Epidemiology of Infections with SARS-CoV-2 Omicron BA.2 Variant, Hong Kong, January–March 2022

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Our analysis of data collected from multiple epidemics in Hong Kong indicated a shorter serial interval and generation time of infections with the SARS-CoV-2 Omicron variant. The age-specific case-fatality risk for Omicron BA.2.2 case-patients without complete primary vaccination was comparable to that of persons infected with ancestral strains in earlier waves.

Several SARS-CoV-2 variants of concern have caused large outbreaks of infection, including deaths, after the emergence of the ancestral strain in late 2019. First detected in South Africa in November 2021, the Omicron variants quickly became dominant across the world, even in countries with high SARS-CoV-2 vaccination coverage (*1*), probably attributable to enhanced immune escape and increased transmissibility (*2*).

Hong Kong (population 7.4 million), a special administrative region of China, applied intensive public health and social measures to control 4 epidemic waves during 2020–2021, in which 9,403 locally infected (non-imported) cases (1.3 cases/1,000 population) and 207 fatalities occurred. During December 31, 2021–May 21, 2022, a total of 9,148 deaths and >1 million cases largely caused by Omicron were reported in the fifth pandemic wave (Figure 1, panel A, B, https://wwwnc.cdc.gov/EID/article/28/9/22-0613-F1.htm). The COVID-19 vaccination program in Hong Kong began in late February 2021 and uses the mRNA vaccine BNT162b2 (Pfizer-BioNTech, https://www.pfizer.com) and the inactivated vaccine CoronaVac (Sinovac, https://www.sinovac.com). Approximately 10% of the population had been vaccinated with 1 dose by late April 2021, and coverage slowly increased thereafter. The Omicron variant (BA.1) was first detected in Hong Kong among 2 travelers in hotel quarantine in November 2021 (*3*), and a small community outbreak occurred in early January 2022, linked to 2 aircrew members infected overseas (*4*). Subsequently, Omicron BA.2.2 cases were reported in another quarantine hotel in mid-January in an arriving traveler who was reaching the end of a 21-day quarantine (*5*). Ultimately, a large fifth wave dominated by BA.2.2 peaked in early March 2022 after rising exponentially for ≥1 month, with a doubling time of 3.1 days (Figure 1, panel C). Virus sequencing conducted throughout the epidemic indicated that the last local BA.1 cases were detected in mid-January and 1 sporadic local Delta detection occurred in late March (Leo Poon, University of Hong Kong, pers. comm., email, May 28, 2022).

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The Study

We analyzed contact-tracing data on reverse transcription PCR–confirmed COVID-19 cases reported during December 31, 2021–January 22, 2022, to estimate the serial interval and generation time for Omicron (Appendix, https://wwwnc.cdc.gov/EID/article/28/9/22-0613-App1.pdf). Given the 207 deaths that occurred in 9,403 locally infected case-patients in the first 4 epidemic waves and 106 deaths among 4,604 case-patients discharged from hospital isolation in the early period of wave 5, we estimated the age-specific case-fatality risk (CFR) for case-patients infected with ancestral strains compared with Omicron-infected case-patients.

By using information on 80 case-patients (57 infected with BA.1 and 23 with BA.2) with known

exposure and symptom onset information, we estimated the mean (±SD) incubation periods to be 4.58 (±1.72) days for Omicron BA.1 and 4.42 (±1.42) days for Omicron BA.2 (Appendix Table 1). For 43 symptomatic infector–infectee pairs, we estimated the mean (±SD) serial interval for BA.1 infections (n = 30) as 3.30 (±1.95) days; median was 3.17 days. For BA.2 (n = 13), the estimated mean (±SD) serial interval was 2.72 (±1.51) days; median was 2.52 days. We used gamma distribution for estimates of BA.2 accounting for the potential for epidemic phase bias (*6*) with a growth rate of 0.25, because data were collected during the early growth phase of the BA.2 epidemic.

In the early period of the fifth wave (on or before February 15, 2022), all reported COVID-19 cases were only confirmed through reverse transcription PCR conducted by Hong Kong's Public Health Laboratory Services, as in earlier waves (Figure 1; Appendix Figure 1). After accounting for unresolved outcomes in some persons, we estimated that the age-specific CFR for case-patients without completion of a primary series of vaccination in wave 5 was comparable to that of case-patients confirmed in waves 1–4 across all age groups (Figure 2; Appendix Table 2). The highest fatality risk observed in waves 1–4 for patients ≥80 years of age (24.9% [95% CI 20.9%–29.3%]) was similar to that for unvaccinated persons at the same age from wave 5 (21.7% [95% CI 17.1%–26.8%]) (Figure 2). The CFR for persons ≥80 years of age who had not completed a primary series of vaccination in wave 5 was approximately double the risk for persons in the same age group who had completed a primary series (11.1% [95% CI 4.2–22.6]). Among case-patients 65–79 years of age, the CFR was 5.2% (95% CI 4.1%–6.5%) in waves 1–4, 6.7% (4.3%–9.8%) in wave 5 with incomplete primary series, and 0.7% (0.1%–2.4) with complete primary series (Figure 2; Appendix Table 2). The 8 deaths that occurred in adults ≥65 years of age with a complete primary series of vaccination were all in persons who had received 2 or 3 doses of CoronaVac vaccine.

Conclusions

Our study estimated a relatively shorter serial interval and generation time of the Omicron BA.2 subvariant in Hong Kong compared with earlier variants (*7*), which would have contributed to faster spread in the population along with the higher intrinsic transmissibility. Our analysis was conducted on a relatively small number of case pairs in the fifth wave. Similar studies conducted in South Korea and the Netherlands reported shorter mean incubation periods as low as 3.2 days (*8*) and serial intervals of 2.8–3.0 days (*8*,*9*). The peak of the fifth epidemic in Hong Kong in early March despite no major change in social distancing measures probably indicates sufficient infections to create herd immunity, at least temporarily, with subsequent infections overshooting that threshold (*11*).

Among all the deaths in persons whose age was recorded through May 21 in Hong Kong, 92.7% (8,482/9,146) occurred in persons ≥65 years of age and 71.1% (6,500/9,146) in persons ≥80 years of age. We found a generally similar fatality risk for unvaccinated case-patients across age groups in the early period of the fifth wave compared with earlier waves, although the CFR for Omicron cases in person ≥80 years of age without complete primary vaccination series might be slightly lower than persons infected with ancestral strains. This finding indicates that the intrinsic severity of BA.2 may not be much lower than the ancestral strain. Nonetheless, only 106 fatal cases that occurred in the fifth wave were applied in the analysis. Infections with the Omicron variant were reported to have milder severity in South Africa (*12*) and elsewhere (*13*,*14*), where most of the population were either exposed to previous infections or had been vaccinated. However, our estimates might slightly overestimate the fatality risk of Omicron in

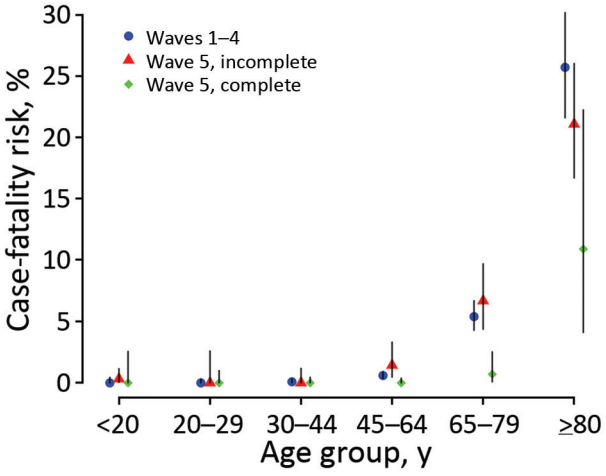

Figure 2. Age-stratified estimates of the case-fatality risk for COVID-19 in epidemic waves 1–4 and wave 5 in Hong Kong by vaccination status. Case-patients were classified as having a complete primary series if they had received ≥2 doses of COVID-19 vaccines ≥2 weeks before symptom onset (for symptomatic case-patients) or ≥3 weeks before laboratory confirmation of the infection (for symptomatic case-patients with a missing onset date or asymptomatic case-patients), otherwise as having an incomplete primary series. The COVID-19 vaccines available in Hong Kong included BNT162b2 (Pfizer-BioNTech, https://www.pfizer.com) and CoronaVac (Sinovac, https://www.sinovac.com) vaccines.

Hong Kong because a small number of cases of Delta infection, including fatal cases, might have been included in the analysis and some milder COVID-19 cases might not have been diagnosed and isolated yet during the early period of the fifth wave.

The relatively high number of deaths in Hong Kong's fifth wave can be attributed to the high incidence of infections within a short period and the low level of vaccination coverage in older adults. Although the overall vaccination coverage was 70% at the start of the fifth wave, only 50% of persons ≥65 years of age and 20% of persons ≥80 years of age had completed a primary series of vaccination. Vaccine hesitancy in older adults in Hong Kong appeared to be associated with low confidence in the government and the concern about the risk for adverse events after vaccination among persons with underlying medical conditions (*15*). Overall, our findings highlight the importance of achieving high vaccination coverage, especially in older adults, and the need to reassess public health and social measures in response to any more transmissible SARS-CoV-2 variant in the future.

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Y.M.M., P.W., and B.J.C. conceived the study. Y.M., D.C., H.B., Y.L., J.K.C., J.Y.W., S.T.A., and E.H.Y. collected the data and conducted the analysis. Y.M. and P.W. drafted the manuscript. All authors critically reviewed and revised the manuscript and approved the final version.

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Appendix

Data Sources

We obtained all confirmed cases with SARS-CoV-2 infections in Hong Kong from the Department of Health and the Hospital Authority of the Government of Hong Kong Special Administrative Region from 23 January 2020 to 17 March 2022. Case information includes age, sex, time of symptom onset, sample collection, laboratory confirmation, report, admission, discharge and death, severity status (mild-to-moderate, severe or critical, fatal), SpO_2 levels, time and vaccination and type of vaccine for each dose. We also collected contact tracing data published by the Government or from media reports that quoted government statements on some of the confirmed case clusters (*1*). The contact tracing data provided information on demographics (age and sex), date of exposure, symptom onset date, case category (symptomatic /asymptomatic), type of SARS-CoV-2 variant, and vaccination status. The confirmed cases in a cluster either had a single exposure date or a reported interval of exposure defined by the earliest and latest dates of exposure to an index case. In Hong Kong a COVID-19 case can be confirmed by the real-time reverse transcription-polymerase chain reaction (real-time RT-PCR) assay (since the emergence of SARS-CoV-2 in 2020) or by a rapid antigen test (RAT) since 26 February 2022.

Epidemiologic Parameters Definition

We define that the incubation period is the time interval between initial contact with a confirmed SARS-CoV-2 case and symptom onset, serial interval is the time interval between symptom onset of the infector and the infectee in a transmission pair, and generation time is the time interval between exposure time of the infector and the infectee in a transmission pair.

Transmission Pair Construction

We constructed infector-infectee transmission pairs with laboratory-confirmed SARS-CoV-2 omicron infection using contact tracing data published on the Web site of the Department of Health, the Government of the Hong Kong Special Administrative Region, and media reports that quoted government statements.

We constructed transmission pairs for estimating mean serial interval and generation time if the infector had direct contact with its infectee. A transmission pair was defined as two confirmed COVID-19 cases identified in the epidemiologic investigation by showing a clear epidemiologic link with each other, which is the infector needs to have direct contact with the infectee. The 'infector' was defined as the primary case, with an identified source of exposure occurring before their encounter with the 'infectee'. The 'infectee' was defined as the secondary case whose exposure was solely by the infector. In the same chain of transmission, the same infector could generate more than one pair if they infected more than one individual. In a large case cluster with multiple generations of transmission, an infectee in a transmission pair might also be an infector in another pair.

For serial interval calculation, as there is established evidence of asymptomatic/ presymptomatic transmission of SARS-CoV-2 (*2,3*), infector-infectee pairs were determined regardless of the order of their onset dates. The infectors-infectees order were determined by who were first exposed to suspected source of infection and induced further infection spread to his/her own network, especially in the case of household or workplace transmission setting. However, to be conservative, in a cluster where the serial interval between index case to off-spring case was larger than 6 days (C. Kremer et al., unpub. data, https://doi.org/10.1101/2022.01.28.22269756), such transmission pairs were excluded as this was suggestive of possible intermediate transmission.

For exposure time that was not explicitly recorded in the government document, we constructed exposure interval based on the following assumptions:

1. The latest exposure time (lower bounds of the exposure interval) is symptom onset date or isolation/quarantine date or confirmation date (if asymptomatic) of the infector

2. The earliest exposure time (upper bounds of the exposure interval) is the infector's exposure date if the infector was a local family member or the infector's arrival date if the infector was an imported family member.

Statistical Analysis

Estimation of Serial Interval and Generation Time

We fitted the parametric distributions of Lognormal, Weibull, and Gamma models to the time intervals data and estimated the distributions of incubation period, serial interval and generation time using the maximum likelihood method (*4,5*) (N. Gozzi et al., unpub. data, https://doi.org/10.1101/2022.01.04.22268721). We accounted for the interval censoring of exposure windows in estimation of the incubation period and generation time. The best fitted model was determined by the smallest value of Akaike's Information Criterion. Estimates of the mean, standard deviation (SD), median and 95% percentiles were derived from the models. The corresponding 95% confidence intervals (CIs) of each estimate were constructed using the parametric bootstrap method with 1000 bootstrapped samples. Because data on serial interval included zero value, we shifted data by adding 1 day to each serial interval so that we could fit distributions. Furthermore, Omicron BA.2 parameters estimations were also made using gamma distribution accounting for the sampling bias that could happen when parameters estimation made using data collected during the initial growth phase of the outbreak (*6*). In our calculation, sampling bias correction was made based on the computed exponential growth rate ($r = 0.25$) of BA.2 using data collected from 15–23 January 2022.

Estimation of Case-Fatality-Risk (CFR)

The COVID-19 case line list obtained from the Hospital Authority was used for estimation of the CFR. Cases confirmed after 15/02/2022 in the fifth wave were excluded from the analysis, and fatal cases were identified with the date of death indicated in the dataset as of 23 March 2022. COVID-19 patients who were not fatal and with a date of discharge were defined as recovered cases. Hong Kong has started COVID-19 vaccination programme since later February 2021 which allow us to analyze the CFR in patients with and without vaccination. Cases who had two or more doses of the mRNA vaccine BNT162b2 (BioNTech/Fosun Pharma/Pfizer) and the inactivated vaccine CoronaVac (Sinovac) ≥14 days before symptom

onset were classified as completing the primary vaccination series while the rest including without vaccination or being vaccinated with 1 dose or 2 doses within 14 days before onset were referred to as incomplete primary vaccination series. Cases without information on the vaccination status or age were excluded from the analysis.

In estimation of the CFR, we classified all the COVID-19 cases confirmed on or before 15 February into three groups, i.e., cases occurred in Waves 1 to 4 (before 01/01/2022), and cases with a complete and incomplete primary vaccination series for the early period of Wave 5 (between 01/01/2022 and 15/02/2022). The CFR was then calculated for six age groups (<20, 20–29, 30–44, 45–64, 65–79, 80+ years) considering vaccination status of cases with the equation: CFR = death/ (death + recovered) allowing for the potential delay from admission to death. The confidence intervals were calculated using a binomial (n,p) test with n = the number of deaths and p = the number of deaths + the number of recovered cases.

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Appendix Table 1. Estimated mean and percentiles of incubation period, serial interval and generation time of infections with SARS-CoV-2 Omicron BA.1 and BA.2 subvariants, 31 December 2021 to 22 January 2022, Hong Kong.

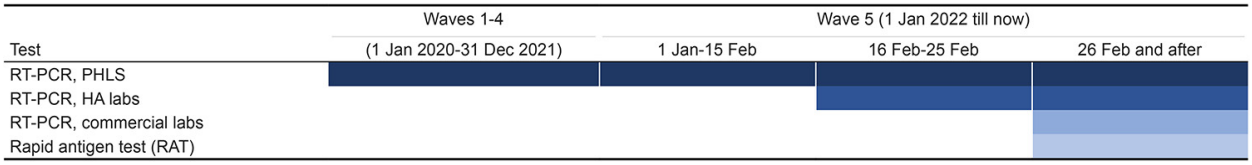
Omicron subvariant	Parameters (sample size)	Best fitted distribution	Mean (95% CI)	SD (95% CI)	Median (95% CI)	95 percentile (95% CI)
BA.1	Incubation period (57)	Gamma	4.58 (4.1–5.08)	1.72 (1.32–2.07)	4.38 (3.88–4.87)	7.73 (6.72–8.71)
	Serial Interval (30)	Weibull	3.30 (2.65–4.01)	1.96 (1.42–2.41)	3.15 (2.49–3.92)	6.76 (5.36–8.16)
	Generation time (45)	Weibull	2.36 (2.01–2.77)	0.59 (0.38–0.90)	2.38 (2.01–2.80)	3.28 (2.79–3.97)
BA.2	Incubation period (23)	Weibull	4.03 (3.19–4.80)	1.12 (0.46–1.51)	4.05 (3.21–4.84)	5.82 (4.37–6.76)
		Gamma*	4.42 (3.40–5.21)	1.42 (0.36–1.99)	4.27 (3.29–5.02)	6.93 (4.85–8.80)
	Serial Interval (13)	Weibull	2.23 (1.53–2.90)	1.26 (0.72–1.63)	2.17 (1.46–2.91)	4.40 (2.99–5.31)
		Gamma*	2.72 (1.80–3.88)	1.51 (0.76–2.43)	2.52 (1.68–3.55)	5.50 (3.31–8.25)

* Estimation accounted for the potential epidemic phase bias since Omicron BA.2 were data collected during the early growth phase of BA.2 outbreak. The exponential growth rate was estimated to be 0.25 based on data collected from 15–23 January 2022.

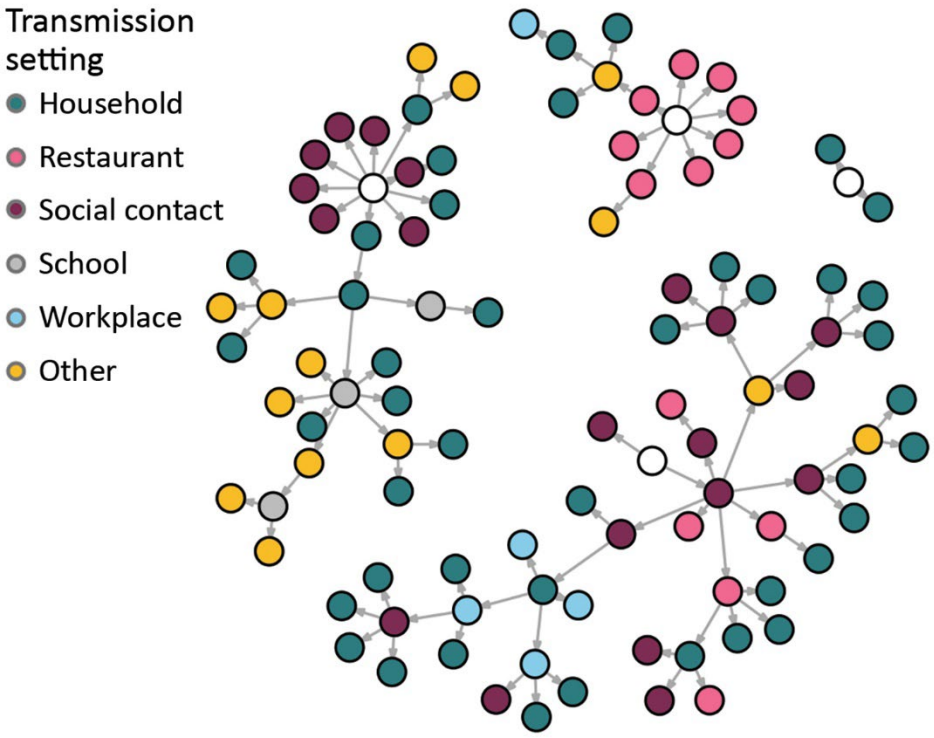
Appendix Table 2**.** Estimated case-fatality-risk among the COVID-19 cases confirmed in the first 1–4 waves in comparison to cases with and without complete primary series who were identified in the early period of wave 5 (1 January – 15 February 2022) in Hong Kong.

	Waves 1 to 4			Wave 5 (Incomplete primary series) ‡			Wave 5 (Complete primary series)*		
Age group, y	Deaths	Recovered	CFR, % Mean (95% CI)	Deaths	Recovered	CFR, % Mean (95% CI)	Deaths	Recovered	CFR, % mean (95% CI)
<20	0	813	0.00 (0.00–0.45)	2	620	0.32 (0.04–1.16)	0	142	0.00 (0.00–2.56)
20–29	0	1,146	0.00 (0.00–0.32)	0	140	0.00 (0.00–2.60)	0	364	0.00 (0.00–1.01)
30–44	2	2,255	0.09 (0.01–0.32)	0	309	0.00 (0.00–1.19)	0	804	0.00 (0.00–0.46)
45–64	20	3,318	0.60 (0.37–0.92)	5	343	1.44 (0.47–3.32)	0	956	0.00 (0.00–0.39)
65–79	77	1,349	5.40 (4.28–6.70)	25	349	6.68 (4.37–9.71)	2	281	0.71 (0.09–2.53)
≥80	108	312	25.71 (21.60–30.18)	66	247	21.09 (16.70–26.03)	6	49	10.91 (4.11–22.25)

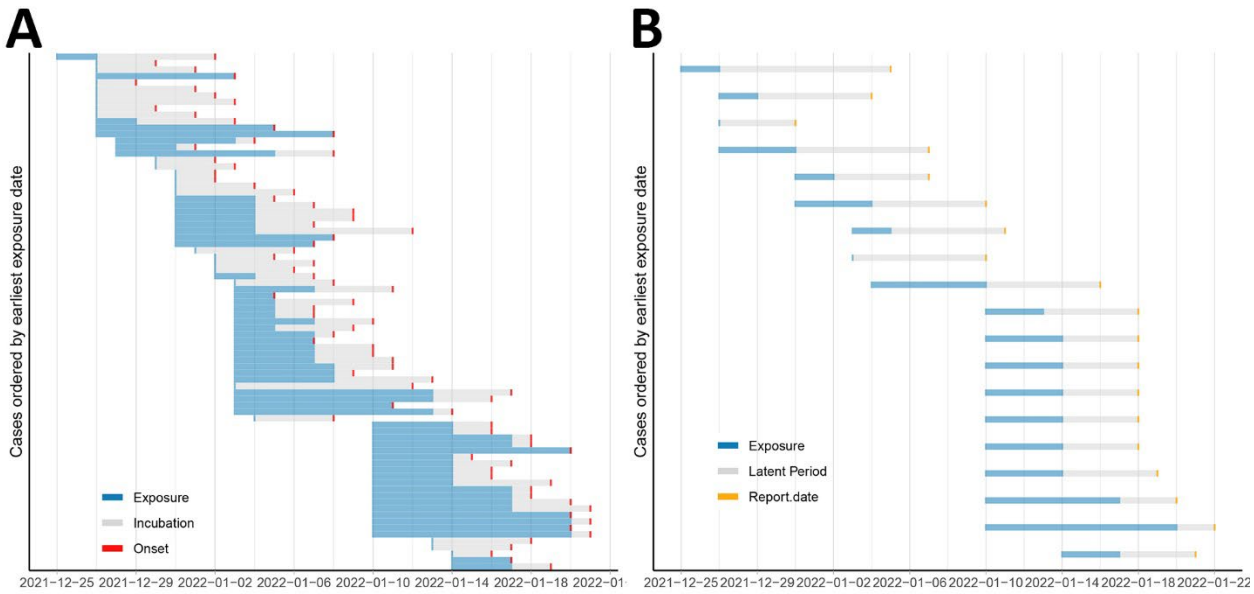
*Cases with complete primary series are individuals who have received at least 2 doses of COVID-19 vaccines before confirmation of infection, and cases with incomplete vaccinated refer to those without receiving any vaccine or with only one dose of vaccine.



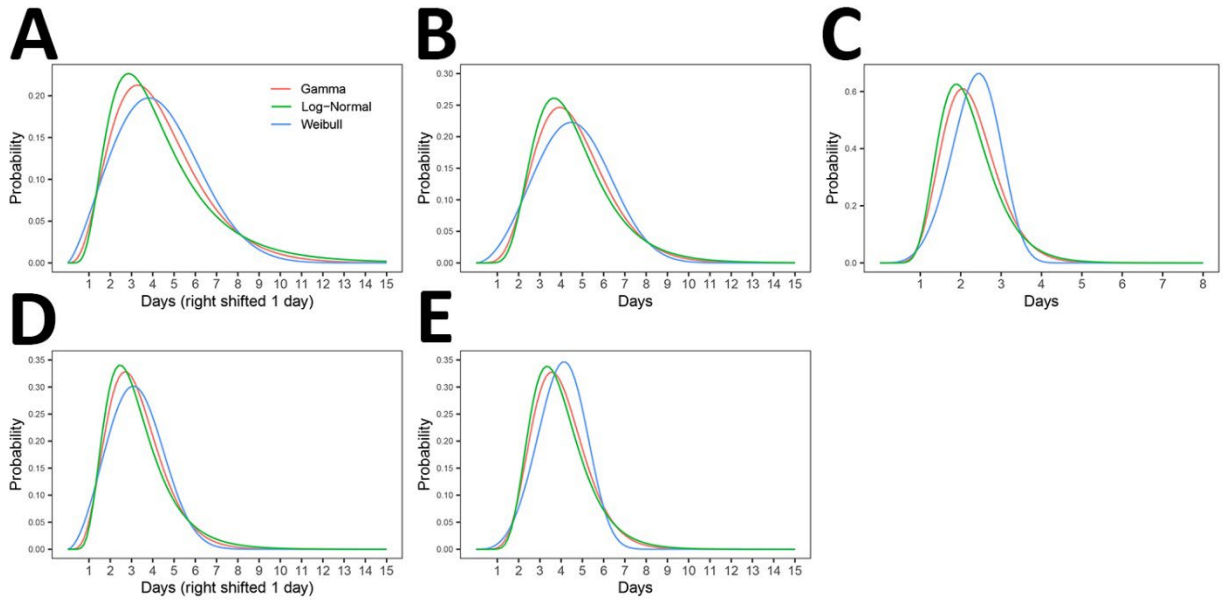
Appendix Figure 1. Laboratory confirmation of COVID-19 in Hong Kong over the epidemic waves since 2020. PHLS: The Public Health Laboratory Services Branch of Centre for Health Protection provides clinical diagnostic and public health laboratory services to the public and private health sectors for both patient care and public health functions. HA: The Hospital Authority is a statutory body managing all the government hospitals and institutes in Hong Kong.



Appendix Figure 2. Transmission chains by transmission settings of SARS-CoV-2 Omicron infections associated with four imported cases in Hong Kong, 31 December 2021 to 22 January (n=98).



Appendix Figure 3. Cases (n=98) studied to estimate incubation period, serial interval and generation time of SARS-CoV-2 Omicron variant. Figure A refers to symptomatic cases and Figure B refers to asymptomatic cases. In each row, red shaded point indicates the dates of onset date, orange shaded point indicates confirmation date, blue shaded area indicates the period of exposure and that in grey indicates the incubation period.



Appendix Figure 4. The estimated distributions of the incubation period, serial interval and generation time for infections occurred in infections with Omicron variant BA.1 and Omicron BA.2 in wave 5 in Hong Kong.