

Supplementary Appendix

Supplement to: Tan SHX, Cook AR, Heng D, Ong B, Lye DC, Tan KB. Effectiveness of BNT162b2 vaccine against omicron in children 5 to 11 years of age. *N Engl J Med*. DOI: 10.1056/NEJMoa2203209

This appendix has been provided by the authors to give readers additional information about the work.

Supplementary Appendix

Contents

Methods.....	2
Methods: Secondary Analysis 1 – Rates of Infection and Hospitalizations by Time from Vaccination	3
Methods: Secondary Analysis 2 and 3– Analyses of Effectiveness of BNT-162b2 Vaccine Against SARS-CoV-2 Infections and Hospitalizations by Age Group and Time Period.....	4
Methods: Secondary Analysis 4 – Effectiveness of BNT-162b2 Vaccine Against SARS-CoV-2 Infections and Hospitalizations (adjusted for geographical region).....	5
Methods: Secondary Analysis 5 – Matching	6
Figure S1 Incidence of All Confirmed Infections in Unvaccinated Children by Date (red) and Modeled Incidence with 95% Confidence Intervals (black).....	8
Figure S2 Incidence of All Confirmed Infections in Partially Vaccinated Children by Date (blue) and Modeled Incidence with 95% Confidence Intervals (black).....	8
Figure S3 Incidence of All Confirmed Infections in Fully Vaccinated Children by Date (gold) and Modeled Incidence with 95% Confidence Intervals (black).....	9
Figure S4 Distribution of Time Interval between First and Second Vaccine Dose Among Fully Vaccinated Individuals	9
Table S1 Estimated Effectiveness of BNT-162b2 Vaccine Against SARS-CoV-2 Infections and Hospitalizations by Time Since Vaccination.....	10
Table S2 Estimated Effectiveness of BNT-162b2 Vaccine Against SARS-CoV-2 Infections and Hospitalizations by Age Group.....	12
Table S3 Estimated Effectiveness of BNT-162b2 Vaccine Against SARS-CoV-2 Infections and Hospitalizations by Time Period.....	13
Table S4 Estimated Effectiveness of BNT-162b2 Vaccine Against SARS-CoV-2 Infections and Hospitalizations, adjusted for Geographical Region.....	15
Table S5 Estimated Effectiveness of BNT-162b2 Vaccine Against SARS-CoV-2 Infections and Hospitalizations by Matched Analysis.....	16
References	17

Methods

The BNT162b2 (Pfizer-BioNTech) vaccine was first authorized for use in Singapore under the Pandemic Special Access Route (PSAR) in December 2020. Singapore has a high vaccination rate with coverage of over 96% of the population aged 12 years and above since December 2021. Vaccinations for children were administered at 15 designated pediatric vaccination centres islandwide free of charge. Mobile vaccination teams were also deployed to administer vaccines for children enrolled in special education schools. Through the study period from January 21 to April 8, 2022, there was an increasing number of confirmed infections over time up to a peak in end February 2022, which declined thereafter.

Methods: Secondary Analysis 1 – Rates of Infection and Hospitalizations by Time from

Vaccination

The rate of infections and hospitalizations across vaccinated groups by time from vaccination was also assessed (Table S1). Compared to the unvaccinated, vaccine effectiveness for all confirmed infections was 20.9% (95% CI, 16.6 to 25.0), -1.3% (95% CI, -5.1 to 2.4), 2.0% (95% CI, -1.0 to 4.8), 21.9% (95% CI, 18.1 to 25.6), and 35.7% (95% CI, 33.0 to 38.2) 1 to 6 days, 7 to 14 days, 15 to 29 days, 30 or more days after vaccination with one dose, and 1 to 6 days after the second dose respectively. Vaccine effectiveness for all confirmed infections for the fully vaccinated group was 48.8% (95% CI, 46.9 to 50.8), 37.6% (95% CI, 35.7 to 39.3), 28.5% (95% CI, 26.3 to 30.7), and 25.6% (95% CI, 19.3 to 31.5) 7 to 14 days, 15 to 29 days, 30 to 59, and 60 or more days after vaccination with two doses respectively.

Methods: Secondary Analysis 2 and 3– Analyses of Effectiveness of BNT-162b2 Vaccine Against SARS-CoV-2 Infections and Hospitalizations by Age Group and Time Period

A secondary analysis was carried out by age group, with race, sex, housing type and calendar date as covariates. A separate analysis was carried out by time period, with age, race, sex, housing type and calendar date as covariates.

Results of vaccine effectiveness are similar across age groups. Compared to the unvaccinated group, vaccine effectiveness against all confirmed infections after full vaccination was 39.6% (95% CI, 36.8 to 42.3), 37.4% (95% CI, 35.2 to 39.5), and 33.8% (95% CI, 30.6 to 36.9) for children aged 5 to 6 years, 7 to 9 years, and 10 to 11 years respectively. Vaccine effectiveness against hospitalization was 75.7% (95% CI, 46.8 to 88.9), 85.1% (95% CI, 73.3 to 91.6), and 82.9% (95% CI, 66.9 to 91.2) for children aged 5 to 6 years, 7 to 9 years, and 10 to 11 years respectively (Table S2).

Similar estimates of vaccine effectiveness were obtained across time periods (Table S3).

Methods: Secondary Analysis 4 – Effectiveness of BNT-162b2 Vaccine Against SARS-CoV-2

Infections and Hospitalizations (adjusted for geographical region)

A secondary analysis was carried out with constituencies (electoral boundaries), a proxy for residential/geographical region, as a covariate, in addition to age, race, sex, housing type and calendar date. The map of constituencies in Singapore is available [here](#).¹

Results on vaccine effectiveness (Table S4) are similar to that reported without the inclusion of constituencies as a covariate (Table 2).

Methods: Secondary Analysis 5 – Matching

We conducted a matching approach following Dagan et al.,² comparing the risk of matched individuals rather than deriving regression-adjusted rates based on person-days in our main method.

Separately for individuals who have been fully vaccinated (at least 7 days after their second dose) and those who have been partially vaccinated (1 day after their first dose to 6 days after their second dose), we matched those who were vaccinated with those who had not been vaccinated. We matched individuals on a 1:1 basis on the following characteristics: age (in years), race, sex, and housing-type as a proxy for socio-economic status. Vaccinated individuals had their observation period started 7 days after their second dose (fully vaccinated), or 1 day after their first vaccine dose (partially vaccinated). Matched unvaccinated individuals also had their observation periods starting on similar dates. Individuals in a pair were followed up until time of infection, and were censored at the end of the study, or at the time the unvaccinated individual received the first dose, or past the 6th day after the partially vaccinated individual received the second dose.

After matching fully and partially vaccinated individuals to unvaccinated controls using age, race, sex and housing-type, we estimated a proportional hazards model using a Cox regression method, using time to infection or to the end of the study period as the outcome, to obtain the hazard ratios for the fully vaccinated group vis-à-vis the unvaccinated group, and the partially vaccinated group vis-à-vis the unvaccinated group. The vaccine effectiveness estimates are derived based on one minus the respective hazard ratio

estimates. We do this separately for the 3 outcomes of interest. We calculated the 95% CIs using a percentile bootstrap method with 200 runs, with all analysis done using STATA v16.

For the matched analysis, compared to the unvaccinated group, the estimated vaccine effectiveness against all confirmed infections was 4.4% (95% CI, 2.7 to 6.1) for the partially vaccinated group and 30.6% (95%, 28.2 to 32.9) for the fully vaccinated group. The estimated vaccine effectiveness for PCR-confirmed infections was 18.9% (95% CI, 14.4 to 22.9) for the partially vaccinated group and 66.4% (95%, 62.1 to 70.2) for the fully vaccinated group. The estimated vaccine effectiveness against hospitalization was 49.9% (95% CI, 40.4 to 59.2) for the partially vaccinated group and 77.9% (95% CI, 66.6 to 85.4) for the fully vaccinated group.

Figure S1 Incidence of All Confirmed Infections in Unvaccinated Children by Date (red) and Modeled Incidence with 95% Confidence Intervals (black)
Saturdays and Sundays are indicated in gray.

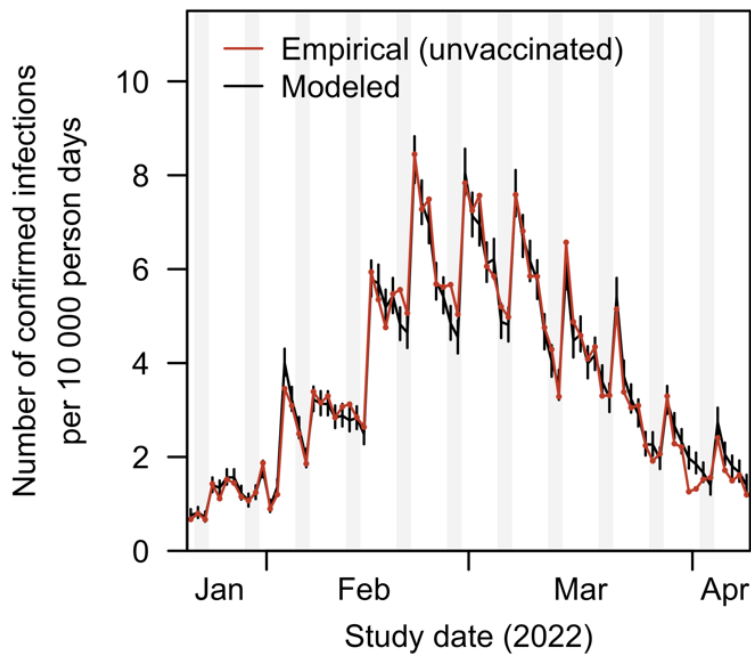


Figure S2 Incidence of All Confirmed Infections in Partially Vaccinated Children by Date (blue) and Modeled Incidence with 95% Confidence Intervals (black)
Saturdays and Sundays are indicated in gray.

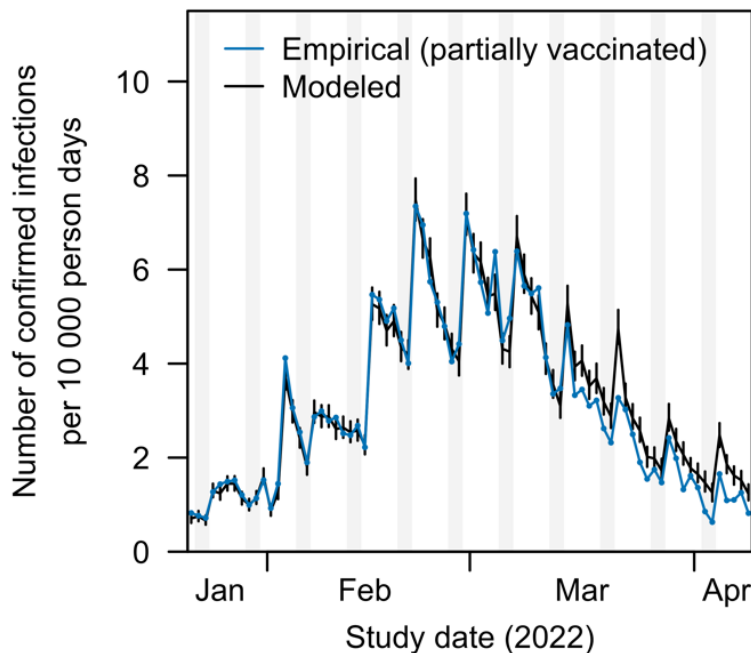


Figure S3 Incidence of All Confirmed Infections in Fully Vaccinated Children by Date (gold) and Modeled Incidence with 95% Confidence Intervals (black)
 Saturdays and Sundays are indicated in gray.

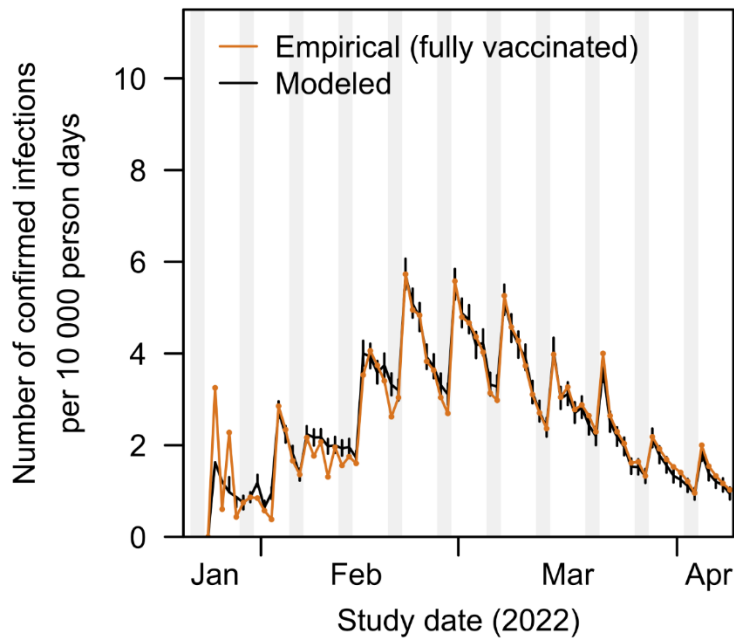


Figure S4 Distribution of Time Interval between First and Second Vaccine Dose Among Fully Vaccinated Individuals

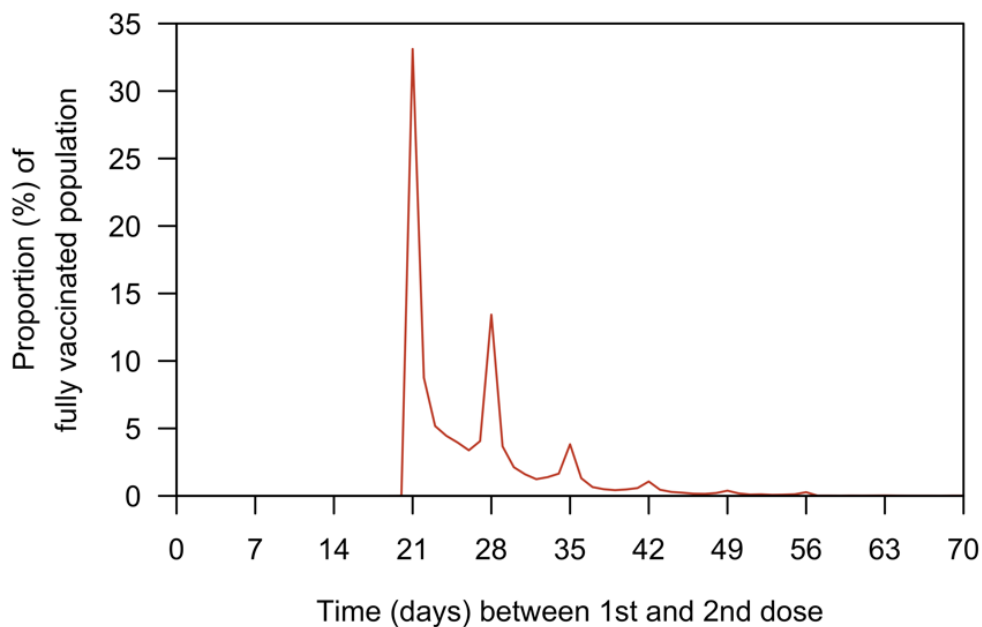


Table S1 Estimated Effectiveness of BNT-162b2 Vaccine Against SARS-CoV-2 Infections and Hospitalizations by Time Since Vaccination

Group	Person-Days At Risk*	No. of Cases (events)			Crude Incidence Rates (events/ 1,000,000 person-days)			Relative Vaccine Effectiveness (95%) [†] (percent)		
		All confirmed cases‡	PCR-confirmed cases	Hospitalizations	All confirmed cases ‡	PCR-confirmed cases	Hospitalizations	All confirmed cases‡	PCR-confirmed cases	Hospitalizations
Unvaccinated	5,118,468	16,909	2,425	146	3303.5	473.8	30.0	Reference	Reference	Reference
Partially vaccinated										
1 - 6 days after first dose	622,268	1,494	211	12	2400.9	339.1	19.4	20.9 (16.6—25.0)	35.3 (25.5—43.8)	34.5 (-18.5—63.8)
7 - 14 days after first dose	1,126,655	3,397	537	29	3015.1	476.6	26.0	-1.3 (-5.1—2.4)	10.4 (1.5—18.6)	15.7 (-26.5—43.8)
15 - 29 days after first dose	1,965,252	6,314	905	36	3212.8	460.5	18.6	2.0 (-1.0—4.8)	14.6 (7.5—21.1)	44.2 (18.9—61.6)
≥ 30 days after first dose	569,063	1,970	204	10	3461.8	358.5	19.3	21.9 (18.1—25.6)	13.7 (0.0 —25.5)	51.6 (7.1—74.8)
1-6 days after second dose	1,056,967	2,831	232	13	2678.4	219.5	12.5	35.7 (33.0—38.2)	58.1 (51.9—63.5)	64.7 (37.3—80.2)
Fully vaccinated										
7 - 14 days after second dose	1,362,912	3,338	196	6	2449.2	143.8	4.5	48.8 (46.9—50.8)	70.6 (65.9—74.7)	87.8 (72.2—94.7)
15 - 29 days after second dose	2,324,406	7,647	318	14	3289.9	136.8	6.4	37.6 (35.7—39.3)	66.3 (61.7—70.2)	84.5 (72.7—91.2)
30 - 59 days after second dose	3,236,817	8,787	288	20	2714.7	89.0	7.6	28.5 (26.3—30.7)	60.2 (54.1—65.5)	80.4 (67.0—88.4)
≥ 60 days after second dose	480,931	742	26	2	1542.8	54.1	10.9	25.6 (19.3—31.5)	42.7 (12.0—62.7)	N.A.§

* Person-days at risk for the hospitalization outcome was 4,869,127 for the unvaccinated group, 617,703 for the partially vaccinated (1 to 6 days post first dose) group, 1,117,349 for the partially vaccinated (7 to 14 days post first dose) group, 1,938,929 for the partially vaccinated (15 to 29 days post first dose) group, 516,969 for the partially vaccinated (30 or more days post first dose) group, and 1,040,403 for the partially vaccinated (1 to 6 days after the second dose) group. For the fully vaccinated group, the person-days at risk for the hospitalization outcome was 1,326,630 for the group that was 7 to 14 days post the second dose,

2,194,985 for the group that was 15 to 29 days post the second dose, 2,633,706 for the group that was 30 to 59 days post the second dose, and 182,843 for the group 60 or more days post the second dose.

† Vaccine effectiveness is calculated from 1 minus the incidence rate ratio (IRR). IRR is obtained from the exponentiated coefficients of separate Poisson regressions on all confirmed infections, infections confirmed via PCR testing only, and severe infections resulting in hospitalization. The following covariates: age (5 to 11 years), race (Chinese, Indian, Malay, Others), sex (male, female), housing type (1–2 room, 3 room, 4 room, 5 room public housing, private housing and others), and calendar dates were included in the regression to control for potential confounding. Vaccine effectiveness for partially vaccinated and fully vaccinated groups were reported with the unvaccinated group as a reference. Confidence intervals have not been adjusted for multiplicity and should not be used to infer statistical significance.

‡ All confirmed cases refer to all reported SARS-CoV-2 infections confirmed by polymerase chain reaction testing or antigen rapid testing.

§ Not applicable. Due to the small number of individuals in the group, our sample sizes are too small to obtain meaningful comparisons.

Table S2 Estimated Effectiveness of BNT-162b2 Vaccine Against SARS-CoV-2 Infections and Hospitalizations by Age Group

Group	Person-Days At Risk*	No. of Cases (events)			Crude Incidence Rates (events/ 1,000,000 person-days)			Relative Vaccine Effectiveness (95% CI)†		
		All confirmed cases ‡	PCR-confirmed cases	Hospitalizations	All confirmed cases ‡	PCR-confirmed cases	Hospitalizations	All confirmed cases ‡	PCR-confirmed cases	Hospitalizations
5-6 years old										
Unvaccinated	2,530,548	8,187	1,242	65	3235.3	490.8	27.1	Reference	Reference	Reference
Partially Vaccinated	1,366,442	4,544	511	22	3325.4	374.0	16.6	12.5 (9.2—15.7)	23.5 (15.0—31.3)	43.3 (7.0—65.4)
Fully Vaccinated	1,259,615	3,014	95	8	2392.8	75.4	7.8	39.6 (36.8—42.3)	69.9 (62.4—75.9)	75.7 (46.8—88.9)
7-9 years old										
Unvaccinated	1,878,876	6,304	852	57	3355.2	453.5	31.8	Reference	Reference	Reference
Partially Vaccinated	2,554,508	7,704	1,005	48	3015.8	393.4	19.1	14.4 (11.5—17.2)	22.6 (15.1—29.4)	43.6 (16.7—61.8)
Fully Vaccinated	3,427,332	9,645	364	17	2814.1	106.2	5.8	37.4 (35.2—39.5)	67.4 (62.7—71.6)	85.1 (73.3—91.6)
10-11 years old										
Unvaccinated	709,044	2,418	331	24	3410.2	466.8	35.5	Reference	Reference	Reference
Partially Vaccinated	1,419,255	3,758	573	30	2647.9	403.7	21.4	15.7 (11.2—19.9)	23.5 (12.2—33.3)	40.6 (-2.9—65.7)
Fully Vaccinated	2,718,119	7,855	369	17	2889.9	135.8	7.1	33.8 (30.6—36.9)	62.6 (56.0—68.2)	82.9 (66.9—91.2)

* For children aged 5 to 6 years old, the person-days at risk for the hospitalization outcome was 2,398,998 for the unvaccinated group, 1,322,821 for the partially vaccinated group, and 1,025,330 for the fully vaccinated group. For children 7 to 9 years old, the person-days at risk for the hospitalization outcome was 1,793,908 for the unvaccinated group, 2,509,465 for the partially vaccinated group, and 2,930,475 for the fully vaccinated group. For children 10 to 11 years old, the person-days at risk for the hospitalization outcome was 676,221 for the unvaccinated group, 1,399,067 for the partially vaccinated group, and 2,382,359 for the fully vaccinated group.

† Vaccine effectiveness is calculated as 1 minus the incidence rate ratio (IRR). IRR is obtained from the exponentiated coefficients of separate Poisson regressions on all confirmed infections, infections confirmed via PCR testing only, and severe infections resulting in hospitalization. The following covariates: race (Chinese, Indian, Malay, Others), sex (male, female), housing type (1–2 room, 3 room, 4 room, 5 room public housing, private housing and others), and calendar dates were included in the regression to control for potential confounding. Vaccine effectiveness for partially vaccinated and fully vaccinated groups were reported with the unvaccinated group as a reference. Confidence intervals have not been adjusted for multiplicity and should not be used to infer statistical significance.

‡ All confirmed cases refer to all reported SARS-CoV-2 infections confirmed by polymerase chain reaction testing or antigen rapid testing.

Table S3 Estimated Effectiveness of BNT-162b2 Vaccine Against SARS-CoV-2 Infections and Hospitalizations by Time Period

Group§	Person-Days At Risk*	No. of Cases (events)			Crude Incidence Rates (events/ 1,000,000 person-days)			Relative Vaccine Effectiveness (95% CI)† (percent)		
		All confirmed cases ‡	PCR-confirmed cases	Hospitalizations	All confirmed cases ‡	PCR-confirmed cases	Hospitalizations	All confirmed cases ‡	PCR-confirmed cases	Hospitalizations
January 21 to February 11, 2022										
Unvaccinated	2,355,894	4,193	1,371	58	1779.8	581.9	24.6	Reference	Reference	Reference
Partially Vaccinated	2,801,916	5,151	1,244	54	1838.4	444.0	19.3	12.6 (8.7—16.4)	21.3 (14.4—27.6)	30.2 (-4.2—53.2)
Fully Vaccinated	391,213	655	87	1	1674.3	222.4	2.6	46.0 (41.0—50.6)	61.9 (52.1—69.7)	91.5 (37.3—98.9)
February 12 to February 25, 2022										
Unvaccinated	984,275	5,166	570	29	5248.5	579.1	29.5	Reference	Reference	Reference
Partially Vaccinated	1,194,665	5,537	521	22	4634.8	436.1	18.4	15.5 (12.1—18.7)	27.5 (18.1—35.9)	47.2 (6.9—70.0)
Fully Vaccinated	1,177,765	4,254	239	12	3611.9	202.9	10.2	42.4 (39.7—44.9)	67.3 (61.4—72.2)	73.5 (45.7—87.1)
February 26 to March 11, 2022										
Unvaccinated	701,841	4,334	303	36	6175.2	431.7	51.3	Reference	Reference	Reference
Partially Vaccinated	671,541	3,655	242	11	5442.7	360.4	16.4	14.0 (10.1—17.8)	19.5 (4.4—32.2)	70.2 (41.0—84.9)
Fully Vaccinated	1,759,550	7,061	223	3	4013.0	126.7	1.7	38.8 (36.2—41.3)	73.9 (68.7—78.3)	97.3 (91.1—99.2)
March 12 to March 25, 2022										
Unvaccinated	569,020	2,276	133	18	3999.9	233.7	31.6	Reference	Reference	Reference
Partially Vaccinated	428,685	1,318	73	11	3074.5	170.3	25.7	25.1 (19.8—30.0)	24.5 (-0.7—43.5)	17.7 (-75.9—61.5)
Fully Vaccinated	1,961,496	5,385	193	22	2745.4	98.4	11.2	32.6 (29.0—36.1)	56.8 (45.1—66.0)	65.4 (32.1—82.4)
March 26 to April 8, 2022 (to April 1, 2022 for hospitalization outcome)										
Unvaccinated	507,438	940	48	5	1852.4	94.6	19.4	Reference	Reference	Reference
Partially Vaccinated	243,398	345	9	2	1417.4	37.0	14.9	25.1 (15.2—33.8)	61.8 (21.9—81.3)	23.3 (-301.0—85.3)
Fully Vaccinated	2,115,042	3,159	86	4	1493.6	40.7	3.8	19.5 (13.1—25.5)	58.9 (39.7—71.9)	79.0 (14.4—94.9)

* For January 21 to February 11, 2022, the person-days at risk for the hospitalization outcome was 2,355,894 for the unvaccinated group, 2,801,916 for the partially vaccinated group, and 391,213 for the fully vaccinated group. For February 12 to February 25, 2022, the person-days at risk for the hospitalization outcome was 984,275 for the unvaccinated group, 1,194,665 for the partially vaccinated group, and 1,177,765 for the fully vaccinated group. For February 26 to March 11, 2022, the person-days at risk for the hospitalization outcome was 701,841 for the unvaccinated group, 671,541 for the partially vaccinated group, and 1,759,550 for the fully vaccinated group. For March 12 to March 25, 2022, the person-days at risk for the hospitalization outcome was 569,020 for the unvaccinated group, 428,685 for the partially vaccinated group, and 1,961,496 for the fully vaccinated group. For March 26 to April 1, 2022, the person-days at risk for the hospitalization outcome was 258,097 for the unvaccinated group, 134,546 for the partially vaccinated group, and 1,048,140 for the fully vaccinated group.

† Vaccine effectiveness is calculated as 1 minus the incidence rate ratio (IRR). IRR is obtained from the exponentiated coefficients of separate Poisson regressions on all confirmed infections, infections confirmed via PCR testing only, and severe infections resulting in hospitalization. The following covariates: age (5 to 11 years), race (Chinese, Indian, Malay, Others), sex (male, female), housing type (1–2 room, 3 room, 4 room, 5 room public housing, private housing and others), and calendar dates were included in the regression to control for potential confounding. Vaccine effectiveness for partially vaccinated and fully vaccinated groups were reported with the unvaccinated group as a reference. Confidence intervals have not been adjusted for multiplicity and should not be used to infer statistical significance.

‡ All confirmed cases refer to all reported SARS-CoV-2 infections confirmed by polymerase chain reaction testing or antigen rapid testing.

Table S4 Estimated Effectiveness of BNT-162b2 Vaccine Against SARS-CoV-2 Infections and Hospitalizations, adjusted for Geographical Region

Group	Person-Days At Risk*	No. of Cases (events)			Crude Incidence Rates (events/ 1,000,000 person-days)			Relative Vaccine Effectiveness (95%)† (percent)		
		All confirmed cases‡	PCR-confirmed cases	Hospitalizations	All confirmed cases ‡	PCR-confirmed cases	Hospitalizations	All confirmed cases‡	PCR-confirmed cases	Hospitalizations
Unvaccinated	5,118,468	16,909	2,425	146	3303.5	473.8	30.0	Reference	Reference	Reference
Partially vaccinated	5,340,205	16,006	2,089	100	2997.3	391.2	19.1	13.7 (11.8—15.6)	24.8 (20.0—29.3)	41.2 (23.2—55.0)
Fully vaccinated	7,405,066	20,514	828	42	2770.3	111.8	6.6	36.8 (35.3—38.3)	65.5 (62.1—68.5)	82.6 (74.5—88.2)

* Person-days at risk for the hospitalization outcome was 4,869,127 for the unvaccinated group, 5,231,353 for the partially vaccinated group, and 6,338,164 for the fully vaccinated group.

† Vaccine effectiveness is calculated as 1 minus the incidence rate ratio (IRR). IRR is obtained from the exponentiated coefficients of separate Poisson regressions on all confirmed infections, infections confirmed via PCR testing only, and severe infections resulting in hospitalization. The following covariates: age (5 to 11 years), race (Chinese, Indian, Malay, Others), sex (male, female), housing type (1–2 room, 3 room, 4 room, 5 room public housing, private housing and others), geographical region (constituency), and calendar dates were included in the regression to control for potential confounding. Vaccine effectiveness for partially vaccinated and fully vaccinated groups were reported with the unvaccinated group as a reference. Confidence intervals have not been adjusted for multiplicity and should not be used to infer statistical significance.

‡ All confirmed cases refer to all reported SARS-CoV-2 infections confirmed by polymerase chain reaction testing or antigen rapid testing.

Table S5 Estimated Effectiveness of BNT-162b2 Vaccine Against SARS-CoV-2 Infections and Hospitalizations by Matched Analysis

Group	Relative Vaccine Effectiveness (95%)* (percent)		
	All confirmed cases†	PCR-confirmed cases	Hospitalizations
Unvaccinated	Reference	Reference	Reference
Partially vaccinated	4.4 (2.7–6.1)	18.9 (14.4–22.9)	49.9 (40.4–59.2)
Fully vaccinated	30.6 (28.2–32.9)	66.4 (62.1–70.2)	77.9 (66.6–85.4)

* After matching fully and partially individuals to unvaccinated controls using age (5 to 11 years), race (Chinese, Indian, Malay, Others), sex (male, female), and housing type (1–2 room, 3 room, 4 room, 5 room public housing, private housing and others), we estimated a proportional hazards model using a Cox regression method, using time to infection or to the end of the study period as the outcome, to obtain the hazard ratios for the fully vaccinated group vis-à-vis the unvaccinated group, and the partially vaccinated group vis-à-vis the unvaccinated group. Vaccine effectiveness is calculated as 1 minus the hazards ratio (HR). Confidence intervals have not been adjusted for multiplicity and should not be used to infer statistical significance.

† All confirmed cases refer to all reported SARS-CoV-2 infections confirmed by polymerase chain reaction testing or antigen rapid testing.

References

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2. Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting. N Engl J Med 2021;384:1412-23.