Supplemental Online Content

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eAppendix 1. Definitions of SARS-CoV-2 Infections, Close Contacts, and Transmission Pairs

All COVID-19 cases were defined as individuals who received a positive testing outcome (with Ct value < 40) from real-time reverse transcription polymerase chain reaction (RT-PCR) assay for genetic segments of SARS-CoV-2 strains using ORF1ab gene or N gene detection kit.

The definition of clinical severity after SARS-CoV-2 infection was as follows. For a symptomatic case, it was defined as a case presenting one of the relevant clinical symptoms, including fever, respiratory symptoms, and radiographic evidence of pneumonia. The asymptomatic or mildly symptomatic SARS-CoV-2 infection, which was classified as "asymptomatic" in this study, was defined as a case presenting one of the relevant clinical symptoms for less than 7 days, including fever, or respiratory symptoms, and without a radiographic evidence of pneumonia. Since most of confirmed cases (92.7%) were asymptomatic or mildly symptomatic, which was classified as "asymptomatic" in this study, we avoided to further classify the clinical severity of cases into more detailed levels due to limited samples.

We defined close contacts of a confirmed COVID-19 case as individuals having an epidemiologic link to a COVID-19 case, i.e., this individual has been exposed to another individual with test-positive status for SARS-CoV-2 infection. As a considerable amount of transmission could occur at very early stage after infection [1, 2], individuals who had been exposed to a case within 4 days before the test-positive date of the case would also be counted as close contacts. In this study, we categorized the These individuals who had exposure risk were considered as close contacts (of confirmed cases). Close contacts included, but were not limited to, COVID-19 cases'

- household contacts (i.e., household members regularly living within the same or close space, or relatives who had close contact with case)
- workplace or school contacts (i.e., a work colleague or classmate), and
- community contacts (i.e., healthcare-givers and patients in the same ward, persons sharing a vehicle or restaurant, and community workers having contact with case in public places).

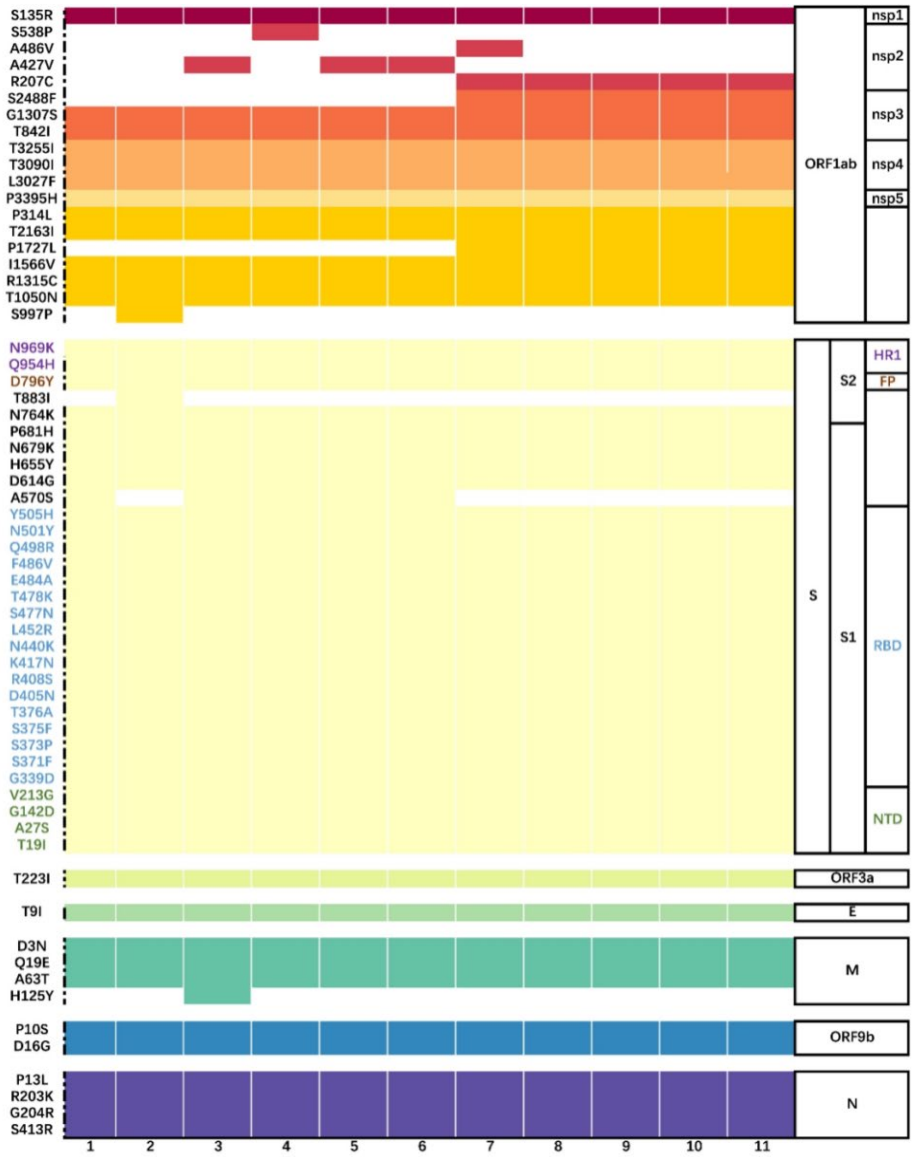
For those contacts who were (eventually) test-positive for COVID-19, we treated these contacts as infectee, and their source case (who were confirmed with COVID-19 in the first place) as infector. We extracted this epidemiologically linked infector and infectee in pairs, and collected their individual-based data for all these transmission pairs.

If it was unclear who was the source case (e.g., more than one infectors were linked to a close contact), this contact would be excluded from analysis. In our study, none of such situation occurs in the dataset.

eAppendix 2. Confirmation of Genetic Sequence

Among the nasopharyngeal or oropharyngeal swabs collected from confirmed COVID cases in the first few days of the outbreak, 11 (out of 38, 28.9%) specimen samples were sent out for whole-genome sequencing. Multiple sequence alignments were performed using MAFFT program. The phylogenetic relationship was explored using maximum likelihood heuristic search and the GTR + CAT nucleotide substitution model in FastTree (version 2.1.11). According to Phylogenetic Assignment of Named Global Outbreak (PANGO) lineage designation, the samples were classified as SARS-CoV-2 Omicron BA.5.2 sub-lineage.

There were a total of 62 amino acid (AA) substitutions in different genetic segments of SARS-CoV-2, including 31 AA substitutions in spike (S) protein, 19 in non-structural proteins (NSPs) ORF1a and ORF1b (S135R, T842I, S538P, A427V, R207C, G1307S, A486V, L3027F, T3090I, S2488F, T3255I, P3395H, P314L, T1050N, S997P, R1315C, I1566V, T2163I and P1727L), 4 in membrane protein (M) (D3N, Q19E, A63T and H125Y), 4 in nucleocapsid (N) (P13 L, R203K, G204R and S413R), 3 in auxiliary proteins ORF3a and ORF9b (T223I, P10S and D16G), and 1 in envelope protein (E) (T9I). The key non-synonymous mutations in these 11 genetic sequence samples were presented in Figure S2.1.



eFigure 1. Key Amino Acid Substitutions in Genetic Sequence Samples From 11 Individuals With COVID-19

Cases labeled as integer from 1 to 11 on the horizontal axis. The colors of text at the left-hand side represented the AA substitutions in NTD (green), RBD (blue), FP (brown), and HR1 (purple).

eAppendix 3. Key Time Intervals of Transmission

S3.1 Generation interval

Generation interval (GI) is defined as the mean duration between time of infection of a secondary infectee and the time of infection of its primary infector [3, 4]. We included transmission pairs with known exposure time for infectors and infectees to estimate the GI. The generation interval together with the reproduction number governs the progression of an epidemic. We denoted G_i as the generation interval (GI) of the ith transmission pair, and we assumed the GI of the Omicron BA.5.2 followed a gamma distribution, denoted by $h(.)$. The GI can change over the course of an outbreak due to sampling bias [5]. In particular, the observed GIs was more likely to be shorter during an exponential growth phase (infectees with more recent exposure to an infector are more likely to be identified) but tend to be longer during the exponential decay phase of the outbreak [5]. In our study, the transmission pairs were collected during a whole epidemic wave that covering both increasing and decreasing phase, and thus our GI estimates would not suffer from such bias. We also considered the right-truncation of the time interval [6-8] that is, the generation interval generated by each infector is truncated due to the PHSMs that could curb the transmission (e.g., contact tracing and case isolation). Thus, the truncation-adjusted distribution function was

$$h_{\text{adjust}}(G_i) = \frac{h(G_i)}{H(T_i)}$$

Here, the $H(.)$ is the cumulative density function of $h(.)$. The T_i is the isolation delay (i.e., the time interval between the isolation and symptom onset) of the infector for the i-th transmission pair. The likelihood functions with and without truncation adjusted are given by:

$$L_{\text{GI}} = \prod_{i}^{n} h(G_i)$$

$$L_{\text{GI\_adjust}} = \prod_{i}^{n} h_{\text{adjust}}(G_i)$$

S3.2 The period from exposure to viral shedding

The period from exposure to viral shedding was defined as the time interval between exposure and the first appearance of viral shedding, which may be considered a proxy for latent period. To estimate the distribution of the period from exposure to viral shedding, we included cases with known exposure date and RT-PCR test-positive dates. As serial intensive RT-PCR testing were conducted for each confirmed case during the study period, we considered the time that the i-th case start to shed viral genetic particles was bounded by the first test-positive date (denoted by S_{ui}) and the last test-negative date (denoted by S_{li}) of that case. Therefore, the observed period from exposure to viral shedding was interval-censored, which needs to be corrected in the estimation [9]. We excluded cases with a prior to his/her exposure date, which possibly indicating recall bias. We assumed the period from exposure to viral shedding followed a gamma distribution. We denoted E_i as the exposure date of ith case, S_i as the start date of viral shedding, and $w(.)$ as the gamma distribution of the period from exposure to viral shedding. Then the interval-censored likelihood function is constructed as follow:

$$L_{latent} = \prod_{i}^{n} \int_{S_{li}}^{S_{ui}} w(S_i - E_i)\, \mathrm{d}S$$

S3.3 Viral shedding period

Confirmed COVID-19 cases with known serial RT-PCR testing date were used to calculate the viral shedding period, which may be considered a proxy for infectious period. Considering the last date for the ith case to shed viral genetic particles was also bounded between the last test-positive date (denoted by R_{li}) and the first test-negative date (denoted by R_{ui}) after infection, the observed viral shedding period was doubly interval-censored [10, 11]. All included cases had an R_{li} later than S_{ui}. We assumed the viral shedding period was gamma distributed, denoted by $u(.)$. Then. we constructed the doubly interval-censored likelihood function as follow:

$$L_{infectious} = \prod_{i}^{n} \int_{S_{li}}^{S_{ui}} \int_{R_{li}}^{R_{ui}} u(R_i - S_i)\, \mathrm{d}R\, \mathrm{d}S$$

S3.4 Incubation period

The incubation period is the duration between the exposure and symptoms onset. We only included symptomatic cases with known exposure date to estimate the incubation period. We denoted V_i as the incubation period of the ith case, and we assumed it followed a gamma distribution, denoted by $k(.)$. The likelihood function is given by:

$$L_{incubation} = \prod_{i}^{n} k(V_i)$$

A graph to show the relationship of GI, incubation period, period from exposure to viral shedding and viral shedding period in Figure S3.1 (see below).

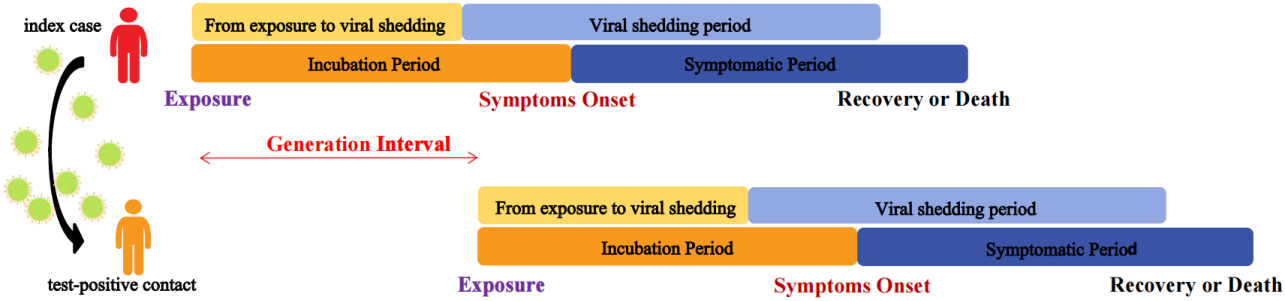


Figure S3.1. The relationship among generation interval (GI), incubation period, period from exposure to viral shedding, and viral shedding period in the context of a typical transmission chain.

S3.5 Parameter estimation

For each key time interval, the parameters of gamma distribution were estimated by using the Metropolis-Hastings algorithm, which is a Markov chain Monte Carlo (MCMC) method, with non-informative prior distributions. The marginal posterior distribution was obtained from 10 000 iterations, among which the first 5 000 samples were discarded as for burn-in. The convergence of each MCMC chain was checked by using the trace plot and Gelman-Rubin-Brooks convergence diagnostic [12]. The median and 95% credible intervals (CrI) were obtained from the converged posterior distributions of each parameter.

S3.6 Supplementary results

The estimations of the key time interval distributions were summarized in Table S3.1.

As for results, we found that the mean GI was shorter in household settings than in non-household settings, which could be attributed to the depletion of susceptible people within household (i.e., a lower potential for observing a longer GI) [13]. The mean GI decreased after the implementation of the lockdown measures, implicitly suggesting that the PHSMs contribute to trimming down the infectiousness profiles of individual cases. An early modelling study indicated that a delay of case isolation was positively associated with the duration of the serial interval [14], a metrics that metric used as a proxy of GI, which means the GI could be shortened on the basis of how quickly fast cases were isolated. Therefore, the GI estimates should also be interpreted in the context of different settings, and our GI estimates would be more generalizable for settings that had the same public health capacity as Urumqi.

eTable. Estimated Mean, SD, Median, and 95th Percentile of Key Time Intervals for Transmission of SARS-CoV-2 Omicron BA.5.2 Variants
All estimates were summarized in "median (95% CrI)" form in the table below.

Time interval	stratification	sample size	Mean	SD	Median	95% percentile
Generation interval	**Overall without truncation**	178	2.8 (2.4, 3.5)	3.7 (3.0, 4.8)	1.4 (1.1, 1.9)	10.4 (8.5, 13.0)
	Overall with truncation	79	4.3 (2.6,6.9)	6.7 (4.2,11.1)	1.5 (0.9,2.8)	17.8 (11.1,28.9)
	contact setting					
	household	88	2.3 (1.7, 3.3)	3.8 (2.7, 5.3)	0.8 (0.4, 1.3)	9.9 (7.2, 13.9)
	non-household	90	3.2 (2.6, 4.0)	3.4 (2.6, 4.5)	2.2 (1.7, 2.7)	10.0 (8.0, 13.0)
	epidemic period					
	before lockdown	83	3.9 (3.0, 5.1)	4.9 (3.7, 6.7)	2.2 (1.5, 3.0)	13.8 (10.6, 18.4)
	after lockdown	95	1.8 (1.4, 2.4)	2.3 (1.7, 3.2)	1.0 (0.7, 1.4)	6.4 (5.0, 8.7)
period from exposure to viral shedding	**overall**	709	3.3 (3.0, 3.6)	2.9 (2.6, 3.1)	2.5 (2.3, 2.8)	8.9 (8.1, 9.8)
	age group					
	0-15	130	3.6 (3.0, 4.3)	3.4 (2.7, 4.3)	2.6 (2.2, 3.2)	10.3 (8.5, 12.8)
	16-65	519	3.3 (3.0, 3.5)	2.8 (2.5, 3.1)	2.5 (2.2, 2.7)	8.7 (7.9, 9.8)
	>65	60	3.1 (2.5, 3.8)	2.7 (2.1, 3.6)	2.4 (1.9, 3.0)	8.5 (6.7, 10.8)
	Symptom status					
	symptomatic	59	2.8 (2.2, 3.7)	2.5 (2.0, 3.7)	2.1 (1.5, 2.6)	7.8 (6.1, 11.1)
	asymptomatic	650	3.3 (3.1, 3.6)	2.9 (2.5, 3.2)	2.6 (2.3, 2.8)	8.9 (8.1, 10.0)
	vaccine dose					
	0-1	92	3.3 (2.8, 4.0)	2.9 (2.3, 3.6)	2.5 (2.0, 3.1)	9.1 (7.3, 11.1)
	2	179	3.5 (3.1, 4.0)	3.1 (2.6, 3.6)	2.7 (2.3, 3.1)	9.5 (8.2, 11.2)
	3	438	3.2 (2.9, 3.5)	2.8 (2.5, 3.2)	2.4 (2.2, 2.7)	8.8 (7.7, 9.8)
viral shedding period	**overall**	770	6.7 (6.4, 7.1)	3.7 (3.4, 4.0)	6.1 (5.7, 6.4)	13.7 (12.7, 14.7)
	age group					
	0-15	136	6.3 (5.7, 7.0)	3.7 (3.2, 4.3)	5.6 (4.9, 6.3)	13.3 (11.8, 15.1)
	16-65	574	7.0 (6.6, 7.3)	3.7 (3.4, 4.1)	6.3 (5.9, 6.7)	13.9 (12.9, 15.0)
	>65	60	5.7 (4.9, 6.5)	3.3 (2.7, 4.1)	5.0 (4.2, 5.8)	12.0 (10.1, 14.3)
	symptom status					
	symptomatic	53	6.0 (5.1, 7.0)	3.3 (2.6, 4.3)	5.4 (4.6, 6.3)	12.3 (10.2, 14.9)
	asymptomatic	717	6.8 (6.5, 7.2)	3.8 (3.4, 4.1)	6.1 (5.7, 6.5)	14.0 (13.0, 15.1)
	vaccine dose					
	0-1	90	6.5 (5.6, 7.4)	4.3 (3.6, 5.4)	5.5 (4.7, 6.4)	14.8 (12.7, 17.9)
	2	188	6.2 (5.7, 6.7)	3.3 (2.9, 3.9)	5.6 (5.1, 6.1)	12.6 (11.3, 14.0)
	3	492	7.0 (6.6, 7.4)	3.6 (3.3, 3.9)	6.4 (6.0, 6.8)	13.8 (12.8, 14.8)
Incubation period	**overall**	60	5.7 (4.8, 6.6)	3.7 (2.9, 4.7)	4.9 (4.0, 5.6)	12.8 (10.7, 15.6)

eAppendix 4. Epidemic Growth and Reproduction Number

The exponential growth (or decay) was frequently used to capture the pattern of epidemic curve [15, 16]. We fitted the observed daily cumulative number of COVID-19 cases denoted by $C(t)$ to an exponential growth model to estimate the growth rate (γ).

Given the estimated growth rate and GI, we estimated the reproduction number (R) by using the formula as per [17]:

$$R = \frac{1}{M(-\gamma)},$$

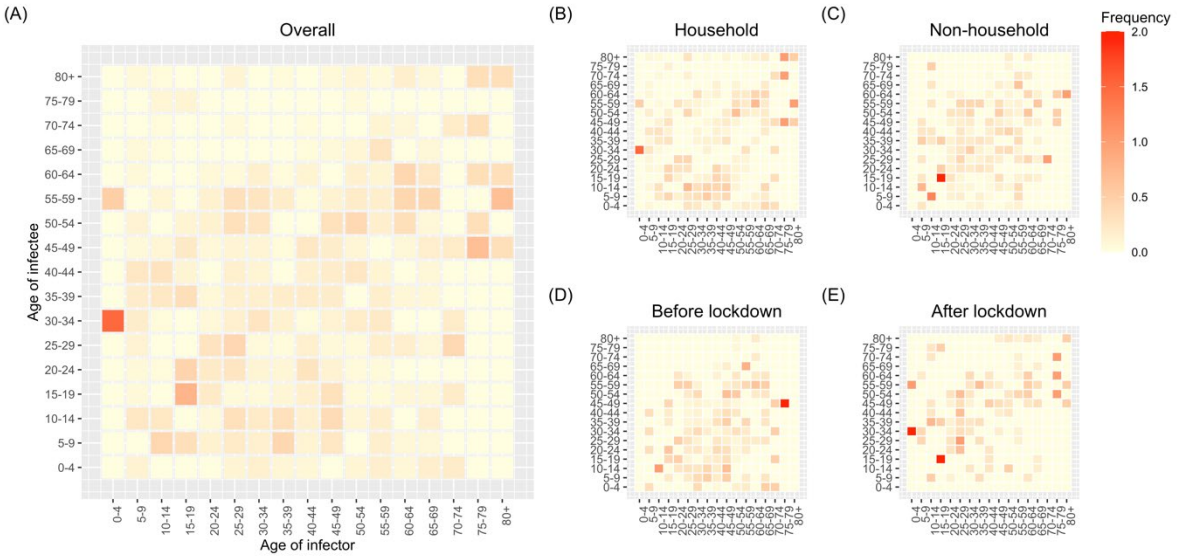
where the function $M(\cdot)$ was the moment generation function (MGF) of the probability density function (PDF) of GI. For GI following a gamma distribution with parameters shape α and rate β, then the R can be simplified as follows:

$$R = (1 + \frac{\gamma}{\beta})^{\alpha}.$$

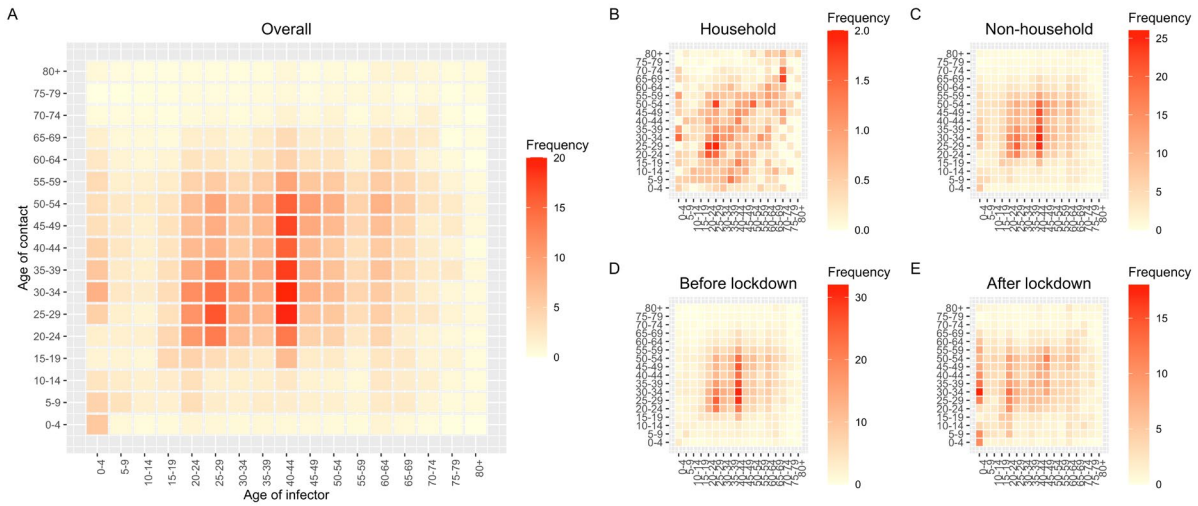
eAppendix 5. Contact Matrix and Mean Number of Offspring Infections by Age of Individuals Spreading and Receiving Infection

We relied on contact tracing data to characterize the age-specific contact matrixes and "who acquired infections from whom" (WAIFW) matrixes [18] for the infected individuals and their close contacts. A contact matrix comprised infectors and all of their close contacts (including both test-positive and test-negative individuals), whereas a WAIFW matrix only contains infectors and their test-positive contacts.

All cases were classified into 16 age groups according to their ages (i.e., 0 to 4 years, 5 to 9 years, 10 to 14 years, 15 to 19 years, 20 to 24 years, 25 to 29 years, 30 to 34 years, 35 to 39 years, 40 to 44 years, 45 to 49 years, 50 to 54 years, 55 to 59 years, 60 to 64 years, 65 to 69 years, 70 to 74 years, 75 to 79 years, and 80 years or older), to generate the age-specific contact and WAIFW matrixes. In addition, the age-specific contact and WAIFW matrixes stratified by contact settings and epidemic period (i.e., before and after lock down) were also constructed (see Figure S5.1). The constructed contact matrixes were shown in Figure S5.2.



eFigure 2. Who Acquires Infection From Whom Matrix Between Source and Offspring Infections Stratified by age groups (panel A), and stratified by contact settings including (panel B) household, and (panel C) non-household, and stratified by epidemic periods including the periods (panel D) before city lockdown, and (panel E) after city lockdown.



eFigure 3. Contact Matrix Between Individuals Who Were Sources of Infections and Their Close Contacts

Stratified by age groups (panel A), and stratified by contact settings including (panel B) household, and (panel C) non-household, and stratified by epidemic periods including the periods (panel D) before city lockdown, and (panel E) after city lockdown.

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