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Effectiveness of BNT162b2 and Sinovac vaccines against the transmission of SARS-CoV-2 during Omicron-predominance in Hong Kong: A retrospective cohort study of COVID-19 cases

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ABSTRACT

Background: In 2022, SARS-CoV-2 Omicron variants circulated globally, generating concerns about increased transmissibility and immune escape. Hong Kong, having an infection-naive population with a moderate 2-dose vaccine coverage (63% by the end of 2021), experienced a COVID-19 epidemic largely seeded by Omicron BA.2 variants that led to the greatest outbreak in the region to date. Little remains known about the protection of commonly-administered vaccines against transmission of Omicron BA.2 variants.

Methods: In this retrospective cohort study, we identified 17 535 laboratory-confirmed COVID-19 cases using contact tracing information during the Omicron-predominant period between January and June 2022 in Hong Kong. Demographic characteristics, time from positive test result to case reporting, isolation, or hospital admission, as well as contact tracing history and contact setting were extracted. Transmission pairs were reconstructed through suspected epidemiological links according to contact tracing history, and the number of secondary cases was determined for each index case as a measurement for risk of transmission. The effectiveness of mRNA vaccine (BNT162b2) and inactivated vaccine (Sinovac) against transmission of BA.2 variants was estimated using zero-inflated negative binomial regression models.

Results: Vaccine effectiveness against transmission for patients who received the 2-dose BNT162b2 vaccine was estimated at 56.2% (95% CI: 14.5, 77.6), 30.6% (95% CI: 13.0, 44.6), and 21.3% (95% CI: 2.9, 36.2) on 15 – 90, 91 – 180, and 181 – 270 days after vaccination, respectively, showing a significant decrease over time. For 3-dose vaccines, vaccine effectiveness estimates were 41.0% (95% CI: 11.3, 60.7) and 41.9% (95% CI: 6.1, 64.0) on 15 – 180 days after booster doses of Sinovac and BNT162b2, respectively. Although significant vaccine effectiveness was detected in household settings, no evidence of such protective association was detected in non-household settings for either Sinovac or BNT162b2.

Conclusion: Moderate and significant protection against Omicron BA.2 variants' transmission was found for 2 and 3 doses of Sinovac or BNT162b2 vaccines. Although protection by 2-dose BNT162b2 may evidently wane with time, protection could be restored by the booster dose. Here, we highlight the importance of continuously evaluating vaccine effectiveness against transmission for emerging SARS-CoV-2 variants.

1. Introduction

A challenge in COVID-19 pandemic control is the continuous emergence of various genetic variants of SARS-CoV-2 posing a threat to public health [1]. In November 2021, the SARS-CoV-2 Omicron variants, i.e., B.1.1.529 lineage (PANGO), was first reported to World Health

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Organization (WHO) in South Africa [2], and was recognized as a variant of concern (VoC). The global circulation of Omicron variants was considered to be an outcome of an increase in transmissibility [3] and immune escape associated with novel genetic mutations [4–6]. Owing to disease elimination strategy, COVID-19 outbreaks in Hong Kong were kept under control with a low incidence rate until December 2021 [7]. Then, a large-scale community outbreak seeded by Omicron BA.2 variant occurred in early January, this fifth wave peaked with a daily incidence of over 50 000 laboratory-confirmed cases in early March, and subsided in May 2022 [8]. While public health and social measures including active contact tracing, case isolation, and temporary treatment facilities were tightened in the early phase of the fifth wave, the high number of cases overwhelmed the public health system and disrupted local healthcare.

Besides non-pharmaceutical interventions, mass vaccination was prioritized. Globally, over 12 billion doses of vaccine were administered by July 2022. Although an increasing number of studies have found that vaccines reduce risk of infection by and developing severe clinical outcomes from Omicron variants [6,9,10], few studies have evaluated vaccine effectiveness (VE) against risk of transmission of Omicron variants among different demographic groups. A US-based observational study found a lower household transmission rate for index cases of Omicron with 2- or 3-dose of vaccine compared to non-vaccinated index cases; a similar reduction in attack rate was detected among index cases with previous SARS-CoV-2 infection versus those without [11]. A systematic review and meta-analysis showed that full vaccination led to a reduction in both infectiousness of index cases and susceptibility to Omicron infection [12]. A Spanish study of household contacts of COVID-19 index cases found a household attack rate of 80.9% during the Omicron-dominant period compared with 58.2% during the Delta-dominant period, but an insignificant association between vaccination status (71.8% received BNT162b2) and attack rate during Omicron-dominant period [13]. Another Israeli study assessed VE against infectiousness after confirmed SARS-CoV-2 infection with Delta variants, and found no evident protection for BNT162b2 in the household setting [14]. In contrast, a cohort study in England found moderate but significant VE of BNT162b2 and ChAdOx1 nCoV-19 against transmission of Alpha and Delta variants [15]. Similarly, a Chinese cohort study reported a moderate and significant VE of 48.5% for 3-dose BBIBP-CorV within 15–90 days against Omicron BA.5 transmission, but no evident protection was detected after 90 days [16]. Evaluating the real-world effectiveness of different vaccines against Omicron variants' transmission is important given the continued global circulation of Omicron variants and their genetic decedents.

In Hong Kong, a COVID-19 vaccination program was launched in February 2021 for both Pfizer mRNA BNT162b2 vaccine (Comirnaty, Fosun Pharma-BioNTech) and Sinovac inactivated vaccine (CoronaVac). A subsequent booster vaccine program (i.e., third dose) was initialized first for priority groups (mostly the elderly) in November 2021 and then for the general population aged 18 years and above on January 1, 2022, given 6 months or more after the second dose [17]. While mRNA vaccines have been widely-used as the main type of COVID-19 vaccines in developed countries, inactivated vaccines have been mainly used in developing countries; it is thus important to evaluate the protective performance of both.

With a largely infection-naive (i.e., $<$ 0.2% previously infected) general population in Hong Kong under the moderate coverage of 2-dose vaccines (and in the near future, also for 3-dose vaccines), we assessed VE and waning protection of different doses of BNT162b2 and Sinovac against the transmission of SARS-CoV-2 Omicron BA.2 variants.

2. Methods

2.1. Study design, setting, participants, and data

We performed a retrospective cohort study based on COVID-19 cases in Hong Kong. The study period was from January 1 to June 19, 2022, during which Omicron BA.2 variants were dominant with coverage over 99% among the detected circulating SARS-CoV-2 strains [18]. By the end of 2021, the 2-dose vaccine coverage (i.e., fully vaccinated) reached 64.0% among the general population with 40.3% for BNT162b2 and 23.7% for Sinovac. By the end of April 2022, this 2-dose coverage increased to 84.2% (48.3% for BNT162b2, 35.9% for Sinovac) with a net growth of 21.2% within 4 months during the fifth epidemic wave in Hong Kong. For 3-dose vaccine, the coverage was 29.8% for BNT162b2 and 14.3% for Sinovac on April 30, 2022. We assessed the VE of BNT162b2 and Sinovac against the transmission (i.e., infectiousness rather than infection) of SARS-CoV-2.

In Hong Kong, real-time quantitative polymerase chain reaction (RT-qPCR) tests for SARS-CoV-2 infections were accessible and conducted in healthcare facilities and communities without substantial time or financial costs. All RT-qPCR test-positive SARS-CoV-2 cases were documented individually by the Centre for Health Protection of Hong Kong. Contact tracing was performed extensively before mid-February 2022, but only a small fraction of cases was traced after this time point. The cessation of contact tracing was largely due to the limited human resources given the large number of cases. Contact history data were referred to when identifying transmission pairs between index cases and their associated test-positive close contacts (i.e., secondary cases, see **Appendix S1**) A visualization of the epidemic curve during study period can be found in **Fig S4.1**.

The study population was RT-qPCR test-positive SARS-CoV-2 cases (both symptomatic and asymptomatic cases were included) aged 7 years and above with available contact tracing history. Baseline information for each case was provided by the Hong Kong Hospital Authority, a public sector corporation responsible for all public hospitals in Hong Kong where all COVID-19 patients were referred for admission. Contact tracing histories were obtained from the population-based surveillance data provided by CHP. Because of the prevailing COVID-19 elimination strategy, epidemic waves before 2022 were at relatively low levels with average daily cases $<$ 20 accounting for less than 0.2% of the population, which means the chance of re-infection was negligible.

Data, variables, and inclusion and exclusion criteria are detailed in **Appendix S2**.

2.2. Statistical analysis

Zero-inflated negative binomial (ZINB) log-linear regression models were adopted to fit the secondary cases. The secondary case number of each index case was the outcome variable and the vaccine status was the variable of interest. As a frequently adopted approach in the analysis of count data, the choice of ZINB model was based on its advantage of capturing situations where the number of zeros occur more frequently than expected, which was likely for the secondary cases number under intensive disease control measures [19]. We accounted for the effects of time-varying disease control measures or self-protective behaviors that could reduce transmission risk and lead to zero secondary cases. We adjusted for test-positive date, an importation factor in each index case because COVID-19 control measures varied during different phases of outbreak. We estimated VE after adjusting for sex, age, residential district, and test-positive date. The natural cubic spline was adopted to control the possible nonlinear association from numerical confounding variables (e.g., age, and calendar date). Technical details for ZINB regression models can be found in **Appendix S3**.

Risk ratio (RR) was calculated for various vaccine status regarding 0 dose as the reference level. V) was calculated as 1 minus RR. Using a maximum likelihood estimation approach, we summarized the point estimates and the 95% confidence interval (CI) was constructed using point estimate plus and minus 1.96-fold of the standard error. When RR, or any side of its 95% CI was larger than 1, the VE was transformed as $-[1-(1/\mathrm{RR})]\times 100\%$ [20]. The two-sided p-value was calculated using Wald's test, and statistical significance was claimed when p-value $<$

0.05.

Subgroup analyses were carried out by contact setting (household and non-household transmission), stratifying secondary cases according to vaccine doses received before infection, and age group of index cases (school-age teenager: 7–17 years, adults: 18–64 years, and the elderly >64 years). The vaccine lag effect was formulated as categorical variables according to 15–90, 91–180, 180–270, and >270 days since last dose, and the reference level was set as 0 dose.

All statistical analyses were performed using **R** statistical software (version 3.6.1). Fitting the ZINB model was achieved by using **R** function "*zeroinfl*" in package "*pscl*" [21].

2.3. Role of the funding source

The funder of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

3. Results

17 535 cases were identified with detailed contact history allowing extraction of number of secondary cases (Fig. 1). Summary statistics are shown in Table 1. The interpretation of these descriptive statistics can be found in **Appendix S5**. The epidemic curve of local cases (excluding imported cases) is shown in Fig 2 and stratified by vaccine status (0, 1, 2, or 3 doses) and number of secondary cases generated (0 or > 0 cases). Due to the exponential increase in the number of cases during February 2022 (see **Appendix S4**), mass contact tracing to investigate all cases and identify non-household contacts was stopped in mid-February. Amongst the 13 631 infected individuals generating no secondary cases, 3803 (27.9%) and 953 (7.0%) received 0 or 1 dose of vaccine, while 7383 (54.2%) and 1492 (10.9%) received 2 or 3 doses, respectively. By contrast, among the 1489 infected individuals with at least one secondary case, 569 (38.2%) and 98 (6.6%) received 0 or 1 dose, while 716 (48.1%) and 106 (7.1%) received 2 or 3 doses, respectively. As such, the crude VE against generating secondary case of Omicron BA.2 variant was 35% (95% CI: 27, 42) and 53% (95% CI: 41, 62) for infected individuals that received 2- or 3-doses, respectively, versus no vaccine.

After excluding cases with missing information or without eligible age or vaccine status (see Fig. 1) 15 526 were included for further statistical analyses. Among eligible index cases, the average number of secondary cases showed a decreasing trend with increasing doses of vaccine for both Sinovac ($p = 0.023$) and BNT162b2 ($p = 0.019$), see Fig. 3. Age sub-group analysis showed a similar significant negative association between vaccine dose and number of secondary cases in the 18 – 64 age group, but not in school-age teenagers. Among older individuals, secondary case number was negatively associated with number of doses of BNT162b2 vaccine ($p = 0.025$), but not for Sinovac ($p = 0.947$). No association was detected for asymptomatic cases.

The dose-dependent vaccine protection against generating secondary cases for infected individuals who received 2 or 3 doses of vaccine were converted to VE (see Table 2). For 2-dose Sinovac, VE was estimated of 62.6% (95% CI: 21.8, 82.1), 13.5% (95% CI: 1.1, 32.8), and 31.1% (95% CI: 10.0, 47.2) on 15 – 90, 91 – 180, 181 – 270 days after vaccination, respectively, under household contact setting. However, no evidence for positive VE was found regardless of contact settings on 15 –

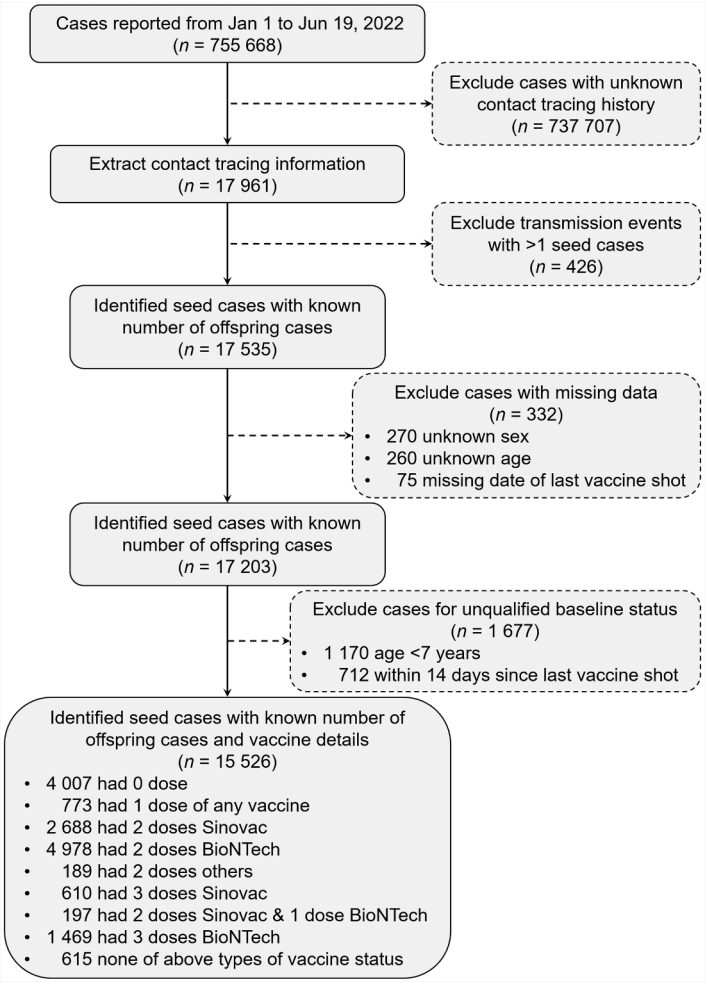

Fig. 1. Flowchart for sample selection. All 17 535 (out of a total of 755 668, 2.3%) identified index cases (including both symptomatic and asymptomatic index cases) with known number of secondary cases (including those index cases with 0 secondary case, i.e., terminal and sporadic cases) were included for summary of baseline characteristics. Among them, a total of 15 526 eligible index cases without missing data of key variables were included for statistical analysis.

Note: The counting of secondary cases was based on the RT-qPCR testing status of close contacts, and only test-positive contacts were considered as secondary cases, which means both symptomatic and asymptomatic secondary cases were involved.

Table 1
Summary of the baseline characteristics of identified index cases (i.e., infector, n = 17 535) with known number of secondary cases.

	Number of index cases (row%) Vaccine status			
	0 dose	1 dose	2 doses	3 doses
All (n = 17,535)	4607 (26.3%)	1102 (6.3%)	8725 (49.8%)	3101 (17.7%)
Those with gender information (n = 17,265)				
Female (n = 9249)	2479 (26.8%)	615 (6.6%)	4606 (49.8%)	1549 (16.7%)
Male (n = 8016)	2040 (25.4%)	475 (5.9%)	3976 (49.6%)	1525 (19.0%)
Those with age information (n = 17,275)				
Age from 0 to 6 years (n = 1170)	500 (42.7%)	77 (6.6%)	501 (42.8%)	92 (7.9%)
Age from 7 to 17 years (n = 1183)	414 (35%)	77 (6.5%)	584 (49.4%)	108 (9.1%)
Age from 18 to 64 years (n = 12,726)	2931 (23%)	778 (6.1%)	6444 (50.6%)	2573 (20.2%)
Age of or over 65 years (n = 2196)	681 (31%)	158 (7.2%)	1064 (48.5%)	293 (13.3%)
Those with information of case classification (n = 17,535)				
Local (n = 14,587)	4301 (29.5%)	1029 (7.1%)	7765 (53.2%)	1492 (10.2%)
Imported (n = 2948)	306 (10.4%)	73 (2.5%)	960 (32.6%)	1609 (54.6%)
Those with information of residential district (n = 13,100)				
Hong Kong Island (n = 1515)	351 (23.2%)	82 (5.4%)	752 (49.6%)	330 (21.8%)
Kowloon (n = 5014)	1435 (28.6%)	351 (7%)	2637 (52.6%)	591 (11.8%)
New Territories (n = 6571)	1823 (27.7%)	473 (7.2%)	3487 (53.1%)	788 (12.0%)
Epidemic period when test positive for COVID-19 (n = 17,535)				
Epidemic growth period from Jan 1 to Mar 3, 2022 (n = 15,120)	4372 (28.9%)	1051 (7.0%)	8099 (53.6%)	1598 (10.6%)
Epidemic decline period from Mar 4 to May 13, 2022 (n = 762)	132 (17.3%)	19 (2.5%)	223 (29.3%)	388 (50.9%)
Epidemic growth period from May 14 to Jun 19, 2022 (n = 1653)	103 (6.2%)	32 (1.9%)	403 (24.4%)	1115 (67.5%)
Those with SARS-CoV-2 genetic variant information (n = 14,427)				
Delta variant (n = 389)	122 (31.4%)	31 (8.0%)	207 (53.2%)	29 (7.5%)
Omicron variant (n = 14,038)	3699 (26.3%)	909 (6.5%)	7311 (52.1%)	2119 (15.1%)
Period from last vaccine dose to test positive for COVID-19				
from 0 to 14 days (n = 844, excluding 0 dose)	NA	250 (29.6%)	169 (20.0%)	425 (50.3%)
from 15 to 28 days (n = 857, excluding 0 dose)		378 (44.1%)	110 (12.8%)	369 (43.0%)
from 29 to 90 days (n = 1993, excluding 0 dose)		276 (13.8%)	497 (24.9%)	1220 (61.3%)
From 91 to 180 days (n = 4400, excluding 0 dose)		145 (3.3%)	3344 (76.0%)	911 (20.7%)
Over 180 days (n = 4759, excluding 0 dose)		50 (1.1%)	4554 (95.7%)	155 (3.3%)

90, or 91 – 180 days after vaccination. For 2-dose BNT162b2, VE was estimated of 56.2% (95% CI: 14.5, 77.6), 30.6% (95% CI: 13.0, 44.6), and 21.3% (95% CI: 2.9, 36.2) for 15 – 90, 91 – 180, 181 – 270 days after vaccination, respectively, where a significant decreasing trend was detected with p-value < 0.001. For 3-dose vaccine, VEs were estimated of 41.0% (95% CI: 11.3, 60.7) and 41.9% (95% CI: 6.1, 64.0) for those receiving Sinovac and BNT162b2 within 15 - 180 days, respectively. Under non-household contact setting, no evidence of positive VE was detected for either Sinovac or BNT162b2.

4. Discussion

Using detailed individual-level surveillance and contact tracing data of COVID-19 cases, we estimated the VE of Sinovac and BNT162b2 against transmission of Omicron BA.2 variants in a largely infection-naive but highly vaccinated population during the fifth COVID-19 wave in Hong Kong. In the final dataset, there were 49.8% index cases that received 2-dose vaccine prior to infection, which was a vaccine coverage lower than in general population (66.0% for 2-dose as of January 2022) [17], reflecting protection of vaccine against SARS-CoV-2 infection. Both 2- and 3-dose Sinovac and BNT162b2 were associated with a range of protection against the risks of generating secondary cases (Table 2). VE against household transmission of Omicron BA.2 was estimated at 62.6% or 45.3% within 15 - 90 days for 2 doses of Sinovac or BNT162b2, respectively. Our estimated VE appeared slightly lower than previous estimates of 76% for Alpha variants [22,23] but similar to previous estimates of 40% for Delta variants [24]. For 3-dose vaccinees, VE was estimated at 41.0% or 41.9% within 15 - 180 days for Sinovac or BNT162b2, consistent with 32.3% found previously [12]. We performed sensitivity analysis by restricting our dataset to identified Omicron cases (we excluded those with Delta infection or without VoC identification). We found that these VE estimates were similar to our main results, especially for the point estimates, but with slightly wider 95% CIs, likely due to the reduced sample size.

Households are an ideal setting for evaluating viral transmission and the effectiveness of vaccination [25]. In Hong Kong in 2022, the housing density was extremely high with a population density of 6747 people per square kilometre. Contact tracing was straightforward to perform in household settings and information of exposure history could be identified with relatively high certainty. VE was detected in household transmission settings but was unclear in non-household settings. The scale of VE for household settings was similar to overall VE estimates. Among all index cases, the mean number of offspring cases was estimated at 0.14 (95% CI: 0.13, 0.16) or 0.04 (95% CI: 0.03, 0.05) for household and non-household settings, respectively. Despite relatively lower transmissibility for non-household settings, transmissibility had a relatively higher scale of statistical dispersion in terms of coefficient of variation (CV) at 16.8 compared to 5.9 for household setting. Higher heterogeneity in transmission implies that the majority of transmission events were driven by superspreading [26–28]. As such, the reduction in transmission associated with vaccine may be difficult to identify in the context of superspreading events. By contrast, household settings were less likely to facilitate super spreader events because the number of household contacts for each individual was relatively stable. From the standpoint of contact tracing surveillance, household contacts were straightforward to identify, whereas the identifying contacts in non-household settings (e.g., workplace, community, or school) were usually subject to the uncertainty from self-reporting and memory recall. The household setting has been widely adopted in previous studies in assessing VE against transmission of Omicron variants [11,13,29] and earlier SARS-CoV-2 strains [12,22,23,30,31], as well as other diseases [32]. Hence, we considered VE estimates in household settings to be a reliable measure of the true effect of vaccine against Omicron BA.2 variants' transmission.

We found a significant reduction in VE for 2-dose BNT162b2 recipients from 56.2% to 7.4% as the time lag increased from 15 – 90 to over 270 days since the second dose. To the best of our knowledge, this waning effect against transmission of BA.2 variants was first reported using real-world observations and was also suggested for the waning of VE against infectiousness after confirmed infection with Delta variants [14]. Although waning protection was detected, our estimate of VE for 3-dose BNT162b2 recipients was 50.4% which approached the VE of 56.2% for 2-dose BNT162b2 at early stage after vaccination. This finding suggested that the waning protection of 2-dose BNT162b2 could be restored by a third dose of BNT162b2. A similar phenomenon in that the protective effect of 2-dose vaccines could be restored by a booster dose was previously reported for VE against SARS-CoV-2 infections [6,33,34] and severe illness with COVID-19 [35,36], but we are unaware of a similar finding regarding VE against transmission of Omicron BA.2 variants. As the 3-dose vaccine program was initiated before the fifth

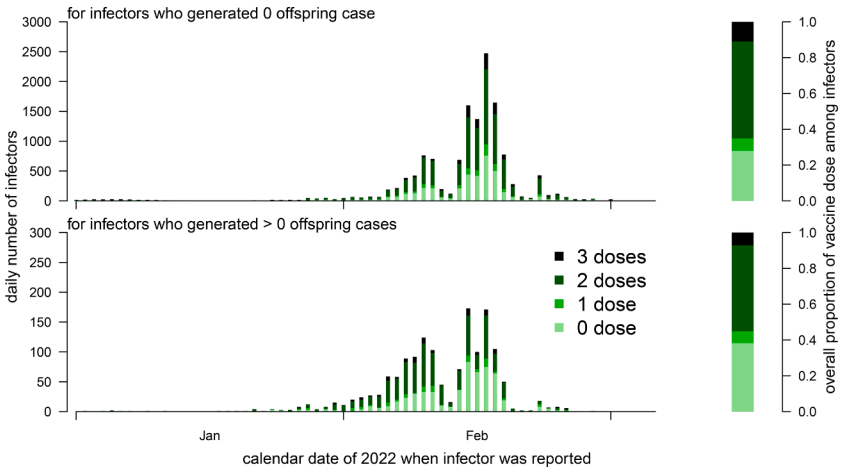

Fig. 2. Daily number of identified infectors reported during the growing phase of the fifth epidemic wave in Hong Kong, stratified by number of vaccine dose received before SARS-CoV-2 infection. The top panels showed the epidemic curve, and cumulative distribution of vaccine status for cases WHO generated 0 secondary case (i.e., terminal and sporadic cases). The bottom panels showed the epidemic curve, and cumulative distribution of vaccine status for cases WHO generated > 0 secondary cases (i.e., those index cases leading to critical and supercritical transmission).

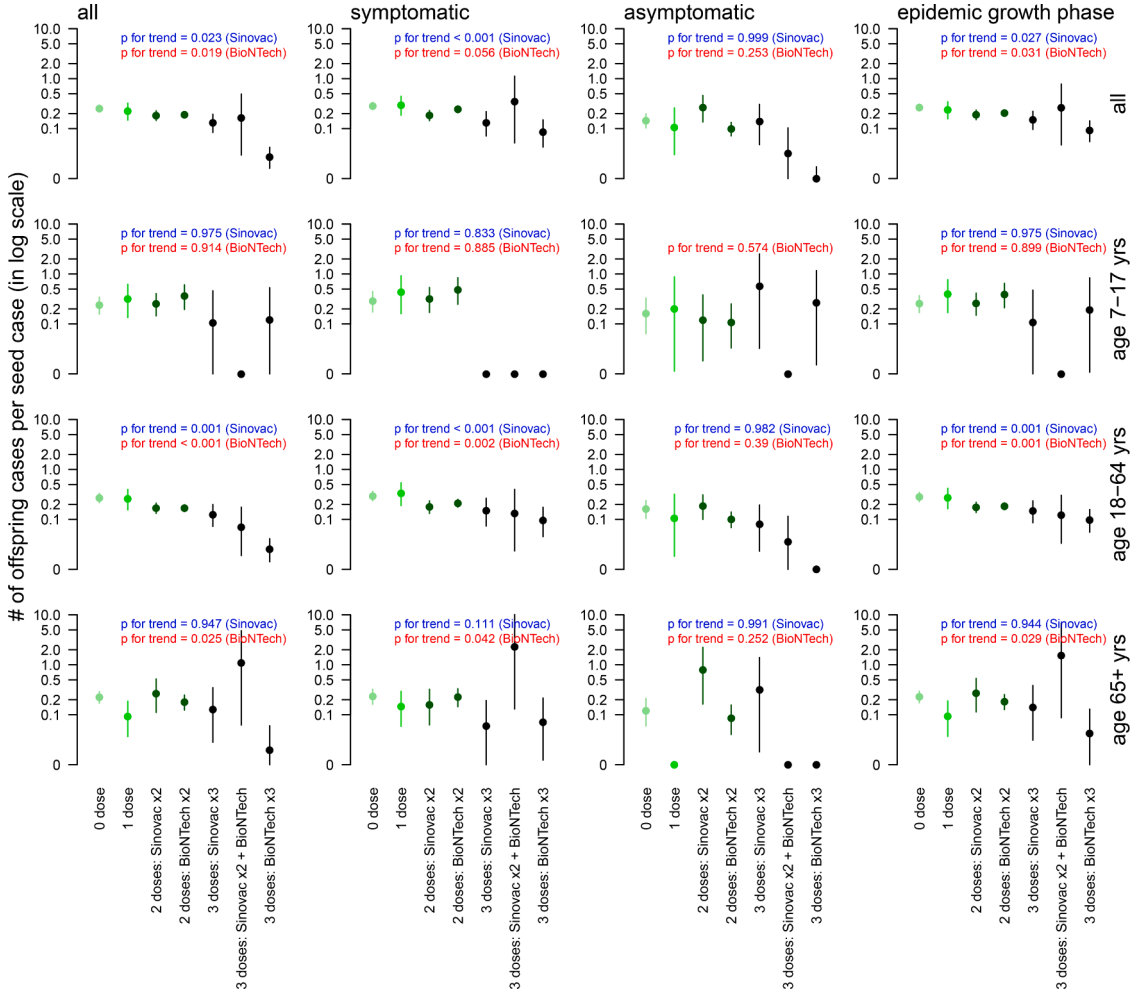

Fig. 3. Summary statistics of number of secondary cases per index case, stratified by vaccination status, age groups, symptom status, and epidemic phase of index cases. In each panel, the dots were the mean secondary case number per index case, bars were 95% CIs, and the vertical axis was in log scale. The *p*-values for trend measured the statistical significance for the decreasing trend of secondary case numbers against the dose of vaccine with age, sex, calendar week, living region, importation status, and symptom status adjusted.
Note: The "epidemic growth phase" here in the last column were the period from January 1 to February 15, 2022, which covered the period with a relatively high contact tracing intensity.

COVID-19 wave, we were only able to estimate the VE of three doses for a relatively short period since the its uptake. Among the 2655 3-dose vaccine recipients vaccinated more than 15 days before infection, 1589 (59.8%) were vaccinated within 90 days before infection. We attempted to estimate 3-dose VE over 180 days since the last dose, but no evidence for a reduction in transmission was detected for three doses of

Table 2
Summary of vaccine effectiveness (VE, in%) estimates against generating secondary cases, stratified by vaccine doses and combination of vaccine types of infector, lag from last dose, and contact settings (i.e., household, and non-household).

Vaccine dose of index case	Lag from last dose to test positive	Sample size	VE against generating secondary cases (95% CI)[a]		
			Categorized by contact setting		Overall
			Household	Non-household	
0 dose	NA	4003	Reference		
1 dose					
any	15 – 90 d	593	7.4 (−21.3, 32.5)	54.6 (−40.1, 87.7)	18.7 (−15.2, 43.9)
	> 90 d	180	−19.4 (−52.2, 26.4)	9.7 (−79.5, 83.3)	−14.4 (−52.8, 35.7)
2 doses					
Sinovac × 2	15 – 90 d	229	62.6 (21.8, 82.1)	−17.8 (−78.6, 68.2)	44.9 (−10.3, 72.7)
	91 – 180 d	1083	13.5 (1.1, 32.8)	17.6 (−46.6, 63.7)	15.1 (−11.8, 36.4)
	181 – 270 d	1195	31.1 (10.0, 47.2)	23.7 (−44.2, 67.5)	29.8 (4.8, 48.3)
	> 270 d	181	11.4 (−38.3, 51.6)	52.4 (−79.1, 95.3)	21.5 (−39.2, 62.5)
BioNTech × 2	15 – 90 d	304	45.3 (2.7, 69.2)	81.4 (−46.0, 98.1)	56.2 (14.5, 77.6)
	91 – 180 d	1921	37.2 (21.7, 49.6)	4.8 (−40.0, 45.6)	30.6 (13.0, 44.6)
	181 – 270 d	2266	21.7 (4.6, 35.7)	18.9 (−31.0, 54.6)	21.3 (2.9, 36.2)
	> 270 d	487	−3.2 (−38.2, 33.9)	43.7 (−63.0, 88.3)	7.4 (−34.6, 43.9)
3 doses					
Sinovac × 3	15 – 180 d	593	41.0 (11.3, 60.7)	48.2 (−51.5, 87.0)	43.6 (8.5, 65.2)
	> 180 d	17	not calculated[b]		
Sinovac × 2 + BioNTech	15 – 180 d	183	61.1 (−3.7, 85.4)	−67.8 (−98.7, 12.3)	−10.8 (−56.5, 45.3)
	> 180 d	14	not calculated[b]		
BioNTech × 3	15 – 180 d	757	41.9 (6.1, 64.0)	77.8 (−39.0, 97.0)	50.4 (9.7, 72.8)
	> 180 d	66	35.3 (−91.5, 96.4)	24.3 (−95.4, 97.4)	42.9 (−91.6, 97.3)

[a] Adjusted for sex, age, calendar week, living region, importation status.
[b] The VE estimates was not calculated due to insufficient samples with size < 50.

Sinovac or BNT162b2, or two doses of Sinovac followed by one dose of BNT162b2. As such, the duration of the protection from the booster dose remains unclear.

To further control for the protective effect of vaccine against infection, we divided the cases into four groups according to the vaccine dose they received prior to infection (0, 1, 2, or 3 doses of any vaccine; 1 dose not shown due to limited sample size), see **Appendix S6**. For index cases who received 2-dose BNT162b2 within 15 – 90 days of infection, the estimated VE ranged from 47.6% to 87.9% for reduction in transmissibility to secondary cases who received 0 – 3 doses of any vaccine. Thus, we found evidence of the protective effects of vaccines after accounting for the vaccine status of secondary cases. For either vaccine, no evident trend was detected for VE against Omicron BA.2 variants' transmission across various doses of vaccine received by the secondary cases.

Another explanation for the association between the vaccinated index case and a lower risk to spread SARS-CoV-2 is that close contacts of vaccinated index cases were more likely to have been vaccinated. To avoid this undesired association, we performed sensitivity analysis to stratify the number of secondary cases by vaccine status (**Appendix S6.1**). We found the scale and trend of VE estimates were largely consistent with our main findings for index cases generating secondary cases vaccinated with 2 or 3 doses of any vaccine. For stratification by different age groups of index cases, evidence for the protection of both Sinovac or BNT162b2 was found only among adult index cases with age 18–64 years (**Appendix S6.2**). Insignificant VE estimates for individuals age 7–17 and the age >64 years are likely due to a relatively small sample size. As such, we cannot conclude whether 2- or 3-dose vaccines received by an index case who was a teenager or an older adult provided protection against transmission. The results of VE estimates stratified by symptom status of index case are summarized in **Appendix S6.3**; VE for symptomatic index case were largely consistent with the main results. For asymptomatic index cases, significant protection was detected among those aged 18–64 years with 2-dose BNT162b2; insignificant VE estimates in other age groups may be due to limited sample size.

Immune escape might contribute to the high transmissibility of Omicron variants in populations with moderate coverage of vaccines such as in Hong Kong. The Omicron variants appears to evade immunity developed from both prior infection and vaccination in terms of low neutralizing antibody titer [4,37,38] and three doses of BNT162b2 provided nearly ineffective protection against symptomatic infection at > 20 weeks after booster dose [13,39]. These findings highlight the importance of continuous monitoring of the epidemiologic characteristics of and vaccine effectiveness against emerging SARS-CoV-2 variants in communities regardless of vaccine coverage or infection rate of previous epidemics [1,40]. Two-dose vaccination plus a booster showed moderate significant protection against COVID-19 transmission, and was recommended first for the elderly, people with high-risk factors, and then the general population in Hong Kong [17]. Considering the increased selection advantage of Omicron variants compared with other strains [2,41–43], developing vaccines with long-term protection and transmission of COVID-19 was desired. Although the clinical severity after infected Omicron variants was lower compared to previous VoCs [44–46], high transmission was of concern [47]. PHSMs such as using of facemasks focused on high-risk groups including vulnerable populations, those with high chance of exposure, and contact settings with poor ventilation or hygiene were suggested during the -19 pandemic, accompanied by the promotion of vaccines.

4.1. Limitations

This study has several limitations. First, we cannot exclude the possibility that misclassification of index cases versus secondary cases might have occurred, which was difficult to eliminate from the existing dataset. Since the analyses relied on surveillance data of contact tracing history, any degree of recalling bias and case underreporting during contact tracing could affect the accuracy of identified transmission pairs and thus might dilute our VE estimates. Due to lack of genomic analysis, transmission pairs were reconstructed through suspected epidemiological link according to contact tracing history, which was not definitive. Second, we were only able to investigate the effectiveness of 3-dose vaccines for a relatively short period of time as the third dose vaccine program was initiated close to the start of the fifth COVID-19 wave. Most cases that had received the booster dose were vaccinated within 90 days before infection. While the insignificant VE of 3-dose Sinovac or BNT162b2 over 90 or 180 days might imply a decay in effect, the waning protection of booster vaccine against the transmission of Omicron BA.2

variants was largely unassessed due to lack of data with longer post-vaccination period. Third, our analysis did not adjust for immunocompromised status, which has been shown to be an important determinant of vaccine performance [6,48]. Fourth, due to a lack of test-negative control group, we choose number of transmitted cases as the outcome. Thus, the vaccine status of transmitted cases cannot be directly adjusted, which was accounted for in sensitivity analysis (**Appendix S6.1**). Fourth, this study was based on the contact tracing data from January to June 2022, but the contact tracing information was scarce after mid-February 2022 due to the limited human resources and large number of cases. Overall, roughly 2% of total cases were traced. After mid-February 2022, contact tracing procedures in Hong Kong may bias towards the patients infected by cases that were previously traced and were symptomatic or imported cases. These patients were likely to self-isolate, and more likely to accept COVID-19 tests or show symptoms so their close contacts were aware of the risk of transmission. Thus, index cases identified at a later stage may have generated a smaller number of secondary cases than those not identified. As shown in the panels in the last column of Fig. 3, index cases identified at an earlier stage generated a slightly higher number of secondary cases (see first column). Thus, while we have adjusted both time-varying effects of policy changes and importation status, our VE estimates might be overestimated. Similarly, comparing two recent studies based on data in Israel [14] and mainland China [16], where mainland China has a relatively intensive COVID-19 control, the reduction in infectiousness associated with vaccine is likely to be detected in the context with strict disease control measures. This may be because multiple times, high-level or long-duration of exposure risks from seed case to secondary cases were like to occur under relaxed control strategies, such that vaccine protection might become marginal. Therefore, as control policies in Hong Kong were relatively strict, the change in contact tracing coverage in our dataset is unlikely to affect our main findings. Other technical limitations re discussed in **Appendix S7**. Finally, since Omicron BA.2 variants were dominant in Hong Kong during the study period, we restricted interpretation of our findings to BA.2 variants; further investigations were needed for other emerging or circulating genetic variants of SARS-CoV-2 and sub-lineages of Omicron BA.5.

5. Conclusions

Using real-world observations, significant protection against the transmission of SARS-CoV-2 Omicron BA.2 variants was found for index cases who received 2 or 3 doses of Sinovac or BNT162b2 vaccines. A reduction in VE was reported from 56.2% to 7.4% for 2-dose BNT162b2 recipients as the time lag increased since the second dose. This research highlights the importance of continuously evaluating VE against emerging SARS-CoV-2 variants as they evolve regardless of existing vaccine coverage.

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The funders of the study had no role in study design, data collection, data analysis, data interpretation, writing of the manuscript, or the decision to submit for publication. All authors had full access to all the data in the study and were responsible for the decision to submit the manuscript for publication.

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Data sharing statement

The cases' surveillance data were extracted from electronic records in the system managed by the Hong Kong Hospital Authority. The vaccine history and contact tracing databases were extracted from the COVID-19 surveillance database provided by the Department of Health in Hong Kong. Restrictions apply to the availability of these data.

Author's contributions

All authors critically reviewed the manuscript, and gave final approval for publication.

Ethics approval and consent to participate

This was an observational study based on identity-masked datasets provided by the Department of Health, the Government of the Hong Kong Special Administrative Region. Either ethics approval or informed consent for conducting this study was waived by the Hong Kong Hospital Authority.

Consent for publication

Not applicable.

CRediT authorship contribution statement

Shi Zhao: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Visualization, Project administration. **Zihao Guo:** Software, Validation, Data curation, Writing – review & editing. **Shengzhi Sun:** Writing – review & editing. **Chi Tim Hung:** Writing – review & editing. **Eman Yee Man Leung:** Writing – review & editing. **Yuchen Wei:** Data curation, Writing – review & editing. **Huwen Wang:** Writing – review & editing. **Kehang Li:** Writing – review & editing. **Carrie Ho Kwan Yam:** Data curation. **Tsz Yu Chow:** Data curation. **Jian Gao:** Writing – original draft. **Katherine Min Jia:** Writing – original draft. **Ka Chun Chong:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing, Supervision, Funding acquisition. **Eng-Kiong Yeoh:** Resources, Writing – review & editing, Supervision, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

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References

[1] M.U.G. Kraemer, O.G. Pybus, C. Fraser, S. Cauchemez, A. Rambaut, B.J. Cowling, Monitoring key epidemiological parameters of SARS-CoV-2 transmission, Nat. Med. 27 (11) (2021) 1854–1855.

[2] R. Viana, S. Moyo, D.G. Amoako, H. Tegally, C. Scheepers, C.L. Althaus, U. J. Anyaneji, P.A. Bester, M.F. Boni, M. Chand, Rapid epidemic expansion of the SARS-CoV-2 Omicron variant in southern Africa, Nature 603 (7902) (2022) 679–686.

[3] K.P.Y. Hui, J.C.W. Ho, M-c Cheung, K-c Ng, R.H.H. Ching, K-l Lai, T.T. Kam, H. Gu, K.Y. Sit, M.K.Y. Hsin, et al., SARS-CoV-2 Omicron variant replication in human bronchus and lung ex vivo, Nature 603 (7902) (2022) 715–720.

[4] D. Planas, N. Saunders, P. Maes, F. Guivel-Benhassine, C. Planchais, J. Buchrieser, W.H. Bolland, F. Porrot, I. Staropoli, F. Lemoine, Considerable escape of SARS-CoV-2 Omicron to antibody neutralization, Nature 602 (7898) (2022) 671–675.

[5] S. Collie, J. Champion, H. Moultrie, L-G Bekker, G. Gray, Effectiveness of BNT162b2 vaccine against Omicron variant in South Africa, N. Engl. J. Med. 386 (5) (2022) 494–496.

[6] H.F. Tseng, B.K. Ackerson, Y. Luo, L.S. Sy, C.A. Talarico, Y. Tian, K.J. Bruxvoort, J. E. Tubert, A. Florea, J.H. Ku, Effectiveness of mRNA-1273 against SARS-CoV-2 Omicron and Delta variants, Nat. Med. 28 (5) (2022) 1063–1071.

[7] P.H.H. Cheung, C.P. Chan, D-Y Jin, Lessons learned from the fifth wave of COVID-19 in Hong Kong in early 2022, Emerg. Microbes Infect. 11 (1) (2022) 1072–1078.

[8] Z. Du, L. Tian, D-Y Jin, Understanding the impact of rapid antigen tests on SARS-CoV-2 transmission in the fifth wave of COVID-19 in Hong Kong in early 2022, Emerg. Microbes Infect. (2022) 1–19, just-accepted.

[9] Y.M. Bar-On, Y. Goldberg, M. Mandel, O. Bodenheimer, O. Amir, L. Freedman, S. Alroy-Preis, N. Ash, A. Huppert, R. Milo, Protection by a fourth dose of BNT162b2 against Omicron in Israel, N. Engl. J. Med. 386 (18) (2022) 1712–1720.

[10] M.E. McMenamin, J. Nealon, Y. Lin, J.Y. Wong, J.K. Cheung, E.H.Y. Lau, P. Wu, G. M. Leung, B.J. Cowling, Vaccine effectiveness of one, two, and three doses of BNT162b2 and CoronaVac against COVID-19 in Hong Kong: a population-based observational study, Lancet Infect. Dis. 22 (10) (2022) 1435–1443.

[11] J.M. Baker, J.Y. Nakayama, M. O'Hegarty, A. McGowan, R.A. Teran, S.M. Bart, K. Mosack, N. Roberts, B. Campos, A. Paegle, SARS-CoV-2 B 1.1. 529 (Omicron) variant transmission within households—Four US jurisdictions, November 2021–February 2022, Morb. Mortal. Wkly. Rep. 71 (9) (2022) 341.

[12] Z.J. Madewell, Y. Yang, I.M. Longini, M.E. Halloran, N.E. Dean, Household secondary attack rates of SARS-CoV-2 by variant and vaccination status: an updated systematic review and meta-analysis, JAMA Netw. Open 5 (4) (2022), e229317 e229317.

[13] I. López-Muñoz, A. Torrella, O. Pérez-Quílez, A. Castillo-Zuza, E. Martró, A. E. Bordoy, V. Saludes, I. Blanco, L. Soldevila, O. Estrada, SARS-CoV-2 secondary attack rates in vaccinated and unvaccinated household contacts during replacement of delta with Omicron variant, Spain, Emerging Infect. Dis. 28 (10) (2022) 1999–2008.

[14] O. Prunas, J.L. Warren, F.W. Crawford, S. Gazit, T. Patalon, D.M. Weinberger, V. E. Pitzer, Vaccination with BNT162b2 reduces transmission of SARS-CoV-2 to household contacts in Israel, Science 375 (6585) (2022) 1151–1154.

[15] D.W. Eyre, D. Taylor, M. Purver, D. Chapman, T. Fowler, K.B. Pouwels, A. S. Walker, T.E.A. Peto, Effect of Covid-19 vaccination on transmission of alpha and delta variants, N. Engl. J. Med. 386 (8) (2022) 744–756.

[16] K. Wang, Z. Guo, T. Zeng, S. Sun, Y. Lu, J. Wang, S. Li, Z. Luan, H. Li, J. Zhang, et al., Transmission characteristics and inactivated vaccine effectiveness against transmission of SARS-CoV-2 Omicron BA.5 Variants in Urumqi, China, JAMA Netw. Open 6 (3) (2023), e235755 e235755.

[17] Hong Kong Vaccination Dashboard [https://www.covidvaccine.gov.hk/en/dashboard].

[18] Y. Mesfin, D. Chen, H. Bond, V. Lam, J. Cheung, J. Wong, Ali ST, E. Lau, P. Wu, G. Leung, Epidemiology of infections with SARS-CoV-2 Omicron BA. 2 variant in Hong Kong, January-March 2022, medRxiv (2022).

[19] Y. Lu, Z. Guo, T. Zeng, S. Sun, Y. Lu, Z. Teng, M. Tian, J. Wang, S. Li, X. Fan, Case clustering, contact stratification, and transmission heterogeneity of SARS-CoV-2 Omicron BA. 5 variants in Urumqi, China: an observational study, J. Glob. Health 13 (2023) 06018.

[20] S. Greenland, K. Drescher, Maximum likelihood estimation of the attributable fraction from logistic models, Biometrics (1993) 865–872.

[21] A. Zeileis, C. Kleiber, S. Jackman, Regression models for count data in R, J. Stat. Softw. 27 (8) (2008) 1–25.

[22] B. de Gier, S. Andeweg, R. Joosten, R. Ter Schegget, N. Smorenburg, J. van de Kassteele, S.J.M. Hahné, S. van den Hof, H.E. de Melker, M.J. Knol, Vaccine effectiveness against SARS-CoV-2 transmission and infections among household and other close contacts of confirmed cases, the Netherlands, February to May 2021, Eurosurveillance 26 (31) (2021), 2100640.

[23] S. Gazit, B. Mizrahi, N. Kalkstein, A. Neuberger, A. Peretz, M. Mizrahi-Reuveni, A. Ben-Tov, T. Patalon, BNT162b2 mRNA vaccine effectiveness given confirmed exposure: analysis of household members of coronavirus disease 2019 patients, Clin. Infect. Dis. 75 (1) (2022) e734–e740.

[24] B. de Gier, S. Andeweg, J.A. Backer, S.J.M. Hahné, S. van den Hof, H.E. de Melker, M.J. Knol, Vaccine effectiveness against SARS-CoV-2 transmission to household contacts during dominance of Delta variant (B. 1.617. 2), the Netherlands, August to September 2021, Eurosurveillance 26 (44) (2021), 2100977.

[25] V.E. Pitzer, T. Cohen, Household studies provide key insights on the transmission of, and susceptibility to, SARS-CoV-2, Lancet Infect. Dis. 20 (10) (2020) 1103–1104.

[26] D.C. Adam, P. Wu, J.Y. Wong, E.H.Y. Lau, T.K. Tsang, S. Cauchemez, G.M. Leung, B.J. Cowling, Clustering and superspreading potential of SARS-CoV-2 infections in Hong Kong, Nat. Med. 26 (11) (2020) 1714–1719.

[27] S. Zhao, M.K.C. Chong, S. Ryu, Z. Guo, M. He, B. Chen, S.S. Musa, J. Wang, Y. Wu, D. He, et al., Characterizing superspreading potential of infectious disease: decomposition of individual transmissibility, PLoS Comput. Biol. 18 (6) (2022), e1010281.

[28] J.O. Lloyd-Smith, S.J. Schreiber, P.E. Kopp, W.M. Getz, Superspreading and the effect of individual variation on disease emergence, Nature 438 (7066) (2005) 355–359.

[29] D.S. Lim, Y.J. Choe, Y.M. Kim, S.E. Lee, E.J. Jang, J. Kim, Y.J. Park, Household secondary attack rates of SARS-CoV-2 Omicron variant, South Korea, February 2022, Emerg. Infect. Dis. 28 (8) (2022) 1731.

[30] O.T. Ng, V. Koh, C.J. Chiew, K. Marimuthu, N.M. Thevasagayam, T.M. Mak, J. K. Chua, S.S.H. Ong, Y.K. Lim, Z. Ferdous, Impact of Delta variant and vaccination on SARS-CoV-2 secondary attack rate among household close contacts, Lancet Reg. Health-Western Pacific 17 (2021), 100299.

[31] M. Layan, M. Gilboa, T. Gonen, M. Goldenfeld, L. Meltzer, A. Andronico, N. Hozé, S. Cauchemez, G. Regev-Yochay, Impact of BNT162b2 vaccination and isolation on SARS-CoV-2 transmission in Israeli households: an observational study, Am. J. Epidemiol. 191 (7) (2022) 1224–1234.

[32] S.E. Ohmit, J.G. Petrie, R.E. Malosh, B.J. Cowling, M.G. Thompson, D.K. Shay, A. S. Monto, Influenza vaccine effectiveness in the community and the household, Clin. Infect. Dis. 56 (10) (2013) 1363–1369.

[33] N. Andrews, J. Stowe, F. Kirsebom, S. Toffa, T. Rickeard, E. Gallagher, C. Gower, M. Kall, N. Groves, A.M. O'Connell, Covid-19 vaccine effectiveness against the Omicron (B. 1.1. 529) variant, N. Engl. J. Med. 386 (16) (2022) 1532–1546.

[34] H. Chemaitelly, H.H. Ayoub, S. AlMukdad, P. Coyle, P. Tang, H.M. Yassine, H. A. Al-Khatib, M.K. Smatti, M.R. Hasan, Z. Al-Kanaani, Duration of mRNA vaccine protection against SARS-CoV-2 Omicron BA. 1 and BA. 2 subvariants in Qatar, Nat. Commun. 13 (1) (2022) 1–12.

[35] S. Collie, J. Nayager, L. Bamford, L-G Bekker, M. Zylstra, G. Gray, Effectiveness and durability of the BNT162b2 vaccine against Omicron sublineages in South Africa, N. Engl. J. Med. (2022).

[36] S.Y. Tartof, J.M. Slezak, L. Puzniak, V. Hong, F. Xie, B.K. Ackerson, S.R. Valluri, L. Jodar, J.M. McLaughlin, Durability of BNT162b2 vaccine against hospital and emergency department admissions due to the Omicron and delta variants in a large health system in the USA: a test-negative case–control study, Lancet Respir. Med. (2022).

[37] N.P. Hachmann, J. Miller, A-rY Collier, J.D. Ventura, J. Yu, M. Rowe, E.A. Bondzie, O. Powers, N. Surve, K. Hall, et al., Neutralization escape by SARS-CoV-2 Omicron subvariants BA.2.12.1, BA.4, and BA.5, N. Engl. J. Med. 387 (1) (2022) 86–88.

[38] J. Ai, H. Zhang, Y. Zhang, K. Lin, Y. Zhang, J. Wu, Y. Wan, Y. Huang, J. Song, Z. Fu, Omicron variant showed lower neutralizing sensitivity than other SARS-CoV-2 variants to immune sera elicited by vaccines after boost, Emerg. Microbes Infect. 11 (1) (2022) 337–343.

[39] Public Health England: COVID-19 vaccine surveillance report Week 15 (14 April 2022). In.; 2022.

[40] L. Cao, J. Lou, S.Y. Chan, H. Zheng, C. Liu, S. Zhao, Q. Li, C.K.P. Mok, R.W.Y. Chan, M.K.C. Chong, Rapid evaluation of COVID-19 vaccine effectiveness against symptomatic infection with SARS-CoV-2 variants by analysis of genetic distance, Nat. Med. 28 (8) (2022) 1715–1722.

[41] J.A. Backer, D. Eggink, S.P. Andeweg, I.K. Veldhuijzen, N. van Maarseveen, K. Vermaas, B. Vlaemynck, R. Schepers, S. van den Hof, C.B. Reusken, et al., Shorter serial intervals in SARS-CoV-2 cases with Omicron BA.1 variant compared with Delta variant, the Netherlands, 13 to 26 December 2021, Euro surveillance 27 (6) (2022), 2200042.

[42] K. Ito, C. Piantham, H. Nishiura, Relative instantaneous reproduction number of Omicron SARS-CoV-2 variant with respect to the Delta variant in Denmark, J. Med. Virol. 94 (5) (2022) 2265–2268.

[43] M.T. Sofonea, B. Roquebert, V. Foulongne, D. Morquin, L. Verdurme, S. Trombert-Paolantoni, M. Roussel, J.C. Bonetti, J. Zerah, S. Haim-Boukobza, Analyzing and modeling the spread of SARS-CoV-2 Omicron lineages BA. 1 and BA. 2, France, September 2021–February 2022, Emerg. Infect. Dis. 28 (7) (2022) 1355.

[44] N. Wolter, W. Jassat, S. Walaza, R. Welch, H. Moultrie, M. Groome, D.G. Amoako, J. Everatt, J.N. Bhiman, C. Scheepers, Early assessment of the clinical severity of the SARS-CoV-2 Omicron variant in South Africa: a data linkage study, Lancet 399 (10323) (2022) 437–446.

[45] X. Chen, X. Yan, K. Sun, N. Zheng, R. Sun, J. Zhou, X. Deng, T. Zhuang, J. Cai, J. Zhang, Estimation of disease burden and clinical severity of COVID-19 caused by Omicron BA. 2 in Shanghai, February-June 2022, Emerg. Microbes Infect. (2022) 1–10, just-accepted.

[46] A.S. Lauring, M.W. Tenforde, J.D. Chappell, M. Gaglani, A.A. Ginde, T. McNeal, S. Ghamande, D.J. Douin, H.K. Talbot, J.D. Casey, Clinical severity of, and effectiveness of mRNA vaccines against, Covid-19 from Omicron, delta, and alpha SARS-CoV-2 variants in the United States: prospective observational study, BMJ (2022) 376.

[47] E. Mahase, Covid-19: hospital admission 50-70% less likely with Omicron than delta, but transmission a major concern, BMJ 375 (2021) n3151.

[48] L. Corey, C. Beyrer, M.S. Cohen, N.L. Michael, T. Bedford, M. Rolland, SARS-CoV-2 variants in patients with immunosuppression, N. Engl. J. Med. 385 (6) (2021) 562–566.