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Original Article

Vaccine effectiveness against Delta, Omicron BA.1, and BA.2 in a highly vaccinated Asian setting: a test-negative design study

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ABSTRACT

Objectives: We compared the vaccine effectiveness over time of the primary series and booster against infection and severe disease with the Delta, Omicron BA.1, and BA.2 variants in Singapore, an Asian setting with high vaccination coverage.

Methods: We conducted a test-negative case-control study on all adult residents in Singapore who underwent PCR testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in acute hospitals. Individuals with a negative PCR from 1 September, 2021, to 30 November, 2021, and 1 December, 2021, to 25 April, 2022, served as controls for the Delta and Omicron variants respectively, and PCR-positive individuals within these two time periods served as cases. Associations between vaccination status and SARS-CoV-2 infection and severe disease with the Delta or Omicron variants were measured using Poisson regressions. Vaccine effectiveness was calculated by taking 1 minus risk ratio.

Results: There were 68 114 individuals comprising 58 495 controls and 9619 cases for the Delta period, of whom 53 093 completed the primary series and 9161 were boosted. For the Omicron period, 104 601 individuals comprising 80 428 controls, 8643 BA.1 cases, and 15 530 BA.2 cases were included, of whom 29 183 and 71 513 were vaccinated with the primary series and boosted, respectively. The primary series provided greater protection against infection with Delta (45%, 95% CI 40−50%) than against infection with Omicron (21%, 95% CI 7−34% for BA.1; 18%, 95% CI 6−29% for BA.2) at <2 months from vaccination. Vaccine effectiveness of the booster was similar against infection with BA.1 (44%, 95% CI 38−50%) and BA.2 (40%, 95% CI 35−40%). Protection against severe disease by the booster for BA.1 (83%, 95% CI 76−88%) and BA.2 (78%, 95% CI 73−82%) was comparable to that by the primary series for Delta (80%, 95% CI 73−85%).

Conclusion: Our findings support the use of a booster dose to reduce the risk of severe disease and mitigate the impact on the healthcare system in an Omicron-predominant epidemic. **Celine Y. Tan, Clin Microbiol Infect 2022;▪:1**

Introduction

The Delta variant (B.1.617.2) of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first detected in India in October 2020 and became the dominant strain causing coronavirus disease 2019 (COVID-19) globally by mid-2021. In November 2021, the Omicron variant (B.1.1.529) was designated a variant of concern by the WHO after being reported in South Africa and quickly

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replaced Delta as the most prevalent strain worldwide. While the BA.1 sublineage accounted for the majority of Omicron cases initially, BA.2 became the dominant sublineage worldwide by March 2022 and is associated with increased transmissibility compared with BA.1 [1].

Singapore, a city-state with a population of 5.5 million, faced a surge in cases caused by Delta from May 2021, peaking at >5000 cases daily in October 2021 [2]. This was followed by the Omicron variant, first detected on 2 December, 2021 [3], which became the dominant strain by January 2022. Despite high vaccination and booster rates, with more than 90% of the population vaccinated with the primary series and 70% receiving a booster dose under the COVID-19 National Vaccination Programme [4], Singapore endured an Omicron wave which peaked at >26 000 cases daily on 22 February, 2022 [2]. The wave was initially driven by BA.1 from 2 December, 2021, to 4 February, 2022, followed by a period of co-dominance, then predominantly by BA.2 from 17 February, 2022. Despite the lower severity of Omicron [5–7] and higher proportion of boosted individuals in Singapore, the Omicron wave resulted in higher strain on acute hospital resources compared with the Delta wave.

Ensuring that we have sufficient healthcare resources to manage variants of concern requires understanding of the effectiveness of mitigation measures, in particular the impact of vaccines in reducing the incidence of SARS-CoV-2 infections. Data comparing vaccine effectiveness (VE) against infection (VE-I) and against severe disease (VE-S) among cases with BA.1 and BA.2 are currently limited. A study from the United Kingdom found no evidence that VE against symptomatic disease differed between the two sublineages [8], whereas a Swedish study found that VE-S was comparable between BA.1 and BA.2 among those who received three doses but decreased markedly against BA.2 among those who received only two doses [9]. Studies of relative VEs against the Delta and Omicron variants within Asian populations are also lacking.

To address these knowledge gaps, this study aims to compare VE-I and VE-S among cases with Delta, Omicron BA.1, and BA.2 in Singapore, an Asian setting with high vaccination coverage. Using a test-negative design, our analysis focuses on individuals presenting at acute hospitals because these are symptomatic cases which impose a high burden on healthcare resources available to manage patients with COVID-19.

Methods

We conducted a test-negative case-control study to compare VE against PCR-confirmed infection and severe disease among the Delta, Omicron BA.1, and BA.2 variants. The test-negative design was adopted as recommended by WHO to evaluate COVID-19 VE [10]. The study population comprised Singapore residents aged ≥18 years without previous SARS-CoV-2 infection who underwent a PCR test at any acute hospital in Singapore. PCR tests are conducted on individuals who present to a hospital with clinical suspicion of COVID-19, such as acute respiratory symptoms, or require admission for any reason. Only individuals who presented to acute hospitals were included to minimize selection bias caused by differential health-seeking behaviour and changing protocols for PCR testing in the community during the pandemic.

Individuals who tested PCR-negative from 1 September, 2021, to 30 November, 2021, served as controls for the Delta variant, and those who tested PCR-negative from 1 December, 2021, to 25 April, 2022, served as controls for the Omicron variant. For individuals with multiple PCR-negative results, only the most recent record was used. Individuals with a positive PCR within these two time periods served as cases. Severe disease was defined as requiring oxygen supplementation in hospital, admission to the intensive care unit, or death. Individuals who completed two doses of Pfizer-BioNTech BNT162b2 or Moderna mRNA-1273 or three doses of Sinovac-CoronaVac or Sinopharm BBIBP-CorV were considered fully vaccinated with the primary series, and those who received an additional dose of mRNA vaccine were considered boosted.

Poisson regressions were used to estimate relative risk ratios (RR) of PCR-confirmed infection and severe disease, adjusting for sex, age, race, housing type (as a proxy for socioeconomic status), and calendar week (to account for varying force of infection across time). The reference group comprised unvaccinated and partially vaccinated individuals. VE was calculated by taking 1 minus the relative risk [11], with the lower bound set as 0%.

Two sets of analyses were done; the first set using only cases with variant confirmed by whole genome sequencing (WGS) or screened by S-gene target failure (SGTF) testing. In line with the time periods of the Delta and Omicron waves in Singapore, we assumed that all SGTF-negative cases reported on or prior to 15 January, 2022, were of the Delta variant, and SGTF-negative cases after 15 January, 2022, were of the BA.2 variant. SGTF-positive cases were assumed to be of the BA.1 variant during the Omicron period.

In the second set of analyses, all cases were used, including those without WGS and SGTF results. For these cases, the variant was imputed based on reporting date; all cases reported before 1 December, 2021, were assumed to be of the Delta variant (because all cases sequenced during that period were Delta), and cases from 1 December, 2021, could be of the Delta or Omicron variant. To impute the sublineage of Omicron cases, regression imputation was used, specifically a logistic regression model based on age and residency status or the reporting date. Further details can be found in the supplementary material.

Data were collected from official databases maintained by the Ministry of Health, Singapore, including national records of all confirmed SARS-CoV-2 infections, severe COVID-19 cases, and vaccines administered. The study was conducted as part of the national public health response under the Infectious Diseases Act, Singapore, with exemption from ethics review. Analysis was performed using Stata Statistical Software Release 17 (StataCorp LP, College Station, TX, USA).

Results

In total, 68 114 individuals with PCR tests done in acute hospitals in Singapore were included for the Delta variant period, comprising 58 495 controls with a negative PCR and 9619 cases with a positive PCR, of whom 191 had the variant confirmed by WGS and/or SGTF screening (Table 1). 5860 (8.6%) were unvaccinated or partially vaccinated, 53 093 (77.9%) completed the primary series, and 9161 (13.4%) were boosted. For the Omicron variant period, 104 601 individuals were included, comprising 80 428 controls, 8643 BA.1 cases, and 15 530 BA.2 cases. Among these, 3287 BA.1 cases and 2921 BA.2 cases had WGS and/or SGTF testing results. 3905 (3.7%), 29 183 (27.9%) and 71 513 (68.4%) were unvaccinated or partially vaccinated, fully vaccinated with the primary series, and boosted, respectively. The distribution of vaccines received by the study population is presented in Table S1.

Vaccine effectiveness against infection

From analysis of all cases, including those with the variant imputed, completion of the primary series reduced the risk of infection with Delta to a greater extent compared with BA.1 and BA.2 (Table 2). The adjusted RR of infection with Delta was 0.55 (95% CI 0.50–0.60) at <2 months from vaccination. Comparatively, the primary series provided less protection against infection with Omicron. The risk of infection with BA.1 and BA.2 was 0.79 (95% CI

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Table 1
Distribution of vaccination status and variant type of cases and controls

Vaccination status	Interval since vaccination (mo)	Delta variant (n = 68 114), n (%)			Omicron BA.1 variant (n = 89 071), n (%)			Omicron BA.2 variant (n = 95 958), n (%)		
		Negative controls (n = 58 495)	Cases		Negative controls (n = 80 428)	Cases		Negative controls (n = 80 428)	Cases	
			WGS/SGTF subset (n = 191)	All cases (n = 9619)		WGS/SGTF subset (n = 3287)	All cases (n = 8643)		WGS/SGTF subset (n = 2921)	All cases (n = 15 530)
Unvaccinated/ partially vaccinated		4368 (7.5%)	38 (19.9%)	1492 (15.5%)	2616 (3.3%)	150 (4.6%)	411 (4.8%)	2616 (3.3%)	200 (6.8%)	878 (5.7%)
Vaccinated with primary series	<2	7480 (12.8%)	22 (11.5%)	847 (8.8%)	1615 (2.0%)	83 (2.5%)	189 (2.2%)	1615 (2.0%)	66 (2.3%)	233 (1.5%)
	2–4	11,957 (20.4%)	32 (16.8%)	2174 (22.6%)	5064 (6.3%)	246 (7.5%)	618 (7.2%)	5064 (6.3%)	207 (7.1%)	844 (5.4%)
	4–5	7508 (12.8%)	28 (14.7%)	1148 (11.9%)	5200 (6.5%)	261 (7.9%)	617 (7.1%)	5200 (6.5%)	167 (5.7%)	713 (4.6%)
	5–6	6930 (11.8%)	25 (13.1%)	1474 (15.3%)	4090 (5.1%)	341 (10.4%)	793 (9.2%)	4090 (5.1%)	172 (5.9%)	816 (5.3%)
	≥6	12,143 (20.8%)	38 (19.9%)	1432 (14.9%)	6261 (7.8%)	320 (9.7%)	874 (10.1%)	6261 (7.8%)	198 (6.8%)	1256 (8.1%)
Vaccinated with primary series and boosted	<2	7756 (13.3%)	8 (4.2%)	1019 (10.6%)	16,737 (20.8%)	566 (17.2%)	1533 (17.7%)	16,737 (20.8%)	379 (13.0%)	2344 (15.1%)
	2–4	351 (0.6%)	0 (0.0%)	30 (0.3%)	22,073 (27.4%)	955 (29.1%)	2219 (25.7%)	22,073 (27.4%)	616 (21.1%)	3257 (21.0%)
	4–5	1 (0.0%)	0 (0.0%)	2 (0.0%)	8130 (10.1%)	332 (10.1%)	1236 (14.3%)	8130 (10.1%)	479 (16.4%)	2724 (17.5%)
	≥5	1 (0.0%)	0 (0.0%)	1 (0.0%)	8642 (10.7%)	33 (1.0%)	153 (1.8%)	8642 (10.7%)	437 (15.0%)	2465 (15.9%)

COVID-19, coronavirus disease 2019; SGTF, S-gene target failure; WGS, whole genome sequencing.

0.66–0.93) and 0.82 (95% CI 0.71–0.94), respectively, at <2 months from vaccination. The VE-I of the primary series against Delta was 45% (95% CI 40–50%) at <2 months from vaccination and 26% (95% CI 21–32%) at 5–6 months from vaccination compared with 3% (95% CI 0–14%) to 21% (95% CI 7–34%) against BA.1, and 9% (95% CI 0–17%) to 18% (95% CI 6–29%) against BA.2 (Fig. 1).

Similarly, among those who received the booster dose, the risk of infection with Delta was lower than that with both Omicron sublineages. Adjusted RR was 0.32 (95% CI 0.29–0.35), 0.56 (95% CI 0.50–0.62), and 0.60 (95% CI 0.56–0.65) for Delta, BA.1, and BA.2, respectively, within the first 2 months of the booster. A slight booster waning effect was observed, with RR for BA.1 and BA.2 increasing to 0.64 (95% CI 0.52–0.77) and 0.70 (95% CI 0.64–0.75), respectively, ≥5 months from the booster. The VE-I of the booster was 68% (95% CI 65–71%) against Delta compared with 28% (95% CI 19–35%) to 44% (95% CI 38–50%) against BA.1, and 28% (95% CI 23–34%) to 40% (95% CI 35–44%) against BA.2. When the analysis was restricted to cases who had WGS and/or SGTF results, similar patterns were observed, although the RR estimates were lower (with wider CIs).

Vaccine effectiveness against severe disease

Analysis of all cases, including those with variant imputed, found that the primary series conferred greatest protection against severe disease from Delta. Among those who completed the primary series <2 months prior, adjusted RR of severe disease with Delta variant was 0.20 (95% CI 0.15–0.27) relative to those who were unvaccinated or partially vaccinated. This was markedly lower than adjusted RRs of 0.59 (95% CI 0.39–0.89) and 0.64 (95% CI 0.46–0.91) for BA.1 and BA.2, respectively (Table 3). Boosters also provided most significant risk reduction against severe illness for Delta, with an adjusted RR of 0.04 (95% CI 0.03–0.06) compared with 0.17 (95% CI 0.12–0.24) and 0.22 (95% CI 0.18–0.27) for BA.1 and BA.2, respectively, within 2 months from the booster dose.

A minimal waning effect of the primary series and boosters was observed against all three variants. The VE-S of the primary series ranged from 80% (95% CI 73–85%) to 86% (95% CI 80–90%) against Delta compared with 39% (95% CI 18–55%) to 60% (95% CI 43–72%) and 29% (95% CI 12–43%) to 53% (95% CI 41–62%) against BA.1 and BA.2, respectively. Boosters generally provided good protection

Table 2
Relative risk ratios of COVID-19 infection

Vaccination status	Interval since vaccination (mo)	Subset of cases which were sequenced and/or tested for SGTF, RR (95% CI)			All cases, including those with variant imputed, RR (95% CI)		
		Delta	Omicron BA.1	Omicron BA.2	Delta	Omicron BA.1	Omicron BA.2
Unvaccinated/ partially vaccinated		1 [Ref]	1 [Ref]	1 [Ref]	1 [Ref]	1 [Ref]	1 [Ref]
Vaccinated with primary series	<2	0.43 (0.25–0.73)	0.82 (0.63–1.08)	0.84 (0.64–1.11)	0.55 (0.50–0.60)	0.79 (0.66–0.93)	0.82 (0.71–0.94)
	2–4	0.39 (0.24–0.64)	0.85 (0.69–1.04)	0.90 (0.74–1.10)	0.65 (0.60–0.69)	0.82 (0.72–0.93)	0.88 (0.80–0.96)
	4–5	0.52 (0.32–0.87)	0.87 (0.71–1.06)	0.88 (0.72–1.09)	0.63 (0.58–0.68)	0.80 (0.71–0.91)	0.87 (0.78–0.96)
	5–6	0.41 (0.24–0.68)	1.03 (0.85–1.25)	0.85 (0.69–1.04)	0.74 (0.68–0.79)	0.97 (0.86–1.10)	0.91 (0.83–1.00)
	≥6	0.47 (0.30–0.76)	0.89 (0.73–1.09)	0.62 (0.51–0.75)	0.56 (0.52–0.60)	0.87 (0.78–0.99)	0.82 (0.75–0.89)
Vaccinated with primary series and boosted	<2	0.10 (0.04–0.21)	0.55 (0.46–0.66)	0.43 (0.36–0.52)	0.32 (0.29–0.35)	0.56 (0.50–0.62)	0.60 (0.56–0.65)
	2–4	—	0.66 (0.55–0.78)	0.49 (0.41–0.57)	—	0.61 (0.55–0.68)	0.62 (0.58–0.67)
	4–5	—	0.72 (0.60–0.88)	0.54 (0.46–0.64)	—	0.72 (0.65–0.81)	0.72 (0.66–0.77)
	≥5	—	0.61 (0.41–0.91)	0.50 (0.42–0.59)	—	0.64 (0.52–0.77)	0.70 (0.64–0.75)

COVID-19, coronavirus disease 2019; RR, relative risk ratio; SGTF, S-gene target failure.

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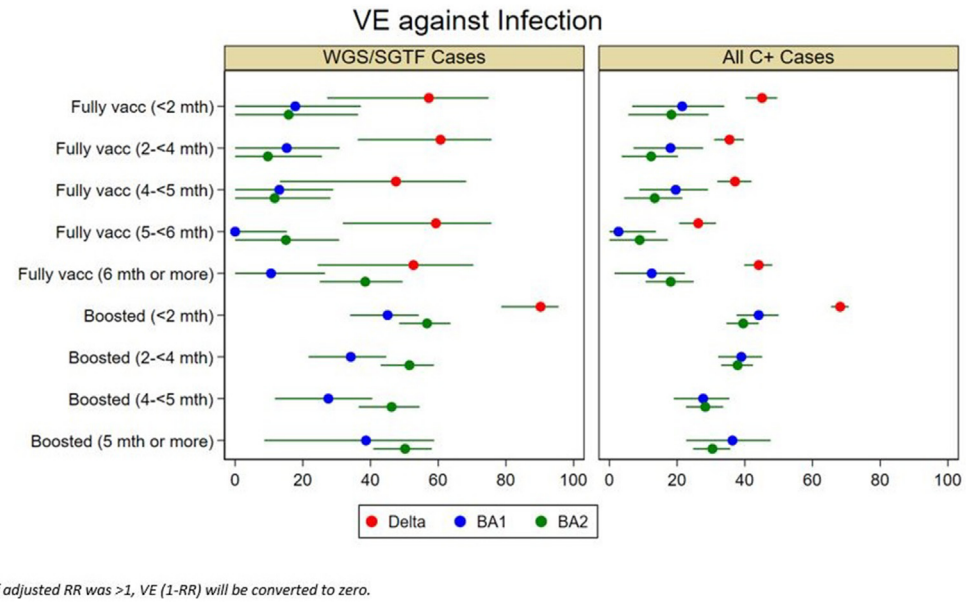

Fig. 1. Vaccine effectiveness against infection (VE-I) over time by vaccination status and variant type. If adjusted relative risk ratio (RR) was >1, VE (1-RR) will be converted to zero.

against severe disease, with VE-S of 96% (95% CI 94–97%) against Delta, 83% (95% CI 76–88%) to 86% (95% CI 74–92%) against BA.1, and 76% (95% CI 71–81%) to 81% (95% CI 77–85%) against BA.2 (Fig. 2). Results from the analysis restricted to cases which were sequenced and/or tested for SGTF were concordant, with RR estimates lower for VE-S of the primary series but largely similar for boosters.

Discussion

In this study, we found VE-I of the primary series and booster to be consistently higher against Delta compared with BA.1 and BA.2, congruous with numerous studies comparing the effectiveness of various vaccines (BNT162b2, mRNA-1273, and AstraZeneca ChAdOx1 nCoV-19) against infection with Delta and Omicron [12–14]. These results are aligned with *in vitro* neutralization assays showing greater immune evasion in Omicron [15–17] and lower infection rates during the Delta wave compared with that during the Omicron wave in Singapore.

Our results showed that the primary series had little-to-no efficacy against BA.1 or BA.2 infection, with 95% CIs close to or crossing 1. A study in Qatar similarly found that two-dose vaccination had negligible effectiveness against either Omicron sublineage [18]. While the researchers had attributed the findings to most individuals receiving their second doses >8 months earlier, our findings were consistent across various intervals from vaccination. In addition to the greater infectivity and vaccine-escape capability by Omicron [15–17], individuals in Singapore who were not fully vaccinated were subject to vaccination-differentiated measures designed to reduce exposure to settings at high risk of transmission, which could confer some protection against infection and contribute to the limited risk reduction observed.

While VE-S of the primary series and booster was consistently higher against Delta than BA.1 and BA.2, the level of protection provided by the booster against severe illness with BA.1 and BA.2 was comparable to that of the primary series against Delta. This was consistent with a U.S. study which found that three vaccine doses were required to achieve similar protection against Omicron to that provided by two doses against Delta [19]. Because of the staggered rollout of boosters in Singapore, the booster coverage was only about 10% during the Delta wave but increased to >60% by February 2022 at the peak of the Omicron wave [4], allowing the population to maintain adequate levels of protection against severe disease.

Table 3
Relative risk ratios of severe disease from COVID-19

Vaccination status	Interval since vaccination (mo)	Subset of cases which were sequenced and/or tested for SGTF, RR (95% CI)			All cases, including those with variant imputed, RR (95% CI)		
		Delta	Omicron BA.1	Omicron BA.2	Delta	Omicron BA.1	Omicron BA.2
Unvaccinated/partially vaccinated		1 [Ref]	1 [Ref]	1 [Ref]	1 [Ref]	1 [Ref]	1 [Ref]
Vaccinated with primary series	<2	0.20 (0.04–0.90)	0.58 (0.32–1.06)	0.46 (0.26–0.83)	0.20 (0.15–0.27)	0.59 (0.39–0.89)	0.64 (0.46–0.91)
	2–4	0.06 (0.01–0.48)	0.59 (0.37–0.93)	0.71 (0.51–0.99)	0.16 (0.13–0.20)	0.61 (0.45–0.82)	0.71 (0.57–0.88)
	4–5	0.18 (0.04–0.84)	0.35 (0.20–0.61)	0.47 (0.31–0.71)	0.14 (0.10–0.20)	0.40 (0.28–0.57)	0.63 (0.49–0.80)
	5–6	0.28 (0.09–0.86)	0.38 (0.22–0.67)	0.55 (0.38–0.79)	0.19 (0.15–0.24)	0.42 (0.29–0.61)	0.64 (0.51–0.81)
	≥6	0.19 (0.05–0.69)	0.40 (0.24–0.66)	0.38 (0.27–0.55)	0.16 (0.13–0.21)	0.50 (0.36–0.68)	0.47 (0.38–0.59)
Vaccinated with primary series and boosted	<2	0.03 (0.00–0.23)	0.17 (0.11–0.28)	0.18 (0.12–0.25)	0.04 (0.03–0.06)	0.17 (0.12–0.24)	0.22 (0.18–0.27)
	2–4	—	0.15 (0.10–0.23)	0.14 (0.10–0.20)	—	0.15 (0.11–0.20)	0.19 (0.15–0.23)
	4–5	—	0.14 (0.08–0.22)	0.22 (0.16–0.30)	—	0.14 (0.10–0.20)	0.24 (0.19–0.29)
	≥5	—	0.11 (0.05–0.27)	0.14 (0.10–0.19)	—	0.14 (0.08–0.26)	0.19 (0.16–0.24)

COVID-19, coronavirus disease 2019; RR, relative risk ratio; SGTF, S-gene target failure.

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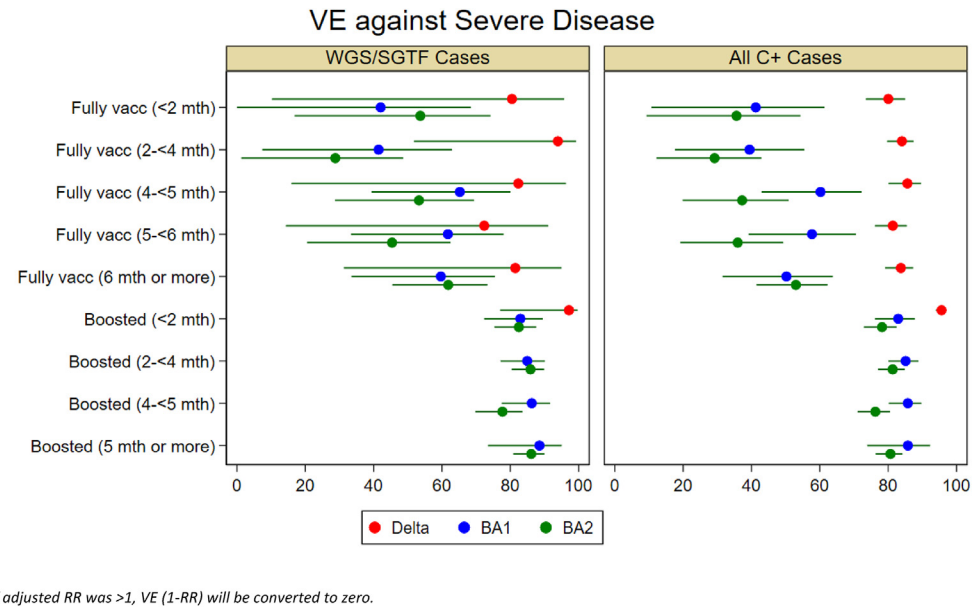

Fig. 2. Vaccine effectiveness against severe disease (VE-S) over time by vaccination status and variant type. If adjusted relative risk ratio (RR) was >1, VE (1-RR) will be converted to zero.

Coupled with the lower intrinsic severity of Omicron compared with Delta [20], Singapore observed lower rates of severe disease and case fatality during the Omicron wave.

In a comparison of BA.1 and BA.2, while the primary series provided varying degrees of protection against infection and severe disease in our study, VE-I and VE-S of the booster were similar against both sublineages. Results from a study in Qatar similarly found that three doses of BNT162b2 or mRNA-1273 (without prior infection) provided comparable levels of protection against symptomatic BA.1 and BA.2 infections. Boosters with BNT162b2 also had comparable efficacies against severe, critical, or fatal disease among cases infected with BA.1 (97.5%, 95% CI 71.7—99.8%) and BA.2 (98.2%, 95% CI 91.9—99.6%) [18]. The markedly higher VE-S observed in Qatar could be due to their unusually young demographics, with only 9% of residents ≥50 years old, compared with Singapore which has a significantly older population, comprising 38% of residents aged ≥50 years old [21], with higher risk of severe disease. Studies also found that neutralising titres by vaccine-elicited sera were similar against the two sublineages, with median titres only slightly lower for BA.2, suggesting that the growth advantage of BA.2 over BA.1 is probably related to other factors, such as increased transmissibility, rather than enhanced immune evasion by BA.2 [22—24].

Of note, while we observed a slight booster waning effect against BA.1 and BA.2 infection, this was not observed for VE-S. Findings from the United Kingdom also showed that VE of the booster against infection with both Omicron sublineages declined at a similar rate, but provided longer lasting protection against severe disease [8], suggesting that boosters remain relevant in providing sustained protection against severe BA.1 and BA.2 illnesses.

The key strength of this study is the application of a test-negative case-control design on national level data on all individuals presenting at acute hospitals. This reduces confounding and selection bias from differential healthcare-seeking behaviour, compared to other VE estimation methods [10,25]. Our study relies on healthcare administrative system and lab-reported data, and does not suffer from potential recall bias of self-reported studies. Access to healthcare is generally universal in Singapore because of government subsidy in public hospitals and mandatory health insurance and savings for all residents.

Despite these strengths, this study has several limitations. First, there is possible misclassification of variant type from imputation because not all cases were sequenced or SGTF-screened. However, we show that an analysis of subset of cases with variant confirmed by WGS and/or SGTF screening produced similar results. Second, the study population only included individuals who presented to acute hospitals; hence, the results may not be generalisable to cases with milder symptoms. Third, there might be residual confounding from co-morbidities or other factors affecting vaccination status or disease severity.

Conclusion

Our study conducted in a highly vaccinated Asian population adds to the body of evidence that boosters confer greater protection against Delta and Omicron variants compared with primary series alone, and VE-I and VE-S of boosters is greater against Delta compared with Omicron but comparable between BA.1 and BA.2. VE-S of the booster against both Omicron sublineages was comparable to that of the primary series against Delta, highlighting the utility of boosters in maintaining sustained protection against severe COVID-19. With the emergence of BA.4 and BA.5, future studies are needed to estimate VE against these Omicron sublineages. Although the Omicron variant causes milder COVID-19, our data support similar studies in the benefit of a booster dose to reduce the impact on public healthcare and individual morbidity and mortality from an Omicron epidemic.

Author contributions

C.Y.T. and C.J.C. were involved in the study conception and writing of the manuscript. D.P. was involved in the study conception, data analysis, and writing of the manuscript. V.L. and B.O. were involved in the study conception and provided supervision. D.C.L. was involved in the study conception and critical revision of the

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manuscript. K.B.T. was involved in the study conception, verification of data analysis, and critical revision of the manuscript.

Transparency declaration

The authors declare that they have no conflict of interest.

Appendix B. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2022.08.002.

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