

SARS-CoV-2 Variants and Age-Dependent Infection Rates among Household and Nonhousehold Contacts

Reiko Miyahara, Kosuke Tamura, Tomoko Kato, Mineko Nakazaki, Kanako Otani, Yura K. Ko, Taro Kamigaki, Yuzo Arima, Hideki Tani, Kazunori Oishi, Motoi Suzuki

To determine the effects of age and variants of concern on transmission of SARS-CoV-2, we analyzed infection rates among close contacts over 4 periods in Toyama Prefecture, Japan. Among household contacts, odds of infection were 6.2 times higher during the period of the Omicron variant than during previous periods, particularly among children and adolescents.

SARS-CoV-2 has been spreading globally since 2019; new variants of concern (VOCs) caused several epidemic waves during 2020–2022. According to a meta-analysis, the overall household secondary attack rates were higher for the Omicron variant (42.7%) than for the Alpha (36.4%) and Delta (29.7%) variants (1). The transmissibility and age-dependent susceptibility for Omicron and Delta exhibited significant heterogeneity among studies (1,2), and children were identified as being more vulnerable than adults to new variants (2). Infection rates among close contacts, determined by SARS-CoV-2 diagnostic tests, can vary according to study design, site settings, nonpharmacological control measures, and contact patterns (3). Thus, assessing infection rates among household and nonhousehold contacts within the same geographic area and population by using consistent methods over time could provide more reliable and valid information about changes in the effects of age and VOCs on transmission risk. With this study, we aimed to analyze the effects of age and VOCs on SARS-CoV-2 transmission by using contact tracing data of index

case-patients and household and nonhousehold contacts in a city in Toyama Prefecture, Japan.

The Study

We analyzed COVID-19 cases recorded in a city in Toyama Prefecture, Japan, over 4 periods, dominated by each of the 4 main virus variants: July 1–October 31, 2020 (pre-VOC period), April 1–30, 2021 (Alpha period), July 3–August 15, 2021 (Delta period), and January 3–23, 2022 (Omicron period) (Appendix Figure 1, <https://wwwnc.cdc.gov/EID/article/29/8/22-1582-App1.pdf>). Health center staff conducted telephone interviews with all COVID-19 case-patients, including those who were asymptomatic, to collect clinical information and recent activity history. According to the contact tracing guidelines of the National Institute of Infectious Diseases (Japan Ministry of Health, Labour and Welfare), we defined a close contact as someone who had contact with a COVID-19 case-patient during the period from 2 days before symptom onset until diagnosis (4). Close contacts were divided into household contacts (those who resided in the same household) and nonhousehold contacts (others who had contact with a confirmed COVID-19 case-patient for ≥ 15 minutes within a 1-meter distance without wearing any personal protective equipment). All contacts received SARS-CoV-2 PCR testing regardless of symptom status. If the PCR result for the first test was negative, contacts received PCR testing again if COVID-19–associated symptoms developed. We excluded from analysis close contacts with no PCR results.

All data management and analyses were conducted as part of the public health response in Toyama Prefecture and the National Institute of Infectious Diseases, and we used registered data collected according to the Infectious Diseases Law of Japan. Ethics approval was not required for this study.

Author affiliations: National Institute of Infectious Diseases, Tokyo, Japan (R. Miyahara, K. Otani, T. Kamigaki, Y. Arima, M. Suzuki); Toyama Institute of Health, Toyama, Japan (K. Tamura, M. Nakazaki, H. Tani, K. Oishi); Takaoka Health and Welfare Center, Toyama (T. Kato); Tohoku University Graduate School of Medicine, Miyagi, Japan (Y.K. Ko)

DOI: <https://doi.org/10.3201/eid2908.221582>

First, we determined the baseline characteristics of the index case-patients and close contacts for each of the 4 periods. Second, we calculated infection rates stratified by the characteristics of index case-patients (age, sex, history of contact with COVID-19 case-patients before diagnosis, and symptom status) and close contacts (age, sex, and interval between diagnosis of index case-patients and PCR results of contacts). To adjust for clustering effects, we calculated infection rates as the total number of positive contacts divided by the total number of close contacts (with 95% CIs) by using the `svyset` command in Stata (Stata-Corp LLC, <https://www.stata.com>). To account for clustering among contacts exposed to the same index case-patients, we analyzed odds ratios of the infection rates (with 95% CIs) by using GEE (generalized estimating equations) logistic regression models with exchangeable correlations. We adjusted the models for the characteristics of both the index case-patients and their close contacts. Third, we described the contact matrix for the average number of contacts and infection rates based on the age of the index case-patients and contacts. We used Stata version 16.0 and R version 4.2.1 (The R Project for Statistical Computing, <https://www.r-project.org>) software to perform statistical analyses.

We enrolled 1,057 patients and 3,820 contacts: 123 index case-patients and 530 close contacts, in the pre-VOC period; 246 index case-patients and 988 close contacts in the Alpha period; 304 index case-patients and 984 close contacts in the Delta period; and 384 index case-patients and 1,318 close contacts in the Omicron period (Appendix Table 1). We excluded close contacts without PCR results: 45 (8.5%) persons from the pre-VOC period, 29 (2.9%) from the Alpha period, 111 (11.3%) from the Delta period, and 173 (13.1%) from the Omicron period. Infection rates during the Omicron period were 35.0% (95% CI 28.3–42.2) for household contacts and 15.1% (95% CI 10.0–22.5) for nonhousehold contacts. After adjustment for age, symptoms, sex, contact history, interval from diagnosis of index case-patient to PCR test, and household size, the odds ratios for infection were 6.22 times higher among household contacts and 3.55 times higher among nonhousehold contacts during the Omicron period than during the pre-VOC period (Table; Appendix Table 2). The risk for infection among household contacts 0–19 years of age increased significantly, from 3% in the pre-VOC period to 38% during the Omicron period (Appendix Figure 2). In contrast, during the study period, infection rates for nonhousehold contacts in this age group were

Table. Infection rates of SARS-CoV-2 infection among household and nonhousehold contacts in study of SARS-CoV-2 variants and age-dependent infection rates

Variable	Household contacts				Nonhousehold contacts			
	Total no.	No. PCR positive	Infection rate, %	Adjusted odds ratio (95% CI)*	Total no.	No. PCR positive	Infection rate, %	Adjusted odds ratio (95% CI)*
Total	1,144	294	25.7		2,318	302	13.0	
Period								
Pre-VOC	155	20	12.9	Referent	330	36	10.9	Referent
Alpha	251	48	19.1	1.91 (0.94–3.90)	708	71	10.0	1.47 (0.86–2.50)
Delta	329	83	25.2	3.75 (1.84–7.61)	544	84	15.4	2.34 (1.37–3.98)
Omicron	409	143	35.0	6.22 (3.04–12.70)	736	111	15.1	3.55 (2.09–6.06)
Index case-patient age, y								
0–19	214	54	25.2	0.42 (0.20–0.86)	852	34	4.0	0.16 (0.08–0.34)
20–39	493	111	22.5	0.36 (0.20–0.66)	973	182	18.7	0.42 (0.25–0.73)
40–59	309	84	27.2	0.45 (0.24–0.83)	317	48	15.1	0.40 (0.22–0.72)
≥60	129	45	35.2	Referent	176	38	21.6	Referent
Close contact age, y								
0–19	295	80	27.1	1.06 (0.70–1.62)	831	45	5.4	0.67 (0.39–1.17)
20–39	259	79	30.5	1.33 (0.89–2.00)	721	162	22.5	1.09 (0.70–1.71)
40–59	359	84	23.4	1.14 (0.78–1.68)	353	38	10.8	0.52 (0.31–0.85)
≥60	227	51	22.5	Referent	257	51	19.8	Referent
Unknown	4	0	0	NA	156	6	3.8	0.22 (0.07–0.66)

* Odds ratios were adjusted for age, sex, symptoms of index case-patients at the time of diagnosis, contact history, interval from diagnosis of index case-patient to PCR tests, and number of persons in the same household. NA, not applicable; VOC, variant of concern.

lower, despite a higher number of contacts compared with nonhousehold contacts in other age groups (Appendix Figure 3). Infection rates among household contacts ≥ 60 years of age decreased during the Delta period (12%) but increased again during the Omicron period (29%). Regarding infectivity throughout all time periods, the risk for infection from index case-patients ≥ 60 years of age was higher than that from index case-patients of other ages (Appendix Figure 2).

Conclusions

Our study showed that odds of infection were 6.2 times higher for household contacts during the Omicron period than during the pre-VOC period and that children and adolescents were particularly vulnerable (2). Despite increased nonhousehold contact among persons 0–19 years of age, nonphysical contact (5) and nonpharmacological control measures (6) in school and daycare centers may have led to lower infection rates and fewer large outbreaks in schools.

In addition, infection rates for contacts ≥ 60 years of age decreased during the Delta period but increased again during the Omicron period, potentially because of waning immunity associated with SARS-CoV-2 vaccination and the attenuated effect on the Omicron variant (7), even with high vaccination rates (93%) among persons >65 years of age during the Omicron period (Appendix Figure 1). In addition, the infectivity of elderly persons tended to be higher than that of persons in other age groups even after vaccine introduction (8), possibly because of close contact, such as caregiving and nursing care. The value of protecting those who care for elderly case-patients should thus be emphasized.

A limitation of this study was the varied timing and frequency of PCR testing. As the number of days from symptom onset to diagnosis decreased over time, infection rates were associated with the timing of testing and symptoms at the time of testing. We might have missed asymptomatic infections and potentially overcounted infected case-patients among contacts who might have been exposed to other places or infected persons.

Our finding of increased odds of infection among household contacts during the period of the Omicron variant, particularly among children and adolescents, highlights the need for periodic surveys to investigate comparative infectivity by epidemic strain as well as susceptibility and trends by age group over time in the same area and population. Such studies would account for variations in local conditions such as control regulation, contact tracing strategy, population age structure, and vaccination coverage.

Acknowledgments

We thank the public health centers and prefectural offices in Toyama Prefecture for data access.

This work was supported by grants from the National Center for Global Health and Medicine (20A2002D).

About the Author

Dr. Miyahara is a researcher at the Center for Surveillance, Immunization, and Epidemiologic Research, National Institute of Infectious Diseases, Tokyo, Japan. Her primary research interests are the clinical and genetic epidemiology of infectious diseases, including tuberculosis and COVID-19.

References

1. Madewell ZJ, Yang Y, Longini IM Jr, Halloran ME, Dean NE. Household secondary attack rates of SARS-CoV-2 by variant and vaccination status: an updated systematic review and meta-analysis. *JAMA Netw Open*. 2022;5:e229317. <https://doi.org/10.1001/jamanetworkopen.2022.9317>
2. Chen F, Tian Y, Zhang L, Shi Y. The role of children in household transmission of COVID-19: a systematic review and meta-analysis. *Int J Infect Dis*. 2022;122:266–75. <https://doi.org/10.1016/j.ijid.2022.05.016>
3. Madewell ZJ, Yang Y, Longini IM Jr, Halloran ME, Dean NE. Factors associated with household transmission of SARS-CoV-2: an updated systematic review and meta-analysis. *JAMA Netw Open*. 2021;4:e2122240. <https://doi.org/10.1001/jamanetworkopen.2021.22240>
4. National Institute of Infectious Diseases. Guidelines for active epidemiological investigation in patients with novel coronavirus infection [in Japanese] [cited 2022 Oct 8]. <https://www.niid.go.jp/niid/ja/diseases/ka/coronavirus/2019-ncov/2484-idsc/9357-2019-ncov-02.html>
5. Munasinghe L, Asai Y, Nishiura H. Quantifying heterogeneous contact patterns in Japan: a social contact survey. *Theor Biol Med Model*. 2019;16:6. <https://doi.org/10.1186/s12976-019-0102-8>
6. Budzyn SE, Panaggio MJ, Parks SE, Papazian M, Magid J, Eng M, et al. Pediatric COVID-19 cases in counties with and without school mask requirements – United States, July 1–September 4, 2021. *MMWR Morb Mortal Wkly Rep*. 2021;70:1377–8. <https://doi.org/10.15585/mmwr.mm7039e3>
7. Jalali N, Brustad HK, Frigessi A, MacDonald EA, Meijerink H, Feruglio SL, et al. Increased household transmission and immune escape of the SARS-CoV-2 Omicron compared to Delta variants. *Nat Commun*. 2022;13:5706. <https://doi.org/10.1038/s41467-022-33233-9>
8. Lyngse FP, Mortensen LH, Denwood MJ, Christiansen LE, Møller CH, Skov RL, et al. Household transmission of the SARS-CoV-2 Omicron variant in Denmark. *Nat Commun*. 2022;13:5573. <https://doi.org/10.1038/s41467-022-33328-3>

Address for correspondence: Reiko Miyahara, Center for Surveillance, Immunization, and Epidemiologic Research, National Institute of Infectious Diseases, 1-23-1 Toyama, Shinjuku-ku, Tokyo 162-8640, Japan; email: rmiyahara@niid.go.jp

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

SARS-CoV-2 Variants and Age-Dependent Infection Rates among Household and Nonhousehold Contacts

Appendix

Appendix Table 1. Characteristics of index patients and contacts in the pre-VOC period, the Alpha period, the Delta period and the Omicron period

Category	Subcategory	pre-VOC period	Alpha period	Delta period	Omicron period
		July 2020 – October 2020	April 2021	July-August 2021	January 2022
Index case-patients		n = 123	n = 246	n = 304	n = 384
Age (years), n (%)	0–19	4 (3.3)	29 (11.8)	32 (10.5)	81 (21.1)
	20–39	56 (45.5)	95 (38.6)	171 (56.3)	184 (47.9)
	40–59	26 (21.1)	65 (26.4)	83 (27.3)	78 (20.3)
	≥60	37 (30.1)	57 (23.2)	18 (5.9)	41 (10.7)
Sex, n (%)	Male	70 (56.9)	153 (62.2)	175 (57.6)	209 (54.4)
	Female	53 (43.1)	93 (37.8)	129 (42.4)	175 (45.6)
Variants of concern, n (%)	Non-VOC	123 (100)	47 (19.1)		
	Alpha		145 (58.9)	31 (10.2)	
	Delta			273 (89.8)	13 (3.4)
	Omicron				68 (17.7)
	Unclassified / untested case-patients		54 (7.3)		303 (78.9)
Symptomatic at time of diagnosis, n (%)	Yes	104 (84.6)	202 (82.1)	294 (96.7)	351 (91.4)
Contact history, n(%)	Yes	77 (62.6)	174 (70.7)	186 (61.2)	184 (47.9)
Days from symptom onset to diagnosis	Mean days (SD)	5.31 (4.67)	3.82 (3.17)	2.80 (2.09)	2.13 (2.27)
Index case who had close contacts, n(%)	Yes	99 (80.5)	161 (65.4)	195 (64.1)	253 (65.9)
Number of close contacts	Mean (median)	5.35 (3)	6.14 (3)	5.05 (3)	5.21 (3)
Number of familial contacts	Mean (median)	1.58 (1)	1.57 (1)	1.69 (2)	1.73 (2)
Contacts		n = 530	n = 988	n = 984	n = 1,318
Age (years), n (%)	0–19	61 (11.5)	383 (38.8)	219 (22.3)	478 (36.3)

Category	Subcategory	pre-VOC period	Alpha period	Delta period	Omicron period
		July 2020 – October 2020	April 2021	July-August 2021	January 2022
	20–39	166 (31.3)	252 (25.5)	326 (33.1)	292 (22.2)
	40–59	130 (24.5)	173 (17.5)	235 (23.9)	206 (15.6)
	≥60	95 (17.9)	132 (13.4)	98 (10.0)	175 (13.3)
	Unknown	78 (14.7)	48 (4.9)	106 (10.8)	167 (12.7)
Sex, n (%)	Male	269 (50.8)	542 (54.9)	490 (49.8)	585 (44.4)
	Female	217 (10.9)	442 (44.7)	428 (43.5)	603 (45.8)
	Unknown	44 (8.3)	4 (0.4)	66 (6.7)	130 (9.9)
Symptomatic at time of PCR test, n (%)	Yes	94 (17.7)	250 (25.3)	181 (18.4)	261 (19.8)
PCR test result, n (%)	Negative	429 (80.9)	840 (85.0)	706 (71.8)	891 (67.6)
	Positive	56 (10.6)	119 (12.0)	167 (17.0)	254 (19.3)
	Untested/Unknown	45 (8.5)	29 (2.9)	111 (11.3)	173 (13.1)
Type of contact, n (%)	Household	156 (29.4)	253 (25.6)	332 (33.7)	437 (33.2)
	Non-household	375 (70.6)	735 (74.4)	652 (66.3)	881 (66.8)
Place of contact, n (%)	Home	235 (44.3)	357 (36.1)	444 (45.1)	566 (42.9)
	School	0 (0)	141 (14.3)	93 (9.5)	194 (14.7)
	Hospital/Nursing home	46 (8.7)	22 (2.2)	19 (1.9)	80 (6.1)
	Nursery	0 (0)	197 (19.9)	45 (4.6)	135 (10.2)
	Restaurants/eating	110 (20.8)	93 (9.4)	140 (14.2)	168 (12.8)
	Work place	87 (16.4)	93 (9.4)	171 (17.4)	66 (5.0)
	Outside	6 (1.1)	30 (3)	24 (2.4)	35 (2.7)
	Inside	10 (1.9)	23 (2.3)	25 (2.5)	8 (0.6)
	Others	36 (6.8)	32 (3.2)	23 (2.3)	66 (5)
Interval from diagnosis of index case to PCR test, n (%)	0–1day	276 (52.1)	286 (29.0)	185 (18.8)	210 (15.9)
	2–3 d	163 (30.8)	412 (41.7)	557 (56.6)	543 (41.2)
	4–5 d	9 (1.7)	26 (2.6)	63 (6.4)	298 (22.6)
	6–10 d	9 (1.7)	27 (2.7)	59 (6.0)	58 (4.4)
	≥11 d	1 (0.2)	29 (2.9)	8 (0.8)	9 (0.7)
	Untested/Unknown	72 (13.6)	208 (21.1)	112 (11.4)	200 (15.2)
Symptomatic case-patients among PCR positive contacts		38/56 (67.9%)	91/119 (76.5%)	145/167 (86.8%)	204/254 (80.3%)

Appendix Table 2. Infection rates of SARS-CoV-2 infection among household and non-household contacts

Category	Sub-category	Household contacts					Non-household contacts				
		Number N=1,144	PCR positive N=294	Infection rates(%) 25.7	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Number N=2,318	PCR positive N=302	Infection rates (%) 13.0	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)
Index case characteristics											
Time period	pre-VOC	155	20	12.9	ref	ref	330	36	10.9	ref	ref
	Alpha	251	48	19.1	1.41 (0.73, 2.74)	1.91 (0.94, 3.90)	708	71	10.0	1.15 (0.61,2.17)	1.47 (0.86,2.50)
	Delta	329	83	25.2	1.91 (1.02, 3.58)	3.75 (1.84,7.61)	544	84	15.4	1.67 (0.92,3.06)	2.34 (1.37,3.98)
	Omicron	409	143	35.0	2.77 (1.51, 5.05)	6.22 (3.04,12.70)	736	111	15.1	2.18 (1.22, 3.92)	3.55 (2.09,6.06)
Symptomatic at the time of diagnosis	No	72	13	18.1	ref	ref	207	5	2.4	ref	ref
	Yes	1,073	281	26.2	1.77 (0.81, 3.90)	1.59 (0.66,3.83)	2,111	297	14.1	2.20 (0.73, 6.67)	2.32 (0.78,6.89)
Age (years)	0-19	214	54	25.2	0.55 (0.29,1.04)	0.42 (0.20,0.86)	852	34	4.0	0.23 (0.11,0.46)	0.16 (0.08,0.34)
	20-39	493	111	22.5	0.54 (0.32,0.92)	0.36 (0.20,0.66)	973	182	18.7	0.73 (0.45,1.16)	0.42 (0.25,0.73)
	40-59	309	84	27.2	0.64 (0.37,1.11)	0.45 (0.24,0.83)	317	48	15.1	0.71 (0.41,1.24)	0.40 (0.22,0.72)
	≥60	129	45	35.2	ref	ref	176	38	21.6	ref	ref
Sex	Male	713	186	26.1	ref	ref	1,419	187	13.2	ref	ref
	Female	432	108	25.0	0.91 (0.64,1.30)	0.98 (0.67,1.42)	899	115	12.8	0.85 (0.59, 1.23)	0.84 (0.60,1.18)
Contact history	No	620	196	31.6	ref	ref	1,431	214	15.0	ref	ref
	Yes	525	98	18.7	0.56 (0.39,0.79)	0.67 (0.46,0.99)	887	88	9.9	0.60 (0.41,0.88)	0.70 (0.49,0.99)
Close contact characteristics											
Age (years)	0-19	295	80	27.1	0.86 (0.61,1.22)	1.06 (0.70,1.62)	831	45	5.4	0.45 (0.28,0.72)	0.67 (0.39,1.17)
	20-39	259	79	30.5	1.23 (0.87,1.73)	1.33 (0.89,2.00)	721	162	22.5	0.96 (0.66,1.40)	1.09 (0.70,1.71)
	40-59	359	84	23.4	0.99 (0.72,1.37)	1.14 (0.78,1.68)	353	38	10.8	0.52 (0.33,0.80)	0.52 (0.31,0.85)
	≥60	227	51	22.5	ref	ref	257	51	19.8	ref	ref
	Unknown	4	0	0	-	-	156	6	3.8	0.10 (0.03,0.30)	0.22 (0.07,0.66)
Sex	Male	492	119	24.2	ref	ref	1,287	179	13.9	ref	ref
	female	646	175	27.1	1.17 (0.94,1.45)	1.18 (0.91,1.51)	954	121	12.7	0.97 (0.78,1.20)	1.00 (0.76,1.33)
	Unknown	7	0	0	-	-	77	2	2.6	0.06 (0.01,0.57)	0.25 (0.04,1.85)
Interval from diagnosis of index case to PCR test	0-1day	387	111	28.7	ref	ref	567	129	22.8	Ref	ref
	2-3 days	501	102	20.4	0.53 (0.37,0.76)	0.37 (0.24,0.56)	1,174	116	9.9	0.33 (0.24,0.45)	0.28 (0.20,0.38)
	4-5 days	170	35	20.6	0.55 (0.34,0.90)	0.29 (0.17,0.50)	226	27	11.9	0.45 (0.27,0.75)	0.34 (0.20,0.59)
	6-10 days	57	30	52.6	1.17 (0.67,2.05)	0.91 (0.49,1.68)	96	16	16.7	0.81 (0.42,1.57)	0.63 (0.31,1.26)
	≥11 days	28	15	53.6	0.89 (0.42,1.92)	0.78 (0.34,1.78)	19	9	47.4	1.04 (0.37,2.95)	1.34 (0.46,3.88)
	Unknown	1	1	100.0	-	-	236	5	2.1	0.09 (0.02,0.37)	0.46 (0.15,1.40)

Category	Sub-category	Household contacts					Non-household contacts				
		Number	PCR positive	Infection rates(%)	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Number	PCR positive	Infection rates (%)	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)
		N=1,144	N=294	25.7			N=2,318	N=302	13.0		
Number of people in the same household	1-2	427	126	29.5	ref	ref					
	3-5	625	150	24.0	0.70 (0.49,1.00)	0.74 (0.51,1.08)					
	over 6	92	18	19.6	0.57 (0.20,1.62)	0.52 (0.19,1.43)					

Appendix Table 3a. Infection rates of SARS-CoV-2 infection among household and non-household contacts, pre-VOC period

Category	Sub-category	Household contacts					Non-household contacts				
		Number	PCR positive	Infection rate (%)	Odds Ratio (95% CI)	Adjusted Odds ratio (95% CI)	Number	PCR positive	Infection rate (%)	Odds Ratio (95% CI)	Adjusted Odds ratio (95% CI)
Total		N=155	N=20	12.9			N=330	N=36	10.9		
Index case characteristics											
Age (years)	0-19	32	0	0	-	-	1	0	0	-	-
	20-39	75	5	6.7	0.25 (0.08,0.75)	0.24 (0.05,1.12)	171	19	11.1	0.41 (0.16,1.03)	0.16 (0.04,0.72)
	40-59	28	4	14.3	0.57 (0.16,2.00)	0.55 (0.11,2.83)	97	3	3.1	0.22 (0.05,0.88)	0.08 (0.01,0.53)
	≥60	49	11	22.4	ref	ref	61	14	23.0	ref	ref
Sex	Male	94	13	13.8	ref	ref	204	23	11.3	ref	ref
	Female	61	7	11.5	0.79 (0.29,2.15)	0.49 (0.10,2.53)	126	13	10.3	1.28 (0.5,3.29)	0.68 (0.23,1.99)
Symptomatic	No	20	3	15.0	ref	ref	17	1	5.9	ref	ref
	Yes	135	17	12.6	0.82 (0.21,3.12)	2.04 (0.25,16.82)	313	35	11.2	1.78 (0.22,14.44)	1.92 (0.17,22.25)
Contact history	No	70	10	14.3	ref	ref	196	26	13.3	ref	ref
	Yes	85	10	11.8	0.81 (0.31,2.09)	0.79 (0.23,2.72)	134	10	7.5	0.42 (0.16,1.14)	0.19 (0.06,0.60)
Close contact characteristics											
Age	0-19	34	1	2.9	0.16 (0.02,1.35)	0.38 (0.04,3.97)	27	0	0	-	-
	20-39	33	8	24.2	1.66 (0.54,5.1)	4.02 (0.94,17.2)	120	19	15.8	0.64 (0.28,1.49)	1.21 (0.34,4.27)
	40-59	40	4	10.0	0.60 (0.16,2.15)	0.73 (0.14,3.80)	87	3	3.4	0.23 (0.08,0.67)	0.29 (0.07,1.09)
	≥60	44	7	15.9	ref	ref	48	14	29.2	ref	ref

Category	Sub-category	Household contacts					Non-household contacts				
		Number	PCR positive	Infection rate (%)	Odds Ratio (95% CI)	Adjusted Odds ratio (95% CI)	Number	PCR positive	Infection rate (%)	Odds Ratio (95% CI)	Adjusted Odds ratio (95% CI)
Sex	Unknown	4	0	0	-	-	48	0	0	-	-
	Male	67	9	13.4	ref	ref	178	18	10.1	ref	ref
	female	87	11	12.6	0.92 (0.36,2.35)	1.12 (0.28,4.39)	124	18	14.5	1.07 (0.57,2.03)	0.98 (0.44,2.19)
Interval from diagnosis of index case to PCR test	Unknown	1	0	0	-	-	28	0	0	-	-
	0-1day	124	14	11.3	ref	ref	152	25	16.4	ref	ref
	2-3 days	26	2	7.7	0.66 (0.14,3.08)	0.37 (0.06,2.17)	137	10	7.3	0.67 (0.28,1.58)	0.72 (0.25,2.07)
	4-5 days	3	2	66.7	15.7 (1.34,184.62)	4.34 (0.24,79.14)	6	1	16.7	0.55 (0.04,7.08)	0.90 (0.07,11.88)
	6-10 days	1	1	100	-	-	9	0	0	-	-
	≥11 days	1	1	100	-	-	26	0	0	-	-
Number of same household	1-2	62	13	21.0	ref	ref					
	3-5	85	5	5.9	0.23 (0.08,0.67)	0.39 (0.10,1.45)					
	over 6	8	2	25.0	1.28 (0.29,5.63)	0.74 (0.07,8.02)					

Appendix Table 3b. Infection rates of SARS-CoV-2 infection among household and non-household contacts, Alpha period

Category	Sub-category	Household contacts					Non-household contacts				
		Number	PCR positive	Infection rate (%)	Odds Ratio (95% CI)	Adjusted Odds ratio (95% CI)	Number	PCR positive	Infection rate (%)	Odds Ratio (95% CI)	Adjusted Odds ratio (95% CI)
Total		251	48	19.1			708	71	10		
Index case characteristics											
Age	0-19	58	6	10.3	0.16 (0.04,0.61)	0.26 (0.05,1.30)	329	9	2.7	0.29 (0.07,1.19)	0.20 (0.04,1.07)
	20-39	77	8	10.4	0.20 (0.06,0.59)	0.17 (0.05,0.64)	227	38	16.7	0.77 (0.31,1.89)	0.32 (0.10,1.03)
	40-59	80	20	25.0	0.55 (0.22,1.39)	0.44 (0.14,1.39)	70	13	18.6	1.20 (0.44,3.27)	0.78 (0.25,2.46)
	≥60	36	14	38.9	ref	ref	82	11	13.4	ref	ref
Sex	Male	159	26	16.4	ref	ref	524	55	10.5	ref	ref
	Female	92	22	23.9	1.42 (0.67,2.99)	1.46 (0.62,3.45)	184	16	8.7	0.68 (0.29,1.58)	0.51 (0.22,1.17)
Symptomatic	No	22	2	9.1	ref	ref	182	3	1.6	ref	ref

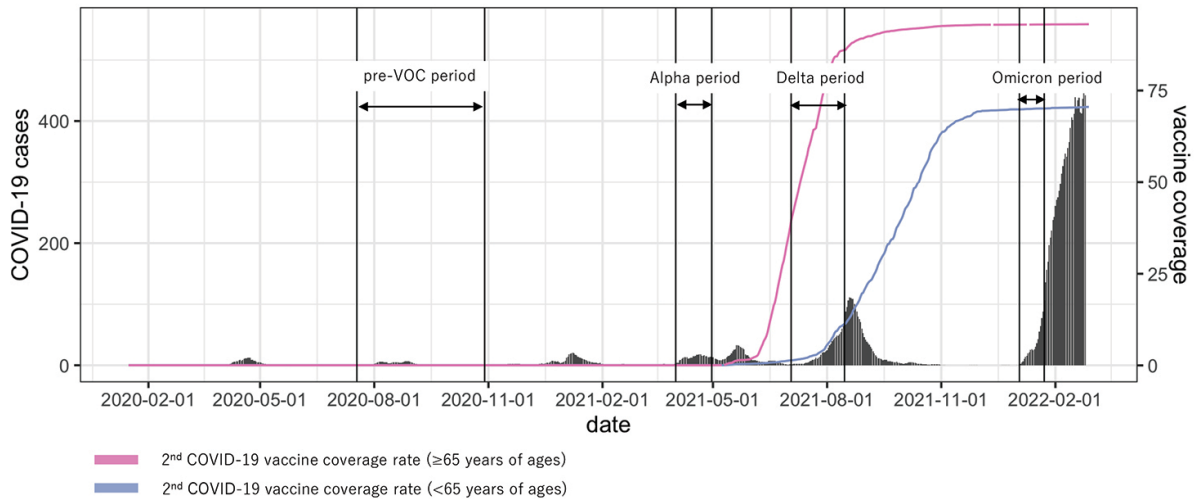
Category	Sub-category	Household contacts					Non-household contacts				
		Number	PCR positive	Infection rate (%)	Odds Ratio (95% CI)	Adjusted Odds ratio (95% CI)	Number	PCR positive	Infection rate (%)	Odds Ratio (95% CI)	Adjusted Odds ratio (95% CI)
	Yes	229	46	20.1	2.73 (0.49,15.19)	2.28 (0.40,13.10)	526	68	12.9	1.98 (0.39,10.12)	2.72 (0.48,15.41)
Contact history	No	100	29	29.0	ref	ref	275	34	12.4	ref	ref
	Yes	151	19	12.6	0.41 (0.20,0.86)	0.76 (0.33,1.74)	433	37	8.5	0.85 (0.39,1.83)	1.26 (0.61,2.61)
Close contact characteristics											
Age	0-19	59	8	13.6	0.42 (0.17,1.05)	0.99 (0.29,3.35)	321	13	4.0	0.98 (0.34,2.83)	2.63 (0.65,10.73)
	20-39	65	9	13.8	0.47 (0.19,1.15)	0.82 (0.26,2.59)	175	37	21.1	1.15 (0.48,2.77)	1.88 (0.64,5.51)
	40-59	72	16	22.2	0.82 (0.39,1.75)	1.51 (0.52,4.38)	97	9	9.3	0.74 (0.29,1.91)	0.92 (0.32,2.70)
	≥60	55	15	27.3	ref	ref	76	12	15.8	ref	ref
	Unknown	0	0	0	-	-	39	0	0	-	-
Sex	Male	112	18	16.1	ref	ref	412	53	12.9	ref	ref
	female	139	30	21.6	1.28 (0.71,2.33)	1.21 (0.56,2.63)	293	18	6.1	0.81 (0.53,1.24)	0.78 (0.40,1.52)
	Unknown	0	0	0	-	-	3	0	0	-	-
Interval from diagnosis of index case to PCR test	0-1day	112	22	19.6	ref	ref	171	29	17.0	ref	ref
	2-3 days	104	11	10.6	0.47 (0.20,1.11)	0.47 (0.18,1.20)	308	17	5.5	0.22 (0.11,0.47)	0.20 (0.09,0.42)
	4-5 days	9	5	55.6	5.08 (1.12,22.93)	8.08 (1.30,50.14)	17	7	41.2	1.75 (0.58,5.28)	1.73 (0.53,5.65)
	6-10 days	13	5	38.5	2.12 (0.58,7.67)	1.73 (0.40,7.41)	14	9	64.3	4.76 (1.55,14.6)	4.27 (1.26,14.51)
	≥11 days	13	5	38.5	1.55 (0.42,5.78)	1.90 (0.47,7.65)	16	9	56.3	1.86 (0.59,5.89)	2.36 (0.73,7.69)
Number of same household	1-2	108	26	24.1	ref	ref					
	3-5	112	20	17.9	0.66 (0.31,1.41)	1.05 (0.42,2.59)					
	over 6	31	2	6.5	0.23 (0.02,2.29)	0.48 (0.06,3.68)					

Appendix Table 3c. Infection rates of SARS-CoV-2 infection among household and non-household contacts, Delta period

Category	Sub-category	Household contacts					Non-household contacts				
		Number	PCR positive	Infection rate (%)	Odds Ratio (95% CI)	Adjusted Odds ratio (95% CI)	Number	PCR positive	Infection rate (%)	Odds Ratio (95% CI)	Adjusted Odds ratio (95% CI)
Total		329	83	25.2			544	84	15.4		
Index case characteristics											
Age	0-19	31	9	29.0	0.74 (0.14,3.86)	0.85 (0.11,6.33)	134	7	5.2	0.29 (0.05,1.76)	1.50 (0.20,11.45)
	20-39	183	42	23.0	0.56 (0.14,2.21)	0.41 (0.08,2.22)	283	57	20.1	0.99 (0.22,4.49)	1.31 (0.25,6.81)
	40-59	93	23	24.7	0.53 (0.13,2.26)	0.39 (0.07,2.22)	111	16	14.4	0.55 (0.11,2.78)	0.72 (0.13,3.92)
	≥60	22	9	40.9	ref	ref	16	4	25.0	ref	ref
Sex	Male	208	50	24.0	ref	ref	345	51	14.8	ref	ref
	Female	121	33	27.3	1.22 (0.64,2.35)	1.40 (0.65,2.99)	199	33	16.6	0.80 (0.41,1.56)	1.14 (0.56,2.32)
Symptomatic	No	4	1	25.0	ref	ref	3	0	0	-	-
	Yes	325	82	25.2	0.60 (0.05,7.47)	0.54 (0.02,14.7)	541	84	15.5	-	-
Contact history	No	171	47	27.5	ref	ref	306	61	19.9	ref	ref
	Yes	158	36	22.8	0.82 (0.43,1.55)	0.70 (0.33,1.47)	238	23	9.7	0.50 (0.26,0.98)	0.38 (0.19,0.75)
Close contact characteristics											
Age	0-19	76	23	30.3	1.21 (0.57,2.56)	1.39 (0.60,3.22)	142	5	3.5	0.41 (0.10,1.59)	0.34 (0.08,1.50)
	20-39	72	27	37.5	1.87 (0.93,3.77)	1.53 (0.70,3.31)	29	57	23.8	2.39 (0.89,6.38)	1.91 (0.66,5.54)
	40-59	131	27	20.6	1.09 (0.55,2.17)	1.15 (0.53,2.46)	100	15	15.0	1.46 (0.51,4.21)	1.21 (0.40,3.63)
	≥60	50	6	12.0	ref	ref	44	5	11.4	ref	ref
Sex	Unknown	0	0	0	-	-	19	2	10.5	1.22 (0.24,6.18)	0.56 (0.07,4.81)
	Male	140	34	24.3	ref	ref	327	49	15.0	ref	ref
	female	189	49	25.9	1.14 (0.76,1.70)	1.23 (0.78,1.95)	210	34	16.2	0.95 (0.57,1.57)	1.14 (0.61,2.11)
Interval from diagnosis of index case to PCR test	Unknown	0	0	0	-	-	7	1	14.3	1.20 (0.17,8.35)	-
	0-1day	83	34	41.0	ref	ref	102	31	30.4	ref	ref
	2-3 days	198	33	16.7	0.24 (0.12,0.47)	0.21 (0.10,0.45)	359	44	12.3	0.22 (0.12,0.39)	0.19 (0.10,0.36)
	4-5 days	24	4	16.7	0.19 (0.05,0.74)	0.13 (0.03,0.55)	39	7	17.9	0.31 (0.11,0.88)	0.28 (0.09,0.82)
Number of same household	6-10 days	19	9	47.4	0.55 (0.19,1.57)	0.40 (0.13,1.24)	40	1	2.5	0.24 (0.04,1.59)	0.40 (0.04,4.04)
	≥11 days	5	3	60.0	0.53 (0.10,2.92)	0.41 (0.07,2.51)	3	0	0	-	-
Number of same household	1-2	118	40	33.9	ref	ref					
	3-5	187	38	20.3	0.49 (0.25,0.96)	0.39 (0.18,0.83)					
	over 6	24	5	20.8	0.49 (0.08,3.14)	0.32 (0.03,3.62)					

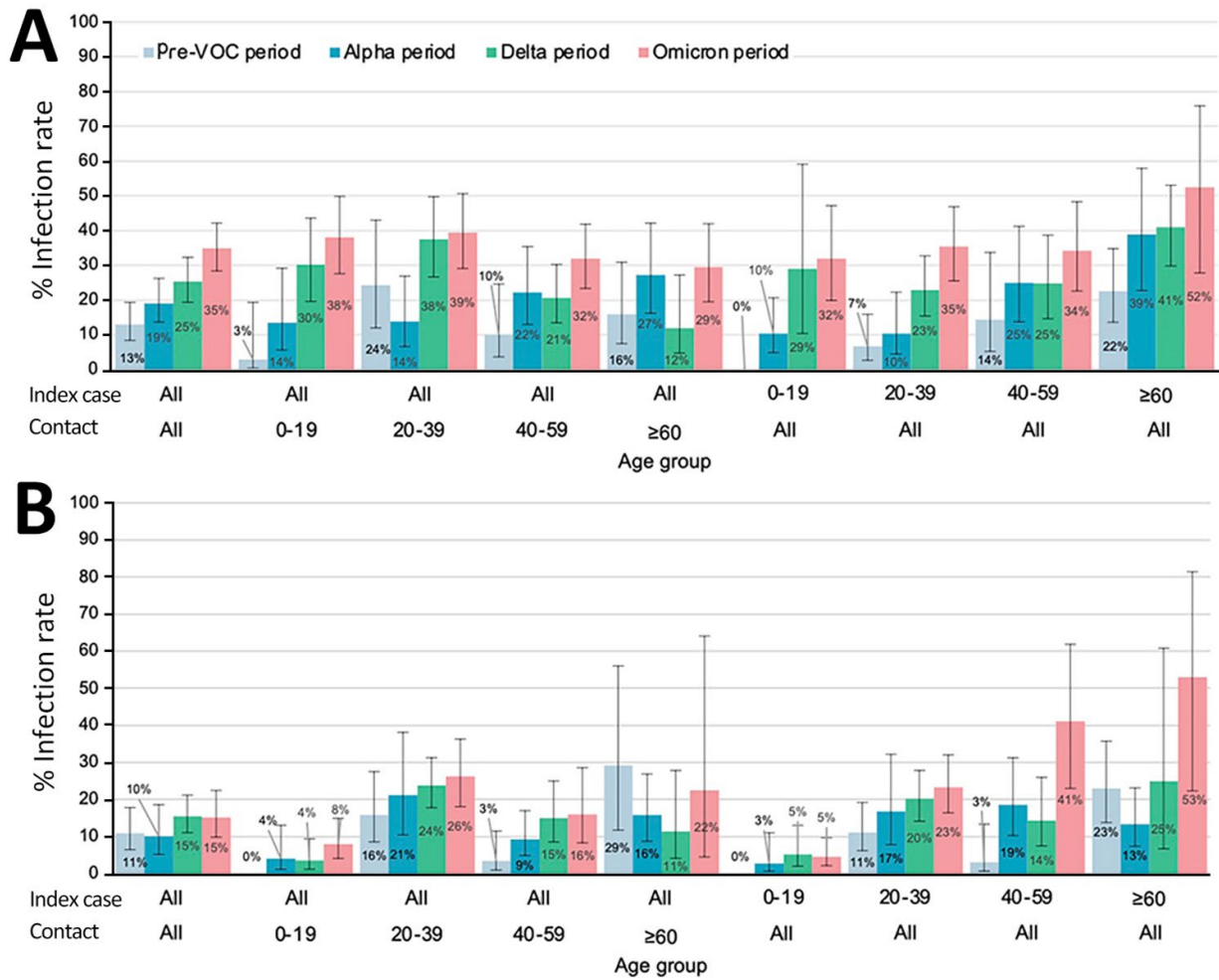
Appendix Table 3d. Infection rates of SARS-CoV-2 infection among household and non-household contacts, Omicron period

Category	Sub-category	Household contacts					Non-household contacts				
		Number	PCR positive	Infection rate (%)	Odds Ratio (95% CI)	Adjusted Odds ratio (95% CI)	Number	PCR positive	Infection rate (%)	Odds Ratio (95% CI)	Adjusted Odds ratio (95% CI)
Total		409	143	35.0			736	111	15.1		
Index case characteristics											
Age	0-19	122	39	32.0	0.39 (0.13,1.24)	0.44 (0.12,1.62)	388	18	4.6	0.06 (0.02,0.2)	0.04 (0.01,0.22)
	20-39	158	56	35.4	0.51 (0.17,1.51)	0.51 (0.15,1.67)	292	68	23.3	0.25 (0.09,0.72)	0.12 (0.03,0.49)
	40-59	108	37	34.3	0.45 (0.14,1.40)	0.51 (0.15,1.75)	39	16	41.0	0.60 (0.18,2.00)	0.29 (0.06,1.39)
	≥60	21	11	52.4	ref	ref	17	9	52.9	ref	ref
Sex	Male	251	97	38.6	ref	ref	346	58	16.8	ref	ref
	Female	158	46	29.1	0.62 (0.35,1.12)	0.70 (0.37,1.33)	390	53	13.6	0.81 (0.43,1.52)	1.10 (0.57,2.13)
Symptomatic	No	26	7	26.9	ref	ref	5	1	20.0	ref	ref
	Yes	383	136	35.5	1.87 (0.50,6.90)	1.40 (0.32,6.07)	731	110	15.0	0.93 (0.09,9.31)	5.16 (0.45,59.14)
Contact history	No	279	110	39.4	ref	ref	654	93	14.2	ref	ref
	Yes	130	33	25.4	0.50 (0.27,0.95)	0.52 (0.25,1.07)	82	18	22	0.96 (0.46,1.99)	0.69 (0.31,1.53)
Close contact characteristics											
Age	0-19	126	48	38.1	1.03 (0.62,1.70)	1.07 (0.60,1.91)	341	27	7.9	0.53 (0.29,0.98)	1.19 (0.47,3.01)
	20-39	89	35	39.3	1.28 (0.75,2.16)	1.11 (0.61,2.01)	187	49	26.2	0.55 (0.30,1.00)	1.41 (0.58,3.43)
	40-59	116	37	31.9	1.14 (0.70,1.85)	1.17 (0.67,2.04)	69	11	15.9	0.27 (0.13,0.57)	0.60 (0.21,1.69)
	≥60	78	23	29.5	ref	ref	89	20	22.5	ref	ref
	Unknown	0	0	0	-	-	50	4	8.0	0.10 (0.03,0.36)	0.68 (0.14,3.36)
Sex	Male	173	58	33.5	ref	ref	370	59	15.9	ref	ref
	female	230	85	37.0	1.24 (0.92,1.67)	1.28 (0.90,1.82)	327	51	15.6	0.96 (0.72,1.29)	0.93 (0.59,1.45)
	Unknown	6	0	0	-	-	39	1	2.6	-	-
Interval from diagnosis of index case to PCR test	0-1day	66	41	60.3	ref	ref	142	44	31.0	ref	ref
	2-3 days	173	56	32.4	0.30 (0.16,0.58)	0.31 (0.15,0.60)	370	45	12.2	0.22 (0.13,0.40)	0.22 (0.12,0.4)0
	4-5 days	134	24	17.9	0.18 (0.09,0.36)	0.17 (0.08,0.34)	164	12	7.3	0.12 (0.05,0.30)	0.12 (0.05,0.32)
Number of same household	6-10 days	25	16	64.0	0.50 (0.21,1.18)	0.51 (0.20,1.27)	33	6	18.2	0.22 (0.06,0.80)	0.21 (0.06,0.76)
	≥11 days	11	6	66.7	0.44 (0.13,1.45)	0.40 (0.11,1.38)	0	0	0	-	-
Number of same household	1-2	139	47	33.8	ref	ref					
	3-5	241	87	36.1	0.97 (0.55,1.71)	1.28 (0.68,2.40)					
	over 6	29	9	31.0	0.88 (0.16,4.87)	1.06 (0.18,6.22)					

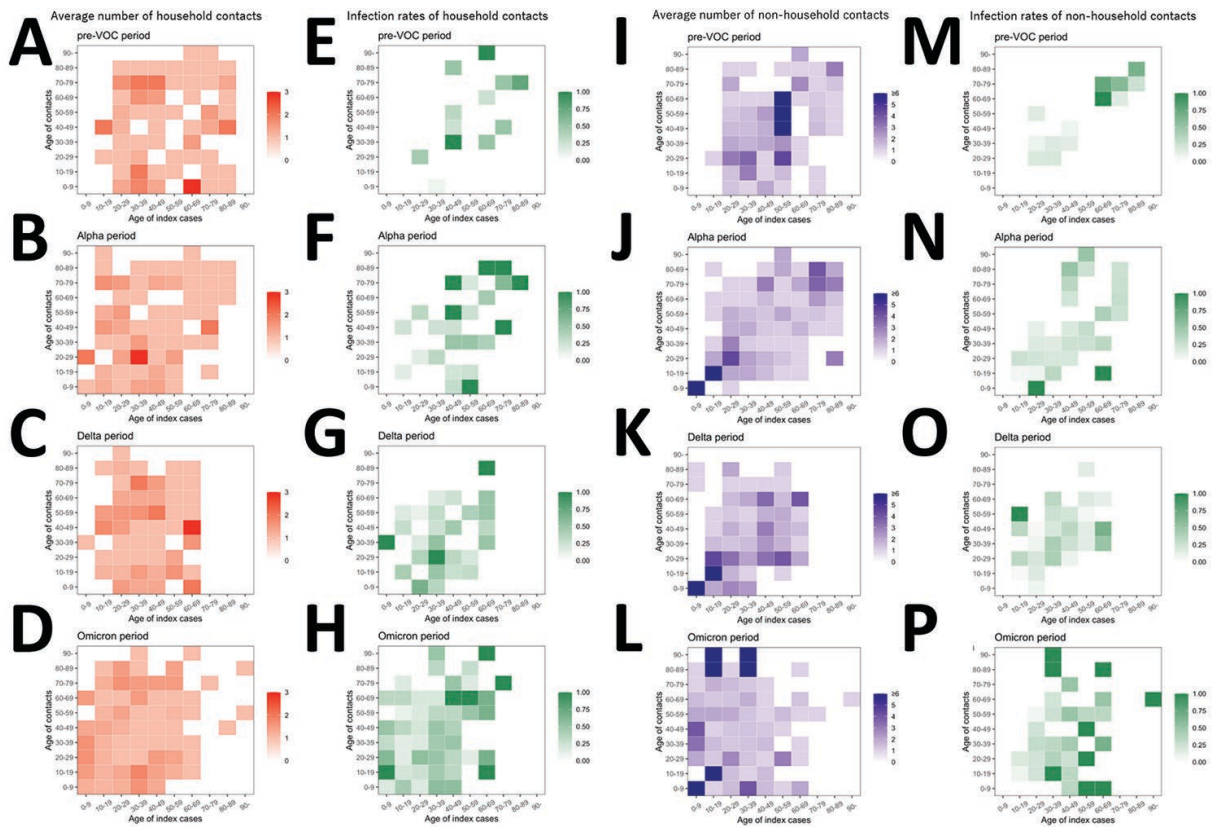


Appendix Figure 1. COVID-19 case-patients and vaccination coverage rates in Toyama Prefecture

Vaccination coverage was defined as the percentage of people in the population who received the 2nd dose of COVID-19 vaccine. The number of people receiving the 2nd dose of COVID-19 vaccines in Toyama prefecture were reported in the Web site of the Digital Agency, Japan (<https://info.vrs.digital.go.jp/opendata>). The denominator used for vaccine coverage was the total number of population as of October 1, 2020, published in the Web site of e-Stat <https://www.e-stat.go.jp>. COVID-19 case-patients were reported from the Toyama prefecture. We downloaded the database from NHK, openly available at <https://www3.nhk.or.jp/news/special/coronavirus/data>.



Appendix Figure 2. Age -specific infection rates according to age of the index case-patient and contact stratified by household contacts (A) and nonhousehold contacts (B) in study of SARS-CoV-2 variants and age-dependent infection rates. Age groups were categorized as 0–19, 20–39, 40–59, and ≥60 years. “All” includes all age groups. The upper row of the age group shows the age of index case-patients, and the lower row shows the age of contacts. Error bars indicate 95% CIs.



Appendix Figure 3. Age-structured matrices for the average number of contacts and infection rates of SARS-CoV-2 infection in household contacts and nonhousehold contacts in study of SARS-CoV-2 variants and age-dependent infection rates over 4 study periods. A–D) Average number of household contacts per index case-patient. E–H) Infection rates for each age group among household contacts. I–J) Average number of nonhousehold contacts per index case-patient. M–P) Infection rates for each age group among nonhousehold contacts.