Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Effectiveness of primary series and booster vaccination against SARS-CoV-2 infection and hospitalisation among adolescents aged 12–17 years in Singapore: a national cohort study

Calvin J Chiew, M Premikha, Chia Yin Chong, Wycliffe E Wei, Benjamin Ong, David Chien Lye, Derrick Heng, Vernon J Lee, Kelvin Bryan Tan

Summary

Background Singapore offered the BNT162b2 vaccine (tozinameran; Pfizer-BioNTech) to adolescents aged 12–17 years in May 18, 2021, and extended booster vaccines to this group in Jan 21, 2022. Literature on the effectiveness of primary series and booster vaccination among adolescents is scarce outside of Europe and North America. We aimed to determine primary series and booster vaccine effectiveness against SARS-CoV-2 infection and hospitalisation among adolescents in Singapore.

Methods For this national cohort study, we assessed the incidence of confirmed SARS-CoV-2 infection and hospitalisation among adolescents aged 12–17 years vaccinated with BNT162b2 in Singapore from Sept 1 to Dec 15, 2021, during the delta (B.1.617.2) variant wave, and from Jan 21 to April 28, 2022, during the omicron (B.1.1.529) variant wave. Data were collected from official databases maintained by the Ministry of Health of Singapore. Individuals were classified as partly vaccinated (those who had received one dose and those who had received the second dose no more than 7 days previously), fully vaccinated (8 days after receiving a second dose), or boosted (8 days after receiving a third dose) and compared with unvaccinated individuals.

Findings 249 763 individuals aged 12–17 years were included in the study, contributing over 56·2 million person-days of observation. Compared with unvaccinated individuals, two vaccine doses achieved vaccine effectiveness of 66% (95% CI 63–69) against infection with the delta variant and 25% (21–29) against infection with the omicron variant, and 83% (74–89) against delta variant-associated hospitalisation and 75% (56–86) against omicron variant-associated hospitalisation. Booster vaccination with a third dose achieved vaccine effectiveness of 56% (53–58) against infection with the omicron variant and 94% (86–97) against omicron-associated hospitalisation, compared with unvaccinated adolescents. Vaccine effectiveness against infection for both variants after two doses waned over time, whereas vaccine effectiveness against hospitalisation for both variants remained stable; both were increased after three doses.

Interpretation Among adolescents aged 12–17 years, vaccine effectiveness against confirmed SARS-CoV-2 infection after two doses of BNT162b2 decreased over time and increased after a third dose. Boosted adolescents were also the most protected from hospitalisation compared with fully vaccinated, partly vaccinated, and unvaccinated adolescents. Therefore, the booster dose of BNT162b2 can help to reduce the burden on the health-care system and individual morbidity during an omicron wave.

Funding None.

Copyright © 2022 Elsevier Ltd. All rights reserved.

Lancet Infect Dis 2022

Published Online September 28, 2022 https://doi.org/10.1016/S1473-3099(22)00573-4

Public Health Group (C J Chiew MPH, W E Wei MPH, Prof D Heng MPhil, Prof V J Lee PhD), **Crisis Strategy and Operations Group** (M Premikha MBBS, K B Tan PhD), **and DMS Office** (Prof B Ong MBBS), **Ministry of Health, Singapore; Department of Infectious Diseases, KK Women's and Children's Hospital, Singapore** (C Y Chong MBBS); **Yong Loo Lin School of Medicine** (C Y Chong, Prof B Ong, Prof D C Lye MBBS) **and Saw Swee Hock School of Public Health** (Prof D Heng, Prof V J Lee, K B Tan), **National University of Singapore, Singapore; Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore** (C Y Chong, Prof D C Lye); **Duke-NUS Medical School, Singapore** (C Y Chong); **National Centre for Infectious Diseases, Singapore** (Prof D C Lye); **Department of Infectious Diseases, Tan Tock Seng Hospital, Singapore** (Prof D C Lye)

Correspondence to: Dr Calvin J Chiew, Communicable Diseases Division, Ministry of Health, Singapore 169852 **calvin_chiew@moh.gov.sg**

Introduction

Although SARS-CoV-2 infection in children and adolescents is generally milder compared with that in adults and older people,[1,2] cases of severe disease (ie, requiring oxygen or intensive care) in this age group have been reported, including multisystem inflammatory syndrome, possibly progressing to death.[3] Additionally, risk factors such as medical comorbidities and obesity further predispose some children and adolescents to severe COVID-19 disease.[3,4] In a cohort of paediatric patients hospitalised with COVID-19 in the USA, nearly a third had severe disease, with an increased risk of severe disease in younger children aged 2–11 years compared with adolescents aged 12–18 years.[5]

Singapore had a large wave of SARS-CoV-2 infections from September to December, 2021, driven by the delta (B.1.617.2) variant, followed by an even larger wave from January to April, 2022, driven by the omicron (B.1.1.529) variant. Excluding imported cases, adolescents aged 12–17 years comprised 2·4% of the overall case numbers (5044 of 206 181) during the delta variant wave, and 5·0% of the overall case numbers (43 734 of 872 489) during the omicron variant wave.

To protect adolescents from SARS-CoV-2 infection, as they spend much of their time in communal settings

Research in context

Evidence before this study

We searched PubMed for reports from start of the database up to June 15, 2022, using the keywords ("COVID-19" OR "SARS-CoV-2") AND ("vaccine*" OR "vaccination*") AND ("effect*" OR "efficacy") AND "adolescent*", with no restrictions on language. We identified 20 studies reporting the effectiveness of COVID-19 vaccination in adolescents, of which 11 were observational studies in real-world settings, while the remaining were randomised controlled trials, systematic reviews, or meta-analyses. Among the observational studies, almost all were done in North America, except for three reports from Israel, South Korea, and Malaysia. Only two studies (both from the USA) evaluated the effectiveness of boosters and examined data from a period of omicron (B.1.1.529) variant predominance.

Added value of this study

We studied the effectiveness of primary series and booster vaccination in preventing SARS-CoV-2 infection and hospitalisation among adolescents aged 12–17 years during the delta (B.1.617.2) variant and omicron waves in Singapore using comprehensive national data. Our findings add to the existing body of evidence showing that primary series vaccine effectiveness against SARS-CoV-2 infection was lower for omicron than for delta, and gradually waned over time for both variants. Additionally, we showed that a booster dose provided the greatest protection against both infection and hospitalisation. Specifically for omicron, the booster increased protection against hospitalisation to levels similar to those against delta after the primary series.

Implications of all the available evidence

These findings highlight the usefulness of the booster dose in reducing stress on health-care systems and maintaining individual protection against severe disease in an omicron-dominated wave. Waning of immunity after the booster dose should be evaluated over a longer term in further studies.

such as schools, Singapore offered the BNT162b2 vaccine (tozinameran; Pfizer-BioNTech) to individuals aged 12–17 years under the National Vaccination Programme starting in May 18, 2021. Booster vaccines were extended to this group on Jan 21, 2022, for those who had received their second dose 5 months previously. As of April 28, 2022, 98% of adolescents (196 364 of 199 865) aged 12–17 years in Singapore have been fully vaccinated with two doses of BNT162b2, the only vaccine available to this age group under the National Vaccination Programme, and 83% of adolescents (164 979) have received a third dose.

See Online for appendix

Although BNT162b2's clinical trial suggested that vaccine efficacy was 100% against SARS-CoV-2 infection in adolescents aged 12–15 years who received two doses,[6] literature on primary series and booster vaccine effectiveness among adolescents is scarce, especially outside of Europe and North America. Therefore, we aimed to determine the vaccine effectiveness in preventing SARS-CoV-2 infection and hospitalisation among adolescents to guide policy recommendations on vaccination and public health measures.

Methods

Study design and participants

For this national cohort study, we analysed the incidence of all reported SARS-CoV-2 infections confirmed by PCR or antigen rapid testing and hospitalisations for COVID-19 among adolescents aged 12–17 years in Singapore, from Sept 1 to Dec 15, 2021, and from Jan 21 to April 28, 2022, separately. The first period coincided with the time when delta was the predominant variant, while the second period covered the time when omicron was predominant. We excluded the period between Dec 16, 2021, and Jan 20, 2022, because both delta and omicron were circulating during this time. The cutoff dates and predominant variant of each infection wave were determined on the basis of whole-genome sequencing results from a representative sample of cases systematically selected under the national genomic surveillance programme for COVID-19 (appendix p 1).

Adolescents whose 12th birthday was after Sept 1, 2021, were included in the study so that unvaccinated person-days before their vaccination eligibility date could be observed. Adolescents whose 18th birthday was before Sept 1, 2021, were excluded as they were eligible to receive mRNA vaccinations other than BNT162b2.

Testing for SARS-CoV-2 infection was done on all individuals who presented with symptoms of acute respiratory infection to a health-care facility, and all positive cases were required by law to be notified to the Ministry of Health of Singapore (MOH) under the Infectious Diseases Act. Additionally, all public hospitals were required to report patient-level information on all SARS-CoV-2-related hospitalisations to the MOH. Need for hospitalisation was assessed by physicians on the basis of clinical presentation and risk factors such as comorbidities.

Data were collected from official databases maintained by the MOH including national records of all confirmed SARS-CoV-2 infections, hospitalisations, and vaccines administered.[7] The study was done as part of national public health research under the Infectious Diseases Act, Singapore, to support policy decision making and evaluation of the public health response to COVID-19; hence, a separate ethics review by an Institutional Review Board was not required.

Outcomes

Adolescents with no previous history of SARS-CoV-2 infection and who had received one, two, or three doses of BNT162b2 were compared with those unvaccinated for the outcomes of confirmed infection and hospitalisation. Individuals were classified as partly vaccinated from the day after their first dose until 7 days after receiving their second dose, and fully vaccinated 8 days after their second dose to allow for sufficient immune response.[8] Similarly, individuals were classified as boosted 8 days after their third dose. Classification within these groups was dynamic, with those unvaccinated becoming partly vaccinated, fully vaccinated, or boosted subsequently, similar to a published booster effectiveness analysis.[9]

Statistical analysis

Using a Poisson regression model, we estimated the incidence rate ratio (IRR) of confirmed SARS-CoV-2 infection and hospitalisation, controlling for age, gender, ethnicity, housing type (a marker of socioeconomic status), and varying force of infection (exposure risk) across time (by including daily calendar date dummy variables in the model). In counting person-time, we accounted for the time-varying nature of vaccination status: the same individual could contribute person-time to unvaccinated, partly vaccinated, fully vaccinated, and boosted groups depending on time. Vaccine effectiveness was calculated by taking 1 minus the relative risk in relation to the unvaccinated group, with the lower bound set at 0%. We calculated 95% CIs on the basis of Wald statistics, assuming that the over-dispersion parameter was one. We report estimates of vaccine effectiveness during the delta wave and the omicron wave separately. Estimates of booster effectiveness were only available for the omicron wave.

We also present estimates from a modified Poisson regression with robust error variance using a sandwich estimator and estimates from a cluster variance estimator using unique individuals as the cluster variable in the appendix (p 2). We evaluated model fit by comparing modelled incidences of infections with empirically observed ones. The analysis was done with Stata, version 17.

Role of the funding source

There was no funding source for this study.

Results

249 763 individuals aged 12–17 years were included in the study cohort (appendix p 4); of these, 127 379 (51·0%) were boys and 122 384 (49·0%) were girls, and median age was 15 years (IQR 13–16). These adolescents contributed over 56·2 million person-days of observation, of which about 9·4 million (16·7%) were boosted, 42·8 million (76·1%) were fully vaccinated, 1·1 million (2·0%) were partly vaccinated, and 2·9 million (5·2%) were unvaccinated (table 1). Median time interval was 35 days (28–42) between the first and second dose, and 211 days (201–224) between the second and third dose. 49 921 adolescents developed SARS-CoV-2 infection over the study period, of whom 372 (0·7%) were hospitalised for COVID-19. None of the adolescents had a reinfection within the study period. There was one severe case of a 16-year-old female individual requiring intubation in an intensive care unit, and one case of multisystem inflammatory syndrome in a 12-year-old male individual. Both were vaccinated with two doses and were infected during the omicron wave.

After adjusting for age, gender, ethnicity, socioeconomic status, and daily infection rate, two doses of vaccination achieved vaccine effectiveness of 66% (95% CI 63–69) against delta infection and 25% (21–29) against omicron infection, and 83% (74–89) against delta hospitalisation and 75% (56–86) against omicron hospitalisation (table 2). Booster vaccination with a third dose achieved a vaccine effectiveness of 56% (53–58) against omicron infection

	Unvaccinated, person-days at risk	Partly vaccinated*, person-days at risk	Fully vaccinated†, person-days at risk	Boosted‡, person-days at risk
Total person-days at risk	2 916 869	1 099 953	42 838 791	9 425 598
Gender				
Boys	1 537 813 (52·7%)	581 176 (52·8%)	21 928 993 (51·2%)	4 694 049 (49·8%)
Girls	1 379 056 (47·3%)	518 777 (47·2%)	20 909 798 (48·8%)	4 731 549 (50·2%)
Age distribution, years				
11	1 813 270 (62·2%)	636 511 (57·9%)	3 109 844 (7·3%)	217 696 (2·3%)
12	303 015 (10·4%)	121 371 (11·0%)	7 180 186 (16·8%)	1 423 354 (15·1%)
13	221 040 (7·6%)	90 771 (8·3%)	7 435 059 (17·4%)	1 568 785 (16·6%)
14	192 342 (6·6%)	74 691 (6·8%)	7 192 709 (16·8%)	1 572 825 (16·7%)
15	161 626 (5·5%)	67 613 (6·1%)	7 046 434 (16·4%)	1 685 486 (17·9%)
16	149 641 (5·1%)	65 370 (5·9%)	6 841 893 (16·0%)	1 658 798 (17·6%)
17	75 935 (2·6%)	43 626 (4·0%)	4 032 666 (9·4%)	1 298 654 (13·8%)
Ethnicity				
Chinese	2 032 024 (69·7%)	747 042 (67·9%)	28 790 570 (67·2%)	6 493 360 (68·9%)
Malay	349 395 (12·0%)	138 544 (12·6%)	5 306 060 (12·4%)	1 118 044 (11·9%)
Indian	395 418 (13·6%)	172 286 (15·7%)	6 951 905 (16·2%)	1 395 842 (14·8%)
Others§	140 032 (4·8%)	42 081 (3·8%)	1 790 256 (4·2%)	418 352 (4·4%)
Housing type				
1–2-room public housing	79 675 (2·7%)	39 868 (3·6%)	1 295 819 (3·0%)	240 468 (2·6%)
3-room public housing	466 347 (16·0%)	169 454 (15·4%)	5 875 470 (13·7%)	1 241 808 (13·2%)
4-room public housing	910 565 (31·2%)	340 384 (30·9%)	13 089 812 (30·6%)	2 809 701 (29·8%)
5-room public housing	829 121 (28·4%)	319 141 (29·0%)	12 503 353 (29·2%)	2 756 032 (29·2%)
Private housing	564 652 (19·4%)	199 370 (18·1%)	8 630 597 (20·1%)	2 048 150 (21·7%)
Others	66 509 (2·3%)	31 736 (2·9%)	1 443 740 (3·4%)	329 439 (3·5%)

Data are n or n (%). *Partial vaccination was defined as having received one dose of BNT162b2 or two doses with 7 days or fewer after the second dose. †Full vaccination was defined as having received two doses of BNT162b2 with 8 days elapsed after the second dose to allow for sufficient immune response. ‡Boosted was defined as having received a third dose of BNT162b2 at least 5 months after the second dose, and 8 days after the third dose. §Includes individuals of other ethnicities or mixed ethnicities.

Table 1: **Demographic characteristics of the study cohort by vaccination status**

	Unvaccinated	Partly vaccinated*	Fully vaccinated†	Boosted‡
Confirmed SARS-CoV-2 infection, delta-variant wave				
Number of cases	997	163	3884	NA
Incidence, per million person-days	449	204	169	NA
Adjusted IRR§ (95% CI)	1 (ref)	0·41 (0·35–0·49)	0·34 (0·31–0·37)	NA
Adjusted VE§ (95% CI)	(ref)	0·59 (0·51–0·65)	0·66 (0·63–0·69)	NA
Confirmed SARS-CoV-2 infection, omicron-variant wave				
Number of cases	1254	388	30 866	11 226
Incidence, per million person-days	3159	2768	2721	1198
Adjusted IRR§ (95% CI)	1 (ref)	0·78 (0·69–0·87)	0·75 (0·71–0·79)	0·44 (0·42–0·47)
Adjusted VE§ (95% CI)	(ref)	0·22 (0·13–0·31)	0·25 (0·21–0·29)	0·56 (0·53–0·58)
Hospitalisation, delta-variant wave				
Number of cases	70	7	112	NA
Incidence, per million person-days	31	9	5	NA
Adjusted IRR§ (95% CI)	1 (ref)	0·28 (0·13–0·61)	0·17 (0·11–0·26)	NA
Adjusted VE§ (95% CI)	(ref)	0·72 (0·39–0·87)	0·83 (0·74–0·89)	NA
Hospitalisation, omicron-variant wave				
Number of cases	15	5	131	12
Incidence, per million person-days	40	37	12	1
Adjusted IRR§ (95% CI)	1 (ref)	0·67 (0·24–1·87)	0·25 (0·14–0·44)	0·06 (0·03–0·14)
Adjusted VE§ (95% CI)	(ref)	0·33(0·00–0·76)	0·75 (0·56–0·86)	0·94 (0·86–0·97)

The delta-variant wave occurred between September and December, 2021. The omicron-variant wave occurred between January and April, 2022. IRR=incidence rate ratio. NA=not applicable. VE=vaccine effectiveness. *Partial vaccination was defined as having received one dose of BNT162b2 or two doses with 7 days or fewer after the second dose. †Full vaccination was defined as having received two doses of BNT162b2 with 8 days elapsed after the second dose to allow for sufficient immune response. ‡Boosted was defined as having received a third dose of BNT162b2 at least 5 months after the second dose, and 8 days after the third dose. §Adjusted for age, gender, ethnicity, housing type, and date of reporting (to control for daily infection rate) with Poisson regression.

Table 2: **Primary series and booster vaccine effectiveness against confirmed SARS-CoV-2 infection and hospitalisation among adolescents, stratified by time period**

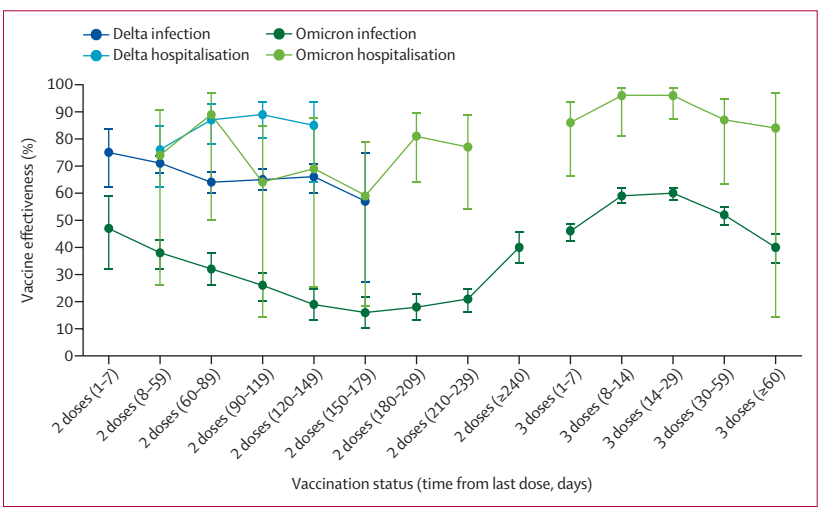

Figure: **Vaccine effectiveness over time against SARS-CoV-2 infection and hospitalisation by variant**
Error bars are 95% CIs. Vaccine effectiveness is adjusted for age, gender, ethnicity, housing type, and date of reporting (to control for daily infection rate) using Poisson regression. Unvaccinated individuals were used as the reference group. Vaccine effectiveness estimates for booster dose were only available during the omicron wave. Vaccine effectiveness estimates with wide 95% CIs (that cross 0%) due to small sample sizes are not shown.

and 94% (86–97) against omicron hospitalisation, compared with unvaccinated adolescents. Estimates using a sandwich and cluster variance estimators yield similar point estimates and 95% CIs (appendix p 2). Modelled incidences of infections among unvaccinated, fully vaccinated, and boosted adolescents were similar to empirically observed incidences (appendix pp 6–7).

For both variants, vaccine effectiveness against infection among fully vaccinated individuals waned over time, from an initial 75% after completion of the second dose to 57% after 150–179 days for delta, and from 47% to 16% over a similar duration for omicron (figure). However, among those boosted, vaccine effectiveness against omicron infection increased to 60% 14–29 days after the third dose, before declining to 40% after 60 days.

Vaccine effectiveness against hospitalisation among fully vaccinated individuals remained stable, ranging between 76% and 89% from 8 days up to 149 days after the second dose for delta, and fluctuating between 59% and 89% from 8 days up to 239 days after the second dose for omicron. This effectiveness against hospitalisation was further increased among those boosted to 84–96% up to 60 days after the third dose for omicron.

Discussion

Our study found that the two-dose vaccine effectiveness against SARS-CoV-2 infection among adolescents was lower for omicron than for delta, corroborating existing studies comparing the efficacy of numerous vaccines against these two variants in adults.[10–12] This finding is probably due to greater immune evasion by omicron and

is supported by higher incidence of infections observed during the omicron wave in Singapore compared with the delta wave (appendix p 5).[13,14]

We also showed that a booster dose provided the greatest protection against SARS-CoV-2 infection and hospitalisation. Among boosted adolescents, our observed vaccine effectiveness of 56% against omicron infection was lower than the 71·1% vaccine effectiveness reported by a US study involving adolescents aged 12–15 years during omicron predominance.[15] Our observed vaccine effectiveness of 66% against delta infection among fully vaccinated adolescents was also lower than the 90% vaccine effectiveness against delta reported by a study in Israel involving similar-age adolescents.[16] Another study in the USA found a vaccine effectiveness of 93% against SARS-CoV-2 hospitalisation for fully vaccinated adolescents during delta predominance, higher than our observed vaccine effectiveness of 83% against delta hospitalisation.[17] The lower vaccine effectiveness against SARS-CoV-2 infection and hospitalisation in our study could be a result of vaccination-differentiated social distancing measures implemented in Singapore from Aug 10 2021, which restricted the access of unvaccinated individuals to settings with potentially higher risk of SARS-CoV-2 transmission such as eateries, shopping malls, and religious and recreational facilities. This could have reduced the exposure risk of unvaccinated individuals.

Our findings also suggest a gradual waning of immunity over 5 months from completion of the second dose for both variants, which supports the need for a booster dose. A study of individuals aged older than 12 years in the USA similarly showed that vaccine effectiveness against delta infections declined from 93% during the first month after full vaccination to 53% after 4 months.[18] Another US study showed that vaccine effectiveness against omicron infections rapidly declined from 59·5% during the first month after full vaccination to 16·6% after 2 months.[15] A slight waning of vaccine effectiveness over 2 months after the third dose was also observed in our study, and should be evaluated over a longer term in further studies.

Despite waning immunity against infection over time, vaccine effectiveness against hospitalisation remained stable among those fully vaccinated up to 4 months after the second dose for delta. Protection against hospitalisation was slightly lower against omicron compared with delta after two doses but increased to similar levels after the booster dose. This aligns with a US study that found that three doses were required to achieve similar protection against omicron hospitalisation compared with two doses against delta hospitalisation,[19] highlighting the benefit of a booster dose in reducing stress on the health-care system and maintaining individual protection against severe disease in an omicron wave.

Our study is based on comprehensive national data on paediatric COVID-19 vaccinations and infections. However, there are a few limitations. First, despite our adjustments for demographic, socioeconomic, and time variables that might affect exposure risk, there might be residual confounding from comorbidities and other unknown factors that influence an adolescent's vaccination status or health-care-seeking behaviour. Second, admission to hospital is a clinical decision, and thus a subjective measure of disease severity. Lastly, as genomic sequencing was not routinely done on all confirmed cases of SARS-CoV-2 infection, variant type was assumed on the basis of case-reporting date and predominant variant of each infection wave in Singapore. As both delta and omicron were codominant between Dec 16, 2021, and Jan 20, 2022, cases reported during this period were omitted from the analysis.

Among adolescents aged 12–17 years, vaccine effectiveness against confirmed SARS-CoV-2 infection after two doses of BNT162b2 decreased over time and increased after a third dose. Boosted adolescents were also most protected from hospitalisation, compared with fully vaccinated, partly vaccinated, and unvaccinated adolescents.

Contributors

CJC and PM contributed to literature search, data analysis, and writing of the manuscript. CYC, WEW, BO, DCL, DH, and VJL contributed to critical review and editing of the manuscript. BO, DCL, DH, and VJL provided supervision. KBT contributed to study design, data collection, data analysis and editing of the manuscript. All authors had full access to all the data in the study and take responsibility for the decision to submit for publication. CJC and KBT directly accessed and verified the underlying data reported in the manuscript.

Declaration of interests

We declare no competing interests.

Data sharing

The databases with individual-level information used for this study are not publicly available due to personal data protection. Deidentified data can be made available for research, subject to approval by the Ministry of Health of Singapore. All inquiries should be sent to the corresponding author.

References

1 Zimmermann P, Curtis N. Why is COVID-19 less severe in children? A review of the proposed mechanisms underlying the age-related difference in severity of SARS-CoV-2 infections. *Arch Dis Child* 2020; **106:** 429–39.

2 Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr* 2020; **109:** 1088–95.

3 Shi Q, Wang Z, Liu J, et al. Risk factors for poor prognosis in children and adolescents with COVID-19: a systematic review and meta-analysis. *EClinicalMedicine* 2021; **41:** 101155.

4 Oliveira EA, Colosimo EA, Simões E Silva AC, et al. Clinical characteristics and risk factors for death among hospitalised children and adolescents with COVID-19 in Brazil: an analysis of a nationwide database. *Lancet Child Adolesc Health* 2021; **5:** 559–68.

5 Preston LE, Chevinsky JR, Kompaniyets L, et al. Characteristics and disease severity of US children and adolescents diagnosed with COVID-19. *JAMA Netw Open* 2021; **4:** e215298.

6 Frenck RW Jr, Klein NP, Kitchin N, et al. Safety, immunogenicity, and efficacy of the BNT162b2 Covid-19 vaccine in adolescents. *N Engl J Med* 2021; **385:** 239–50.

7 Ministry of Health of Singapore. COVID-19 statistics. 2022. https://www.moh.gov.sg/covid-19/statistics (accessed July 15, 2022).

8 Walter EB, Talaat KR, Sabharwal C, et al. Evaluation of the BNT162b2 COVID-19 vaccine in children 5 to 11 years of age. *N Engl J Med* 2022; **386:** 35–46.

9 Bar-On YM, Goldberg Y, Mandel M, et al. Protection of BNT162b2 vaccine booster against COVID-19 in Israel. *N Engl J Med* 2021; **385:** 1393–400.

10 Tseng HF, Ackerson BK, Luo Y, et al. Effectiveness of mRNA-1273 against SARS-CoV-2 omicron and delta variants. *Nat Med* 2022; **28:** 1063–71.

11 Accorsi EK, Britton A, Fleming-Dutra KE, et al. Association between 3 doses of mRNA COVID-19 vaccine and symptomatic infection caused by the SARS-CoV-2 omicron and delta variants. *JAMA* 2022; **327:** 639–51.

12 Andrews N, Stowe J, Kirsebom F, et al. COVID-19 vaccine effectiveness against the omicron (B.1.1.529) variant. *N Engl J Med* 2022; **386:** 1532–46.

13 Cao Y, Wang J, Jian F, et al. Omicron escapes the majority of existing SARS-CoV-2 neutralizing antibodies. *Nature* 2022; **602:** 657–63.

14 Hoffmann M, Krüger N, Schulz S, et al. The omicron variant is highly resistant against antibody-mediated neutralization: implications for control of the COVID-19 pandemic. *Cell* 2022; **185:** 447–56.

15 Fleming-Dutra KE, Britton A, Shang N, et al. Association of prior BNT162b2 COVID-19 vaccination with symptomatic SARS-CoV-2 infection in children and adolescents during omicron predominance. *JAMA* 2022; **327:** 2210–19.

16 Reis BY, Barda N, Leshchinsky M, et al. Effectiveness of BNT162b2 vaccine against delta variant in adolescents. *N Engl J Med* 2021; **385:** 2101–03.

17 Olson SM, Newhams MM, Halasa NB, et al. Effectiveness of Pfizer-BioNTech mRNA vaccination against COVID-19 hospitalization among persons aged 12-18 years—United States, June–September 2021. *MMWR Morb Mortal Wkly Rep* 2021; **70:** 1483–88.

18 Tartof SY, Slezak JM, Fischer H, et al. Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: a retrospective cohort study. *Lancet* 2021; **398:** 1407–16.

19 Lauring AS, Tenforde MW, Chappell JD, et al. Clinical severity of, and effectiveness of mRNA vaccines against, COVID-19 from omicron, delta, and alpha SARS-CoV-2 variants in the United States: prospective observational study. *BMJ* 2022; **376:** e069761.