Effectiveness of BNT162b2 and CoronaVac COVID-19 vaccination against asymptomatic and symptomatic infection of SARS-CoV-2 omicron BA.2 in Hong Kong: a prospective cohort study

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Summary

Background COVID-19 vaccines provide protection against symptomatic infection that might require medical attention and against severe outcomes; however, there is a paucity of evidence regarding the effectiveness of the BNT162b2 and CoronaVac vaccines and their booster regimens against asymptomatic or mild omicron infections in the community. We aimed to measure the effectiveness of BNT162b2 and CoronaVac vaccines against asymptomatic and symptomatic SARS-CoV-2 omicron infections, during a period of omicron BA.2 predominance in Hong Kong.

Methods In this prospective cohort study in a population that was generally infection-naive before the large omicron BA.2 wave between January and late May, 2022, we established a public health surveillance platform to monitor the evolving activity of SARS-CoV-2 infections in the community. We recruited a cohort of individuals aged 5 years and older between March 1 and March 7, 2022, from the general population. Individuals were enrolled from all 18 districts of Hong Kong, according to a predefined age-stratified quota, primarily by random digit dialing (generating suitable eight-digit local telephone numbers by randomly picking sets of the first four digits from a sampling frame, and randomly generating the last four digits), and supplemented by our existing cohorts (which included cohorts for studying influenza vaccination from school-based vaccination programmes and cohorts for SARS-CoV-2 seroprevalence from the community), to ensure representativeness of the population in Hong Kong. Participants did weekly rapid antigen testing with a self-collected pooled nasal and throat swab, regardless of symptom and exposure status, from March 1 to April 15, 2022. Individuals reporting a history of SARS-CoV-2 infection confirmed by laboratory PCR testing before enrolment were excluded from the vaccine effectiveness analysis to avoid potential bias due to infection-induced immunity. The primary outcomes of the study were the incidence of SARS-CoV-2 infection, including asymptomatic and symptomatic infections, and the vaccine effectiveness of BNT162b2 and CoronaVac vaccines. The effectiveness of one, two, and three doses of vaccination was estimated with a Cox proportional hazards regression model with time-dependent covariates, allowing for changes in vaccination status over time, after adjustment for demographic factors and pre-existing medical conditions.

Findings Of the 8636 individuals included in the analysis, 7233 (84%) received at least two doses of vaccine, 3993 (46%) received booster doses, and 903 (10%) reported SARS-CoV-2 infection. Among these infections 589 (65·2%) were symptomatic and 314 (34·8%) were asymptomatic at the time of testing. Statistically significant protection against asymptomatic and symptomatic SARS-CoV-2 omicron infection was found only for those who received a BNT162b2 or CoronaVac booster dose, with a vaccine effectiveness of 41·4% (23·2 to 55·2; p=0·0001) and 32·4% (9·0 to 49·8; p=0·0098), respectively. The vaccine effectiveness of BNT162b2 and CoronaVac boosters was further increased to 50·9% (95% CI 31·0–65·0; p<0·0001) and 41·6% (15·0–59·8; p=0·0049), respectively, for symptomatic omicron infections. A similar pattern of vaccine effectiveness (55·8%, 22·9–74·6; p=0·0040) was also conferred after receipt of a BNT162b2 booster by individuals who received a CoronaVac primary vaccination series.

Interpretation Two doses of either vaccine did not provide significant protection against COVID-19 infection. However, receipt of a BNT162b2 booster or CoronaVac booster was associated with a significantly lower risk of omicron BA.2 infection and symptomatic infection. Our findings confirm the effectiveness of booster doses to protect against mild and asymptomatic infection.

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Introduction

With the current global predominance of the omicron variant of SARS-CoV-2, previous understanding of the effectiveness of different COVID-19 vaccines against the ancestral strain and earlier variants is no longer sufficient to inform the way forward during the evolving COVID-19 pandemic.[1] Literature has generally suggested that a primary series plus booster doses of mRNA vaccine shows

Research in context

Evidence before this study

With the evolving omicron variants of SARS-CoV-2, previous understanding of the effectiveness of COVID-19 vaccines against the ancestral strain and earlier variants is becoming increasingly insufficient. Newer omicron-specific vaccine-effectiveness estimates are needed to inform the way forward, especially for individuals who present with asymptomatic infection, who might either have no symptoms or develop symptoms later (pre-symptomatic), because of the potential public health implications for seeding downstream secondary transmission. We searched PubMed and MedRxiv, with no language restrictions, from database inception up to Sept 14, 2022, using the search terms "((vaccine effectiveness) AND (omicron)) AND (((BNT162b2) OR (Comirnaty)) OR (CoronaVac))", and found 133 published articles and 791 preprints. 118 of these publications reported vaccine effectiveness against omicron outcomes, with 100 studies focused only on symptomatic infection or severe complications. Among the 18 studies that attempted to examine asymptomatic infections, only ten reported aggregated vaccine effectiveness rather than the vaccine effectiveness of specific vaccine types, three used only a risk-based testing approach, which was not optimal in ascertaining asymptomatic infections, and five were of restricted generalisability, as they focused on specific population subgroups (one each on haemodialysis patients, people who were incarcerated, and university students and employees, and two on children). To our knowledge, to date, no study has reported the vaccine effectiveness of the BNT162b2 booster or CoronaVac vaccines and booster regimens against omicron BA.2 asymptomatic infection.

Added value of this study

The population of Hong Kong was generally omicron-infection-naive before a large BA.2 wave extending from January 1 to April 30, 2022, and peaking in early March. Our prospective observational cohort study examined and compared the vaccine effectiveness of BNT162b2 and CoronaVac against asymptomatic and symptomatic SARS-CoV-2 omicron BA.2 infections. The systematic use of weekly SARS-CoV-2 rapid antigen testing for outcome ascertainment, regardless of exposure status and symptoms, allowed for identification of asymptomatic infections, including in those who remained asymptomatic and those who went on to develop symptoms (pre-symptomatic), and improved generalisability to community infections. To our knowledge, our study is the first to report the effectiveness of CoronaVac vaccines against SARS-CoV-2 omicron BA.2 asymptomatic infections.
Our results suggest that no significant protection was observed for one or two doses of BNT162b2 and CoronaVac. Significant protection against SARS-CoV-2 asymptomatic and symptomatic omicron infection was shown for those who received a BNT162b2 booster or CoronaVac booster. A similar pattern of vaccine effectiveness was also conferred by administering a BNT162b2 booster dose to individuals who received a CoronaVac primary vaccination series.

Implications of all the available evidence

Our results suggest that a booster dose of COVID-19 vaccine is needed to achieve significant protection against omicron infection, by either an inactivated or mRNA vaccine, which highlights the importance of achieving high coverage of booster doses. Our study shows the experimental feasibility for examining vaccine effectiveness against asymptomatic and mild infections using a systematic outcome-ascertainment approach, irrespective of exposures status and symptoms.

modest to high effectiveness against severe COVID-19 outcomes, including hospitalisation, mechanical ventilation, and death,[2–7] and effectively prevents symptomatic infections.[4,5,7–9] However, evidence of the effectiveness of vaccines in preventing mild and asymptomatic infections, which have potential public health implications for seeding downstream secondary transmission, are generally lacking.

However, examination of the effectiveness of vaccines in preventing mild and asymptomatic COVID-19 infections is inherently challenging. Common study designs used for studying vaccine effectiveness, including test-negative design, depend on symptomatic cases presenting in various settings.[9] Therefore, such designs can be biased towards the more severe end of the clinical spectrum and might not be generalisable to all cases in the community. Moreover, previous observational vaccine effectiveness studies that do not have a prescribed similar testing schedule might be biased by the potential differential testing frequencies and behaviours among people with different vaccination status.[10,11] Previous vaccine effectiveness studies against omicron infections have focused mainly on various mRNA vaccine candidates, including BNT162b2 (Pfizer–BioNTech) and the mRNA-1273 (Moderna) vaccine, or adenoviral vector vaccines, such as ChAdOx1 nCoV-19 (AstraZeneca),[4,5,7–9,12] and, to our knowledge, the effectiveness of inactivated vaccine (eg CoronaVac [Sinovac]) against omicron infections has yet to be investigated. Although previous studies have reported the effectiveness of BNT162b2 among children and adolescents,[9,12] the comparative effectiveness of BNT162b2 and CoronaVac vaccines among different age groups remains unclear. We did a study examining the effectiveness of BNT162b2 and CoronaVac vaccines against SARS-CoV-2 infection, using a prospective and systematic approach to outcome ascertainment, regardless of risk or symptoms, and therefore capturing

mild and asymptomatic infections, during a period of omicron BA.2 predominance in Hong Kong.

Methods

Study design and participants

From early January to late May, 2022, Hong Kong had its fifth and the largest wave of the COVID-19 pandemic, with daily reported positive SARS-CoV-2 cases rising progressively to a maximum of more than 50 000 per day, and largely caused by the omicron variant sublineage BA.2. From March 1, 2022, we established a public health surveillance platform to monitor the evolving activity of SARS-CoV-2 infections in the community. We recruited a cohort of individuals aged 5 years and older between March 1 and March 7, 2022, from the general population. Individuals were enrolled from all 18 districts of Hong Kong, according to a predefined age-stratified quota, primarily by random digit dialing, and supplemented by our existing cohorts, to ensure representativeness of the population in Hong Kong. Random digit dialing involved generating suitable eight-digit local telephone numbers for recruitment by randomly picking sets of the first four digits from a sampling frame, and randomly generating the last four digits using Microsoft Excel. The existing cohorts included cohorts maintained for studying protection from influenza vaccination in school-based vaccination programmes and cohorts for studying SARS-CoV-2 seroprevalence recruited from the community. Eligible participants had to consent to do regular scheduled rapid antigen tests and be competent at self-reporting testing results to our online system to be recruited to the study. An incentive of supermarket coupon of US$50 would be given to participants submitting 100% of scheduled weekly tests for achieving a high compliance.

Before the study period, COVID-19 infections in the community were confirmed using PCR by either the government laboratory or another officially recognised laboratory in Hong Kong. History of any previous PCR-confirmed infection before joining the study was ascertained by self-reporting in a baseline questionnaire on recruitment. Individuals reporting a history of COVID-19 infection confirmed by laboratory PCR testing before enrolment were excluded from the vaccine effectiveness analysis to avoid potential bias due to natural immunity[13] as, given a very low seroprevalence of infection before the omicron wave,[14] most people reporting a previous infection would have had a recent infection with the omicron BA.2 strain, thus were presumed to be immune to this strain.

The community surveillance programme was reviewed and commissioned by the Health Bureau of the Hong Kong Special Administrative Region Government as an emergency public health initiative during the rapid upswing of the fifth wave of the COVID-19 pandemic in Hong Kong and thus was exempted from a full ethics review. Written informed consent was obtained from all individuals, allowing collection, storage, and use of information for surveillance and anonymised research purposes.

Procedures

Outcome ascertainment of COVID-19 infection was done using a COVID-19 lateral flow rapid antigen test (INDICAID; PHASE Scientific, Hong Kong) for the qualitative detection of SARS-CoV-2 nucleocapsid protein. A rapid antigen test assay brand that met the WHO priority target product profiles for COVID-19 diagnostics (ie, sensitivity ≥80% and specificity ≥97%)[15] and the US Food and Drug Administration (FDA) Emergency Use Authorization[16] was chosen to address the issue of variable sensitivity between assay brands.[17,18] Rapid antigen tests were provided to all consenting individuals for weekly testing with a self-collected pooled nasal and throat swab, regardless of symptom and exposure status, and participants submitted the test results (positive, negative, or invalid) with rapid antigen test photographs to an online platform. Additional rapid antigen tests done at the participants' discretion were also captured. Demographic information, including sex, age, chronic illness history, COVID-19 infection history, household size, housing type, district, and residential address, was collected at enrolment. Corresponding estimates from the overall population were extracted from the 2021 and 2016 Hong Kong Population Census from the Census and Statistics Department. COVID-19 infection was defined as any positive rapid antigen test result reported during the study period, irrespective of symptoms. Symptomatic COVID-19 infections were defined as those receiving a positive rapid antigen test result and reporting at least one of 19 surveyed symptoms (appendix p 1). Asymptomatic infections were defined as positive rapid antigen test without any symptoms at the time point of the test. Participants were stratified into quartiles of socioeconomic levels according to the published monthly domestic household rent of the Hong Kong tertiary planning unit (TPU) that their residential addresses belong to (Q1 [lowest]: ≤HK$1510; Q2: HK$1511–2050; Q3: HK$2051–5300; Q4 [highest]: ≥HK$5301). Vaccination records were collected at baseline and updated regularly and verified by individual official vaccination documents submitted via the same online platform as for rapid antigen test reporting.

See Online for appendix

Outcomes

The primary outcomes of the study were the incidence of SARS-CoV-2 infection, including asymptomatic and symptomatic infections, and the vaccine effectiveness of BNT162b2 and CoronaVac.

Statistical analysis

Cohen's w effect size, defined as

$$w = \sqrt{\sum_{i=1}^{m} \frac{(P_{1i} - P_{0i})^2}{P_{0i}}}$$

—where P_{0i} represents the proportion in cell i posited by the population overall according to the 2021 Population Census from the Hong Kong Census and Statistics Department, P_{0i} represents the proportion in cell i posited by the cohort, and m is the number of cells—was used to estimate the degree of discrepancy between the distribution of our cohort and the Hong Kong population, where a small departure (w=0·1) represents weak discrepancy, a medium departure (w=0·3) represents medium discrepancy, and a larger departure (w=0·5) denotes large discrepancy.[19]

We studied the risk of infection using the community surveillance data during the peak of the epidemic wave in Hong Kong between March 1 and April 15, 2022, to examine the effectiveness of COVID-19 vaccination. Individuals were included in the analysis until the day of infection as confirmed by a positive rapid antigen test, or the end of study period (April 15, 2022), whichever occurred first. Time to infection was measured from the respective date of enrolment for all individuals to control for time-varying confounders (eg, amount of community transmission and prevalence of the omicron variant) when comparing the risk of COVID-19 between vaccinated and unvaccinated people.[20] To address the potential for immortal time bias, we continuously ascertained and updated the classification of the vaccination status of each

	Hong Kong population*	Study cohort			
	Number of individuals (n=7 182 991)	Number of individuals (n=8636)	Effect size†	Negative rapid antigen test (n=7733)	Positive rapid antigen test (n=903)
Gender			0·0001		
Female	3 918 820 (54·6%)	4723 (54·7%)	..	4230 (54·7%)	493 (54·6%)
Male	3 264 171 (45·4%)	3913 (45·3%)	..	3503 (45·3%)	410 (45·4%)
Age group, years	..	..	0·0068	..	..
5–17	738 609 (10·3%)	886 (10·3%)	..	787 (10·2%)	99 (11·0%)
18–59	4 379 236 (61·0%)	6014 (69·6%)	..	5383 (69·6%)	631 (69·9%)
≥60	2 065 146 (28·8%)	1736 (20·1%)	..	1563 (20·2%)	173 (19·2%)
Hong Kong region	..	..	0·0018	..	..
Hong Kong	1 161 636 (16·2%)	1300 (15·1%)	..	1168 (15·1%)	132 (14·6%)
Kowloon	2 166 850 (30·2%)	2482 (28·7%)	..	2204 (28·5%)	278 (30·8%)
New Territories and Marine	3 854 505 (53·7%)	4854 (56·2%)	..	4361 (56·4%)	493 (54·6%)
Hong Kong district	..	..	0·0040	..	..
Central and Western	228 370 (3·2%)	203 (2·4%)	..	179 (2·3%)	24 (2·7%)
Wan Chai	161 585 (2·2%)	118 (1·4%)	..	114 (1·5%)	4 (0·4%)
Eastern	515 623 (7·2%)	648 (7·5%)	..	575 (7·4%)	73 (8·1%)
Southern	256 058 (3·6%)	331 (3·8%)	..	300 (3·9%)	31 (3·4%)
Yau Tsim Mong	298 791 (4·2%)	280 (3·2%)	..	253 (3·3%)	27 (3·0%)
Sham Shui Po	417 242 (5·8%)	451 (5·2%)	..	415 (5·4%)	36 (4·0%)
Kowloon City	397 230 (5·5%)	450 (5·2%)	..	387 (5·0%)	63 (7·0%)
Wong Tai Sin	397 585 (5·5%)	479 (5·5%)	..	423 (5·5%)	56 (6·2%)
Kwun Tong	656 002 (9·1%)	822 (9·5%)	..	726 (9·4%)	96 (10·6%)
Kwai Tsing	482 396 (6·7%)	578 (6·7%)	..	473 (6·1%)	105 (11·6%)
Tsuen Wan	308 481 (4·3%)	462 (5·3%)	..	402 (5·2%)	60 (6·6%)
Tuen Mun	490 910 (6·8%)	598 (6·9%)	..	535 (6·9%)	63 (7·0%)
Yuen Long	643 865 (9·0%)	811 (9·4%)	..	746 (9·6%)	65 (7·2%)
North	300 183 (4·2%)	352 (4·1%)	..	320 (4·1%)	32 (3·5%)
Tai Po	306 046 (4·3%)	347 (4·0%)	..	320 (4·1%)	27 (3·0%)
Sha Tin	672 418 (9·4%)	882 (10·2%)	..	809 (10·5%)	73 (8·1%)
Sai Kung	471 901 (6·6%)	623 (7·2%)	..	571 (7·4%)	52 (5·8%)
Islands and Marine	178 305 (2·5%)	201 (2·3%)	..	185 (2·4%)	16 (1·8%)
Have a chronic illness	1 799 100 (25·0%)	1783 (20·6%)	0·0035	1593 (20·6%)	190 (21·0%)
Median monthly domestic household rent quartile‡	..	..	0·0021	..	..
1 (lowest)	1 738 085/7 334 200 (23·7%)	1966 (22·8%)	..	1711 (22·1%)	255 (28·2%)
2	1 841 942/7 334 200 (25·1%)	2199 (25·5%)	..	1968 (25·4%)	231 (25·6%)
3	1 891 657/7 334 200 (25·8%)	2428 (28·1%)	..	2194 (28·4%)	234 (25·9%)
4 (highest)	1 862 516/7 334 200 (25·4%)	2043 (23·7%)	..	1860 (24·1%)	183 (20·3%)

(Table 1 continues on next page)

	Hong Kong population*	Study cohort			
	Number of individuals (n=7 182 991)	Number of individuals (n=8636)	Effect size†	Negative rapid antigen test (n=7733)	Positive rapid antigen test (n=903)
(Continued from previous page)					
Household size§, people	..	..	0·0298	..	..
1–2	1 307 784/2 674 161 (48·9%)	2146 (24·8%)	..	1975 (25·5%)	171 (18·9%)
3–4	1 097 254/2 674 161 (41·0%)	4689 (54·3%)	..	4167 (53·9%)	522 (57·8%)
≥5	269 123/2 674 161 (10·1%)	1801 (20·9%)	..	1591 (20·6%)	210 (23·3%)
Housing type¶	..	..	0·0055	..	..
Public rental housing	2 120 704/7 047 963 (30·1%)	2414 (28·0%)	..	2032 (26·3%)	382 (42·3%)
Subsidised home ownership scheme housing	1 129 933/7 047 963 (16·0%)	1635 (18·9%)	..	1482 (19·2%)	153 (16·9%)
Private permanent housing	3 710 508/7 047 963 (52·7%)	4356 (50·4%)	..	4005 (51·8%)	351 (38·9%)
Others	86 818/7 047 963 (1·2%)	231 (2·7%)	..	214 (2·8%)	17 (1·9%)
Have COVID-19 symptoms	..	632 (7·3%)	..	43 (0·6%)	589 (65·2%)
Vaccination status‖	..	..	0·0049	..	..
Unvaccinated	731 112/7 394 700 (9·9%)	764 (8·8%)	..	641 (8·3%)	123 (13·6%)
One dose	656 086/7 394 700 (8·9%)	639 (7·4%)	..	545 (7·0%)	94 (10·4%)
Two doses	3 105 353/7 394 700 (42·0%)	3240 (37·5%)	..	2771 (35·8%)	469 (51·9%)
Three doses	2 902 149/7 394 700 (39·2%)	3993 (46·2%)	..	3776 (48·8%)	217 (24·0%)

Data are n (%) or n/N (%), unless otherwise indicated. Only individuals aged 5 years and older were included. *Estimates from the overall population were extracted from the 2021 Hong Kong Population Census from the Census and Statistics Department. †Cohen's w effect size: small 0·1; medium 0·3; large 0·5. ‡Tertiary planning unit-level median monthly domestic household rent was based on the latest available census data in 2016 for the Hong Kong population. §Number of households with the corresponding household size for the Hong Kong population. ¶Total population in domestic households for the Hong Kong population. ‖Total population in 2021, without excluding those younger than 5 years, for the Hong Kong population.

Table 1: **Characteristics of people tested for SARS-CoV-2 with rapid antigen test, according to test positivity or negativity**

individual dynamically, as unvaccinated, first dose, second dose, or third dose during the entire study period. Individuals reported their updated vaccination status and date of vaccination in the weekly scheduled submission. Only vaccine doses completed more than 14 days before the rapid antigen testing were counted.[21]

Since the independent variable (vaccination status) varied over time, univariate and multivariate survival analyses were done with time-dependent covariates (vaccination status) according to the study design. Kaplan-Meier analysis was done for univariate analyses. The association between vaccination and risk of infection was estimated by a multivariate Cox proportional hazards regression model after adjustment for age,[22] gender,[23] coexisting illnesses,[24] and other sociodemographic factors that might confound rapid antigen test positivity—eg, household size, district, housing type, and TPU median monthly domestic household rent—which were associated with test positivity in univariate regression models. All covariates were tested for the proportional hazards assumption by Schoenfeld's global test. 95% CIs were estimated using robust SEs.

We estimated vaccine effectiveness as 1 minus the adjusted hazard ratio (HR), where the adjusted HR was obtained from a multivariate Cox proportional hazards regression model with time-dependent covariates to estimate the risk of rapid antigen test positivity for individuals who were unvaccinated, or who had received one, two, or three doses of vaccination using the Mantel-Byar method.[25] Using information on the time between the start of follow-up and exposure initiation, individuals were followed up from the time of cohort entry, with infection status (rapid antigen test result) and vaccination status updated on a weekly basis. Data from individuals with time-varying vaccination status were split into multiple data segments, each with the corresponding interval of follow-up period for assessing the effectiveness of different vaccination status in the regression model. The effectiveness of one, two, and three doses of vaccination was estimated with unvaccinated people as a reference group. Vaccine effectiveness for the primary series (two doses) was assessed by stratification into either completed within 3 months (14–89 days) or completed 3 months or longer (90 or more days) after the second dose. Most people who received only one dose and those who had received three doses had received their latest dose within the past 3 months so participants were not further stratified. The outcome of infection was ascertained at the time of first rapid antigen test positivity. We estimated vaccine effectiveness for preventing any SARS-CoV-2 infection, irrespective of clinical symptoms (symptomatic and asymptomatic infection), as well as for symptomatic infection. Individual data were censored 14 days after the receipt of a vaccine in the unvaccinated group, after receipt of a further dose in the one-dose and two-dose

	Population				Cohort				
	Total (n=7 394 700)	Aged 0–19 years (n=1 108 900)	Aged 20–59 (n=4 251 700)	Aged ≥60 (n=2 034 100)	Total (n=8636)	Aged 5–17 (n=886)	Aged 18–59 (n=6014)	Aged ≥60 (n=1736)	Effect size*†
Unvaccinated	731 112 (9·9%)	343 882 (31·0%)	36 758 (0·9%)	350 472 (17·2%)	764 (8·8%)	216 (24·4%)	390 (6·5%)	158 (9·1%)	0·0678
One dose	656 086 (8·9%)	274 057 (24·7%)	208 505 (4·9%)	173 524 (8·5%)	639 (7·4%)	287 (32·4%)	232 (3·9%)	120 (6·9%)	0·0055
≥3 months	..	..	..	..	71 (0·8%)	40 (4·5%)	28 (0·5%)	3 (0·2%)	..
<3 months	..	..	..	..	568 (6·6%)	247 (27·9%)	204 (3·4%)	117 (6·7%)	..
Two doses	3 105 353 (42·0%)	412 728 (37·2%)	1 921 045 (45·2%)	771 580 (37·9%)	3240 (37·5%)	323 (36·5%)	2404 (40·0%)	513 (29·6%)	0·0083
≥3 months	..	..	..	..	2308 (26·7%)	133 (15·0%)	1899 (31·6%)	276 (15·9%)	..
<3 months	..	..	..	..	932 (10·8%)	190 (21·4%)	505 (8·4%)	237 (13·7%)	..
Three doses	2 902 149 (39·2%)	78 233 (7·1%)	2 085 392 (49·0%)	738 524 (36·3%)	3993 (46·2%)	60 (6·8%)	2988 (49·7%)	945 (54·4%)	0·0033
≥3 months	..	..	..	..	852 (9·9%)	1 (0·1%)	555 (9·2%)	296 (17·1%)	..
<3 months	..	..	..	..	3141 (36·4%)	59 (6·7%)	2433 (40·5%)	649 (37·4%)	..
One dose BNT162b2	285 584 (3·9%)	143 169 (12·9%)	108 969 (2·6%)	33 446 (1·6%)	329 (3·8%)	152 (17·2%)	145 (2·4%)	32 (1·8%)	0·0042
≥3 months	..	..	..	..	61 (0·7%)	36 (4·1%)	23 (0·4%)	2 (0·1%)	..
<3 months	..	..	..	..	268 (3·1%)	116 (13·1%)	122 (2·0%)	30 (1·7%)	..
One dose CoronaVac	370 502 (5·0%)	130 888 (11·8%)	99 536 (2·3%)	140 078 (6·9%)	310 (3·6%)	135 (15·2%)	87 (1·4%)	88 (5·1%)	0·0060
≥3 months	..	..	..	..	10 (0·1%)	4 (0·5%)	5 (0·1%)	1 (0·1%)	..
<3 months	..	..	..	..	300 (3·5%)	131 (14·8%)	82 (1·4%)	87 (5·0%)	..
Two dose BNT162b2	1 818 926 (24·6%)	232 148 (20·9%)	1 316 777 (31·0%)	270 001 (13·3%)	2353 (27·2%)	175 (19·8%)	1914 (31·8%)	264 (15·2%)	0·0074
≥3 months	..	..	..	..	1884 (21·8%)	124 (14·0%)	1589 (26·4%)	171 (9·9%)	..
<3 months	..	..	..	..	469 (5·4%)	51 (5·8%)	325 (5·4%)	93 (5·4%)	..
Two dose CoronaVac	1 237 279 (16·7%)	175 799 (15·9%)	566 889 (13·3%)	494 591 (24·3%)	875 (10·1%)	146 (16·5%)	481 (8·0%)	248 (14·3%)	0·0063
≥3 months	..	..	..	..	417 (4·8%)	8 (0·9%)	305 (5·1%)	104 (6·0%)	..
<3 months	..	..	..	..	458 (5·3%)	138 (15·6%)	176 (2·9%)	144 (8·3%)	..
Two dose other combinations	49 148 (0·7%)	4781 (0·4%)	37 379 (0·9%)	6988 (0·3%)	12 (0·1%)	2 (0·2%)	9 (0·1%)	1 (0·1%)	0·0042
≥3 months	..	..	..	..	7 (0·1%)	1 (0·1%)	5 (0·1%)	1 (0·1%)	..
<3 months	..	..	..	..	5 (0·1%)	1 (0·1%)	4 (0·1%)	0	..
Three dose BNT162b2	1 580 623 (21·4%)	64 639 (5·8%)	1 213 564 (28·5%)	302 420 (14·9%)	2432 (28·2%)	56 (6·3%)	1913 (31·8%)	463 (26·7%)	0·0036
≥3 months	..	..	..	..	296 (3·4%)	1 (0·1%)	198 (3·3%)	97 (5·6%)	..
<3 months	..	..	..	..	2136 (24·7%)	55 (6·2%)	1715 (28·5%)	366 (21·1%)	..
Three dose CoronaVac	905 449 (12·2%)	5128 (0·5%)	571 478 (13·4%)	328 843 (16·2%)	1050 (12·2%)	0	734 (12·2%)	316 (18·2%)	0·0052
≥3 months	..	..	..	..	371 (4·3%)	0	241 (4·0%)	130 (7·5%)	..
<3 months	..	..	..	..	679 (7·9%)	0	493 (8·2%)	186 (10·7%)	..
Two dose CoronaVac plus BNT162b2	416 077 (5·6%)‡	8466 (0·8%)	300 350 (7·1%)	107 261 (5·3%)	463 (5·4%)	0	310 (5·2%)	153 (8·8%)	0·0070
≥3 months	..	..	..	..	178 (2·1%)	0	112 (1·9%)	66 (3·8%)	..
<3 months	..	..	..	..	285 (3·3%)	0	198 (3·3%)	87 (5·0%)	..
Two dose BNT162b2 plus CoronaVac	..	..	..	..	29 (0·3%)	4 (0·5%)	18 (0·3%)	7 (0·4%)	..
≥3 months	..	..	..	..	3 (<0·1%)	0	2 (<0·1%)	1 (0·1%)	..
<3 months	..	..	..	..	26 (0·3%)	4 (0·5%)	16 (0·3%)	6 (0·3%)	..
Three dose other combinations	..	..	..	..	19 (0·2%)	0	13 (0·2%)	6 (0·3%)	..
≥3 months	..	..	..	..	4 (0·1%)	0	2 (<0·1%)	2 (0·1%)	..
<3 months	..	..	..	..	15 (0·2%)	0	11 (0·2%)	4 (0·2%)	..

Data are n (%), unless otherwise indicated. *Overall effect size for the cohort 0·0084. †Cohen's w effect size: small 0·1; medium 0·3; large 0·5. ‡Included three doses with any vaccine combinations in local population.

Table 2: **Vaccination status by age group**

groups, at 3 months after the second dose if no further doses were received, or at the end of follow-up.

Vaccine effectiveness was also estimated with stratification by age group (children aged 5–17 years, adults aged 18–59 years, and older adults ≥60 years) and vaccine type (BNT162b2 and CoronaVac),[13,26] with the effectiveness of primary series and booster vaccination for different vaccine types (BNT162b2 and CoronaVac)

examined and compared among each age group. Relative vaccine effectiveness was estimated by comparing the relative protection additionally conferred by CoronaVac, using BNT162b2 as a reference. As the local Hong Kong vaccine policy required the same vaccine type to be used in both doses in the primary series, the small proportion of individuals who received the first two doses with different vaccine types from elsewhere were not included in the analysis. As switching to a different vaccine type was allowed for the booster dose, regimens of different vaccine combinations for those who received a third dose were included in the analysis if sample size permitted.

p<0·05 was considered to indicate a statistically significant difference. To achieve 80% power with a 0·05 type I error rate in the survival analysis, 334 positive rapid antigen tests were needed with a HR of 0·60 between vaccinated and unvaccinated groups. All data processing and analyses were done in R (version 4.1.0), using the packages survival and tidyverse.

Role of the funding source

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

Results

1560 (15·3%) of 10 196 individuals in the cohort had reported themselves to be previously infected with SARS-CoV-2 before enrolment and thus were excluded from the vaccine effectiveness analysis. Among the 8636 individuals included in the vaccine effectiveness analysis, 903 (10·5%) were infected during the surveillance period, with a median of 10 days (IQR 6–17) between enrolment and infection; among these infections 589 (65·2%) were symptomatic and 314 (34·8%) were asymptomatic. 7233 (84%) individuals had received at least two doses of vaccine and 3993 (46%) received booster doses. The distribution of positive and negative cases according to sex, age, and comorbidity status was similar (table 1). Sociodemographic factors associated with test positivity included household size, district, housing type, and TPU level median monthly domestic household rent (appendix p 2). High compliance with weekly testing was maintained in 8419 (97·5%) individuals, with a similar pattern across different characteristics (appendix p 3).

764 (8·8%) of 8636 individuals were unvaccinated, 639 (7·4%) had only one dose of vaccine, 3240 (37·5%) had two doses, and 3993 (46·2%) had three doses (table 1). Differences in monthly domestic household rent, housing type, and geographical district were observed between vaccination status; in particular, individuals who received three doses of vaccine had a higher likelihood of being male, older, having a chronic illness, having a smaller household size, and being asymptomatic (appendix p 4). 2308 (71·2%) of 3240 individuals who received two doses of vaccine had received the second dose more than 3 months before testing, so vaccine effectiveness was stratified by those who had completed the second dose within 3 months or 3 months or longer before testing. For the primary series of two vaccine doses, 2353 (27·2%) of 8636 individuals received BNT162b2 and 875 (10·1%) individuals received CoronaVac. For the primary series using BNT162b2, 1884 (21·8%) of 8636 individuals completed the two doses 3 months before testing and 469 (5·4%) completed the

	Total (n=8636)	Test negative (n=7733)	Test positive (n=903)	Positivity (95% CI)*
Unvaccinated	764 (8·8%)	641 (8·3%)	123 (13·6%)	16·1% (13·7–18·9)
One dose	639 (7·4%)	545 (7·0%)	94 (10·4%)	14·7% (12·2–17·7)
≥3 months	71 (0·8%)	58 (0·8%)	13 (1·4%)	18·3% (11·0–28·9)
<3 months	568 (6·6%)	487 (6·3%)	81 (9·0%)	14·3% (11·6–17·4)
Two doses	3240 (37·5%)	2771 (35·8%)	469 (51·9%)	14·5% (13·3–15·7)
≥3 months	2308 (26·7%)	1902 (24·6%)	406 (45·0%)	17·6% (16·1–19·2)
<3 months	932 (10·8%)	869 (11·2%)	63 (7·0%)	6·8% (5·3–8·6)
Three doses	3993 (46·2%)	3776 (48·8%)	217 (24·0%)	5·4% (4·8–6·2)
≥3 months	852 (9·9%)	814 (10·5%)	38 (4·2%)	4·5% (3·3–6·1)
<3 months	3141 (36·4%)	2962 (38·3%)	179 (19·8%)	5·7% (4·9–6·6)
One dose BNT162b2	329 (3·8%)	289 (3·7%)	40 (4·4%)	12·2% (9·1–16·1)
≥3 months	61 (0·7%)	51 (0·7%)	10 (1·1%)	16·4% (9·2–27·6)
<3 months	268 (3·1%)	238 (3·1%)	30 (3·3%)	11·2% (8·0–15·5)
One dose CoronaVac	310 (3·6%)	256 (3·3%)	54 (6·0%)	17·4% (13·6–22·0)
≥3 months	10 (0·1%)	7 (0·1%)	3 (0·3%)	30·0% (10·8–60·3)
<3 months	300 (3·5%)	249 (3·2%)	51 (5·6%)	17·0% (13·2–21·7)
Two dose BNT162b2	2353 (27·2%)	1996 (25·8%)	357 (39·5%)	15·2% (13·8–16·7)
≥3 months	1884 (21·8%)	1561 (20·2%)	323 (35·7%)	17·1% (15·5–18·9)
<3 months	469 (5·4%)	435 (5·6%)	34 (3·8%)	7·3% (5·2–10·0)
Two dose CoronaVac	875 (10·1%)	765 (9·9%)	110 (12·2%)	12·6% (10·5–14·9)
≥3 months	417 (4·8%)	336 (4·3%)	81 (9·0%)	19·4% (15·9–23·5)
<3 months	458 (5·3%)	429 (5·5%)	29 (3·2%)	6·3% (4·4–9·0)
Two dose others	12 (0·1%)	10 (0·1%)	2 (0·1%)	16·7% (4·7–44·8)
≥3 months	7 (0·1%)	5 (0·1%)	2 (0·1%)	28·6% (8·2–64·1)
<3 months	5 (0·1%)	5 (0·1%)	0	0·0% (0·0–43·5)
Three dose BNT162b2	2432 (28·2%)	2322 (30·0%)	110 (12·2%)	4·5% (3·8–5·4)
≥3 months	296 (3·4%)	291 (3·8%)	5 (0·6%)	1·7% (0·7–3·9)
<3 months	2136 (24·7%)	2031 (26·3%)	105 (11·6%)	4·9% (4·1–5·9)
Three dose CoronaVac	1050 (12·2%)	978 (12·6%)	72 (8·0%)	6·9% (5·5–8·6)
≥3 months	371 (4·3%)	352 (4·6%)	19 (2·1%)	5·1% (3·3–7·9)
<3 months	679 (7·9%)	626 (8·1%)	53 (5·9%)	7·8% (6·0–10·1)
Two dose CoronaVac plus BNT162b2	463 (5·4%)	429 (5·5%)	34 (3·8%)	7·3% (5·3–10·1)
≥3 months	178 (2·1%)	164 (2·1%)	14 (1·6%)	7·9% (4·7–12·8)
<3 months	285 (3·3%)	265 (3·4%)	20 (2·2%)	7·0% (4·6–10·6)
Two dose BNT162b2 plus CoronaVac	29 (0·3%)	29 (0·3%)	0	0·0% (0·0–11·7)
≥3 months	3 (<0·1%)	3 (<0·1%)	0	0·0% (0·0–56·2)
<3 months	26 (0·3%)	26 (0 3%)	0	0·0% (0·0–12·9)
Three dose others	19 (0·2%)	18 (0·2%)	1 (0·1%)	5·3% (0·9–24·6)
≥3 months	4 (<0·1%)	4 (0·1%)	0	0·0% (0·0–49·0)
<3 months	15 (0·2%)	14 (0·2%)	1 (0·1%)	6·7% (1·2–29·8)

Data are n (%), unless otherwise indicated. *Overall positivity (95% CI) was 10·5% (9·8–11·1).

Table 3: **Vaccination status and risk of infection**

	Median length of follow-up (person-days)	Total length of follow-up (person-days)	Number of events	Adjusted hazard ratio (95% CI)	Vaccine effectiveness (95% CI)	p value
Asymptomatic and symptomatic infection						
Unvaccinated	31	31166	123	1 (ref)	1 (ref)	..
BNT162b2						
One dose	22	13143	40	0·84 (0·58 to 1·19)	16·5% (–19·5 to 41·6)	0·32
Two doses (≥3 months)	32	85088	323	0·99 (0·80 to 1·22)	1·1% (–22·4 to 20·1)	0·92
Two doses (<3 months)	27	14524	34	0·72 (0·49 to 1·06)	27·6% (–6·3 to 50·7)	0·10
Three doses	32	66787	110	0·59 (0·45 to 0·77)	41·4% (23·2 to 55·2)	0·0001
CoronaVac						
One dose	24	13892	54	1·02 (0·74 to 1·40)	–1·6% (–39·8 to 26·2)	0·92
Two doses (≥3 months)	21	19891	81	0·95 (0·71 to 1·26)	5·4% (–25·6 to 28·8)	0·70
Two doses (<3 months)	21	11367	29	0·77 (0·52 to 1·15)	22·7% (–15·2 to 48·2)	0·21
Three doses	36	32882	72	0·68 (0·50 to 0·91)	32·4% (9·0 to 49·8)	0·0098
CoronaVac plus BNT162b2						
Two-dose CoronaVac plus BNT162b2	36	14809	34	0·69 (0·47 to 1·01)	31·3% (–1·0 to 53·3)	0·056
Two-dose BNT162b2 plus CoronaVac	36	824	0	..	..	..
Other vaccine combination						
One dose	0	0	0	..	..	..
Two doses (≥3 months)	21	377	2	1·17 (0·27 to 5·12)	–16·8% (–412·1 to 73·4)	0·84
Two doses (<3 months)	27	129	0	..	..	..
Three doses	29	537	1	0·77 (0·12 to 4·78)	23·3% (–377·9 to 87·7)	0·78
Symptomatic infection only						
Unvaccinated	31	31166	82	1 (ref)	1 (ref)	..
BNT162b2						
One dose	22	13143	25	0·77 (0·49 to 1·21)	22·9% (–21·4 to 51·0)	0·26
Two doses (≥3 months)	32	85088	219	0·95 (0·73 to 1·24)	4·7% (–23·5 to 26·6)	0·71
Two doses (<3 months)	27	14524	23	0·68 (0·43 to 1·09)	31·6% (–9·3 to 57·2)	0·11
Three doses	32	66787	66	0·49 (0·35 to 0·69)	50·9% (31·0 to 65·0)	<0·0001
CoronaVac						
One dose	24	13892	38	1·09 (0·74 to 1·61)	–9·3% (–60·5 to 25·6)	0·65
Two doses (≥3 months)	21	19891	55	0·94 (0·66 to 1·32)	6·4% (–32·1 to 33·7)	0·71
Two doses (<3 months)	21	11367	22	0·88 (0·55 to 1·40)	12·2% (–40·0 to 44·9)	0·59
Three doses	36	32882	43	0·58 (0·40 to 0·85)	41·6% (15·0 to 59·8)	0·0049
CoronaVac plus BNT162b2						
Two-dose CoronaVac plus BNT162b2	36	14809	15	0·44 (0·25 to 0·77)	55·8% (22·9 to 74·6)	0·0040
Two-dose BNT162b2 plus CoronaVac	36	824	0	..	..	..
Other vaccine combination						
One dose	0	0	0	..	..	..
Two doses (≥3 months)	21	377	1	0·92 (0·12 to 7·08)	7·6% (–608·2 to 88·0)	0·94
Two doses (<3 months)	27	129	0	..	..	..
Three doses	29	537	0	..	..	..

Data are n, unless otherwise indicated. Data were adjusted for age group, gender, chronic illness, household size, district, housing type, Hong Kong tertiary planning unit level, and monthly household rent. Symptomatic infections were defined as those with a positive rapid antigen test result after an individuals reported at least one of 19 surveyed symptoms.

Table 4: **Effectiveness of the BNT162b2 and CoronaVac vaccines against COVID-19 omicron BA.2 infection**

two doses within 3 months of testing (table 2). For the primary series using CoronaVac, 458 (5·3%) of 8636 individuals completed the two doses 3 months before testing and 417 (4·8%) completed the two doses within 3 months of testing (table 2). As switching of vaccine between the two doses was not allowed in the primary series, only 12 (0·1%) of 8636 individuals had two doses with other vaccine combinations, and were not included in the primary analysis (table 2).

For individuals who received three doses of vaccine, 2432 (28·2%) of 8636 received three doses of BNT162b2 and 1050 (12·2%) received CoronaVac. A small proportion of individuals received a combination, either of a primary series of CoronaVac followed by a BNT162b2 booster

(463 [5·4%] of 8636 individuals), or a primary series of BNT162b2 followed by a CoronaVac booster (29 [0·3%] individuals). 19 (0·2%) of 8636 individuals received three vaccine doses in other combinations and were not included in the analysis (table 2).

Among the 886 participants aged 5–17 years, 323 (36·5%) received two doses of vaccine and 287 (32·4%) received one dose of vaccine. As only 60 (6·8%) of 886 individuals aged 5–17 years had received three doses of vaccination, the effectiveness of booster vaccination was not examined in this age group. Among the 6014 individuals aged 18–59 years, 2988 (49·7%) received three doses of vaccine and 2404 (40·0%) received two doses of vaccine. Among the 1736 individuals aged 60 years and older, 945 (54·4%) received three doses of vaccine and 513 (29·6%) received two doses of vaccine. The observed differential distribution of vaccination status by age group was largely consistent with the territory-wide figures of vaccine coverage for the population in Hong Kong (table 2).

Table 3 shows the differential risk of SARS-CoV-2 infection stratified according to vaccination status. The lowest positivity rate was observed among individuals who received three doses (5·4%, 95% CI 4·8–6·2), followed by those who received two doses within 3 months (6·8%, 5·3–8·6). Higher positivity rates were observed among individuals who received only one dose (14·7%, 12·2–17·7) or two doses at least 3 months previously (17·6%, 16·1–19·2). Detailed vaccination status by age group is shown in the appendix were shown in the appendix (pp 5–7). For all age groups, the positivity rate was lower for individuals with a more recent primary series of vaccination within 3 months compared with those who completed vaccination at least 3 months ago.

A potential attenuation of infection severity was shown in those who received a booster BNT162b2 dose compared with unvaccinated individuals, both in terms of a lower number of symptoms (6·21, SD 3·64 *vs* 8·09, 4·13; p=0·0040) and a lower mean severity score was found (8·35, 6·31 *vs* 11·56, 7·93; p=0·0068). No impact on symptom profile was observed for those who received two doses or fewer of BNT162b2 (appendix p 8).

Using unvaccinated people as the reference group in the multivariate model, the first dose of BNT162b2 vaccine provided a vaccine effectiveness of 16·5% (95% CI –19·5 to 41·6; p=0·32) against asymptomatic and symptomatic SARS-CoV-2 omicron infection (table 4). Vaccine effectiveness after two doses (ie, primary series) was not significant (27·6%, –6·3 to 50·7; p=0·10) within 3 months, and point estimates declined to a very low level of 1·1% (–22·4 to 20·1; p=0·92) at 3 months and beyond. A BNT162b2 booster vaccine improved the effectiveness to 41·4% (23·2 to 55·2; p=0·0001; figure; table 4).

A similar pattern of vaccine effectiveness for any SARS-CoV-2 infection, but with a slightly lower magnitude of protection, was given by the CoronaVac vaccine. The first dose of CoronaVac provided a vaccine effectiveness of –1·6% (95% CI –30·8 to 26·2; p=0·92) against asymptomatic and symptomatic SARS-CoV-2 omicron infection (table 4). Vaccine effectiveness after two doses was not significant within 3 months (5·4%, –25·6 to 28·8; p=0·70) or at 3 months and beyond (22·7%, –15·2 to 48·2; p=0·21). A CoronaVac booster improved the vaccine effectiveness to 32·4% (9·0 to 49·8; p=0·0098; figure; table 4). A similar amount of protection was observed for CoronaVac and BNT162b2, with non-significant relative vaccine effectiveness (appendix p 13).

The vaccine effectiveness against any infection of a booster dose using a switched vaccine type was also examined. For people who received a primary series of CoronaVac, the vaccine effectiveness for a booster dose using BNT162b2 was 31·3% (95% CI –1·0 to 53·3; p=0·056), similar to the values for a booster with the same vaccine (table 4). No significant difference in

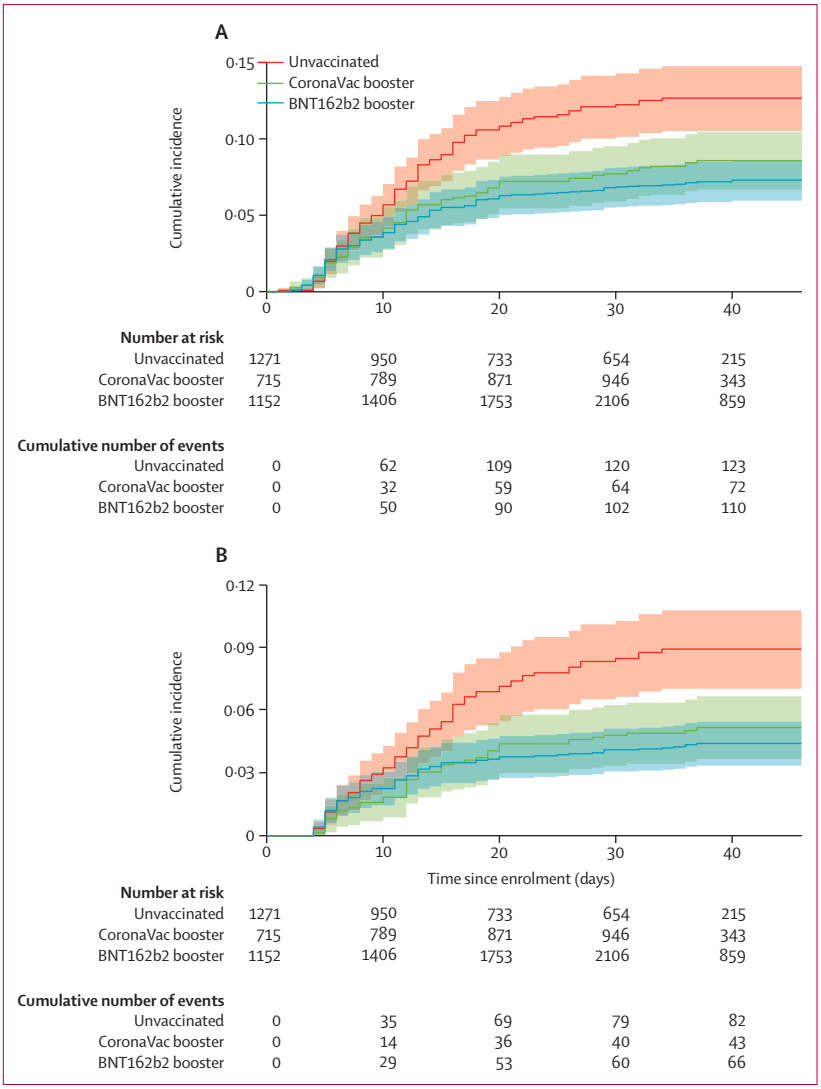

Figure: **Cumulative risk of infection with the SARS-CoV-2 omicron variant according to vaccination status in asymptomatic and symptomatic infection (A) and symptomatic infection only (B)**
Shading indicates 95% CIs.

vaccine effectiveness was found in the estimation of relative effectiveness for the types of booster dose (p=0·86; appendix p 13). The effectiveness of a CoronaVac booster after a primary series of BNT162b2 was not examined because of the small sample size.

For vaccine effectiveness against symptomatic SARS-CoV-2 omicron infection, a booster dose generally showed a similar pattern of effectiveness but conferred a higher level of protection, with vaccine effectiveness of 50·9% (95% CI 31·0–65·0; p<0·0001) for a BNT162b2 booster and 41·6% (15·0–59·8; p=0·0049) for a CoronaVac booster (table 4). A BNT162b2 booster for those who received a primary series of CoronaVac also conferred a similar significant vaccine effectiveness of 55·8% (22·9–74·6; p=0·0040) against symptomatic infection (table 4). The relative vaccine effectiveness against symptomatic infection between CoronaVac and BNT162b2 was not significant (appendix p 13).

To address the potential confounding effect of differential vaccine coverage in subpopulations, the age-specific effectiveness of different vaccine types was further examined. For all SARS-CoV-2 omicron infections, a similar non-significant protection of the first dose and primary series within 3 months was observed across all age groups (appendix pp 17, 20, 23). For adults aged 18–59 years, we observed no significant protection for the first dose of BNT162b2 (20·4%, 95% CI –30·9 to 51·6; p=0·37), first dose CoronaVac (–0·6%, –72·2 to 41·3; p=0·98), two BNT162b2 doses within 3 months (35·3%, –4·2 to 59·8; p=0·073), two CoronaVac doses within 3 months (38·2%, –19·5 to 68·0; p=0·15), or a second dose received beyond 3 months (2·5, –29·0 to 26·2; p=0·86 for BNT162b2 and –3·0, –45·9 to 27·3; p=0·87) for CoronaVac; appendix p 17). Significant protection was only observed for those who received a BNT162b2 booster vaccine, with a vaccine effectiveness of 42·1% (19·5 to 58·4; p=0·0012; appendix p 17). For symptomatic SARS-CoV-2 omicron infection, the significant protection of a BNT162b2 booster was also maintained, with a slightly higher vaccine effectiveness of 51·6% (27·7 to 67·6; p=0·0004) for those receiving a BNT162b2 primary series and 60·0% (20·8 to 79·8; p=0·0085) for those receiving a CoronaVac primary series.

For adults aged 60 years and older, no significant protection against SARS-CoV-2 omicron infection was shown after either one dose of BNT162b2 (–69·7%, 95% CI –353·1 to 36·5; p=0·29), one dose of CoronaVac (–65·0%, –219·6 to 14·8; p=0·14), two BNT162b2 doses within 3 months (–39·3%, –236·4 to 42·4; p=0·46), or two CoronaVac doses within 3 months (–65·7%, –228·5 to 16·5; p=0·15; appendix p 20). A booster vaccine of either BNT162b2 or CoronaVac did not provide significant protection against SARS-CoV-2 omicron infection for this older population, with a vaccine effectiveness of –1·5% (–101·0 to 48·7; p=0·97) and 25·2% (–56·0 to 64·1; p=0·44), respectively (appendix p 20). A similarly negligible protection for older people was observed for symptomatic omicron infection (appendix p 20).

For individuals aged 5–17 years, no significant protection against SARS-CoV-2 omicron infection was shown after one dose of BNT162b2 (32·4%, 95% CI –29·0 to 64·6; p=0·24), one dose of CoronaVac (22·7%, –38·3 to 56·8; p=0·39), two BNT162b2 doses within 3 months (3·2%, –220·7 to 70·8; p=0·96), or two CoronaVac doses within 3 months (55·6%, –50·3 to 86·9; p=0·19; appendix p 23). A similarly negligible protection for this population was observed for symptomatic omicron infection (appendix p 23). The age-specific protection conferred by either a BNT162b2 or CoronaVac booster after a primary series was not examined for those aged 5–17 years because of the small sample size.

Discussion

This prospective cohort study adopted a comprehensive non-symptom and risk-based outcome-ascertainment approach by regular rapid antigen testing to evaluate the vaccine effectiveness of the primary series and booster dose of vaccination against SARS-CoV-2 during omicron BA.2 predominance. A representative cohort that covered different population subgroups by age, gender, monthly income, and district was recruited to increase the generalisability of our findings, and stratified analysis provided an age-specific and vaccine-type-specific estimate for different vaccination statuses. Our surveillance initiative, with regular testing regardless of symptom status or exposure history, allowed assessment of vaccine effectiveness against both symptomatic and asymptomatic infection. The provision of free rapid antigen tests to all enrolled participants helped to minimise the potential effect of changing testing policy and capacity on outcome ascertainment. The exclusion of 15·3% of individuals who were previously infected was consistent with the reported local seroprevalence against BA.2 of 7·3% before the fifth wave of SARS-CoV-2 in November to December, 2021,[27] and 23·4% after the peak of the fifth wave of infection in May, 2022,[28] and might have helped us avoid wrongly attributing protection to previous infection in the vaccine effectiveness analysis. Understanding the updated effectiveness of available vaccines against infection, including asymptomatic infection, in relation to the evolving omicron variants is essential for guiding vaccination policies and informing future vaccine development.

Our findings showed that a booster dose of vaccination conferred substantial protection against SARS-CoV-2 infection by the omicron variant, including mild and asymptomatic cases. Significant protection against infection was observed only for three doses of vaccine. This finding supports the need for a booster dose for protection against the omicron variant, and fits with the current recommendation for booster doses in Hong Kong,[29] Ontario, Canada,[30] Australia,[31] and the USA.[32]

We also observed differential vaccine effectiveness for the booster dose for different age groups. Specifically, moderate and statistically significant protection from a BNT162b2 booster dose was only achieved in those aged 18–59 years, whereas no significant protection was conferred in those aged 60 years and older, which is compatible with the general finding of a lower vaccine effectiveness for older individuals in the literature.[33–36] This differential vaccine effectiveness highlights the need to explore the potential feasibility and benefit of more targeted vaccination regimens for optimising protection of different subpopulations in the community.

For the primary series of two doses of either BNT162b2 or CoronaVac completed within 3 months or at least 3 months ago, our results showed no significant protection was achieved in all age groups. Compared with a previous study on symptomatic omicron infection, our finding of no significant protection from the primary series of BNT162b2 contrasted with that study's finding of high vaccine effectiveness (65·5%, 95% CI 63·9–67·0) assessed at 4 weeks,[8] but was more similar to the study's finding of much lower vaccine effectiveness (8·8%, 7·0–10·5) at 6 months or more after vaccination.[8] Although a BNT162b2 primary series completed within 3 months did not show significant vaccine effectiveness, the higher vaccine effectiveness compared with a course completed 3 or more months ago (27·6% *vs* 1·1%) was compatible with the rapid waning of effectiveness reported in previous studies.[37] This observed difference might also have been partly due to our adjustment for immortal time bias to avoid potential wrongful attribution of protective effects to a more recent vaccination event.

Our findings showed that significant vaccine effectiveness against symptomatic or asymptomatic omicron infection was conferred by a third dose of either BNT162b2 or CoronaVac. The protection conferred by a BNT162b2 or CoronaVac booster was further increased when considering only symptomatic omicron infections. Our results were generally much lower than previously reported vaccine effectiveness of booster doses against the more severe outcomes of omicron infection, including an effectiveness of 86% against hospital admission[2] and more than 90% effectiveness against severe disease or death,[3,38-40] but were consistent with the vaccine effectiveness of 52·2% (95% CI 48·1–55·9) of three doses of BNT162b2 against symptomatic omicron BA.2 infection reported in Qatar, where universal testing allowed detection of cases of all severities.[4] Although our results were lower than the reported vaccine effectiveness in a previous study (70·2–73·5% for BNT162b2 and 32·4–51·0 % for CoronaVac) of patients with mild or moderate COVID-19 who were admitted to hospital during the same epidemic wave in Hong Kong using an ecological study design,[3] our study might capture the milder end of the spectrum of infection in the community, with most individuals not requiring medical attention. With this understanding, our findings are consistent with the overall picture of a rapidly attenuating vaccine effectiveness effect size when the examined outcomes were shifted from the more severe to the milder end of the clinical spectrum in the published literature.[1,4,39] However, as previous studies suggested that vaccination might shorten the viral shedding duration,[41,42] our study design with regular scheduled testing might help to avoid potential differential outcome ascertainment related to the duration of viral shedding, reducing the likelihood of detecting an infection among vaccinated people, and the resultant bias towards an overestimation of the vaccine effectiveness effect size.

Despite the low level of protection against infections with mild or no symptoms, the high proportion of mild infections might still impose a non-trivial collective clinical burden in the community during a rapid surge of an evolving epidemic, as in the fifth SARS-CoV-2 wave in Hong Kong. However, the high proportion of asymptomatic cases that might have been prevented by booster vaccination, which otherwise might have potentially seeded downstream secondary transmission, might help to prevent further propagation of the epidemic in the community due to the shedding of virus in the absence of awareness, appropriate management, isolation, or quarantine measures. This potential public health implication might become even more important as newer SARS-CoV-2 variants with higher transmissibility and milder clinical symptoms emerge,[43] including the new omicron variants.[44,45] Besides the indirect effect on transmission through preventing the incidence of infection, transmission might also be prevented through reduced transmissibility of infection in breakthrough cases in vaccinated people. Although current literature generally regards the vaccine effectiveness of two doses for preventing omicron transmission to be minimal,[44,46] some studies have reported modest effectiveness of a booster dose for reducing secondary transmission related to breakthrough cases in vaccinated people in households or institutional settings,[44,46,47] signifying the value and implications of the vaccine even if effectiveness against mild infection is not high. Although our study did not directly examine the outcome of transmission or viral shedding, our data did reveal a potential attenuation of infection severity in those who received a booster BNT162b2 vaccine compared with unvaccinated individuals, both in terms of a lower number of symptoms and a lower mean severity score. However, similar to the existing literature, no effect on symptom profile was observed for those who received two doses or fewer of vaccine.

The similar magnitude of vaccine effectiveness of the mRNA vaccine (BNT162b2) and inactivated vaccine (CoronaVac) implies that both vaccine types are effective against omicron infection. The similar protection achieved with either the same or different booster regimens also supports the current recommendation of BNT162b2 boosters in Hong Kong and some other countries,[48–50] which might give the advantage of

facilitating higher booster dose uptake, with the enhanced autonomy of personal preference, and lead to less issues with vaccine availability during an evolving pandemic.

This surveillance initiative is an observational study with some possible biases and should be interpreted with caution. As a history of previous PCR-confirmed infection was ascertained by self-reporting, some under-ascertainment of previous infection might have been present and affected our vaccine effectiveness estimation. However, given the straightforward and official nature of the case definition, and the lack of obvious benefit for untruthful reporting, substantial inaccurate recall might be unlikely. Government mandatory testing orders in relation to community exposure risk, which were instituted independent of vaccination status, might serve to capture some people with no symptoms and to prevent substantial differential under-ascertainment among people with different vaccination statuses.

Imperfect performance in terms of suboptimal sensitivity and specificity of rapid antigen testing might cause misclassification of infection status,[18] which is likely to be non-differential, as suggested in a systematic review of 155 studies on rapid antigen test diagnostic performance.[51] This fact might bias the estimation of the HR towards the null, and result in a potentially over-estimated vaccine effectiveness.[52] Adopting rapid antigen test brands that meet the WHO priority target product profiles for COVID-19 diagnostics[15] and FDA Emergency Use Authorization,[16] as in our study, would thus be an important step to minimise potential bias in vaccine effectiveness estimation.

The availability of rapid antigen testing kits for regular self-testing, irrespective of symptom status or exposure risk, should facilitate early identification of both symptomatic and asymptomatic cases.[53] However, case counting on the basis of PCR testing or voluntary rapid antigen test result reporting might underestimate the risk of infection and case ascertainment, as testing can be affected by any change in testing policy, health seeking behaviour, laboratory testing capacity, or incomplete reporting practices due to the fear of isolation or quarantine order being imposed.

As the changing symptom pattern after rapid antigen test positivity was not continuously monitored in our surveillance platform, classification as either symptomatic or asymptomatic in the current study was based primarily on the data at the time of the positive rapid antigen test. As some people who were asymptomatic on original testing might develop symptoms later (ie, pre-symptomatic), this strategy might affect precise estimation of the vaccine effectiveness against symptomatic infection; however, this should have no effect on the estimation of vaccine effectiveness against both symptomatic and asymptomatic infection.

Although behavioural factors, such as wearing a mask and physical distancing, might affect infection risk and be potential residual confounders in this study, a substantial difference between vaccinated and unvaccinated participants, or between individuals who received two doses of vaccine and those who received three doses, was not expected, as universal mask wearing and stringent social distancing requirements were legally required for the whole community during the study period in Hong Kong, irrespective of vaccination.[54] Another limitation was our inability to estimate vaccine effectiveness for some subgroups, due to the relatively small number of individuals who received some vaccine regimens. As the local population had recently started to receive booster doses, and booster doses had only recently been approved for children, the additional protection achievable by a booster dose in children, and the waning effectiveness of booster doses over time, were not evaluated. A further study examining the effect of booster doses on younger age groups and the waning effectiveness of booster doses is warranted, to inform the assessment of and optimise vaccine policy in the evolving pandemic.

In conclusion, we assessed the vaccine effectiveness of the BNT162b2 and CoronaVac vaccines in different regimens and age groups and found that a BNT162b2 or CoronaVac booster dose achieved significant protection against omicron infection in Hong Kong. These updated vaccine effectiveness estimates allow assessment of the public health impact of COVID-19 vaccines for preventing transmission of symptomatic and asymptomatic infections in the community. We found similar effectiveness for both vaccine types, and a potential association of effectiveness with age. Our findings support the use of different booster vaccination regimens from the primary series during the evolving pandemic.

Contributors

GML and DKMI conceived and designed the study. NNYT and HCS collected the data. NNYT and DKMI accessed and verified the data. BJC advised on the statistical analysis. NNYT did the statistical analysis. NNYT and DKMI interpreted the data. NNYT and DKMI wrote the first draft of the manuscript, and all authors provided critical review and revision of the text and approved the final version for publication. All authors had full access to all the data in the study and accept final responsibility for the decision to submit for publication.

Declaration of interests

BJC reports honoraria from AstraZeneca, Fosun Pharma, GlaxoSmithKline, Moderna, Pfizer, Roche, and Sanofi Pasteur. All other authors declare no competing interests.

Data sharing

The data are available from the corresponding author upon reasonable request.

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