429 (23.1)	-0.035	201 (22.3)	201 (22.3)	0.000
50s	152 (14.6)	1142 (18.5)	-0.104	132 (14.6)	131 (14.5)	0.003
60s	110 (10.6)	531 (8.6)	0.068	83 (9.2)	83 (9.2)	0.000
70s	65 (6.3)	252 (4.1)	0.099	42 (4.7)	22 (2.4)	0.120
≥ 80	33 (3.2)	175 (2.8)	0.020	26 (2.9)	19 (2.1)	0.050
Male	411 (39.6)	2764 (44.8)	-0.105	357 (39.6)	324 (35.9)	0.076
Obesity (BMI ≥ 30)	56 (5.4)	328 (5.3)	0.004	47 (5.2)	40 (4.4)	0.036
Comorbidities						
Malignancy	10 (1.0)	91 (1.5)	-0.047	8 (0.9)	5 (0.6)	0.039
Immunocompromised	3 (0.3)	27 (0.4)	-0.025	3 (0.3)	902 (100.0)	0.082
Chronic respiratory diseases	51 (4.9)	243 (3.9)	0.048	43 (4.8)	47 (5.2)	-0.020
Chronic kidney diseases	5 (0.5)	4 (0.1)	0.080	1 (0.1)	2 (0.2)	-0.027
Cardiovascular diseases	16 (1.5)	95 (1.5)	0.000	10 (1.1)	8 (0.9)	0.022
Cerebrovascular diseases	3 (0.3)	2 (0.0)	0.064	1 (0.1)	2 (0.2)	-0.027
Hypertension	108 (10.4)	568 (9.2)	0.041	82 (9.1)	86 (9.5)	-0.015
Diabetes	35 (3.4)	222 (3.6)	-0.012	30 (3.3)	23 (2.6)	0.046
Days since vaccination						
-60	347 (33.4)	284 (4.6)	0.790	235 (26.1)	236 (26.2)	-0.003
61-120	455 (43.8)	1504 (24.4)	0.420	431 (47.8)	424 (47.0)	0.016
121-180	228 (22.0)	2890 (46.8)	-0.542	228 (25.3)	234 (25.9)	-0.015
181-240	8 (0.8)	1381 (22.4)	-0.717	8 (0.9)	8 (0.9)	0.000
241-	0 (0.0)	116 (1.9)	-0.196	0 (0.0)	0 (0.0)	0.000
Previous SARS-CoV-2 infection	17 (1.6)	109 (1.8)	-0.010	14 (1.6)	17 (1.9)	-0.026
Prevalence of symptoms						
Fever				173 (19.2)	375 (41.6)	

Cough	535 (59.3)	528 (58.5)
Sore throat	593 (65.7)	632 (70.1)
Nasal discharge	433 (48.0)	389 (43.1)
Phlegm	301 (33.4)	273 (30.3)
Headache	294 (32.6)	436 (48.3)
Joint or muscle pain	191 (21.2)	287 (31.8)
Decreased food intake	109 (12.1)	190 (21.1)
Severe fatigue	183 (20.3)	265 (29.4)
Dyspnea	98 (10.9)	143 (15.9)
Diarrhea	50 (5.5)	51 (5.7)
Smell or taste disorder	18 (2.0)	24 (2.7)
Number of symptoms, median (IQR)	3 (2-5)	4 (2-5)

Data are n (%) unless otherwise specified.

Absolute value of standardized difference (Std diff) greater than 0.1 is considered as a sign of imbalance.

BMI, body mass index; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation.

Table S7. COVID-19 symptoms prevalence by days since symptom onset in total and subgroups

A. Total individuals (N=157 861)

	Day 0 (onset) (n=22 663)	Day 1 (n=52 383)	Day 2 (n=44 320)	Day 3 (n=22 927)	Day 4 (n=10 635)	Day 5 (n=4933)
	Number (%)					
Fever	12 776 (56.4)	27 645 (52.8)	15 047 (34.0)	4187 (18.3)	1173 (11.0)	390 (7.9)
Cough	11 301 (49.9)	30 683 (58.6)	29 926 (67.5)	16 255 (70.9)	7465 (70.2)	3402 (69.0)
Sore throat	12 257 (54.1)	31 407 (60.0)	28 595 (64.5)	14 837 (64.7)	6195 (58.3)	2547 (51.6)
Nasal discharge	8025 (35.4)	20 927 (40.0)	21 037 (47.5)	11 897 (51.9)	5600 (52.7)	2482 (50.3)
Phlegm	5650 (24.9)	16 476 (31.5)	18 022 (40.7)	10 053 (43.8)	4599 (43.2)	2115 (42.9)
Headache	10 214 (45.1)	24 562 (46.9)	19 063 (43.0)	8215 (35.8)	3124 (29.4)	1247 (25.3)
Joint or muscle pain	6870 (30.3)	17 697 (33.8)	13 345 (30.1)	5451 (23.8)	1891 (17.8)	701 (14.2)
Decreased food intake	7269 (32.1)	17 214 (32.9)	12 372 (27.9)	4958 (21.6)	1837 (17.3)	709 (14.4)
Severe fatigue	7137 (31.5)	16 385 (31.3)	11 495 (25.9)	4699 (20.5)	1791 (16.8)	735 (14.9)
Dyspnea	2824 (12.5)	7293 (13.9)	7353 (16.6)	3916 (17.1)	1758 (16.5)	770 (15.6)
Diarrhea	1310 (5.8)	3811 (7.3)	3928 (8.9)	2024 (8.8)	905 (8.5)	414 (8.4)
Smell or taste disorder	542 (2.4)	1352 (2.6)	1685 (3.8)	1197 (5.2)	662 (6.2)	470 (9.5)

B. Two or fewer vaccinations (N=99 389)

	Day 0 (onset) (n=14 721)	Day 1 (n=33 651)	Day 2 (n=27 878)	Day 3 (n=13 837)	Day 4 (n=6389)	Day 5 (n=2913)
	Number (%)					
Fever	9762 (66.3)	20 767 (61.7)	10 742 (38.5)	2879 (20.8)	864 (13.5)	290 (10.0)
Cough	6623 (45.0)	18 097 (53.8)	17 488 (62.7)	9374 (67.7)	4339 (67.9)	1992 (68.4)
Sore throat	6945 (47.2)	18 136 (53.9)	16 785 (60.2)	8531 (61.7)	3539 (55.4)	1421 (48.8)
Nasal discharge	4747 (32.2)	11 978 (35.6)	11 856 (42.5)	6589 (47.6)	3270 (51.2)	1444 (49.6)
Phlegm	3294 (22.4)	9826 (29.2)	10 907 (39.1)	5976 (43.2)	2738 (42.9)	1220 (41.9)
Headache	6907 (46.9)	16 262 (48.3)	12 184 (43.7)	5075 (36.7)	1942 (30.4)	759 (26.1)
Joint or muscle pain	4540 (30.8)	11 536 (34.3)	8729 (31.3)	3485 (25.2)	1245 (19.5)	445 (15.3)
Decreased food intake	5802 (39.4)	13 439 (39.9)	9362 (33.6)	3612 (26.1)	1346 (21.1)	510 (17.5)
Severe fatigue	4958 (33.7)	11 154 (33.1)	7693 (27.6)	3062 (22.1)	1189 (18.6)	468 (16.1)
Dyspnea	1702 (11.6)	4359 (13.0)	4391 (15.8)	2372 (17.1)	1103 (17.3)	476 (16.3)
Diarrhea	919 (6.2)	2858 (8.5)	3015 (10.8)	1509 (10.9)	686 (10.7)	285 (9.8)
Smell or taste disorder	351 (2.4)	920 (2.7)	1162 (4.2)	752 (5.4)	389 (6.1)	279 (9.6)

C. Three or more vaccinations (N=58 472)

	Day 0 (onset (n=7942))	Day 1 (n=18 732)	Day 2 (n=16 442)	Day 3 (n=9090)	Day 4 (n=4246)	Day 5 (n=2020)
	Number (%)					
Fever	3014 (38.0)	6878 (36.7)	4305 (26.2)	1308 (14.4)	309 (7.3)	100 (5.0)
Cough	4678 (58.9)	12 586 (67.2)	12 438 (75.6)	6881 (75.7)	3126 (73.6)	1410 (69.8)
Sore throat	5312 (66.9)	13 271 (70.8)	11 810 (71.8)	6306 (69.4)	2656 (62.6)	1126 (55.7)
Nasal discharge	3278 (41.3)	8949 (47.8)	9181 (55.8)	5308 (58.4)	2330 (54.9)	1038 (51.4)
Phlegm	2356 (29.7)	6650 (35.5)	7115 (43.3)	4077 (44.9)	1861 (43.8)	895 (44.3)
Headache	3307 (41.6)	8300 (44.3)	6879 (41.8)	3140 (34.5)	1182 (27.8)	488 (24.2)
Joint or muscle pain	2330 (29.3)	6161 (32.9)	4616 (28.1)	1966 (21.6)	646 (15.2)	256 (12.7)
Decreased food intake	1467 (18.5)	3775 (20.2)	3010 (18.3)	1346 (14.8)	491 (11.6)	199 (9.9)
Severe fatigue	2179 (27.4)	5231 (27.9)	3802 (23.1)	1637 (18.0)	602 (14.2)	267 (13.2)
Dyspnea	1122 (14.1)	2934 (15.7)	2962 (18.0)	1544 (17.0)	655 (15.4)	294 (14.6)
Diarrhea	391 (4.9)	953 (5.1)	913 (5.6)	515 (5.7)	219 (5.2)	129 (6.4)
Smell or taste disorder	191 (2.4)	432 (2.3)	523 (3.2)	445 (4.9)	273 (6.4)	191 (9.5)

D. No previous SARS-CoV-2 infection (N=152 094)

	Day 0 (onset) (n=21 715)	Day 1 (n=50 464)	Day 2 (n=42 794)	Day 3 (n=22 117)	Day 4 (n=10 253)	Day 5 (n=4751)
	Number (%)					
Fever	12 337 (56.8)	26 883 (53.3)	14 724 (34.4)	4060 (18.4)	1142 (11.1)	381 (8.0)
Cough	10 833 (49.9)	29 562 (58.6)	28 894 (67.5)	15 679 (70.9)	7209 (70.3)	3259 (68.6)
Sore throat	11 737 (54.1)	30 314 (60.1)	27 632 (64.6)	14 335 (64.8)	5986 (58.4)	2451 (51.6)
Nasal discharge	7611 (35.1)	19 990 (39.6)	20 195 (47.2)	11 431 (51.7)	5396 (52.6)	2381 (50.1)
Phlegm	5447 (25.1)	15 908 (31.5)	17 470 (40.8)	9736 (44.0)	4459 (43.5)	2045 (43.0)
Headache	9826 (45.3)	23 800 (47.2)	18 485 (43.2)	7930 (35.9)	3010 (29.4)	1199 (25.2)
Joint or muscle pain	6684 (30.8)	17 229 (34.1)	13 016 (30.4)	5289 (23.9)	1837 (17.9)	675 (14.2)
Decreased food intake	7039 (32.4)	16 760 (33.2)	12 102 (28.3)	4848 (21.9)	1787 (17.4)	695 (14.6)
Severe fatigue	6894 (31.7)	15 937 (31.6)	11 199 (26.2)	4547 (20.6)	1732 (16.9)	711 (15.0)
Dyspnea	2718 (12.5)	7008 (13.9)	7088 (16.6)	3778 (17.1)	1685 (16.4)	730 (15.4)
Diarrhea	1244 (5.7)	3659 (7.3)	3787 (8.8)	1956 (8.8)	874 (8.5)	401 (8.4)
Smell or taste disorder	515 (2.4)	1311 (2.6)	1637 (3.8)	1149 (5.2)	644 (6.3)	460 (9.7)

E. Previous SARS-CoV-2 infection (N=5767)

	Day 0 (onset) (n=948)	Day 1 (n=1919)	Day 2 (n=1526)	Day 3 (n=810)	Day 4 (n=382)	Day 5 (n=182)
	Number (%)					
Fever	439 (46.3)	762 (39.7)	323 (21.2)	127 (15.7)	31 (8.1)	9 (4.9)
Cough	468 (49.4)	1121 (58.4)	1032 (67.6)	576 (71.1)	256 (67.0)	143 (78.6)
Sore throat	520 (54.9)	1093 (57.0)	963 (63.1)	502 (62.0)	209 (54.7)	96 (52.7)
Nasal discharge	414 (43.7)	937 (48.8)	842 (55.2)	466 (57.5)	204 (53.4)	101 (55.5)
Phlegm	203 (21.4)	568 (29.6)	552 (36.2)	317 (39.1)	140 (36.6)	70 (38.5)
Headache	388 (40.9)	762 (39.7)	578 (37.9)	285 (35.2)	114 (29.8)	48 (26.4)
Joint or muscle pain	186 (19.6)	468 (24.4)	329 (21.6)	162 (20.0)	54 (14.1)	26 (14.3)
Decreased food intake	230 (24.3)	454 (23.7)	270 (17.7)	110 (13.6)	50 (13.1)	14 (7.7)
Severe fatigue	243 (25.6)	448 (23.3)	296 (19.4)	152 (18.8)	59 (15.4)	24 (13.2)
Dyspnea	106 (11.2)	285 (14.9)	265 (17.4)	138 (17.0)	73 (19.1)	40 (22.0)
Diarrhea	66 (7.0)	152 (7.9)	141 (9.2)	68 (8.4)	31 (8.1)	13 (7.1)
Smell or taste disorder	27 (2.8)	41 (2.1)	48 (3.1)	48 (5.9)	18 (4.7)	10 (5.5)

Table S8. Cox regression analysis for the presence of symptoms

A. Fever, cough, sore throat, nasal discharge, phlegm, headache

	Fever	Cough	Sore throat	Nasal discharge	Phlegm	Headache
	Adjusted HR (95% CI)					
BA.5 group (compared with BA.2)	1.67 (1.64 - 1.71)	1.08 (1.06 - 1.09)	1.11 (1.09 - 1.13)	0.96 (0.94 - 0.98)	1.04 (1.02 - 1.06)	1.36 (1.33 - 1.39)
Age						
<10	1.46 (1.43 - 1.50)	0.92 (0.89 - 0.94)	0.40 (0.38 - 0.41)	0.67 (0.69 - 0.66)	0.44 (0.42 - 0.46)	0.51 (0.49 - 0.53)
10s	1.20 (1.17 - 1.24)	0.97 (0.95 - 0.99)	1.00 (0.98 - 1.02)	0.83 (0.85 - 0.81)	0.80 (0.78 - 0.83)	0.95 (0.92 - 0.97)
20s	(reference)	(reference)	(reference)	(reference)	(reference)	(reference)
30s	0.96 (0.94 - 0.99)	0.92 (0.90 - 0.94)	0.94 (0.92 - 0.96)	0.92 (0.94 - 0.90)	0.90 (0.87 - 0.92)	1.05 (1.02 - 1.07)
40s	0.86 (0.84 - 0.89)	0.87 (0.85 - 0.89)	0.89 (0.87 - 0.91)	0.86 (0.88 - 0.84)	0.79 (0.77 - 0.81)	0.98 (0.96 - 1.01)
50s	0.74 (0.72 - 0.77)	0.88 (0.86 - 0.90)	0.86 (0.84 - 0.88)	0.85 (0.87 - 0.83)	0.70 (0.68 - 0.73)	0.90 (0.87 - 0.93)
60s	0.51 (0.49 - 0.54)	0.79 (0.76 - 0.81)	0.72 (0.69 - 0.74)	0.88 (0.91 - 0.85)	0.57 (0.55 - 0.59)	0.62 (0.59 - 0.64)
70s	0.35 (0.32 - 0.38)	0.71 (0.68 - 0.74)	0.56 (0.54 - 0.59)	0.85 (0.88 - 0.81)	0.48 (0.45 - 0.50)	0.38 (0.35 - 0.40)
≥80	0.44 (0.40 - 0.49)	0.74 (0.70 - 0.78)	0.42 (0.39 - 0.45)	0.65 (0.68 - 0.61)	0.51 (0.47 - 0.55)	0.21 (0.19 - 0.24)
Male	1.12 (1.11 - 1.14)	0.98 (0.97 - 0.99)	0.98 (0.97 - 0.99)	0.98 (0.97 - 1.00)	1.01 (0.99 - 1.03)	0.88 (0.86 - 0.89)
Obesity (BMI≥30)	1.01 (0.97 - 1.05)	1.11 (1.07 - 1.14)	0.97 (0.94 - 1.00)	1.22 (1.18 - 1.26)	1.19 (1.15 - 1.23)	1.02 (0.98 - 1.06)
Malignancy	1.28 (1.15 - 1.43)	1.05 (0.97 - 1.13)	1.01 (0.94 - 1.10)	1.01 (0.92 - 1.11)	1.07 (0.97 - 1.19)	1.00 (0.90 - 1.11)
Immuno-compromised	1.01 (0.81 - 1.26)	0.97 (0.83 - 1.13)	0.99 (0.84 - 1.16)	1.03 (0.86 - 1.25)	1.13 (0.93 - 1.38)	1.10 (0.90 - 1.34)
Chronic respiratory diseases	1.05 (1.00 - 1.10)	1.15 (1.12 - 1.19)	1.01 (0.97 - 1.04)	1.21 (1.16 - 1.25)	1.32 (1.27 - 1.38)	1.19 (1.15 - 1.24)
Chronic kidney diseases	1.45 (0.92 - 2.27)	1.42 (1.08 - 1.86)	1.41 (1.05 - 1.90)	1.69 (1.23 - 2.33)	1.24 (0.82 - 1.88)	1.02 (0.62 - 1.70)
Cardiovascular diseases	1.17 (1.06 - 1.29)	1.10 (1.04 - 1.17)	1.09 (1.02 - 1.16)	1.12 (1.04 - 1.21)	1.13 (1.04 - 1.23)	0.98 (0.89 - 1.08)
Cerebrovascular diseases	1.12 (0.74 - 1.68)	0.90 (0.71 - 1.15)	0.92 (0.70 - 1.21)	0.95 (0.70 - 1.30)	0.86 (0.60 - 1.23)	0.72 (0.45 - 1.14)
Hypertension	1.04 (0.99 - 1.09)	1.04 (1.01 - 1.07)	1.01 (0.98 - 1.04)	1.05 (1.01 - 1.09)	1.05 (1.01 - 1.09)	0.93 (0.90 - 0.98)
Diabetes	0.88 (0.82 - 0.95)	0.99 (0.95 - 1.04)	0.96 (0.92 - 1.00)	1.03 (0.98 - 1.08)	0.99 (0.93 - 1.04)	0.91 (0.85 - 0.96)
Vaccination ≥3 doses	0.72 (0.71 - 0.73)	1.19 (1.17 - 1.20)	1.14 (1.12 - 1.16)	1.43 (1.40 - 1.45)	1.08 (1.06 - 1.10)	0.85 (0.83 - 0.86)
Previous SARS-CoV-2 infection	0.62 (0.59 - 0.65)	1.02 (0.99 - 1.06)	1.01 (0.98 - 1.05)	1.21 (1.16 - 1.25)	0.89 (0.85 - 0.94)	0.84 (0.81 - 0.88)

BMI, body mass index; CI, confidence interval; HR, hazard ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

The presence of symptoms on each day was considered as the appearance of symptoms and was set as the outcome of the Cox regression analysis.

B. Joint or muscle pain, decreased food intake, severe fatigue, dyspnea, diarrhea, smell or taste disorder

	Joint or muscle pain	Decreased food intake	Severe fatigue	Dyspnea	Diarrhea	Smell or taste disorder
Adjusted HR (95% CI)						
BA.5 group (compared with BA.2)	1.47 (1.43 - 1.50)	1.64 (1.60 - 1.68)	1.55 (1.51 - 1.59)	1.39 (1.34 - 1.44)	1.27 (1.21 - 1.32)	1.58 (1.47 - 1.70)
Age						
<10	0.26 (0.25 - 0.27)	1.23 (1.20 - 1.27)	0.52 (0.49 - 0.54)	0.28 (0.26 - 0.29)	1.09 (1.02 - 1.15)	0.27 (0.24 - 0.31)
10s	0.60 (0.58 - 0.63)	1.17 (1.13 - 1.20)	0.80 (0.77 - 0.82)	0.64 (0.61 - 0.67)	0.90 (0.84 - 0.96)	0.70 (0.64 - 0.77)
20s	(reference)	(reference)	(reference)	(reference)	(reference)	(reference)
30s	1.15 (1.12 - 1.18)	0.92 (0.89 - 0.95)	1.06 (1.03 - 1.09)	0.82 (0.79 - 0.85)	1.05 (0.99 - 1.11)	0.97 (0.90 - 1.05)
40s	1.08 (1.05 - 1.11)	0.90 (0.87 - 0.93)	0.91 (0.89 - 0.94)	0.70 (0.67 - 0.73)	0.97 (0.91 - 1.03)	0.80 (0.74 - 0.87)
50s	0.97 (0.94 - 1.00)	0.92 (0.88 - 0.95)	0.79 (0.76 - 0.82)	0.68 (0.65 - 0.71)	0.85 (0.79 - 0.91)	0.85 (0.78 - 0.94)
60s	0.67 (0.64 - 0.70)	0.66 (0.62 - 0.70)	0.54 (0.51 - 0.57)	0.48 (0.45 - 0.52)	0.58 (0.52 - 0.65)	0.68 (0.60 - 0.77)
70s	0.42 (0.39 - 0.46)	0.57 (0.53 - 0.62)	0.43 (0.40 - 0.47)	0.36 (0.33 - 0.39)	0.38 (0.33 - 0.45)	0.48 (0.40 - 0.58)
≥80	0.25 (0.22 - 0.29)	0.78 (0.71 - 0.87)	0.55 (0.50 - 0.61)	0.50 (0.45 - 0.57)	0.41 (0.33 - 0.52)	0.38 (0.28 - 0.51)
Male	0.97 (0.95 - 0.98)	0.80 (0.79 - 0.82)	1.10 (1.08 - 1.12)	0.94 (0.92 - 0.97)	1.29 (1.24 - 1.34)	1.14 (1.08 - 1.20)
Obesity (BMI≥30)	1.01 (0.97 - 1.06)	0.88 (0.84 - 0.93)	1.08 (1.03 - 1.13)	1.39 (1.32 - 1.46)	1.46 (1.36 - 1.57)	1.31 (1.18 - 1.45)
Comorbidities						
Malignancy	0.98 (0.87 - 1.11)	1.19 (1.05 - 1.35)	1.13 (1.00 - 1.28)	1.25 (1.08 - 1.44)	0.74 (0.56 - 0.99)	1.42 (1.08 - 1.86)
Immunocompromised	1.18 (0.94 - 1.48)	1.33 (1.06 - 1.67)	1.18 (0.93 - 1.48)	1.23 (0.94 - 1.61)	1.48 (0.90 - 2.42)	1.01 (0.57 - 1.80)
Chronic respiratory diseases	1.27 (1.21 - 1.33)	1.20 (1.15 - 1.26)	1.34 (1.28 - 1.40)	1.97 (1.87 - 2.07)	1.39 (1.28 - 1.51)	1.52 (1.35 - 1.70)
Chronic kidney diseases	0.52 (0.23 - 1.15)	1.54 (0.91 - 2.60)	1.16 (0.69 - 1.97)	1.66 (0.96 - 2.86)	3.17 (1.58 - 6.37)	0.66 (0.09 - 4.71)
Cardiovascular diseases	1.17 (1.06 - 1.29)	1.13 (1.01 - 1.26)	1.30 (1.18 - 1.43)	1.45 (1.30 - 1.62)	1.16 (0.96 - 1.41)	1.03 (0.79 - 1.35)
Cerebrovascular diseases	1.04 (0.67 - 1.62)	1.23 (0.81 - 1.88)	1.03 (0.66 - 1.60)	0.82 (0.47 - 1.45)	2.29 (1.26 - 4.16)	0.56 (0.14 - 2.25)
Hypertension	1.00 (0.96 - 1.05)	0.89 (0.85 - 0.95)	0.97 (0.92 - 1.02)	1.08 (1.02 - 1.15)	1.16 (1.06 - 1.27)	1.03 (0.91 - 1.17)
Diabetes	0.97 (0.91 - 1.04)	0.82 (0.75 - 0.89)	1.00 (0.93 - 1.08)	1.11 (1.02 - 1.20)	1.10 (0.97 - 1.25)	1.00 (0.84 - 1.19)
Vaccination ≥3 doses	0.72 (0.70 - 0.73)	0.53 (0.52 - 0.54)	0.74 (0.72 - 0.76)	0.96 (0.93 - 0.99)	0.60 (0.57 - 0.62)	0.74 (0.70 - 0.78)
Previous SARS-CoV-2 infection	0.68 (0.65 - 0.72)	0.56 (0.53 - 0.60)	0.71 (0.67 - 0.75)	1.01 (0.94 - 1.07)	0.88 (0.80 - 0.96)	0.82 (0.71 - 0.94)

BMI, body mass index; CI, confidence interval; HR, hazard ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

The presence of symptoms on each day was considered as the appearance of symptoms and was set as the outcome of the Cox regression analysis.

Table S9. Propensity score matching analysis of day-of-onset symptoms (grouped with vaccination status)

	Before match			1:1 matched		
	Two or less vaccination	Three or more vaccination	Std diff	Two or less vaccination	Three or more vaccination	Std diff
Total	9767	7936		5630	5630	
BA.5	7264 (74.4)	6898 (86.9)	-0.322	4740 (84.2)	4710 (83.7)	0.015
Age, mean (SD)	22.3 (17.8)	45.5 (17.6)	-0.871	38.7 (14.6)	39.4 (14.5)	-0.048
Age group						
10s	2863 (29.3)	334 (4.2)	0.714	334 (5.9)	334 (5.9)	0.000
20s	2045 (20.9)	1284 (16.2)	0.123	1201 (21.3)	1202 (21.4)	0.000
30s	2041 (20.9)	1601 (20.2)	0.018	1546 (27.5)	1540 (27.4)	0.002
40s	1641 (16.8)	1742 (22.0)	-0.131	1412 (25.1)	1370 (24.3)	0.017
50s	768 (7.9)	1359 (17.1)	-0.283	728 (12.9)	742 (13.2)	-0.007
60s	229 (2.3)	786 (9.9)	-0.319	229 (4.1)	241 (4.3)	-0.011
70s	91 (0.9)	455 (5.7)	-0.270	91 (1.6)	108 (1.9)	-0.023
≥ 80	89 (0.9)	375 (4.7)	-0.232	89 (1.6)	93 (1.7)	-0.006
Male	5288 (54.1)	3447 (43.4)	0.215	2620 (46.5)	2669 (47.4)	-0.017
Obesity (BMI ≥ 30)	498 (5.1)	420 (5.3)	-0.009	331 (5.9)	332 (5.9)	-0.001
Comorbidities						
Malignancy	60 (0.6)	130 (1.6)	-0.097	51 (0.9)	51 (0.9)	0.000
Immunocompromised	11 (0.1)	34 (0.4)	-0.061	9 (0.2)	9 (0.2)	0.000
Chronic respiratory diseases	358 (3.7)	338 (4.3)	-0.030	244 (4.3)	225 (4.0)	0.017
Chronic kidney diseases	1 (0.0)	22 (0.3)	-0.071	1 (0.0)	0 (0.0)	0.019
Cardiovascular diseases	66 (0.7)	167 (2.1)	-0.122	57 (1.0)	58 (1.0)	-0.002
Cerebrovascular diseases	3 (0.0)	8 (0.1)	-0.027	2 (0.0)	3 (0.1)	-0.008
Hypertension	325 (3.3)	857 (10.8)	-0.295	308 (5.5)	321 (5.7)	-0.010
Diabetes	157 (1.6)	316 (4.0)	-0.144	137 (2.4)	143 (2.5)	-0.007
Previous SARS-CoV-2 infection	522 (5.3)	136 (1.7)	0.198	123 (2.2)	130 (2.3)	-0.008
Prevalence of symptoms						
Fever				3300 (58.6)	2194 (39.0)	
Cough				2814 (50.0)	3286 (58.4)	
Sore throat				3427 (60.9)	3902 (69.3)	
Nasal discharge				1735 (30.8)	2420 (43.0)	
Phlegm				1617 (28.7)	1713 (30.4)	

Headache	3188 (56.6)	2461 (43.7)
Joint or muscle pain	2638 (46.9)	1709 (30.4)
Decreased food intake	2064 (36.7)	1031 (18.3)
Severe fatigue	2409 (42.8)	1617 (28.7)
Dyspnea	956 (17.0)	773 (13.7)
Diarrhea	396 (7.0)	284 (5.0)
Smell or taste disorder	189 (3.4)	126 (2.2)
Number of symptoms, median (IQR)	4 (3-6)	4 (2-5)

Data are n (%) unless otherwise specified.

Absolute value of standardized difference (Std diff) greater than 0.1 is considered as a sign of imbalance.

BMI, body mass index; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation.

Table S10. Logistic regression analysis of factors for symptoms adjusting for time since last vaccination

A. Fever, cough, sore throat, nasal discharge, phlegm, headache

	Fever	Cough	Sore throat	Nasal discharge	Phlegm	Headache
	Adjusted OR (95% CI)					
Days since last vaccination						
Unvaccinated	(reference)	(reference)	(reference)	(reference)	(reference)	(reference)
Two doses						
-60	0.38 (0.32 - 0.46)	2.01 (1.69 - 2.40)	1.54 (1.29 - 1.84)	2.21 (1.88 - 2.61)	1.43 (1.20 - 1.70)	0.59 (0.49 - 0.71)
61-120	0.57 (0.51 - 0.64)	1.73 (1.54 - 1.94)	1.37 (1.21 - 1.54)	1.93 (1.73 - 2.16)	1.23 (1.09 - 1.39)	0.73 (0.65 - 0.82)
121-180	0.63 (0.58 - 0.69)	1.72 (1.58 - 1.87)	1.44 (1.32 - 1.56)	1.87 (1.73 - 2.02)	1.26 (1.16 - 1.37)	0.81 (0.75 - 0.88)
181-240	0.76 (0.72 - 0.80)	1.70 (1.62 - 1.80)	1.48 (1.41 - 1.56)	1.93 (1.83 - 2.03)	1.24 (1.17 - 1.30)	0.88 (0.84 - 0.92)
241-	0.93 (0.89 - 0.96)	1.44 (1.40 - 1.50)	1.34 (1.29 - 1.39)	1.52 (1.47 - 1.57)	1.14 (1.10 - 1.18)	0.99 (0.96 - 1.03)
Three doses						
-60	0.31 (0.29 - 0.34)	1.74 (1.64 - 1.85)	1.73 (1.62 - 1.84)	2.55 (2.40 - 2.70)	1.06 (1.00 - 1.13)	0.59 (0.56 - 0.63)
61-120	0.45 (0.43 - 0.47)	1.93 (1.85 - 2.01)	1.61 (1.54 - 1.68)	2.47 (2.38 - 2.57)	1.17 (1.12 - 1.21)	0.64 (0.62 - 0.67)
121-180	0.55 (0.53 - 0.57)	1.85 (1.78 - 1.92)	1.53 (1.47 - 1.59)	2.32 (2.23 - 2.40)	1.18 (1.14 - 1.22)	0.66 (0.64 - 0.68)
181-240	0.50 (0.47 - 0.53)	1.65 (1.55 - 1.74)	1.43 (1.35 - 1.51)	2.00 (1.90 - 2.12)	1.17 (1.11 - 1.23)	0.66 (0.63 - 0.70)
241-	0.52 (0.43 - 0.63)	1.74 (1.43 - 2.12)	1.28 (1.05 - 1.57)	2.22 (1.84 - 2.67)	1.12 (0.92 - 1.36)	0.67 (0.55 - 0.80)
Days since onset						
0	(reference)	(reference)	(reference)	(reference)	(reference)	(reference)
1	0.85 (0.82 - 0.88)	1.40 (1.36 - 1.45)	1.19 (1.15 - 1.23)	1.20 (1.16 - 1.24)	1.34 (1.29 - 1.39)	0.99 (0.96 - 1.02)
2	0.39 (0.37 - 0.40)	2.00 (1.93 - 2.07)	1.33 (1.28 - 1.38)	1.62 (1.56 - 1.68)	1.93 (1.86 - 2.01)	0.78 (0.76 - 0.81)
3	0.17 (0.16 - 0.18)	2.31 (2.22 - 2.41)	1.28 (1.22 - 1.33)	1.94 (1.87 - 2.02)	2.18 (2.09 - 2.27)	0.56 (0.54 - 0.59)
4	0.09 (0.09 - 0.10)	2.22 (2.11 - 2.34)	0.95 (0.91 - 1.00)	2.04 (1.94 - 2.14)	2.12 (2.02 - 2.23)	0.42 (0.40 - 0.44)
5	0.07 (0.06 - 0.08)	2.12 (1.98 - 2.27)	0.72 (0.68 - 0.78)	1.90 (1.78 - 2.03)	2.11 (1.97 - 2.26)	0.35 (0.32 - 0.37)
BA.5 group (compared with BA.2)	2.02 (1.96 - 2.09)	1.06 (1.03 - 1.09)	1.14 (1.10 - 1.17)	0.88 (0.85 - 0.90)	0.97 (0.94 - 1.00)	1.44 (1.40 - 1.49)
Age						
<10	1.16 (1.11 - 1.21)	0.56 (0.54 - 0.59)	0.13 (0.12 - 0.13)	0.92 (0.88 - 0.96)	0.24 (0.23 - 0.25)	0.21 (0.20 - 0.22)
10s	1.18 (1.14 - 1.23)	0.73 (0.70 - 0.76)	0.74 (0.71 - 0.77)	0.84 (0.81 - 0.87)	0.59 (0.57 - 0.62)	0.74 (0.71 - 0.77)
20s	(reference)	(reference)	(reference)	(reference)	(reference)	(reference)
30s	0.92 (0.88 - 0.95)	0.75 (0.73 - 0.78)	0.77 (0.75 - 0.80)	0.82 (0.79 - 0.85)	0.81 (0.78 - 0.84)	1.10 (1.06 - 1.14)
40s	0.78 (0.75 - 0.81)	0.68 (0.65 - 0.70)	0.71 (0.68 - 0.73)	0.66 (0.64 - 0.69)	0.67 (0.65 - 0.70)	1.00 (0.96 - 1.04)
50s	0.63 (0.60 - 0.66)	0.75 (0.72 - 0.79)	0.68 (0.65 - 0.71)	0.62 (0.59 - 0.65)	0.58 (0.55 - 0.60)	0.88 (0.84 - 0.92)
60s	0.45 (0.42 - 0.49)	0.75 (0.70 - 0.79)	0.56 (0.53 - 0.59)	0.52 (0.49 - 0.55)	0.49 (0.46 - 0.52)	0.58 (0.55 - 0.61)

70s	0.31 (0.28 - 0.35)	0.69 (0.63 - 0.75)	0.38 (0.35 - 0.41)	0.36 (0.33 - 0.39)	0.42 (0.39 - 0.46)	0.32 (0.30 - 0.36)
≥80	0.33 (0.28 - 0.38)	0.53 (0.47 - 0.59)	0.17 (0.15 - 0.19)	0.28 (0.24 - 0.31)	0.39 (0.35 - 0.44)	0.12 (0.10 - 0.14)
Male	1.13 (1.11 - 1.16)	0.85 (0.84 - 0.87)	0.84 (0.82 - 0.86)	0.90 (0.89 - 0.92)	0.95 (0.93 - 0.97)	0.72 (0.70 - 0.73)
BMI≥30	1.00 (0.94 - 1.06)	1.37 (1.29 - 1.45)	0.90 (0.85 - 0.95)	1.50 (1.42 - 1.58)	1.37 (1.30 - 1.44)	1.02 (0.97 - 1.08)
Malignancy	1.51 (1.29 - 1.76)	1.17 (1.01 - 1.36)	1.04 (0.91 - 1.20)	1.05 (0.91 - 1.20)	1.19 (1.03 - 1.37)	1.02 (0.88 - 1.18)
Immuno-compromised	0.96 (0.70 - 1.32)	0.80 (0.59 - 1.07)	0.85 (0.64 - 1.14)	0.96 (0.72 - 1.27)	1.16 (0.88 - 1.53)	1.12 (0.84 - 1.50)
Chronic respiratory diseases	1.03 (0.97 - 1.10)	1.47 (1.38 - 1.57)	0.96 (0.90 - 1.02)	1.41 (1.33 - 1.49)	1.58 (1.49 - 1.67)	1.35 (1.28 - 1.44)
Chronic kidney diseases	0.90 (0.44 - 1.83)	0.61 (0.34 - 1.07)	0.78 (0.44 - 1.38)	0.96 (0.54 - 1.73)	0.53 (0.26 - 1.06)	0.43 (0.19 - 0.99)
Cardiovascular diseases	1.17 (1.02 - 1.34)	1.20 (1.06 - 1.36)	1.14 (1.01 - 1.29)	1.23 (1.09 - 1.38)	1.17 (1.04 - 1.32)	0.95 (0.83 - 1.08)
Cerebrovascular diseases	1.34 (0.78 - 2.29)	0.94 (0.59 - 1.49)	0.86 (0.55 - 1.34)	1.12 (0.71 - 1.74)	0.91 (0.57 - 1.45)	0.69 (0.39 - 1.22)
Hypertension	1.03 (0.97 - 1.10)	1.15 (1.08 - 1.21)	1.00 (0.95 - 1.06)	1.08 (1.02 - 1.14)	1.08 (1.03 - 1.15)	0.88 (0.83 - 0.94)
Diabetes	0.87 (0.79 - 0.96)	1.15 (1.06 - 1.25)	1.01 (0.93 - 1.09)	1.11 (1.03 - 1.20)	1.04 (0.96 - 1.12)	0.93 (0.85 - 1.01)
Previous SARS-CoV-2 infection	0.41 (0.38 - 0.43)	1.19 (1.12 - 1.26)	1.14 (1.07 - 1.21)	1.59 (1.51 - 1.68)	0.89 (0.84 - 0.95)	0.75 (0.71 - 0.79)

BMI, body mass index; CI, confidence interval; OR, odds ratio. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

B. Joint or muscle pain, decreased food intake, severe fatigue, dyspnea, diarrhea, smell or taste disorder

	Joint or muscle pain	Decreased food intake	Severe fatigue	Dyspnea	Diarrhea	Smell or taste disorder
Adjusted OR (95% CI)						
Days since last vaccination						
Unvaccinated	(reference)	(reference)	(reference)	(reference)	(reference)	(reference)
Two doses						
-60	0.46 (0.36 - 0.60)	0.42 (0.34 - 0.51)	0.48 (0.37 - 0.61)	1.10 (0.85 - 1.43)	0.60 (0.42 - 0.85)	0.70 (0.40 - 1.23)
61-120	0.62 (0.53 - 0.72)	0.49 (0.43 - 0.55)	0.61 (0.53 - 0.70)	1.14 (0.97 - 1.35)	0.71 (0.58 - 0.88)	0.83 (0.59 - 1.15)
121-180	0.77 (0.70 - 0.84)	0.55 (0.50 - 0.60)	0.72 (0.65 - 0.79)	1.12 (1.00 - 1.25)	0.75 (0.66 - 0.87)	0.81 (0.66 - 1.00)
181-240	0.80 (0.76 - 0.84)	0.60 (0.57 - 0.64)	0.80 (0.76 - 0.85)	1.26 (1.18 - 1.35)	0.68 (0.62 - 0.75)	0.86 (0.75 - 0.98)
241-	0.93 (0.89 - 0.96)	0.69 (0.67 - 0.72)	0.93 (0.90 - 0.96)	1.15 (1.10 - 1.20)	0.74 (0.70 - 0.78)	0.76 (0.71 - 0.83)
Three doses						
-60	0.41 (0.39 - 0.44)	0.24 (0.22 - 0.26)	0.47 (0.43 - 0.50)	0.98 (0.91 - 1.06)	0.42 (0.37 - 0.47)	0.59 (0.50 - 0.69)
61-120	0.49 (0.47 - 0.51)	0.31 (0.30 - 0.33)	0.54 (0.52 - 0.56)	1.04 (0.99 - 1.10)	0.48 (0.45 - 0.52)	0.62 (0.56 - 0.68)
121-180	0.55 (0.53 - 0.57)	0.34 (0.33 - 0.36)	0.59 (0.56 - 0.61)	1.01 (0.96 - 1.06)	0.47 (0.44 - 0.51)	0.65 (0.59 - 0.71)
181-240	0.56 (0.53 - 0.60)	0.36 (0.34 - 0.39)	0.66 (0.62 - 0.69)	0.82 (0.76 - 0.88)	0.51 (0.46 - 0.57)	0.63 (0.54 - 0.72)
241-	0.60 (0.49 - 0.72)	0.32 (0.26 - 0.40)	0.72 (0.59 - 0.87)	0.53 (0.39 - 0.71)	0.40 (0.26 - 0.62)	0.76 (0.48 - 1.20)
Days since onset						
0	(reference)	(reference)	(reference)	(reference)	(reference)	(reference)
1	1.08 (1.04 - 1.12)	1.03 (0.99 - 1.07)	0.94 (0.91 - 0.97)	1.09 (1.03 - 1.14)	1.30 (1.21 - 1.38)	1.04 (0.93 - 1.15)
2	0.82 (0.79 - 0.86)	0.82 (0.79 - 0.85)	0.69 (0.66 - 0.71)	1.27 (1.21 - 1.33)	1.63 (1.52 - 1.74)	1.49 (1.35 - 1.65)
3	0.57 (0.54 - 0.60)	0.59 (0.57 - 0.62)	0.50 (0.48 - 0.52)	1.30 (1.23 - 1.37)	1.67 (1.55 - 1.80)	2.06 (1.85 - 2.29)
4	0.39 (0.37 - 0.42)	0.45 (0.42 - 0.47)	0.39 (0.37 - 0.42)	1.26 (1.18 - 1.35)	1.61 (1.47 - 1.76)	2.50 (2.22 - 2.82)
5	0.30 (0.27 - 0.33)	0.36 (0.33 - 0.39)	0.34 (0.31 - 0.37)	1.20 (1.10 - 1.31)	1.59 (1.41 - 1.79)	4.07 (3.56 - 4.64)
BA.5 group (compared with BA.2)	1.48 (1.43 - 1.53)	1.70 (1.64 - 1.75)	1.54 (1.49 - 1.59)	1.42 (1.36 - 1.48)	1.15 (1.10 - 1.21)	1.53 (1.41 - 1.66)
Age						
<10	0.11 (0.11 - 0.12)	0.77 (0.73 - 0.80)	0.26 (0.25 - 0.28)	0.19 (0.18 - 0.21)	0.76 (0.71 - 0.81)	0.20 (0.17 - 0.22)
10s	0.41 (0.39 - 0.43)	1.06 (1.02 - 1.11)	0.61 (0.59 - 0.64)	0.53 (0.50 - 0.55)	0.79 (0.74 - 0.84)	0.63 (0.57 - 0.69)
20s	(reference)	(reference)	(reference)	(reference)	(reference)	(reference)
30s	1.26 (1.21 - 1.30)	0.90 (0.86 - 0.93)	1.08 (1.04 - 1.12)	0.77 (0.74 - 0.81)	1.08 (1.02 - 1.15)	0.99 (0.91 - 1.07)
40s	1.18 (1.14 - 1.23)	0.89 (0.86 - 0.93)	0.90 (0.86 - 0.93)	0.65 (0.62 - 0.68)	1.02 (0.96 - 1.08)	0.81 (0.75 - 0.89)
50s	1.03 (0.98 - 1.07)	0.94 (0.89 - 0.98)	0.75 (0.72 - 0.79)	0.65 (0.61 - 0.68)	0.89 (0.82 - 0.96)	0.89 (0.80 - 0.98)
60s	0.73 (0.69 - 0.78)	0.72 (0.67 - 0.77)	0.55 (0.51 - 0.59)	0.50 (0.46 - 0.54)	0.67 (0.60 - 0.76)	0.78 (0.68 - 0.89)
70s	0.47 (0.42 - 0.51)	0.70 (0.63 - 0.77)	0.48 (0.43 - 0.53)	0.39 (0.34 - 0.43)	0.49 (0.40 - 0.59)	0.57 (0.46 - 0.71)

≥80	0.20 (0.17 - 0.24)	0.80 (0.70 - 0.91)	0.51 (0.44 - 0.58)	0.52 (0.45 - 0.61)	0.42 (0.32 - 0.57)	0.39 (0.27 - 0.56)
Male	0.88 (0.86 - 0.90)	0.67 (0.66 - 0.69)	1.07 (1.05 - 1.10)	0.89 (0.86 - 0.91)	1.27 (1.23 - 1.32)	1.10 (1.04 - 1.16)
BMI≥30	1.01 (0.96 - 1.07)	0.84 (0.79 - 0.89)	1.12 (1.06 - 1.18)	1.52 (1.43 - 1.62)	1.54 (1.42 - 1.67)	1.33 (1.19 - 1.49)
Malignancy	0.98 (0.84 - 1.14)	1.26 (1.08 - 1.48)	1.22 (1.05 - 1.43)	1.36 (1.14 - 1.61)	0.77 (0.57 - 1.05)	1.50 (1.11 - 2.02)
Immuno-compromised	1.15 (0.85 - 1.56)	1.48 (1.09 - 2.01)	1.14 (0.84 - 1.54)	1.22 (0.88 - 1.71)	1.48 (0.87 - 2.51)	0.89 (0.47 - 1.69)
Chronic respiratory diseases	1.42 (1.34 - 1.51)	1.26 (1.19 - 1.34)	1.51 (1.42 - 1.60)	2.39 (2.24 - 2.54)	1.42 (1.30 - 1.55)	1.51 (1.34 - 1.71)
Chronic kidney diseases	0.14 (0.03 - 0.59)	1.14 (0.55 - 2.38)	0.48 (0.20 - 1.15)	1.01 (0.45 - 2.27)	1.77 (0.63 - 5.01)	N/A*
Cardiovascular diseases	1.19 (1.04 - 1.36)	1.13 (0.99 - 1.30)	1.28 (1.13 - 1.46)	1.54 (1.34 - 1.78)	1.07 (0.86 - 1.33)	0.95 (0.70 - 1.29)
Cerebrovascular diseases	0.95 (0.54 - 1.68)	1.65 (0.98 - 2.78)	1.03 (0.60 - 1.79)	0.94 (0.50 - 1.80)	2.23 (1.10 - 4.51)	0.67 (0.16 - 2.77)
Hypertension	1.00 (0.94 - 1.06)	0.86 (0.80 - 0.92)	0.94 (0.88 - 1.00)	1.09 (1.02 - 1.18)	1.17 (1.06 - 1.30)	1.01 (0.89 - 1.16)
Diabetes	1.03 (0.94 - 1.12)	0.81 (0.73 - 0.90)	1.09 (0.99 - 1.19)	1.14 (1.04 - 1.26)	1.12 (0.97 - 1.29)	1.10 (0.92 - 1.32)
Previous SARS-CoV-2 infection	0.58 (0.54 - 0.62)	0.43 (0.40 - 0.46)	0.62 (0.58 - 0.67)	1.06 (0.98 - 1.14)	0.86 (0.78 - 0.95)	0.80 (0.69 - 0.93)

*Excluded from analysis due to small number of symptomatic individuals for which confidence intervals could not be determined.

BMI, body mass index; CI, confidence interval; OR, odds ratio. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table S11. Prevalence of COVID-19 symptoms by age

	Total (N=157 552)	Age								
		<10 (n=23 219)	10s (n=21 165)	20s (n=26 259)	30s (n=27 665)	40s (n=26 536)	50s (n=16 629)	60s (n=8881)	70s (n=4839)	80 or over (n=2359)
		Number -%								
Fever	61 218 (38.8)	12 614 (54.3)	10 196 (48.2)	10 822 (41.2)	10 591 (38.3)	9052 (34.1)	4899 (29.5)	1833 (20.6)	704 (14.5)	389 (16.5)
Cough	99 032 (62.7)	10 842 (46.7)	12 588 (59.5)	18 283 (69.6)	17 992 (65.0)	16 933 (63.8)	11 223 (67.5)	6170 (69.5)	3361 (69.5)	1453 (61.6)
Sore throat	95 838 (60.7)	5105 (22.0)	13 827 (65.3)	19 271 (73.4)	19 114 (69.1)	17 973 (67.7)	11 236 (67.6)	5642 (63.5)	2644 (54.6)	829 (35.1)
Nasal discharge	69 968 (44.3)	8543 (36.8)	9006 (42.6)	13 293 (50.6)	13 309 (48.1)	11 835 (44.6)	7403 (44.5)	3892 (43.8)	1845 (38.1)	727 (30.8)
Phlegm	56 915 (36.1)	3641 (15.7)	7207 (34.1)	12 491 (47.6)	11 889 (43.0)	10 416 (39.3)	6027 (36.2)	2964 (33.4)	1510 (31.2)	664 (28.1)
Headache	66 425 (42.1)	4926 (21.2)	9392 (44.4)	13 193 (50.2)	14 346 (51.9)	12 942 (48.8)	7416 (44.6)	2840 (32.0)	994 (20.5)	239 (10.1)
Joint or muscle pain	45 955 (29.1)	1910 (8.2)	4444 (21.0)	9528 (36.3)	11 152 (40.3)	10 085 (38.0)	5626 (33.8)	2137 (24.1)	778 (16.1)	199 (8.4)
Decreased food intake	44 359 (28.1)	8060 (34.7)	7436 (35.1)	7988 (30.4)	7345 (26.6)	6702 (25.3)	4076 (24.5)	1496 (16.8)	727 (15.0)	434 (18.4)
Severe fatigue	42 242 (26.8)	3475 (15.0)	5388 (25.5)	8803 (33.5)	9512 (34.4)	7902 (29.8)	4290 (25.8)	1621 (18.3)	757 (15.6)	411 (17.4)
Dyspnea	23 914 (15.1)	1085 (4.7)	2679 (12.7)	5838 (22.2)	5076 (18.3)	4351 (16.4)	2771 (16.7)	1188 (13.4)	545 (11.3)	331 (14.0)
Diarrhea	12 392 (7.9)	1919 (8.3)	1623 (7.7)	2315 (8.8)	2467 (8.9)	2171 (8.2)	1175 (7.1)	444 (5.0)	174 (3.6)	78 (3.3)
Smell or taste disorder	5908 (3.7)	252 (1.1)	687 (3.2)	1322 (5.0)	1322 (4.8)	1060 (4.0)	722 (4.3)	341 (3.8)	147 (3.0)	47 (2.0)

Table S12. Logistic regression analysis of factors for symptoms (set elderly as an explanatory variable)

A. Fever, cough, sore throat, nasal discharge, phlegm, headache

	Fever	Cough	Sore throat	Nasal discharge	Phlegm	Headache
	Adjusted OR (95% CI)					
Days from onset						
0	(reference)	(reference)	(reference)	(reference)	(reference)	(reference)
1	0.84 (0.81 - 0.87)	1.43 (1.38 - 1.47)	1.26 (1.22 - 1.30)	1.21 (1.17 - 1.25)	1.38 (1.33 - 1.43)	1.06 (1.02 - 1.09)
2	0.38 (0.37 - 0.40)	2.09 (2.02 - 2.16)	1.53 (1.48 - 1.59)	1.64 (1.59 - 1.70)	2.06 (1.99 - 2.14)	0.91 (0.88 - 0.94)
3	0.17 (0.16 - 0.17)	2.42 (2.33 - 2.52)	1.54 (1.48 - 1.60)	1.96 (1.88 - 2.03)	2.35 (2.26 - 2.45)	0.68 (0.66 - 0.71)
4	0.09 (0.09 - 0.10)	2.33 (2.22 - 2.45)	1.18 (1.13 - 1.24)	2.04 (1.94 - 2.14)	2.32 (2.21 - 2.44)	0.52 (0.49 - 0.55)
5	0.06 (0.06 - 0.07)	2.19 (2.05 - 2.35)	0.91 (0.86 - 0.97)	1.87 (1.76 - 1.99)	2.30 (2.16 - 2.46)	0.43 (0.40 - 0.46)
BA.5 group (compared with BA.2)	2.13 (2.07 - 2.19)	1.01 (0.99 - 1.04)	1.09 (1.06 - 1.12)	0.81 (0.79 - 0.83)	0.96 (0.94 - 0.99)	1.49 (1.45 - 1.53)
Elderly (age ≥ 65)	0.44 (0.41 - 0.47)	0.88 (0.84 - 0.92)	0.50 (0.47 - 0.52)	0.55 (0.53 - 0.58)	0.64 (0.61 - 0.67)	0.36 (0.34 - 0.38)
Male	1.15 (1.12 - 1.18)	0.85 (0.83 - 0.87)	0.85 (0.83 - 0.86)	0.91 (0.89 - 0.92)	0.95 (0.93 - 0.97)	0.72 (0.70 - 0.73)
Obesity (BMI ≥ 30)	0.94 (0.89 - 0.99)	1.48 (1.40 - 1.56)	1.16 (1.10 - 1.22)	1.51 (1.43 - 1.59)	1.57 (1.50 - 1.66)	1.26 (1.20 - 1.33)
Malignancy	1.27 (1.10 - 1.47)	1.11 (0.97 - 1.26)	1.00 (0.88 - 1.14)	0.91 (0.80 - 1.03)	1.06 (0.93 - 1.21)	1.01 (0.88 - 1.16)
Immuno-compromised	1.01 (0.75 - 1.36)	0.87 (0.66 - 1.14)	0.98 (0.75 - 1.28)	1.06 (0.81 - 1.37)	1.24 (0.96 - 1.61)	1.22 (0.93 - 1.59)
Chronic respiratory diseases	1.01 (0.95 - 1.08)	1.47 (1.38 - 1.56)	0.97 (0.92 - 1.02)	1.38 (1.31 - 1.46)	1.58 (1.50 - 1.67)	1.36 (1.29 - 1.44)
Chronic kidney diseases	0.72 (0.42 - 1.22)	0.77 (0.50 - 1.19)	0.70 (0.45 - 1.07)	1.08 (0.70 - 1.67)	0.73 (0.45 - 1.20)	0.49 (0.28 - 0.87)
Cardiovascular diseases	1.08 (0.95 - 1.22)	1.18 (1.05 - 1.32)	1.04 (0.93 - 1.15)	1.08 (0.97 - 1.20)	1.12 (1.00 - 1.24)	0.87 (0.77 - 0.97)
Cerebrovascular diseases	1.03 (0.62 - 1.73)	0.89 (0.59 - 1.34)	0.81 (0.55 - 1.20)	0.93 (0.62 - 1.40)	0.83 (0.54 - 1.27)	0.59 (0.35 - 0.99)
Hypertension	0.85 (0.80 - 0.90)	1.11 (1.06 - 1.17)	0.98 (0.93 - 1.03)	0.96 (0.91 - 1.01)	0.99 (0.94 - 1.04)	0.86 (0.82 - 0.91)
Diabetes	0.79 (0.72 - 0.86)	1.12 (1.04 - 1.21)	1.00 (0.93 - 1.08)	1.07 (1.00 - 1.15)	0.99 (0.92 - 1.06)	0.92 (0.85 - 0.99)
Vaccination ≥ 3 doses	0.43 (0.41 - 0.46)	1.12 (1.06 - 1.18)	1.02 (0.96 - 1.07)	1.53 (1.45 - 1.62)	0.87 (0.82 - 0.92)	0.73 (0.69 - 0.78)
Previous SARS-CoV-2 infection	0.42 (0.41 - 0.43)	1.65 (1.62 - 1.69)	1.94 (1.90 - 1.99)	1.75 (1.71 - 1.79)	1.28 (1.25 - 1.31)	0.90 (0.88 - 0.92)

The difference from the analysis in Supplementary Table 5 is that the age factor is divided into 65 years and older or not.

BMI, body mass index; CI, confidence interval; OR, odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

B. Joint or muscle pain, decreased food intake, severe fatigue, dyspnea, diarrhea, smell or taste disorder

	Joint or muscle pain	Decreased food intake	Severe fatigue	Dyspnea	Diarrhea	Smell or taste disorder
Adjusted OR (95% CI)						
Days from onset						
0	(reference)	(reference)	(reference)	(reference)	(reference)	(reference)
1	1.16 (1.12 - 1.20)	1.03 (0.99 - 1.06)	0.98 (0.95 - 1.01)	1.13 (1.08 - 1.19)	1.29 (1.21 - 1.37)	1.08 (0.98 - 1.19)
2	0.99 (0.95 - 1.02)	0.82 (0.79 - 0.85)	0.77 (0.74 - 0.79)	1.40 (1.34 - 1.47)	1.63 (1.52 - 1.74)	1.63 (1.48 - 1.80)
3	0.72 (0.70 - 0.76)	0.59 (0.57 - 0.62)	0.57 (0.55 - 0.60)	1.46 (1.39 - 1.54)	1.66 (1.55 - 1.79)	2.30 (2.08 - 2.56)
4	0.51 (0.48 - 0.54)	0.45 (0.42 - 0.48)	0.46 (0.43 - 0.49)	1.42 (1.33 - 1.52)	1.62 (1.49 - 1.77)	2.81 (2.50 - 3.16)
5	0.40 (0.36 - 0.43)	0.36 (0.33 - 0.40)	0.40 (0.37 - 0.43)	1.33 (1.22 - 1.45)	1.61 (1.43 - 1.81)	4.52 (3.97 - 5.13)
BA.5 group (compared with BA.2)	1.58 (1.53 - 1.62)	1.80 (1.74 - 1.85)	1.64 (1.59 - 1.69)	1.38 (1.33 - 1.43)	1.20 (1.15 - 1.26)	1.55 (1.44 - 1.67)
Elderly (age ≥65)	0.45 (0.42 - 0.47)	0.77 (0.72 - 0.81)	0.58 (0.55 - 0.61)	0.63 (0.59 - 0.67)	0.55 (0.49 - 0.61)	0.69 (0.61 - 0.78)
Male	0.86 (0.84 - 0.88)	0.68 (0.66 - 0.69)	1.05 (1.03 - 1.07)	0.88 (0.85 - 0.90)	1.27 (1.22 - 1.31)	1.09 (1.04 - 1.15)
Obesity (BMI≥30)	1.37 (1.30 - 1.44)	0.82 (0.77 - 0.87)	1.34 (1.27 - 1.42)	1.75 (1.65 - 1.86)	1.61 (1.48 - 1.74)	1.52 (1.37 - 1.70)
Malignancy	1.07 (0.92 - 1.23)	1.24 (1.07 - 1.44)	1.18 (1.02 - 1.36)	1.29 (1.10 - 1.52)	0.70 (0.52 - 0.94)	1.45 (1.09 - 1.92)
Immunocompromised	1.31 (0.99 - 1.74)	1.48 (1.11 - 1.97)	1.27 (0.95 - 1.68)	1.29 (0.94 - 1.75)	1.53 (0.91 - 2.56)	1.00 (0.55 - 1.82)
Chronic respiratory diseases	1.46 (1.38 - 1.54)	1.25 (1.18 - 1.33)	1.50 (1.42 - 1.59)	2.36 (2.23 - 2.51)	1.41 (1.29 - 1.54)	1.54 (1.37 - 1.74)
Chronic kidney diseases	0.24 (0.11 - 0.56)	1.04 (0.58 - 1.86)	0.66 (0.37 - 1.17)	1.12 (0.62 - 2.03)	2.10 (1.00 - 4.37)	0.42 (0.06 - 3.04)
Cardiovascular diseases	1.16 (1.03 - 1.30)	1.12 (0.98 - 1.27)	1.34 (1.19 - 1.50)	1.53 (1.35 - 1.74)	1.10 (0.90 - 1.35)	0.98 (0.74 - 1.29)
Cerebrovascular diseases	1.00 (0.60 - 1.65)	1.45 (0.88 - 2.37)	1.06 (0.64 - 1.75)	0.87 (0.47 - 1.60)	2.30 (1.22 - 4.35)	0.54 (0.13 - 2.22)
Hypertension	1.06 (1.00 - 1.12)	0.82 (0.77 - 0.88)	0.89 (0.84 - 0.95)	1.03 (0.97 - 1.10)	1.10 (1.00 - 1.21)	1.04 (0.92 - 1.17)
Diabetes	1.07 (0.99 - 1.16)	0.80 (0.72 - 0.88)	1.03 (0.95 - 1.12)	1.14 (1.04 - 1.24)	1.11 (0.97 - 1.26)	1.04 (0.87 - 1.23)
Vaccination ≥3 doses	0.58 (0.54 - 0.62)	0.46 (0.43 - 0.49)	0.63 (0.59 - 0.67)	1.03 (0.96 - 1.11)	0.90 (0.81 - 0.99)	0.81 (0.70 - 0.94)
Previous SARS-CoV-2 infection	0.86 (0.84 - 0.89)	0.37 (0.36 - 0.38)	0.76 (0.74 - 0.77)	1.10 (1.07 - 1.13)	0.56 (0.53 - 0.58)	0.85 (0.80 - 0.90)

The difference from the analysis in Supplementary Table 5 is that the age factor is divided into 65 years and older or not.

BMI, body mass index; CI, confidence interval; OR, odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table S13. Logistic regression analysis of factors (including number of symptoms) for progression to severe disease

	Age < 65	Age ≥ 65
	Adjusted OR (95% CI)	Adjusted OR (95% CI)
Days from onset		
0	(reference)	(reference)
1	0.81 (0.31 - 2.13)	0.73 (0.43 - 1.25)
2	0.23 (0.06 - 0.91)	0.77 (0.43 - 1.37)
3	0.47 (0.11 - 1.91)	0.63 (0.31 - 1.30)
4	0.71 (0.14 - 3.67)	0.22 (0.07 - 0.76)
5	2.99 (0.78 - 11.52)	1.19 (0.50 - 2.80)
BA.5 (compared with BA.2)	0.86 (0.35 - 2.08)	1.19 (0.63 - 2.26)
Age		
<10	3.06 (0.32 - 28.96)	N/A
10s	2.16 (0.19 - 24.16)	N/A
20s	(reference)	N/A
30s	1.82 (0.16 - 20.11)	N/A
40s	6.18 (0.74 - 51.29)	N/A
50s	10.58 (1.26 - 88.99)	N/A
60s	27.28 (3.03 - 245.41)	(reference)
70s	N/A	2.11 (0.94 - 4.75)
≥80	N/A	10.15 (4.71 - 21.86)
Male	0.89 (0.43 - 1.85)	1.62 (1.07 - 2.44)
Obesity (BMI≥30)	3.82 (1.42 - 10.30)	0.79 (0.21 - 3.01)
Malignancy	13.74 (4.36 - 43.27)	2.55 (1.40 - 4.65)
Immunocompromised	2.52 (0.41 - 15.62)	0.38 (0.07 - 2.01)
Chronic respiratory diseases	1.54 (0.43 - 5.52)	2.97 (1.67 - 5.31)
Chronic kidney diseases	32.57 (3.28 - 323.71)	5.63 (1.54 - 20.51)
Cardiovascular diseases	N/A*	1.05 (0.60 - 1.84)
Cerebrovascular diseases	N/A*	4.02 (1.00 - 16.16)
Hypertension	1.09 (0.35 - 3.37)	0.58 (0.37 - 0.91)
Diabetes	2.93 (0.91 - 9.44)	1.40 (0.82 - 2.39)
Vaccination ≥3 doses	0.38 (0.15 - 0.95)	0.38 (0.25 - 0.59)
Previous SARS-CoV-2 infection	0.87 (0.10 - 7.39)	1.83 (0.38 - 8.81)
Cough	2.22 (0.88 - 5.58)	1.10 (0.70 - 1.73)
Phlegm	1.27 (0.57 - 2.85)	1.03 (0.65 - 1.65)
Headache	0.64 (0.28 - 1.45)	0.62 (0.32 - 1.22)
Joint or muscle pain	0.70 (0.29 - 1.72)	0.53 (0.26 - 1.07)

Diarrhea	0.82 (0.22 - 2.98)	0.88 (0.31 - 2.49)
Smell or taste disorder	1.19 (0.26 - 5.44)	N/A*
Number of upper airway symptoms**		
0	(reference)	(reference)
1	0.44 (0.19 - 1.04)	0.41 (0.26 - 0.65)
2	0.44 (0.16 - 1.22)	0.19 (0.08 - 0.45)
Number of systemic symptoms***		
0	(reference)	(reference)
1	1.07 (0.34 - 3.38)	2.96 (1.72 - 5.11)
2	3.36 (1.20 - 9.43)	7.37 (4.10 - 13.23)
3	4.84 (1.50 - 15.58)	13.86 (6.90 - 27.84)
4	2.50 (0.26 - 24.00)	40.26 (14.60 - 110.98)

*Excluded from analysis due to small number of symptomatic individuals for which confidence intervals could not be determined.

** "Sore throat" and "nasal discharge"

***"Fever", "decreased food intake", "severe fatigue", and "dyspnea"

BMI, body mass index; CI, confidence interval; OR, odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus.

Figure S1

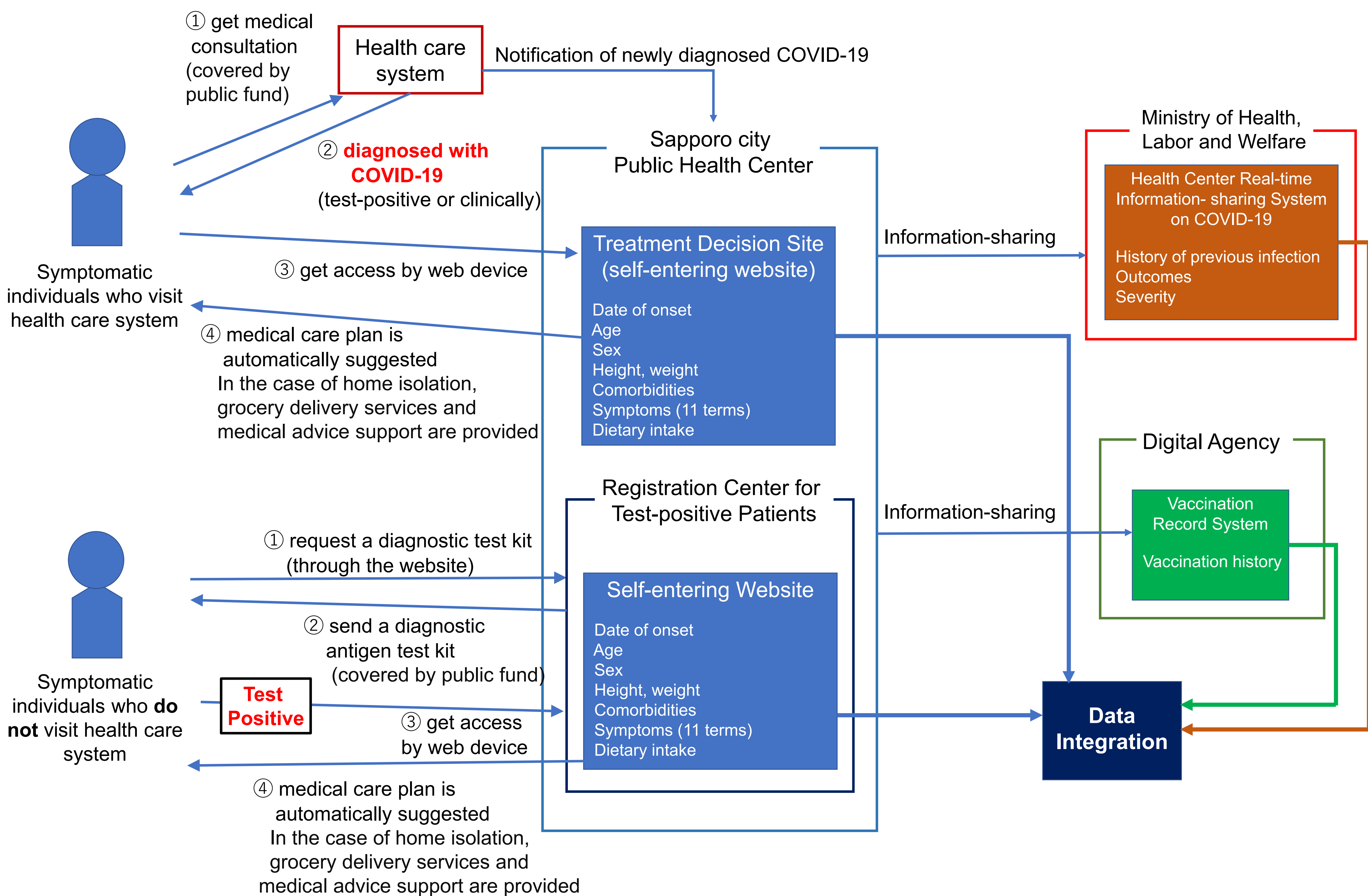


Figure S1. Schema of information registration system for symptomatic COVID-19 patients in Sapporo. Treatment Decision Site (TDS) is an online information registration system set up by Sapporo City Public Health Center. Registration Center for Test-positive Patients (RCPP) is a registration center operated by Sapporo City Public Health Center. The Ministry of Health, Labor and Welfare and Digital Agency are administrative agencies belonging to the Japanese government.

Figure S3

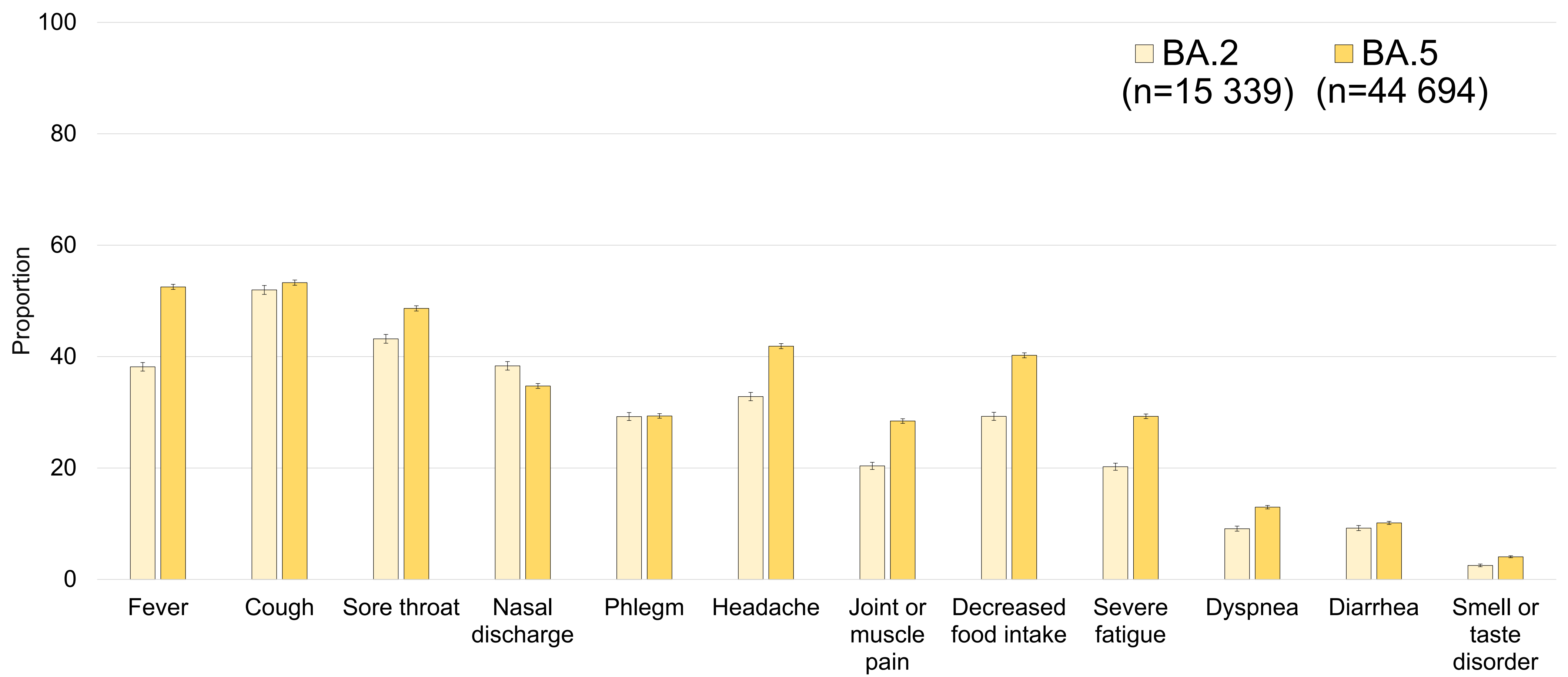


Figure S3. COVID-19 symptom prevalence in unvaccinated individuals. The graph shows the frequencies of 12 symptoms in unvaccinated individuals infected with omicron subvariants BA.2 or BA.5. Error bars indicate 95% confidence intervals.

Figure S4

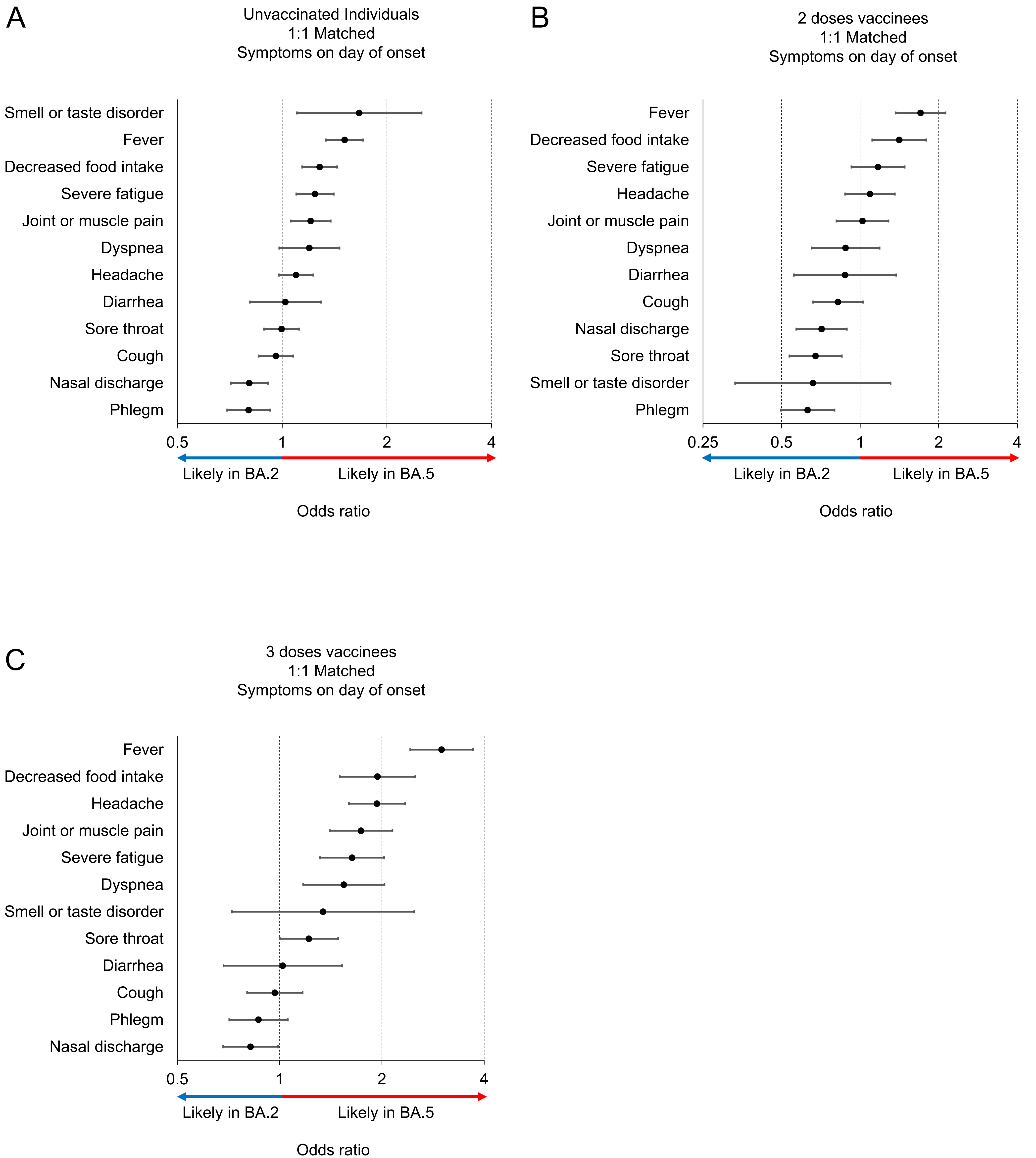


Figure S4. Associations of COVID-19 symptoms with the omicron subvariants BA.2 and BA.5 in subgroups depending on vaccine status. Propensity score 1:1 matching analyses were performed and a propensity score of the type of omicron subvariants was calculated by logistic regression analysis with the variables, including age, sex, obesity, underlying disease, vaccine status, times since last vaccination, and previous SARS-CoV-2 infection. The odds ratios of symptoms for BA.5 to BA.2 are ordered from highest to lowest. The matching was carried out in **A.** unvaccinated, **B.** 2 doses vaccinees and **C.** 3 doses vaccinees. Error bars indicate 95% CI. Detailed results are shown in **Table S6.**

Figure S5

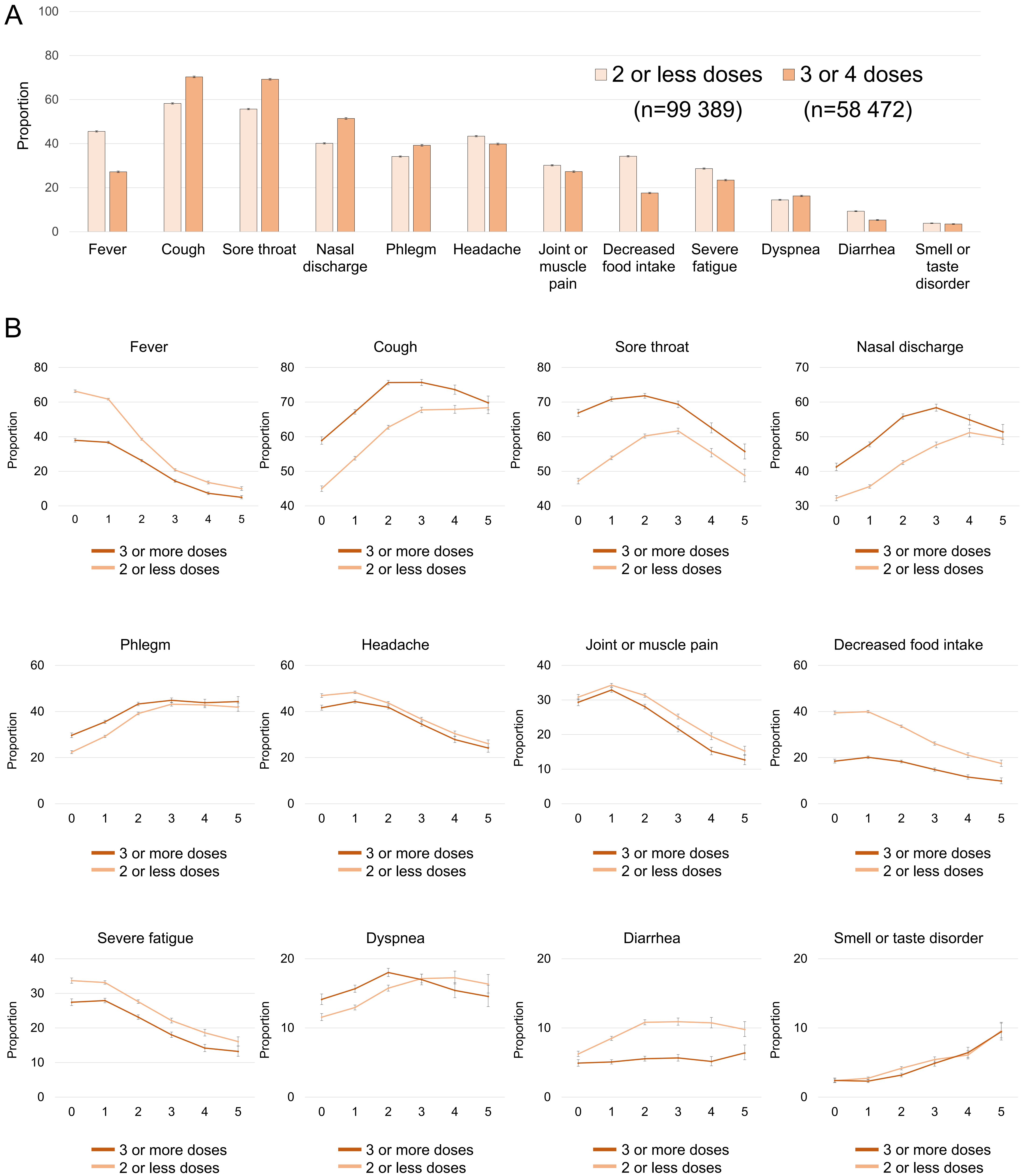


Figure S5. Associations between host vaccine status and COVID-19 symptoms. A. Prevalence of COVID-19 symptoms in individuals with 2 or less doses and 3 or more doses of vaccination. **B.** Prevalence of COVID-19 symptoms by days since symptom onset. Error bars indicate 95% confidence intervals.

Figure S6

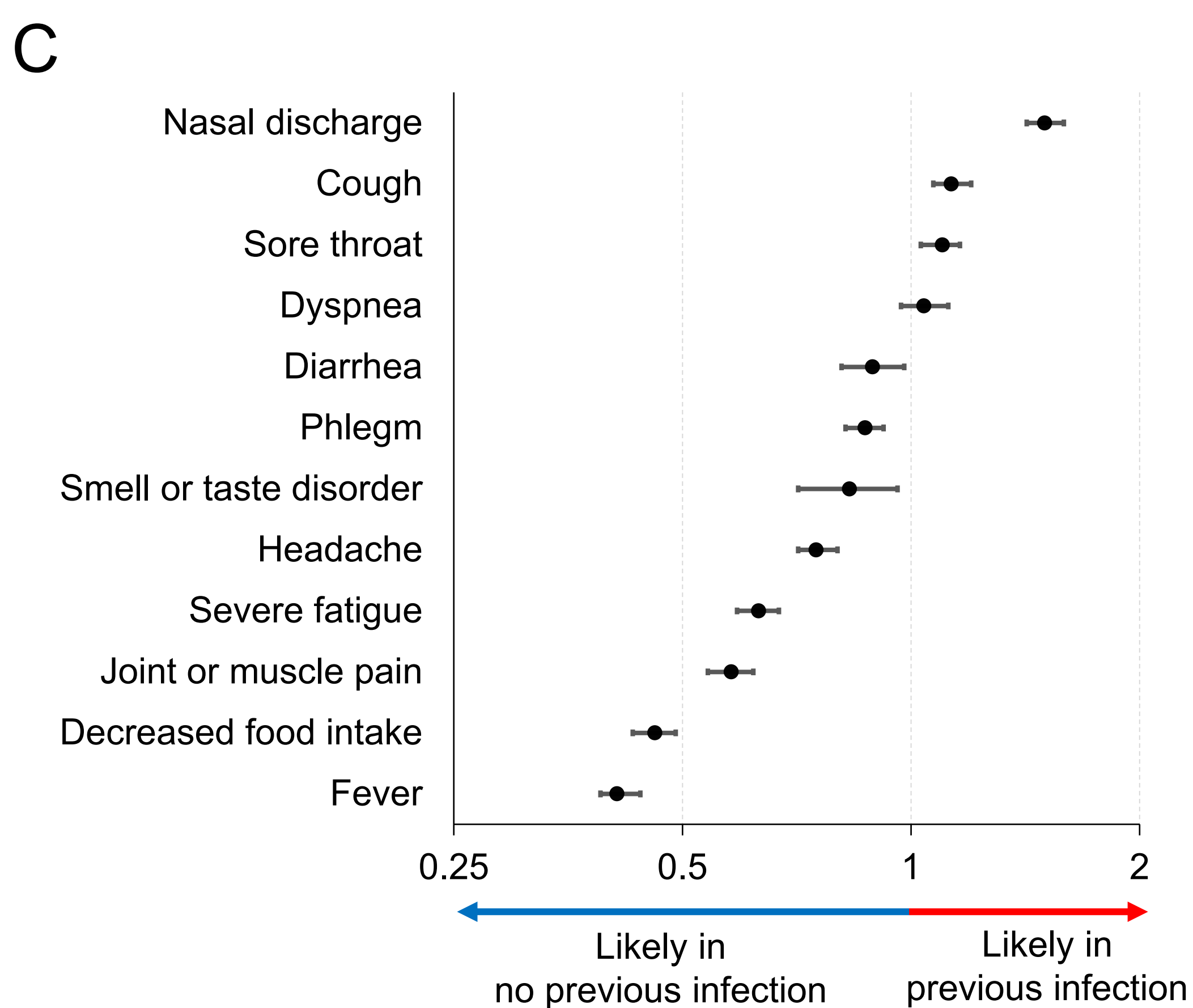
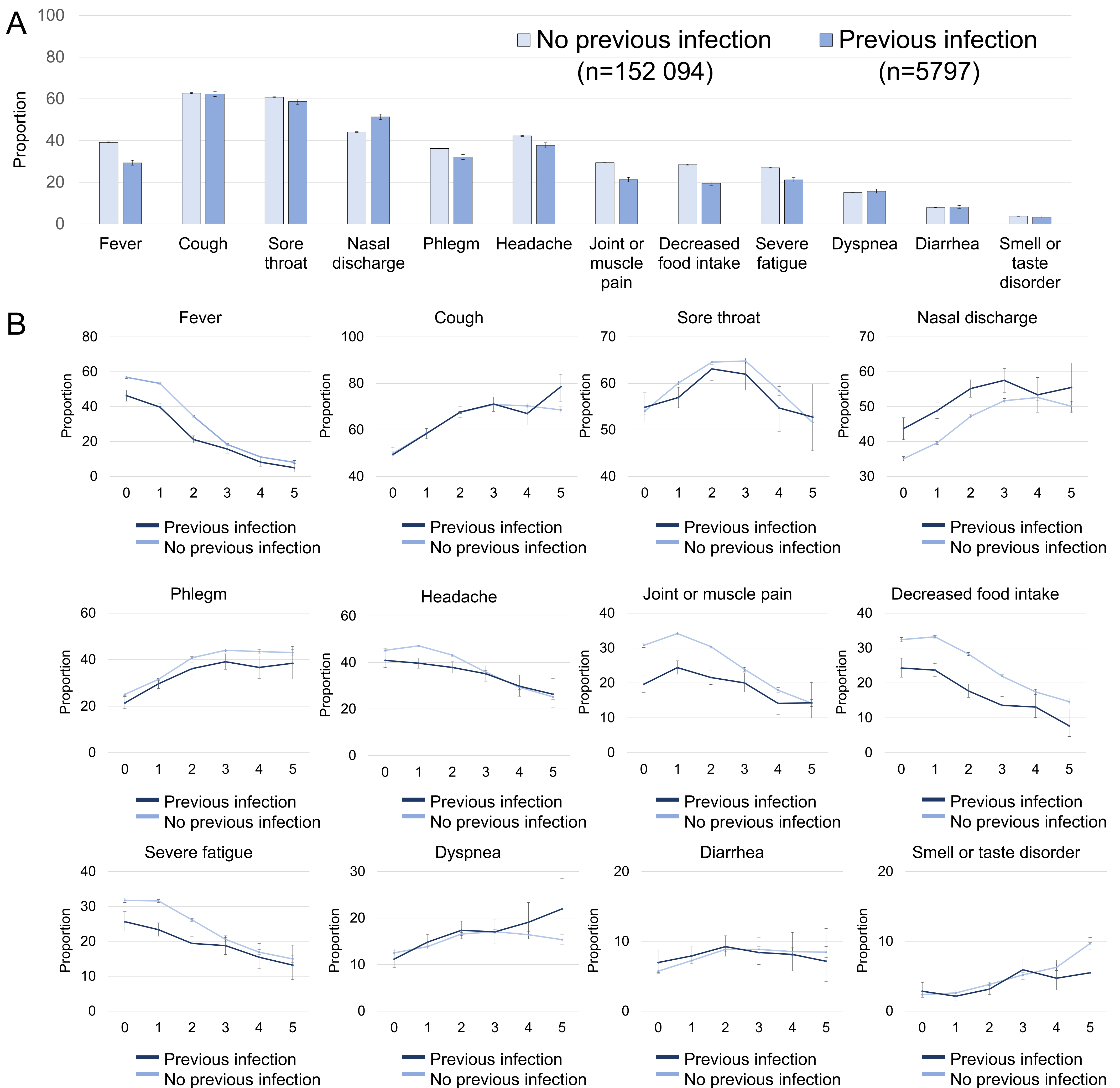


Figure S6. Associations between history of previous infection and COVID-19 symptoms. **A.** Prevalence of COVID-19 symptoms in individuals with or without history of previous infection. **B.** Prevalence of COVID-19 symptoms by days since symptom onset. **C.** Associations between previous COVID-19 infection and symptom likelihood. Multivariable analysis used each symptom as an outcome and mutant strain, age, body mass index, underlying disease, vaccination history, and history of spontaneous infection as explanatory variables. Among the explanatory variables, history of previous SARS-CoV-2 infection and the adjusted odds ratio (OR) for each symptom are arranged from highest to lowest. Points indicate odds ratios, and bars indicate 95% confidence intervals. Detailed results of the multivariate analysis are presented in **Table S4**.