# Effectiveness of the CoronaVac Vaccine on Symptomatic COVID-19 Infection, Severe Disease, ICU/semi-ICU Admission, and Mortality in Samut Sakhon Province: a Test-Negative Case-Control Study

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**Abstract**

A mass vaccination campaign with the inactivated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine, CoronaVac, was implemented in Thailand during the early months of the COVID-19 pandemic. As the Delta variant became the dominant strain in the country, we aimed to evaluate the real-world effectiveness of this particular vaccine among adults in Samut Sakhon Province, Thailand. A test-negative case-control study was conducted from 1 Jun to 31 Jul 2021 to evaluate the effectiveness of CoronaVac against symptomatic COVID-19 infection, severe disease, admission to intensive care unit (ICU)/semi-ICU and mortality. We estimated odds ratios using multiple logistic regression. Among 11,371 participants included in the study, 3,116 (27.4%) tested positive for COVID-19 and 3,333 (29.3%) completed two doses of vaccine. The adjusted vaccine effectiveness of two-dose CoronaVac was 65.8% (95% confidence interval (CI) 61.9–69.3) for the prevention of symptomatic infection, 71.8% (95% CI 58.5–81.6) for severe disease, 72.7% (95% CI 56.6–83.9) for ICU/semi-ICU admission and 86.7% (95% CI 34.8–99.3) for mortality. Results of this study demonstrate that CoronaVac had moderate effectiveness against symptomatic COVID-19 infection, while it was effective in preventing severe disease, ICU/semi-ICU admission and COVID-19 related deaths in a setting where the two variants were circulating.

**Keywords:**  COVID-19, CoronaVac, vaccine effectiveness, test-negative study, Thailand

## Introduction

Since the start of the coronavirus disease 2019 (COVID-19) pandemic, Thailand has recorded over 1 million confirmed cases and almost 10,000 COVID-19 related deaths.[1] In 2020, the government's nation-wide restrictive measures successfully contained the spread of the virus. However, during December 2020, a new outbreak, originating in a seafood market in Samut Sakhon Province, raised the total number of confirmed cases to over 20,000 within three months. Another outbreak, with the epicenter in Bangkok, followed in April 2021. The country's social environment, economy and healthcare system was severely affected despite considerable efforts at controlling the pandemic.

Apart from the lockdown strategy to restrict people's movement and other preventive measures, vaccination is another approach for combating the virus. CoronaVac (Sinovac), an inactivated vaccine developed in China, is known to be 50–65% effective against symptomatic COVID-19 infections based on studies from Brazil and China, while a study from Turkey reported a protective efficacy of 84%.[2–5] A preliminary report from Phuket in Thailand also showed promising results regarding the vaccine effectiveness among high-risk contacts.[6]

Although the first vaccination campaign was rolled out in early February 2021, initially focusing on healthcare workers in affected areas, the number of

confirmed cases reached 10,000 cases per day with over 200 deaths per day. Moreover, concerns were raised over the effectiveness of the CoronaVac vaccine against the different COVID-19 variants circulating around the world, namely B1.117 (Alpha), B.1.351 (Beta) and B.1.617 (Delta). Thus, further studies assessing the vaccine efficacy are warranted to ensure public trust during the ongoing pandemic.

Samut Sakhon Province is a coastal province in central Thailand with a population of approximately 600,000. Over the past decade, the extensive industries in fisheries and seafood processing have brought in a large number of migrant workers from neighboring countries. Currently, it is estimated that over 250,000 migrant workers reside in this province. These characteristics, for example, high population density, dynamic population movement, migrant workers' living conditions, and limited access to healthcare services, pose several challenges in the management of the pandemic.

In light of the Ministry of Public Health's response to the latest COVID-19 outbreak in Samut Sakhon Province, the national policy in directing the vaccine and other resources to the areas of greatest need, combined with 'bubble and seal' measures at factories, effectively suppressed the spreading of the virus. In August 2021 the number of confirmed cases exceeded 50,000 and only 30% of the Sumat Sakhon Province population were vaccinated. A preliminary report found that the proportion of cases infected with the Delta-lineage had increased from 28% to 97% within two months.[7]

Since data regarding the effectiveness of the CoronaVac in Thailand are limited, we aimed to ascertain the real-world effectiveness of the vaccine against symptomatic COVID-19 infections and clinical outcomes of interest, namely severe disease, intensive care unit (ICU)/semi-ICU admissions and mortality among the adult population in Samut Sakhon Province, Thailand.

## Methods

### Study Population and Design

We conducted a retrospective test-negative case-control study. This type of study is widely used to estimate the effectiveness of influenza vaccines as it reduces bias from misclassification and differences in healthcare seeking behavior and access to testing between cases and controls.[8–10]

The study population consisted of residents of Samut Sakhon Province who attended an acute respiratory infection clinic between 1 Jun and 31 Jul 2021 in the three studied hospitals, namely Samutsakhon Hospital, Krathumbaen Hospital and Banphaeo General Hospital, and anyone who was categorized as a patient under investigation, defined by the Department of Disease Control, Ministry of Public Health, Thailand, as a person who had a body temperature ≥37.5 °C and/or any respiratory symptoms, for example, cough, runny nose, sore throat, anosmia, tachypnea, shortness of breath, or difficulty breathing, and with risk factors such as a history of living in an outbreak area or visiting a crowded public area within 14 days prior to symptom onset.[11]

Cases were participants who presented with symptoms of COVID-19 infection and tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by reverse transcription polymerase chain reaction (RT-PCR) within 10 days after symptom onset. Controls were persons who had symptoms compatible with COVID-19 infection but tested negative. We excluded persons who were vaccinated with other COVID-19 vaccines and those who tested positive for COVID-19 within the past six weeks. As the primary target group for the initial CoronaVac vaccination campaign in Samut Sakhon Province was Thai persons aged between 18–59 years, we accordingly excluded participants who were non-Thais and aged less than 18 or over 60 years and the data were collected from 1 Jul to 31 Aug 2021. To calculate a minimum sample size of cases in this study, the following formula was used:[12]

$$N = (z/d)^2 [1/A (1–A) + 1/CP_2 (1–P_2)],$$

where C is the proportion of controls to cases, which was 1 (1:1 case-to-control ratio); $P_2$ is the vaccine coverage, which was 30% in the study population; A is the anticipated vaccine effectiveness, which was 60% according to a previous study, and d is the width of the confidence interval (CI). With 20% desired precision and z value of 1.96, the number of the cases and controls needed in this study was both 801.

### Data Sources

Patient demographic data, clinical data and RT-PCR testing results were extracted from the hospitals' electronic medical record database. Additional data on COVID-19 patient registry and mortality data were collected from Samut Sakhon Provincial Health Office and the Office of Disease Prevention and Control Region 5 Ratchaburi. The COVID-19 vaccination registry data was retrieved from the Strategy and Planning Division of the Office of the Permanent Secretary, Ministry of Public Health. All of the data

sources mentioned above were linked with the 13-digit national identification number.

## Outcomes and Covariates

For vaccination status, we defined fully vaccinated individuals as those who received the second dose of vaccine for at least two weeks. The primary outcomes are RT-PCR confirmed symptomatic COVID-19 infection, severe COVID-19 disease (defined as severe pneumonia requiring oxygen therapy regardless of the type of oxygen delivery devices), admission to ICU/semi-ICU and COVID-19 related deaths. These clinical outcomes were assessed until the end of the study (31 Aug 2021) Covariates assumed to be associated with the risk of exposure to SARS-CoV-2 and likelihood of receiving a vaccine, including age and gender, were also recorded and included in the final model.

## Statistical Analysis

Descriptive statistics were used to summarize frequency distribution, central tendency and variability of study samples. Chi-square and independent t-tests were used to determine the difference in all covariates between cases and controls. We used multiple logistic regression to estimate the odds of being fully vaccinated among all participants. The independent variables were vaccination status, age and gender. Age and gender were included in the multivariate model as they were potential confounders. The vaccine effectiveness was estimated by 1 minus the corresponding odds ratio and the 95% CI was obtained from the adjusted model and expressed as a percentage. Variables with a $p$-value <0.05 were considered significant. Statistical analysis was performed using R version 4.1.1 (Foundation for Statistical Computing, Vienna, Austria).[13]

## Ethics

Ethical approval to conduct the study was obtained from the Research Ethics Committee of Samut Sakhon Provincial Health Office and permission was obtained from the three studied hospitals.

## Funding

## Results

Between 1 Jun and 31 Jul 2021, a total of 11,371 participants who had RT-PCR testing for SARS-CoV-2 at the three studied hospitals were included, of which 3,116 (27.4%) tested positive for COVID-19 and 8,255 (72.6%) tested negative. Figure 1 shows the study diagram and vaccination status (unvaccinated, vaccinated with one dose, or vaccinated with two doses) among cases and controls. Overall, 3,333 (29.3%) participants received 2 doses of the CoronaVac vaccine, 247 (2.2%) received 1 dose, and 7,791 (68.5%) were unvaccinated.
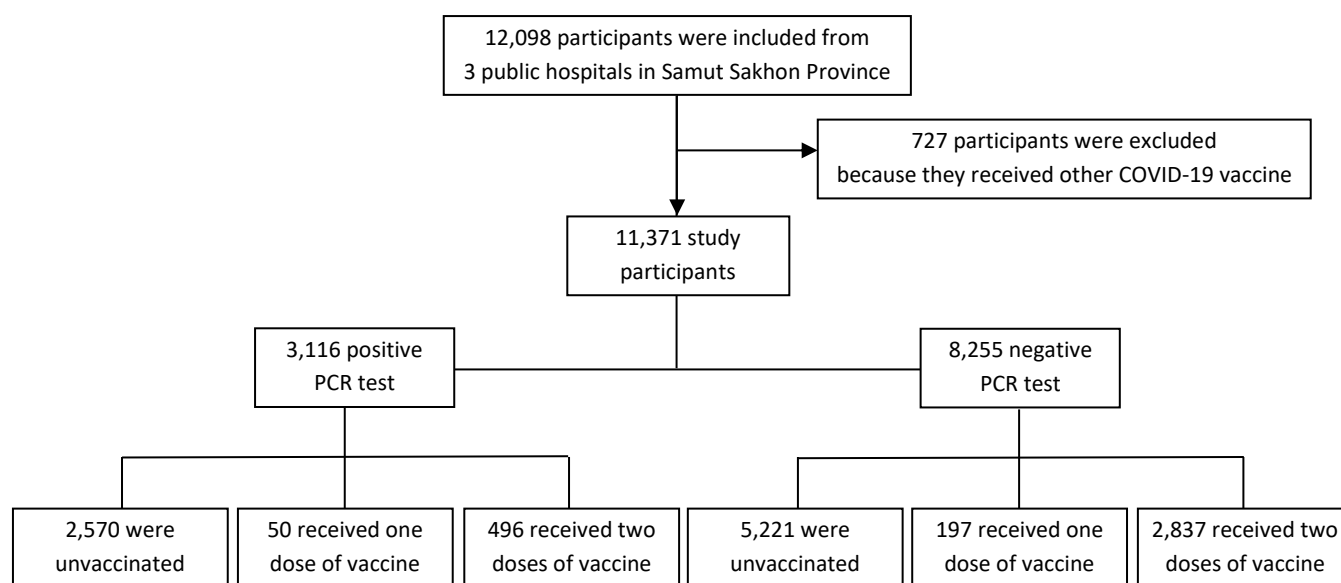


**Figure 1. Flowchart of study population and vaccination status**

Table 1 shows the demographic characteristics of the participants according to the RT-PCR test results and vaccination status. The mean age among those who tested positive and negative was 38.7 and 37.8 years, respectively. More than half of the participants were female among both cases (58.4%) and controls (58.1%) while almost three-quarters of the participants resided in Mueang Samut Sakhon District. The mean age and proportion residing in different districts were statistically different between cases and controls.

Results of the logistic regression analysis in which we estimated the vaccine effectiveness among fully immunized persons compared with unvaccinated individuals are shown in Table 2. The adjusted odds ratios obtained from the models were 0.34 (95% CI 0.31–0.38) for symptomatic infection, 0.28 (95% CI 0.18–0.42) for severe disease, 0.27 (95% CI 0.16–0.43) for ICU or semi-ICU admission, and 0.13 (95% CI 0.01–0.65) for COVID-19 related deaths. The adjusted vaccine effectiveness was 65.8% (95% CI 61.9–69.3) for the prevention of symptomatic infection, 71.8% (95% CI 58.5–81.6) for prevention of severe disease, 72.7% (95% CI 56.6–83.9) for the prevention of ICU/semi-ICU admission and 86.7% (95% CI 34.8–99.3) for the prevention of COVID-19 related deaths.

**Table 1. Demographic characteristics of participants (n=11,371)**

| Characteristic | Cases | Controls | *P*-value | Unvaccinated | Vaccinated with one dose | Vaccinated with two doses |
|---|---|---|---|---|---|---|
| **Total** | **3,116** | **8,255** | | **7,791** | **247** | **3,333** |
| **Age, mean ± SD** | 38.7 ± 11.7 | 37.8 ± 11.5 | <0.01 | 37.3 ± 11.8 | 37.9 ± 10.6 | 39.7 ± 10.9 |
| **Age group (years)** | | | | | | |
| 18–29 | 870 (27.9) | 2,477 (30.0) | <0.01 | 2,521 (32.4) | 67 (27.1) | 759 (22.8) |
| 30–39 | 716 (23.0) | 2,093 (25.4) | | 1,891 (24.3) | 79 (32.0) | 839 (25.2) |
| 40–49 | 788 (25.3) | 1,990 (24.1) | | 1,790 (23.0) | 51 (20.6) | 937 (28.1) |
| 50–59 | 742 (23.8) | 1,695 (20.5) | | 1,589 (20.4) | 50 (20.2) | 798 (23.9) |
| **Gender** | | | | | | |
| Male | 1,296 (41.6) | 3,462 (41.9) | 0.75 | 3,501 (44.9) | 98 (39.7) | 1,159 (34.8) |
| Female | 1,820 (58.4) | 4,793 (58.1) | | 4,290 (55.1) | 149 (60.3) | 2,174 (65.2) |
| **District** | | | | | | |
| Krathum Baen | 654 (21.0) | 1,291 (15.6) | <0.01 | 1,524 (19.6) | 28 (11.3) | 393 (11.8) |
| Ban Phaeo | 261 (8.4) | 786 (9.5) | | 677 (8.7) | 15 (6.1) | 355 (10.7) |
| Mueang Samut Sakhon | 2,201 (70.6) | 6,178 (74.8) | | 5,590 (71.7) | 204 (82.6) | 2,585 (77.6) |

*Note: SD: standard deviation; Data are presented as frequency and percentage unless otherwise specified*

**Table 2. Effectiveness of CoronaVac against symptomatic infection, severe disease, ICU admission and COVID-19 related death**

| | Number of cases | | Number of controls | | Adjusted OR (95% CI)[a] | Effectiveness, % (95% CI) |
|---|---|---|---|---|---|---|
| | Vaccinated | Unvaccinated | Vaccinated | Unvaccinated | | |
| Symptomatic infection | 486 | 2,570 | 2,780 | 5,221 | 0.34 (0.31–0.38) | 65.8 (61.9–69.3) |
| Severe disease | 27 | 204 | 3,239 | 7,587 | 0.28 (0.18–0.42) | 71.8 (58.5–81.6) |
| ICU[b] admission | 18 | 144 | 3,248 | 7,647 | 0.27 (0.16–0.43) | 72.7 (56.6–83.9) |
| Confirmed deaths | 1 | 16 | 3,265 | 7,775 | 0.13 (0.01–0.65) | 86.7 (34.8–99.3) |

*Note: OR: odds ratio. CI: confidence interval. [a]Adjusted for age and gender. [b]Includes semi-ICU admissions*

## Discussion

Our study provides estimates of real-world effectiveness of the CoronaVac vaccine against symptomatic infection and clinical outcomes among those aged 18–59 years who had respiratory symptoms compatible with COVID-19 in Samut Sakhon Province, Thailand. The vaccine effectiveness of two-dose CoronaVac was 65.8% for symptomatic infection, 71.8% for severe disease, 72.7 for ICU/semi-ICU admission and 86.7% for COVID-19 related deaths. It was likely that the circulating variants in Samut Sakhon Province during the study period were mixing between the Alpha- and Delta-lineage viruses as the random sequenced samples demonstrated and increasing proportion of the Delta variant over time, although this could not be directly confirmed. Thus, the vaccine effectiveness reported in this study might not be specific to any particular variant. Our findings are consistent with estimates reported in other studies. The study of a prospective national cohort in Chile demonstrated a high efficacy of CoronaVac in preventing COVID-19 (65.9% [95% CI 65.2–66.6]), hospitalization (87.5% [95% CI 86.7–88.2]), ICU

admission (90.3% [95% CI 89.1–91.4]) and COVID-19 related deaths (86.3% [95% CI 84.5–87.9]), while a randomized phase 3 clinical trial in Brazil among healthcare professionals showed a similar efficacy against symptomatic COVID-19 (50.7% [95% CI 36.0–62.0]), preventing the need for medical treatment (83.7% [95% CI 58.0–93.7]) and moderate/severe disease (100% [95% CI 56.4–100]).[3,13] Our results are somewhat lower than the estimates reported in a randomized phase 3 clinical trial in Turkey (83.5% [95% CI 65.4–92.1]) but significantly higher than the vaccine effectiveness reported in another study from Brazil (36.8% [95% CI 54.9–74.2]).[2,5] These differences in estimates are possibly owing to the dissimilar predominant viral lineage and various national policies on preventive measures implemented during the study period.

Despite the acceptable immunogenicity and safety profiles of CoronaVac, the effectiveness of the vaccine became highly questionable as the Delta variant has been the major variant circulating in Thailand.[15,16] Eventually, the Thai government decided to revoke the 2-dose CoronaVac schedule and endorse a mix-and-match vaccine combination for all Thai adults, known as the CoronaVac-AstraZeneca regimen. Moreover, concern over rapid immunity waning has been suggested by many studies.[17-19] Consequently, the Thailand Ministry of Public Health approved another type of COVID-19 vaccine, Pfizer and AstraZeneca, as a booster dose for every person who already completed 2 doses of CoronaVac, while the World Health Organization recommended a third dose specifically in persons aged over 60 years.[20] Thus, these mixed vaccine regimens are yet to be officially approved by World Health Organization and more evidence on immunogenicity and safety of combining different vaccines types against Delta variant is needed.

Our study has several limitations. First, our results may be subject to unmeasured confounding due to the nature of an observational study. Although we already included age and gender in the adjusted model, some potential confounders that might be associated with the risk of COVID-19 infection and acquiring severe disease, such as underlying medical condition, individual-level protective behavior, were not included. Second, throughout the study period, Thailand's fourth outbreak had severely affected the health system in Samut Sakhon Province. Given limited resources during the crisis (i.e., exceeding ICU/semi-ICU bed capacity, an increasing need for ventilators and medical personnel shortage), a number of patients were not admitted to hospital in a timely fashion and did not receive adequate treatment resulting in increased morbidity and mortality. Therefore, our estimates might not truly reflect the actual vaccine effectiveness. Lastly, our results may not be generalizable to those aged 60 years and above, and since our study population were relatively young and healthy, the need for ICU admission and mortality rate may be different from older and less healthy populations.

In conclusion, we found that the CoronaVac vaccine had moderate efficacy against symptomatic COVID-19 infection, while it was effective in preventing severe disease, ICU/semi-ICU admission and COVID-19 related deaths among Thai adults in a setting where the Delta and Alpha variants were circulating. Viral genetic mutation and waning immunity necessitates continued monitoring of vaccine effectiveness for inactivated SARS-CoV-2 vaccines.

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## Suggested Citation

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