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Real-world Effectiveness of a COVID-19 Vaccine (BNT162b2) against SARS-CoV-2 Infection during the Omicron Variant Predominant Period among Thai Adolescents

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Abstract

This study assessed the real-world vaccine effectiveness (RVE) of a 2-dose schedule of BNT162b2 against the Omicron variant among Thai adolescents aged 12 to 18 in the Eastern Region. A test-negative matched 1:1 case-control design was conducted using nationwide records of RT-PCR tests and vaccination history. Cases were matched with controls by the specimen collection date and residential province. Conditional logistic regression was used to determine the RVE. From January to June 2022, when Omicron prevailed, 7,770 adolescents (3,758 detected and 4,012 undetected) were reported to the system. At the time of the RT-PCR test, 684 (14%), 295 (6%), 3,834 (78%), 104 (2%), and three adolescents had received no, one, two, three, and four doses of any COVID-19 vaccines, respectively. A total of 3,304 eligible adolescents with 2-dose of BNT162b2 with a median (interquartile range (IQR)) age of 16 (14–17) years were analyzed. The median (IQR) interval from the last vaccination to RT-PCR test was 91 (55–125) days. The age-adjusted RVE of BNT162b2 against infection was 22% (95% confidence interval (CI) 5–35%). The highest RVE was 71% (95% CI -9–92%), which occurred 15–29 days after vaccination. We therefore recommend that a booster dose be considered.

Keywords: COVID-19 vaccine, adolescent, Omicron, SARS-CoV-2, vaccine effectiveness

Introduction

In 2022, Omicron became the dominant circulating variant, according to the World Health Organization.[1] In Thailand, the Department of Medical Sciences reported that, since January 2022, more than 93% of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) variants were Omicron.[2] Due to the numerous mutations in the spike protein of this variant, concerns have arisen about a significant reduction in vaccine effectiveness and an increased risk for reinfections.[3–5] Immunization is a pharmaceutical intervention that can decrease the severity of diseases and reduce the risk of infection. However, the first generation of COVID-19 vaccines was developed for the ancestral strain, which may affect its real-world vaccine effectiveness (RVE).[6]

Compared to adults, adolescents experience less severe symptoms when infected with SARS-CoV-2. However, they can develop serious illnesses and complications such as respiratory failure, myocarditis, a multisystem inflammatory syndrome in children and adolescents, and long COVID-19.[7,8] The case fatality rate among Thai adolescents was 8.71% in 2021 and decreased to 0.02% in 2022. In addition, the psychosocial and emotional well-being of adolescents has been negatively affected by the COVID-19 pandemic.[9]

In Thailand, as of January 2022, five COVID-19 vaccines were available, including BNT162b2 (Pfizer BioNTech), mRNA-1273 (Moderna), AZD1222 (AstraZeneca), CoronaVac (Sinovac), and BBIBP-CoV (Sinopharm). However, Thailand primarily uses BNT162b2 in a school-based program for adolescents, with the first and second doses of the primary series implemented four weeks apart, and a booster dose offered three months later. Other vaccines were recommended to other groups, with mRNA-1273 and BBIBP-CoV provided by the private sector. As of 10 Mar 2023, 78% of the Thai population completed the primary series, 39% received a third dose, and 9% received a fourth dose, while among adolescents, 81% completed the primary series, and 25% received a booster dose.[10] Thailand has experienced several SARS-CoV-2 waves dominated by different variants, with the Omicron variant first reported at the end of 2021 and has been predominant since January 2022.[11,12] It is unknown whether the RVE of the primary series against Omicron might affect the community's decision to receive a booster dose.

This study aimed to determine the RVE of a 2-dose BNT162b2 vaccine against SARS-CoV-2 infection among Thai adolescents during Omicron predominance.

Methods

A retrospective test-negative, matched case-control study was conducted. Cases were defined as adolescents who presented to a hospital or healthcare center for SARS-CoV-2 Reverse transcriptase polymerase chain reaction (RT-PCR) testing and had a positive result (detected). Controls were defined as adolescents who tested negative (undetected) for SARS-CoV-2. SARS-CoV-2 RT-PCR results were obtained from the co-laboratory database, which is the national laboratory recording system of the Department of Medical Sciences, Ministry of Public Health (MOPH), and collected laboratory results from both public and private health facilities in Thailand.[13] Vaccination status was ascertained through the National Vaccine Registry database from the MOPH-Immunization Center, which documented vaccine product, vaccine batch, and dates of each vaccination dose.[14]

The inclusion criteria were Thai adolescents aged 12–18 years living in the Eastern Region, including Chonburi, Rayong, Chanthaburi, Trat, Chachoengsao, Prachinburi, and Sa Kaeo Provinces, who were tested by RT-PCR for SARS-CoV-2 from 1 Jan to 30 Jun 2022. Subjects were excluded if 1) the SARS-CoV-2 RT-PCR results were reported as indeterminate or inconclusive, 2) the assay type was missing, 3) there was inconsistent vaccination information, such as missing date or vaccine type, and 4) they had a history of previous SARS-CoV-2 infection within three months.[15] One control was matched to each case from a pool of adolescents who were tested within a 14-day interval and lived in the same province. If a participant had more than one positive RT-PCR result, only the first test was included when calculating the interval between the last vaccination and the RT-PCR test. If a participant had more than one negative RT-PCR result, their most recent test result was used in the matching process. Regarding vaccine exposure, the vaccine received within 14 days prior to lab collection was not counted as a vaccination dose as the peak of immune response typically takes place two weeks after vaccination.[16] Participants who had received a COVID-19 vaccine other than the 2-dose schedule of BNT162b2 were excluded because the sample size was insufficient for an evaluation of protection.

The study was approved by the institutional ethics committee of the Department of Disease Control, MOPH (letterhead: No. FWA 00013622, Ref. No. 65005) and was conducted under the tenets of the Declaration of Helsinki. All individual information was encrypted since the beginning of the data retrieval process. As we used secondary datasets from the MOPH, direct informed consent from the participants was not applicable.

The baseline characteristics of study subjects, including age and location by infection status and history of vaccination, were presented descriptively. We employed conditional logistic regression models to measure the relationship between SARS-CoV-2 infection and the vaccinated and unvaccinated groups, using the odds ratio (OR) and 95% confidence interval (CI). The final vaccine effectiveness (VE) was computed as (1 – OR) x 100%. Subgroup analyses were conducted to investigate the VE in two different age groups (12–15 and 16–18 years). If a case and control from the same matched pair were in a different age group, they were excluded from the calculation. We also examined the VE waning over time by the duration between the last vaccination to RT-PCR testing in four time periods: 15–29, 30–89, 90–179, and ≥180 days. According to the World Health Organization's sample size calculation for vaccine effectiveness for a test-negative case-control study, the study utilized an alpha value of 0.05 and a power of 80%.[17] The predicted vaccine effectiveness against SARS-CoV-2 infection was set at 30%, while the control group was expected to have a vaccine coverage of 65%. To achieve this, we needed 1,605 cases and 1,605 controls. All statistical analyses were conducted using Stata version 17 (Stata Corp., College Station, Texas).

Results

Baseline Characteristics

From January to June 2022, 7,770 adolescents were reported to the co-laboratory system (3,758 were detected, and 4,012 were undetected by RT-PCR). Among them, 4,920 eligible adolescents were included in the study, consisting of 2,460 cases and 2,460 controls. Within this group, 684 (13.9%) had not received any COVID-19 vaccine, while 295 (6.0%), 3,834 (77.9%), 104 (2.1%), and three (0.06%) had received one, two, three, and four doses, respectively. The most common regimen for primary vaccination was two doses of BNT162b2 (90.2%). In order to analyze the RVE of the 2-dose BNT162b2, a subset of 3,304 adolescents was selected, comprising 1,652 cases and 1,652 controls (Figure 1).

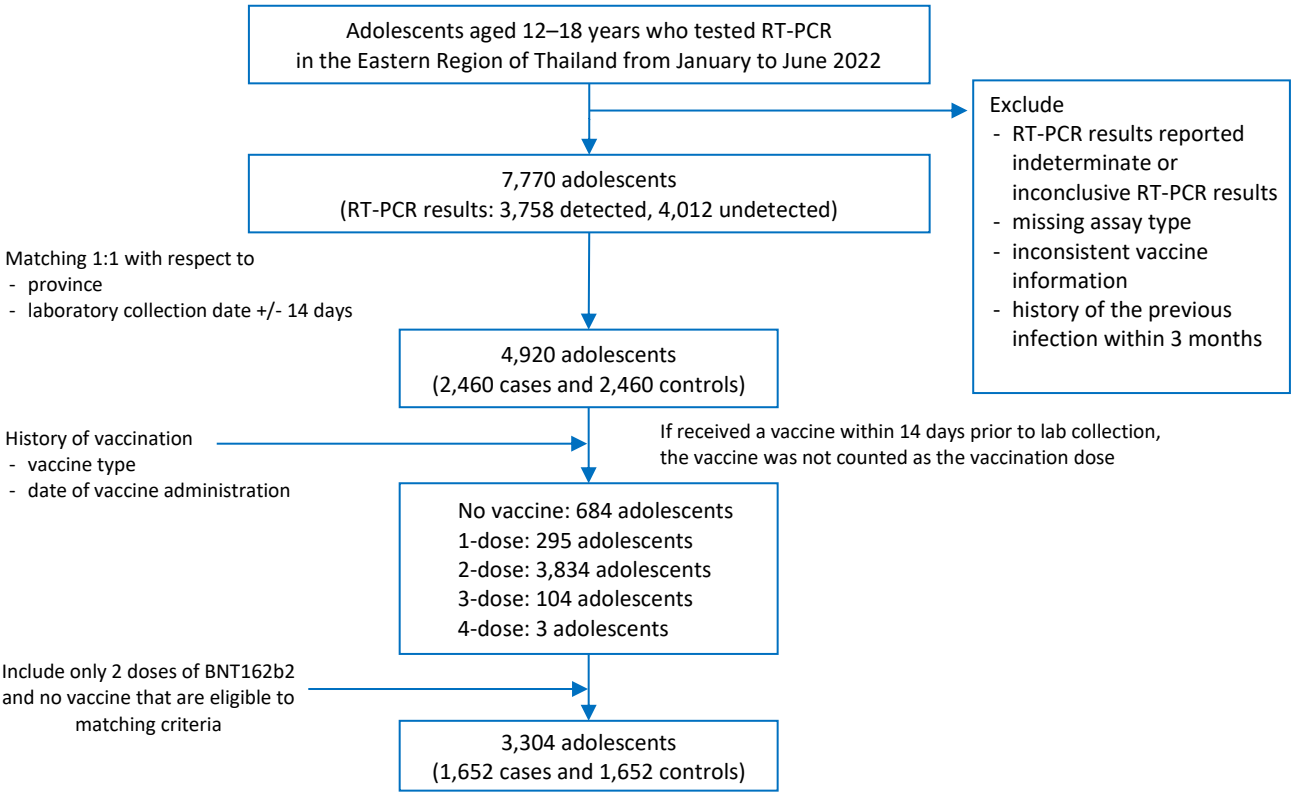

Figure 1. Flow diagram of a test-negative case-control study to determine the real-world effectiveness of 2-dose BNT162b2 against SARS-CoV-2 infection among Thai adolescents during Omicron predominance

The median (interquartile range, IQR) age was 15.8 (13.9–17.3) years, and 53.4% were aged 12–15 years. The median (IQR) interval between the last vaccination and first RT-PCR test was 91 (55–125) days (Table 1).

Table 1. Comparison of baseline characteristics of cases (RT-PCR SARS-CoV-2 detected) and controls (RT-PCR SARS-CoV-2 undetected) in the test-negative case-control study

Characteristic	Overall (n=3,304)	Cases (n=1,652)	Controls (n=1,652)	*P*-value
Age (years), median (IQR)	15.8 (13.9–17.3)	15.7 (13.9–17.3)	15.8 (13.9–17.4)	0.40
Age (years), n (%)				0.14
12–15	1,764 (53.4)	903 (54.7)	861 (52.1)	
16–18	1,540 (46.6)	749 (45.3)	791 (47.9)	
History of vaccination, n (%)				0.01
No	538 (16.3)	243 (14.7)	295 (17.9)	
Yes	2,766 (83.7)	1,409 (85.3)	1,357 (82.1)	
Interval between the last vaccination and RT-PCR test (days), n (%)				0.16
15–29	595 (18)	317 (19.2)	278 (16.8)	
30–89	1,011 (30.6)	516 (31.2)	495 (30)	
90–179	1,541 (46.6)	744 (45.1)	797 (48.2)	
≥180	157 (4.8)	75 (4.5)	82 (5)	

The geographic distribution of participants was as follows: Chonburi (40.2%), Rayong (23.5%), Prachinburi (15.3%), Chachoengsao (14.0%), Trat (4.7%), Sa Kaeo (1.4%), and Chanthaburi (0.9%). The timeline of primary vaccination with BNT162b2 and RT-PCR testing is shown in Figure 2. The first dose of BNT162b2 was administered from October to November 2021, and the second dose was delivered from October to December 2021. The peak of SARS-CoV-2 infection was in January–March 2022. No death was reported during the study period.

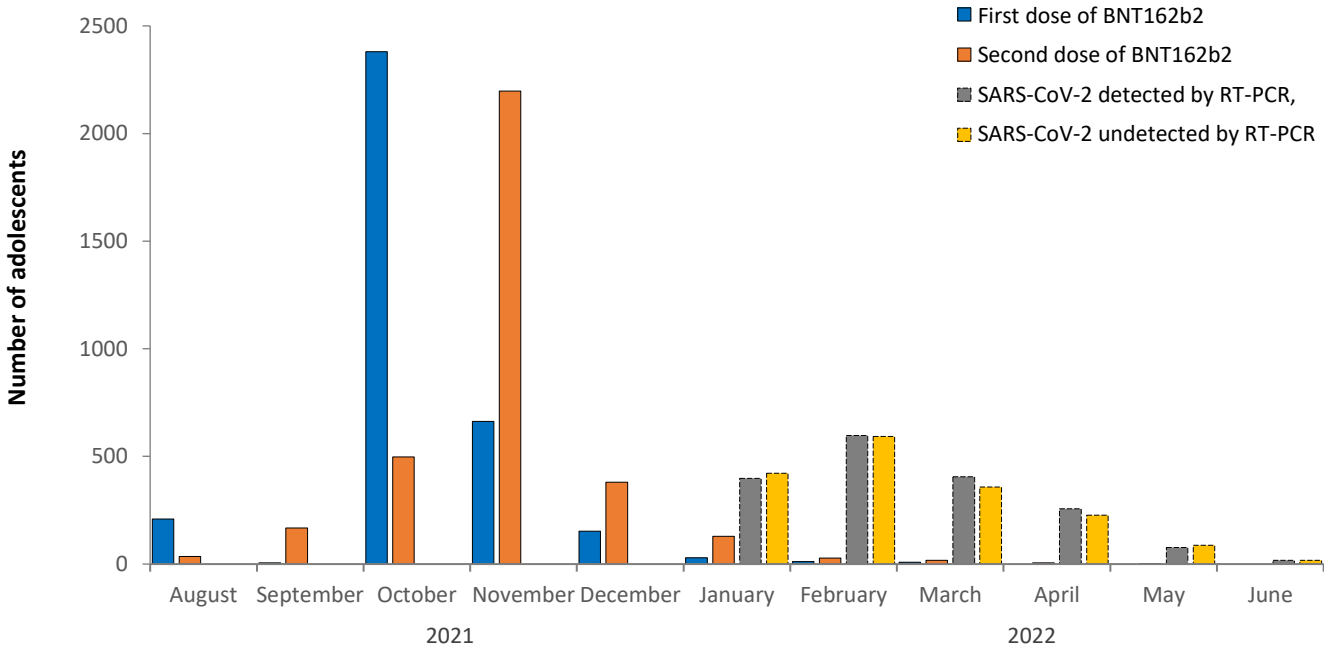

Figure 2. Timeline of the first and second BNT162b2 administration and reported RT-PCR of SARS-CoV-2 results among Thai adolescents in the Eastern Region by month

Real-world Vaccine Effectiveness of 2-dose BNT162b2 against SARS-CoV-2 Infection

The RVE (95% CI) of BNT162b2 against the Omicron infection was 22% (7–34%). Among those aged 12–15 and 16–18 years, the RVE was 19% (-16–48%) and 31% (10–46%), respectively (Table 2). After adjusting for age, the RVE (95% CI) of BNT162b was 22% (5–35%). The RVE (95% CI) against infection over time is shown in Table 3 and reached its highest point (71%) 15–29 days after vaccination.

Table 2. Vaccine effectiveness of 2-dose BNT162b2 against SARS-CoV-2 infection among Thai adolescents stratified by age group

Age group (years)	Odds ratio (95% CI)	Vaccine effectiveness (95% CI)	Vaccine effectiveness (95% CI)†
12–18	0.78 (0.66–0.93)	22% (7–34%)	22% (5–35%)
12–15	0.81 (0.52–1.26)	19% (-26–48%)	NA
16–18	0.69 (0.54–0.90)	31% (10–46%)	NA

†Age adjusted
CI: confidence interval, NA: not applicable

Table 3. Vaccine effectiveness of 2-dose BNT162b2 against SARS-CoV-2 infection among Thai adolescents stratified by the duration of last vaccination and RT-PCR test

Interval between the last vaccination and RT-PCR test (days)	Odds ratio (95% CI)	Vaccine effectiveness (95% CI)
15–29	0.29 (0.08–1.09)	71% (-9–92%)
30–89	0.94 (0.43–2.02)	6% (-100–57%)
90–179	0.66 (0.32–1.35)	37% (-35–65%)
≥180	NA	NA

NA: not applicable (no event to calculate)

Discussion

This study evaluated the RVE of a 2-dose BNT162b2 vaccine against SARS-CoV-2 infection among Thai adolescents aged 12 to 18 years in a period of Omicron predominance. The RVE was 22% and was slightly higher in older adolescents (16–18 years) than in younger ones (12–15 years). These findings are consistent with those of similar studies conducted in the United States and Singapore, which reported VE against infection ranging from 20 to 25% and VE against hospitalization ranging from 40 to 75%.[5,18] Younger adolescents had lower VE than older adolescents, which might be attributed to their less mature immune system or a different immune response to the vaccine.[19] Our findings indicate that the RVE against the Omicron variant was lower compared to the vaccine efficacy against the Alpha variant in a randomized control trial and the RVE against the Delta variant.[19,20] This difference can be attributed to several factors, including the difference in study timelines, the presence of multiple mutations in the spike protein, the increased transmissibility, and its ability to evade the immune response of the Omicron variants.[21–23]

Assessing the performance of COVID-19 vaccines post-licensure is crucial to inform decision-making on their use in national or regional vaccination strategies, including booster dose regimens and effectiveness against new emerging virus variants. This study reported a rapid decline in RVE from 71% within 30 days to values ranging from 6% to 37% after 30 days from the last vaccination. The decline in protection over time has been observed in other studies and is more accelerated with the Omicron variant compared to the Delta variant.[20] Therefore, it is important to consider administering a booster dose. A booster dose of monovalent BNT162b2 among adolescents in a national cohort from Singapore was found to have an increased RVE against Omicron infection (RVE 56%, 95% CI 53–58) and against hospitalization (RVE 94%, 95% CI 86–97%).[15] Another study from the United States reported a higher RVE against symptomatic SARS-CoV2 infection (71%, 95% CI 67–76%) among adolescents during a period of Omicron predominance after receiving a booster dose of BNT162b2.[24]

The strength of this study is the use of a national data registry that links RT-PCR testing and vaccination history; however, there are also some limitations to consider. Firstly, the lack of clinical data limited our ability to distinguish between the RVE for symptomatic or asymptomatic SARS-CoV-2 infection. Secondly, we did not have data on the immune status of participants, which may have affected the RVE in immunocompromised individuals. However, this proportion is relatively small among adolescents. Thirdly, we did not exclude adolescents with previous infection more than three months which may have affected RVE estimates. Prior SARS-CoV-2 infection can affect the estimated VE; people who haven't been vaccinated but have had a previous infection may have immunity resulting from the infection, which could lead to lower VE estimates. On the other hand, individuals who have been vaccinated and had a prior infection may have stronger protection than those who were only vaccinated, resulting in higher VE estimates. However, the Thai guideline recommended to give COVID-19 vaccines after three months of infection. Our results should therefore reflect the RVE in Thailand. Fourthly, there may be a bias between vaccinated and unvaccinated individuals for health care seeking due to the lack of randomization of vaccination, although the test-negative study is designed to minimize this potential bias. Fifthly, there is a risk of misclassification in individuals with COVID-19 who tested negative due to the timing of testing. However, the laboratory results in the study were from RT-PCR, which has high sensitivity and specificity. Lastly, our study solely evaluated the RVE of the 2-dose BNT162b2 regimen against infection, and it might have limited capability to detect the RVE of alternative regimens as well as against severe infection and mortality. Overall, while our study provides important insights into the real-world effectiveness of the BNT162b2 against the Omicron variant, further research is needed to address these limitations and provide a more comprehensive understanding of the RVE against emerging variants of SARS-CoV-2.

Public Health Action and Recommendations

This study highlights the importance of continued monitoring of real-world VE, and it is crucial to communicate the findings to the public. While the RVE of 2-dose BNT162b2 against Omicron infection is relatively low, the marginal effectiveness could provide a non-negligible impact in alleviating the risk of wide-spreading infection, given the fact that adolescents are socially active. Furthermore, it still provides protection against hospitalization and death. Additionally, several meta-analyses have shown that vaccination reduced the risk of long COVID syndrome and multisystem inflammatory syndrome in children and adolescents.[25–26] Based on the results that the rapid decline of RVE of the primary series of BNT162b2 and findings from other studies, it is recommended that a booster dose of the mRNA vaccine be administered to adolescents.[15,24] This booster dose aims to increase the

VE against emerging variants, as they may exhibit immune escape and immunity waning. The public should also be encouraged to continue practicing other preventive measures, such as wearing masks and practicing physical distancing when infectious to reduce the spread of the virus.

Conclusion

Among Thai adolescents aged 12 to 18 years, the age-adjusted RVE against confirmed COVID-19 infection (Omicron variant) after they received two doses of BNT162b2, with a median follow-up time of approximately three months, was 22% (95% CI 5–35%), which was comparable to reports from other countries. A rapid decline in protection was observed; therefore, administering a booster dose of mRNA vaccine may be necessary to enhance the vaccine's effectiveness against the Omicron variant.

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Disclosure

Authors declare no conflict of interest.

Suggested Citation

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