



## SARS-CoV-2 Infections, Vaccination, and Vaccine Effectiveness in Thailand, January 2021–January 2022: Results of a Cohort Study in Four Provinces

Sutthichai Nakphook<sup>1,2</sup>, William W. Davis<sup>3,4</sup>, Kriengkrai Prasert<sup>2,5</sup>, Darunee Ditsungnoen<sup>3</sup>, Hatairat Lerdsamran<sup>6</sup>, Pilaipan Puthavathana<sup>6</sup>, Somrak Sirikhettakon<sup>7</sup>, Kittiphun Chalom<sup>8</sup>, Kusuma Sawangpun<sup>9</sup>, Sopon Iamsirithaworn<sup>1</sup>, Eduardo Azziz-Baumgartner<sup>4</sup>, Beth Skaggs<sup>3,4</sup>, Prabda Praphasiri<sup>2,3\*</sup>, Joshua A. Mott<sup>3,4</sup>

1 Department of Disease Control, Ministry of Public Health, Thailand

2 Faculty of Public Health, Kasetsart University, Chalermprakiat Sakon Nakhon Province Campus, Thailand

3 Thailand MOPH-U.S. CDC Collaboration, Thailand

4 U.S. Centers for Disease Control and Prevention, USA

5 Nakhon Phanom Provincial Hospital, Ministry of Public Health, Thailand

6 Mahidol University, Thailand

7 Institute for Urban Diseases Control and Prevention, Department of Disease Control, Ministry of Public Health, Thailand

8 Chiang Mai Provincial Health Office, Ministry of Public Health, Thailand

9 Phuket Provincial Health Office, Ministry of Public Health, Thailand

\*Corresponding author email: hpu3@cdc.gov

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### Abstract

We implemented a sero-epidemiological survey of SARS-CoV-2 antibodies in an age-stratified sample of people in Thailand. We used two-stage sampling employing stratified random sampling with official residence lists to recruit 1,200 people in three age strata in Bangkok, Chiang Mai, Nakhon Phanom and Phuket provinces. Serum was screened for SARS-CoV-2 antibodies using enzyme-linked immunosorbent assay (ELISA) and microneutralization assay. We collected symptom and vaccination data weekly and tested participants who met a COVID-19-like illness (CLI) case definition by rRT-PCR. Serum for SARS-CoV-2 antibodies was collected and tested again in January 2022. We estimated vaccine effectiveness using multi-level Poisson regression with propensity score stratification to control for differences in healthcare-seeking behavior. Of 1,200 people enrolled in January 2021, 5 (0.4%; 95% confidence interval 0.16–1.16) had antibody detected by ELISA at baseline, and none tested positive by microneutralization. From January 2021 to January 2022, 23% of participants (278/1,200) reported CLI and 18% of CLI cases (50/278) tested positive for SARS-CoV-2 by rRT-PCR. In January 2022, 87% of participants (955/1,101) had SARS-CoV-2 antibodies detected by ELISA. Ninety-eight percent (1,034/1,045) received at least one dose of COVID-19 vaccine and did not get infection. Vaccine effectiveness against hospitalization was 72% for two doses and 98% for three doses of any vaccine. Low SARS-CoV-2 seroprevalence in 2021 suggests that Thailand successfully prevented COVID-19 infections through non-pharmaceutical interventions during the first year of the pandemic. High seroprevalence in 2022 was driven by vaccination.

**Keywords:** antibodies, SARS-CoV-2, seroprevalence, Thailand, vaccine effectiveness

## Background

Thailand was the first country after China to identify a laboratory-confirmed case of severe acute respiratory coronavirus 2 (SARS-CoV-2) infection. Between 13 Jan 2020 and 1 Apr 2021, Thailand reported 28,889 laboratory-confirmed coronavirus disease 2019 (COVID-19) infections.<sup>1</sup> Studies suggest that quarantine for international travelers and other nonpharmaceutical interventions (NPIs) implemented by the government of Thailand, as well as high compliance with NPIs, contributed to limiting transmission of SARS-CoV-2 during the first 15 months of the pandemic.<sup>2-8</sup>

As Thailand transitions from a pandemic to an endemic model of SARS-CoV-2 response, data on antibody profiles and vaccine effectiveness are needed to assess the impact of pharmaceutical and nonpharmaceutical interventions. To gauge the proportion of persons in Thailand with prior SARS-CoV-2 infections or vaccinations and estimate vaccine effectiveness, a sero-epidemiological survey was conducted based on the World Health Organization Unity studies protocol between January 2021 and January 2022 in four major provinces in Thailand.<sup>3</sup>

## Methods

We selected one major province in each of the four regions of Thailand: Chiang Mai, Nakhon Phanom, Bangkok and Phuket provinces. In Bangkok Province, a two-stage sampling was employed. We randomly selected 5 (of 50) districts with probability proportional to size of the population. Stratifying the official list of Thai registered citizens into three age groups (5–18, 19–59, and  $\geq 60$  years), we then conducted simple random sampling within each age group. We recruited 75 persons aged 5–18, 150 persons aged 19–59, and 75 persons aged 60 years and older in each province. If participants could not be contacted or refused, we replaced them with the next person on the official list within the same age group until achieving the specified sample sizes. Estimate sample size equation was,

$$n = \frac{Z_{1-\alpha/2}^2 p(1-p)}{d^2}$$

Where Z (assuming significance 0.05) was 1.96, d was margin of error (0.05), and p was 0.5.

We determined that 300 people in each province would permit seroprevalence estimates of up to 50% prevalence with confidence limits of  $\pm 5\%$ ; 1,200 total participants were thus required for four provinces. We back-calculated power to detect a prevalence of 1% based on the same assumptions, using the formula below:

$$n = \frac{[Z_{1-\alpha/2} + Z_{1-\beta}]^2}{\frac{p_1 - p_0}{\sqrt{p_1(1-p_1)}}}$$

Where  $Z_{1-\alpha/2}$  (assuming significance 0.05) was 1.96,  $Z_{1-\beta}$  (assuming power 80%) was 0.84,  $p_0$  was hypothesized proportion (50% seroprevalence) and  $p_1$  was the measured proportion (1%).

We included people who could communicate in Thai language, were on the official lists and resided in the four provinces at the time of survey enrolment. Exclusion criteria included contraindications to venipuncture and nasopharyngeal or throat swabs.

We collected the blood specimens and the data on demographics, risk factors, mask use, history of COVID-19-like illness (CLI) (presence of one or more of the following: fever, cough, shortness of breath, myalgia, sore throat, loss of taste or smell, or diarrhea) since the beginning of the pandemic, history of positive SARS-CoV-2 rRT-PCR test results since the beginning of the pandemic, and travel history. Blood was again collected from all participants in January 2022.

After enrolment, participants were weekly contacted by phone and asked about CLI symptoms or vaccination in the preceding week. If participants reported CLI, they were asked to visit the nearest health facility for a nasopharyngeal swab, subsequently tested for SARS-CoV-2 by rRT-PCR.

Serum was received within two weeks at Mahidol University and screened within two weeks for SARS-CoV-2 total immunoglobulin using the sandwich enzyme-linked immunosorbent assay (ELISA) (Beijing Wantai Biological Pharmacy Enterprise Co., Ltd., China), which uses the receptor binding domain (RBD) of the SARS-CoV-2 spike protein as the test antigen. Previously tested in a Thai population found sensitivity of the Wantai test to be 100% and specificity 99.2%; multiple studies outside of Thailand reported sensitivities from 62% to 98%.<sup>4-7</sup>

The sandwich ELISA assay was performed per the Wantai kit instructions. Staff at Mahidol University performed cytopathic effect based microneutralization assay following the protocol previously described in a biosafety laboratory level 3.<sup>4</sup>

For descriptive statistics, we computed number and percent of participants by gender and mean with standard deviation by province and age group. P values for analysis of variance were generated. All analyses were performed using STATA 14 (College Station, TX, USA). We calculated the crude seroprevalence and 95% confidence intervals (CI) of SARS-CoV-2 as the percentage of participants with

positive SARS-CoV-2 antibodies. The national seroprevalence estimations were calculated, weighted by age, gender and provincial population size in Thailand, using 2021 population data.<sup>8</sup>

Associations between demographic variables and vaccination, hospitalization were estimated with negative binomial regression. Vaccine effectiveness (VE) was estimated as 100% x (1-rate ratio of rRT-PCR-confirmed COVID-19 infections in vaccinated cohort versus unvaccinated cohort). VE was estimated for infection with fever and infection with hospitalization. These outcomes represented any, mild to moderate, and severe infection.<sup>9</sup> Propensity score stratification was included in the VE estimation to approximate likelihood of accessing and receiving COVID-19 vaccine. To measure time-to-event duration of vaccine dose in multivariable model, the duration of each dose started after receiving the vaccine for 14 days and ended when either the next vaccine dose duration started, developing the study outcome, or loss to follow-up. Propensity scores were constructed using multivariable logistic model that included pre-vaccination variables (age, gender, educational, occupational, smoking status, income, comorbidity, body mass index, history of influenza vaccination in the previous year, and facemask using in public) to estimate the probability of booster 3<sup>rd</sup> dose of COVID-19 vaccination. Poisson regression with log person-time at risk as an offset was used for VE estimate calculation. A multi-level mixed effect model was applied to the Poisson regression to account for propensity score stratification.

The protocol was approved by the Ethical Review Committee for Research related to COVID-19 Disease or Public Health Emergency, Department of Disease Control, Thai Ministry of Public Health.

## Results

During 18 Dec 2020 to 2 Feb 2021, we identified 1,898 people for enrollment. Of those, 440 (23%) people were not available, 33 (8%) refused to participate, and 21 (5%) did not show up at the clinic. In total, 698 (37%) refused or were not available; 384 men and 816 women were included in the survey. Of these 1,200 participants, 452 (37.7%) reported experiencing at least one CLI prior to enrolment, none reported a previous laboratory-confirmed SARS-CoV-2 test result or infection at time of baseline serum collection, and 92% reported “always” or “mostly” wearing masks outside of the home (Table 1).

Serum testing at baseline identified five positive results for total antibody to SARS-CoV-2 by ELISA (0.4%, 95% CI 0.16–1.16), and 5 borderline results. Four of the five positive cases were present in the 19–59-year-old group and one positive in the 60 year and older age group. One positive result was found in each of Nakhon Phanom and Phuket provinces, and three were in Chiang Mai Province. Of note, none of these five ELISA positive cases was confirmed positive for neutralizing antibodies to SARS-CoV-2 by microneutralization assay, suggesting that these were recent infections and neutralizing antibodies had yet to develop.

**Table 1. Baseline characteristics of survey participants in the four provinces, December 2020–January 2021 (n=1,200)**

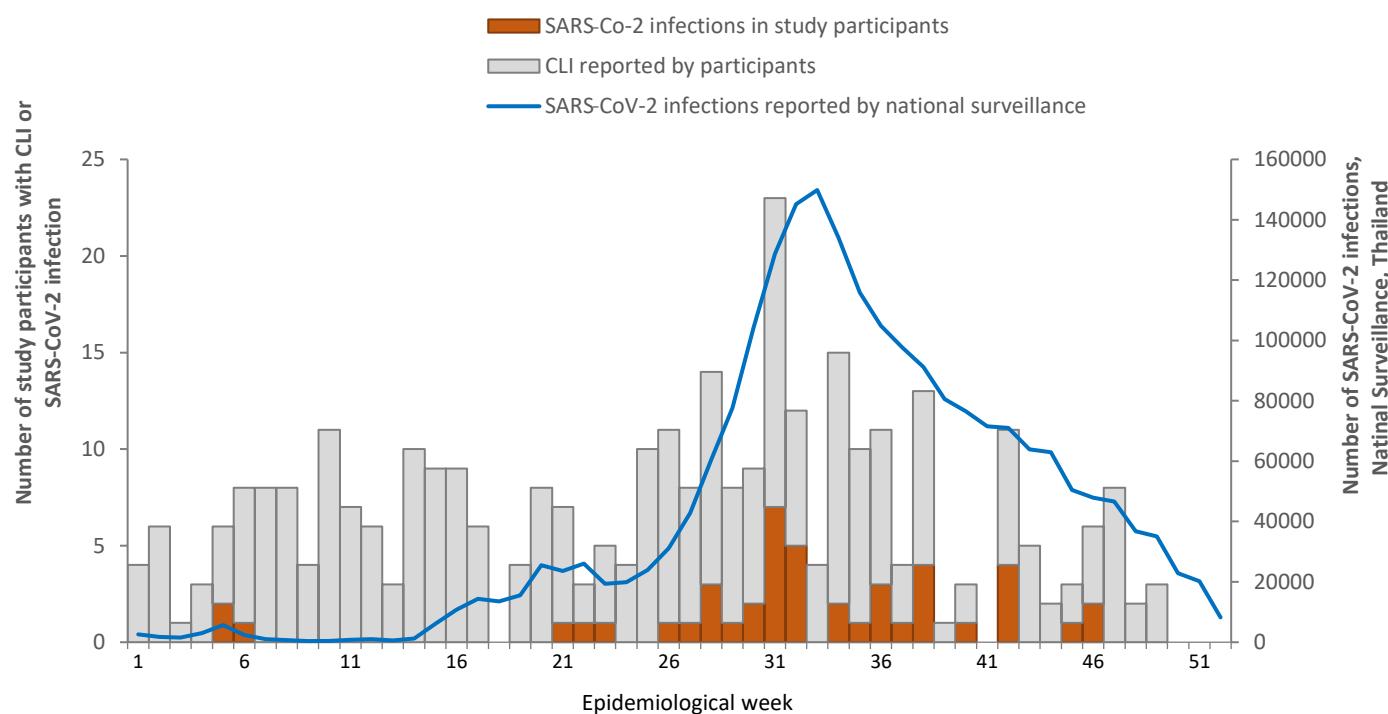
Characteristics	Total (n=1,200)	Bangkok (n=300)	Nakhon Phanom (n=300)	Phuket (n=300)	Chiang Mai (n=300)	P-value
<b>Gender, n (%)</b>						
Male	384 (32.0)	85 (28.3)	103 (34.3)	98 (32.7)	98 (32.7)	0.433 <sup>¶</sup>
Female	816 (68.0)	215 (71.7)	197 (65.7)	202 (67.3)	202 (67.3)	
<b>Age in years, mean (SD)</b>	<b>41.4 (21.4)</b>	<b>40.2 (21.8)</b>	<b>41.5 (21.7)</b>	<b>41.5 (21.0)</b>	<b>42.4 (21.4)</b>	<b>0.926<sup>#</sup></b>
<b>Age group (years), mean (SD)</b>						
5–18	11.9 (3.6)	11.0 (3.7)	12.2 (3.6)	12.0 (3.4)	12.4 (3.7)	0.914 <sup>#</sup>
19–59	43.4 (11.6)	41.5 (12.1)	42.7 (10.8)	43.9 (11.1)	45.4 (12.0)	0.404 <sup>#</sup>
≥60	66.9 (5.4)	66.5 (5.8)	68.6 (5.7)	66.0 (4.8)	66.5 (4.9)	0.195 <sup>#</sup>
<b>Body mass index*, mean (SD)</b>	<b>25.3 (5.0)</b>	<b>24.7 (4.8)</b>	<b>24.7 (4.6)</b>	<b>26.5 (5.9)</b>	<b>25.3 (4.4)</b>	<b>&lt;0.001<sup>#</sup></b>
Obesity <sup>†</sup>	143 (16.1)	28 (12.6)	30 (13.5)	55 (24.6)	30 (13.8)	0.002 <sup>¶</sup>
<b>Face mask—ever used when travelling outside<sup>‡</sup>, n (%)</b>	<b>1,196 (99.7)</b>	<b>299 (99.7)</b>	<b>299 (99.7)</b>	<b>298 (99.3)</b>	<b>300 (100)</b>	<b>0.906<sup>¶</sup></b>
Always	889 (74.8)	253 (84.3)	147 (49.0)	246 (82.0)	243 (81.0)	<0.001 <sup>¶</sup>
Mostly	203 (16.9)	40 (13.3)	75 (25.0)	42 (14.0)	46 (15.3)	<0.001 <sup>¶</sup>
Sometimes	92 (7.7)	6 (2.0)	65 (21.7)	10 (3.3)	11 (3.7)	<0.001 <sup>¶</sup>
Rarely	12 (1.0)	0 (0)	12 (4.0)	0 (0)	0 (0)	-
Never	4 (0.3)	1 (0.3)	1 (0.3)	2 (0.7)	0 (0)	0.906
<b>Change in or loss of taste<sup>§</sup>, n (%)</b>	<b>1 (0.1)</b>	<b>1 (0.3)</b>	<b>0 (0)</b>	<b>0 (0)</b>	<b>0 (0)</b>	<b>1.000<sup>¶</sup></b>
<b>Change in or loss of smell<sup>§</sup>, n (%)</b>	<b>2 (0.2)</b>	<b>0 (0)</b>	<b>2 (0.7)</b>	<b>0 (0)</b>	<b>0 (0)</b>	<b>0.249<sup>¶</sup></b>

\*For age ≥20 years only. <sup>†</sup>Body mass index ≥30 (age ≥20 years). <sup>‡</sup>Self-reported, “ever wear a face mask when travelling outside the home”. <sup>§</sup>Self-reported.

<sup>¶</sup>p-value calculated using Exact probability test. <sup>#</sup>p-value calculated using one-way ANOVA, comparing across participants in each province. SD: standard deviation.

From enrollment to January 2022, 23% (278/1,200) of participants reported CLI. All participants with CLI were tested for SARS-CoV-2 and 18% (50/278) were positive (Table 2). The epidemic curve of CLI and SARS-CoV-2 cases on the cohort approximated the

national curve of cases, both peaking in late July/early August (Figure 1). Among the 50 SARS-CoV-2 cases, the most common symptoms reported were sore throat (62%) cough (60%), and fever (42%), and 78% were hospitalized (Supplementary table 2).



**Figure 1. SARS-CoV-2 infections and cases of COVID-19-like illness among study participants and from national surveillance data, Thailand, 2021**

In January 2022, 1,034 (93%) study participants reported being vaccinated with one to four doses of a combination of Sinovac, Sinopharm, AstraZeneca, Pfizer and Moderna vaccines; participants received 24 different combinations of vaccine (Supplementary figure 1). Of 1,200 participants, 1,003 had received two doses of vaccine by the end of January 2022, and an additional 31 had received one dose.

On 10 Jan 2022, we drew serum from 1,101 participants. ELISA test results indicated that 955 (87%) of participants had SARS-CoV-2 antibodies, suggesting that they had been either infected or vaccinated or both (Table 2). Weighted by age, gender, and population size, we estimated that national overall prevalence was 87% (95% CI 85.0–88.5). Weighted by gender and population size, we estimated that national age-specific prevalence of people with total antibodies to SARS-CoV-2 detectable by ELISA was 64.7 (95% CI 58.8–70.6) for ages 5–18, 94.9 (95% CI 93.0–96.7) for ages 19–59, and 93.0 (95% CI 90.0–96.0) for ages 60 and older. By province, total antibodies were 89.6 (95% CI 86.5–92.7) for Chiang Mai Province, 78.4 (95% CI 73.8–82.9) for Nakhon Phanom Province, 88.7 (95% CI 85.6–91.8) for

Phuket Province and 90.8 (95% CI 85.6–91.8) for Bangkok Province (*p*-value <0.001).

Of 124 participants who were not vaccinated and had not tested positive for COVID-19, 16.1% had antibodies to SARS-CoV-2, suggesting they either did not report symptoms and were not tested or they did not report vaccination, or they had asymptomatic infection (Table 2).

Groups of participants with multiple vaccinations or booster doses tended to have larger proportions of people in the group test positive for SARS-CoV-2 antibodies (Table 2). Of 18 participants who had received one dose of vaccine and had not tested positive for COVID-19, 8 (44%) had SARS-CoV-2 antibodies detected by ELISA. Of participants who received two doses of vaccine and had not tested positive for COVID-19, 93.3% had antibodies to SARS-CoV-2, and of participants who received more than two doses of vaccine, 98.9% had antibodies to SARS-CoV-2. Six of seven (86%) participants who were not vaccinated but tested positive for COVID-19 had SARS-CoV-2 antibodies, and 100% of participants who received one or more doses of vaccine and had also tested positive for COVID-19 by rRT-PCR had SARS-CoV-2 antibodies.

**Table 2. Antibody result stratified by COVID-19 vaccination and SARS-CoV-2 infection (CLI and vaccination update 31 Jan 2022)**

	Not vaccinated (n= 166)		1 dose (n= 31)		2 doses (n= 434)		More than 2 doses (n= 569)		Total
PCR result after CLI	COVID – (n=155)	COVID + (n=11)	COVID – (n=26)	COVID + (n=5)	COVID – (n=413)	COVID + (n=21)	COVID – (n=556)	COVID + (n=13)	1,200
CLI cases, month 0 to 12	36	11	4	5	70	21	118	13	278
Positive ELISA results, month 12	16.1% 20/124*	85.7% 6/7*	44.4% 8/18*	100.0% 4/4*	93.3% 346/371*	100.0% 18/18*	98.9% 540/546*	100.0% 13/13*	86.7% 955/1101
COVID positives with fever, n (%)	-	5 (45.5)	-	2 (40.0)	-	11 (52.4)	-	3 (23.1)	
COVID positives hospitalized, n (%)	-	10 (90.9)	-	5 (100.0)	-	16 (76.2)	-	8 (61.5)	

\*Denominator is participants who could visit for blood draw at 12-month time point. CLI: COVID-19-like illness.

Approximately 4% of participants were exposed to SARS-CoV-2 antigen either through vaccination or infection but did not test positive for SARS-CoV-2 antibodies at the one-year timepoint. For these participants, the median number of days from exposure to the one-year blood draw ranged from 16 (for participants who received only one dose of vaccine) to 189 (in the participant who was infected) (Supplementary table 3).

Of 1,003 participants who had received two or more doses of vaccine, 34 (3.3%) later reported CLI symptoms and tested positive for SARS-CoV-2 by rRT-PCR at least two weeks after the second dose of vaccine. None had multiple infections.

Two doses of any vaccine were 61% (95% CI 10–84%) effective against infection, and three doses were 93% (95% CI 70–99%) effective. Similarly, two doses of vaccine were 72% (95% CI 25–90%) effective against hospitalized infection, and three doses were 98% (95% CI 80–99%) effective. Two or more doses were 80% (95% CI 33–94%) effective against rRT-PCR-confirmed infection with fever (Table 3). We repeated the analysis with common combinations of vaccine. We found the AstraZeneca-AstraZeneca-Pfizer combination to have effectiveness of 94% (95% CI 40–99%) against infection (Supplementary table 4).

**Table 3. VE against laboratory confirmed SARS-CoV-2 infection, infection with hospitalization, and infection with fever\***

	Person-year	Positive PCR <sup>†</sup> n (rate/100 person-year)	Rate ratio <sup>‡</sup> (95% CI)	VE (95% CI)	P-value
<b>Total infection</b>					
Unvaccinated (reference group)	158.69	11 (6.93)	Reference	-	-
Partial vaccinated <sup>¶</sup> (1 dose)	31.21	1 (3.20)	0.42 (0.05, 3.47)	58% (-247, 95%)	0.421
Complete vaccinated (fully 2 dose)	441.77	14 (3.17)	0.39 (0.16, 0.90)	61% (10, 84%)	0.028
Booster 3 dose	449.37	3 (0.67)	0.07 (0.01, 0.30)	93% (70, 99%)	<0.001
Booster 4 dose	124.58	0 (0.00)	-0.07 (-0.11, -0.03) <sup>§</sup>	-	0.001
At least 2 doses	1,015.39	17 (1.67)	0.23 (0.10, 0.52)	77% (48, 90%)	<0.001
At least 3 doses	573.95	3 (0.52)	0.05 (0.01, 0.24)	95% (76, 99%)	<0.001
<b>Hospitalized infection</b>					
Unvaccinated (reference group)	158.69	10 (6.30)	Reference	-	-
Partial vaccinated (1 dose)	31.21	1 (3.20)	0.46 (0.05, 3.89)	54% (-289, 95%)	0.475
Complete vaccinated (fully 2 dose)	441.77	10 (2.26)	0.28 (0.10, 0.75)	72% (25, 90%)	0.011
Booster 3 dose	449.37	1 (0.22)	0.02 (0.002, 0.20)	98% (80, 99.8%)	0.001
Booster 4 dose	124.58	0 (0.00)	-0.06 (-0.10, -0.02) <sup>§</sup>	-	0.003
At least 2 doses	1,015.39	11 (1.08)	0.14 (0.05, 0.36)	86% (64, 95%)	<0.001
At least 3 doses	573.95	1 (0.17)	0.01 (0.001, 0.16)	99% (84, 99.9%)	<0.001

**Table 3. VE against laboratory confirmed SARS-CoV-2 infection, infection with hospitalization, and infection with fever\* (cont.)**

	Person-year	Positive PCR <sup>†</sup> n (rate/100 person-year)	Rate ratio <sup>‡</sup> (95% CI)	VE (95% CI)	P-value
<b>Infection with Fever</b>					
Unvaccinated (reference group)	158.69	5 (3.15)	Reference	-	-
Partial vaccinated (1 dose)	31.21	0 (0.00)	-0.03 (-0.06, -0.004) <sup>§</sup>	-	0.408
Complete vaccinated (fully 2 dose)	441.77	8 (1.81)	0.46 (0.14, 1.54)	54% (-54, 86%)	0.206
Booster 3 dose	449.37	0 (0.00)	-0.03 (-0.06, -0.004) <sup>§</sup>	-	0.001
Booster 4 dose	124.58	0 (0.00)	-0.03 (-0.06, -0.004) <sup>§</sup>	-	0.055
At least 2 doses	1,015.39	8 (0.79)	0.20 (0.06, 0.67)	80% (33, 94%)	0.011
At least 3 doses	573.95	0 (0.00)	-0.03 (-0.06, -0.004) <sup>§</sup>	-	0.005

\*Fever was the main symptom.<sup>11</sup> <sup>†</sup>Vaccinated group, included only episodes which after final vaccination dose >14 days in the analysis. <sup>‡</sup>Multilevel poison regression with propensity score (to booster vaccination) stratification analysis. <sup>§</sup>Rate difference. <sup>¶</sup> To classify the number of vaccination dose, for the first dose was counted after take blood draw at least 14 days, second dose was after first dose 21 days and third dose was after second dose 90 days and fourth dose was after third dose 90 days. VE: vaccine effectiveness = (1 – rate ratio) x 100. CI: confidence interval.

We found no characteristics, including age group or obesity, associated with infection and hospitalization among vaccinated participants. Twenty-two percent of men and 10% of women were unvaccinated, as were 43%

of participants aged 5–18. Factors associated with not being vaccinated were male (rate ratio (RR) 0.67, 95% CI 0.56–0.79), and young age group (age 5–18 RR 0.22, 95% CI 0.18–0.25) (Table 4). (Supplementary tables 5, 6).

**Table 4. Characteristic and prognostic factor for vaccination**

Characteristics	Vaccinated (n=1,034) (n, %)	Not vaccinated (n=166) (n, %)	Rate ratio <sup>§</sup> (95% CI)	P-value
<b>Gender</b>				
Male	296 (28.6)	87 (52.4)	0.67 (0.56, 0.79)	<0.001
Female	738 (71.4)	79 (47.6)	-	-
<b>Age in years, mean (SD)</b>				
<b>Age group (years)</b>	<b>45 (19)</b>	<b>19 (20)</b>	-	<b>&lt;0.001<sup>¶</sup></b>
5–18	172 (16.6)	128 (77.1)	0.22 (0.18, 0.25)	<0.001
19–59	579 (56.0)	22 (13.2)	4.23 (2.85, 6.26)	<0.001
≥60	283 (27.4)	16 (9.6)	2.84 (1.76, 4.57)	<0.001
<b>Body Mass Index*, mean (SD)</b>				
Obesity <sup>†</sup>	25 (5.0)	25 (4.7)	-	<b>0.461<sup>¶</sup></b>
136 (16.0)	6 (16.2)	0.99 (0.47, 2.09)	0.972	
<b>Face mask—ever used when travelling outside<sup>‡</sup></b>				
Always	2 (0.2)	2 (1.2)	0.16 (0.02, 1.13)	0.066
Mostly	784 (75.8)	106 (63.9)	1.19 (1.05, 1.34)	0.005
Sometimes	169 (16.3)	34 (20.5)	0.80 (0.57, 1.11)	0.180
Rarely	70 (6.8)	22 (13.3)	0.51 (0.33, 0.80)	0.003
Never	9 (0.87)	2 (1.20)	0.72 (0.16, 3.31)	0.676
<b>Household income (USD)<sup>#</sup></b>				
<145 USD	146 (14.1)	19 (11.5)	1.03 (0.97, 1.10)	0.317
145–<290 USD	173 (16.7)	31 (18.7)	0.98 (0.92, 1.05)	0.551
290–<581 USD	265 (25.6)	51 (30.7)	0.96 (0.91, 1.02)	0.189
581–<871 USD	171 (16.5)	31 (18.7)	0.98 (0.92, 1.04)	0.512
871–<1,161 USD	120 (11.6)	14 (8.4)	1.05 (0.98, 1.11)	0.175
≥1,161 USD	20 (12.1)	159 (15.4)	1.04 (0.98, 1.10)	0.223

\*For age ≥20 years only. <sup>†</sup>Body mass index ≥30 (age ≥20 years). <sup>‡</sup>Self-reported, “ever wear a face mask when travelling outside the home”.

<sup>§</sup>Rate ratio, negative binomial regression. <sup>¶</sup>t-test. SD: Standard deviation. CI: confidence interval. <sup>#</sup>Based on 1 US dollar (USD) was equivalent to 34.43 Thai Baht (THB).

There were more women in the 19–59 and more than 60 age groups, women in the study had higher risk of being obese (RR 1.53, 95% CI 1.08–2.17), and were more likely to report wearing face masks. (Supplementary table 7).

## Discussion

In January 2022, 955/1,101 (87%) people in the cohort had antibodies to SARS-CoV-2 detected by ELISA. Of the study population, 1,034/1,200 (93%) reported being vaccinated, 50/1,200 (4.2%) had CLI symptoms and rRT-PCR-confirmed infection, and 20/124 (16.1%) who were not vaccinated, did not report CLI symptoms or test positive for COVID-19 by rRT-PCR, had antibodies for SARS-CoV-2 by ELISA. Two doses of any combination of vaccine were 72% (95% CI 25–90%) effective against hospitalized infection, and three doses were 98% (95% CI 80–99%) effective. These results suggest that there is a high degree of immunity in the Thai population, and they highlight the importance of delivering a third booster dose. Continued monitoring of VE and antibody waning will be important in the future.

At baseline we found very low (<1%) prevalence of SARS-CoV-2 antibodies, suggesting that a low proportion of people in Thailand had been infected at the time of data collection.

At the time of baseline data collection, national COVID-19 surveillance had identified 11,649 cumulative COVID-19 cases in Bangkok Province (42.9/100,000 persons), 24 (1.3/100,000 persons) in Chiang Mai Province, 0 in Nakhon Phanom Province, 44 (10.6/100,000 persons) in Phuket Province, and a total of 11,649 (16.8/100,000 persons) cases nationally.<sup>10</sup>

A review of population seroprevalence estimates from 47 studies in several countries worldwide found the range was 0.4–22.1% with a pooled estimate of 3.4% (95% CI 3.10–3.73%).<sup>11</sup> Our point estimates in Thailand in January 2021 (<1%) are at the low end of this range and similar to the global pooled estimate. One reason of high seroprevalence later in 2022 is the omicron variant that render the 2021 non-pharmaceutical intervention not effective. Our findings are consistent with Thai national surveillance data, which indicated a lower cumulative incidence of cases in Thailand during 2020 relative to most other countries in the world, followed by waves of infection and robust vaccination efforts in 2021.<sup>12</sup>

Self-reported vaccine coverage of at least two doses was 84% in the cohort; this was higher than national coverage estimates of ~70% at the time.<sup>13</sup> It is possible that because our study population lived in urban areas, they had better access to vaccine. In January 2022,

87% of participants had antibodies to SARS-CoV-2 by ELISA, while 4% (of vaccinated participants and a natural infected case) had no detectable antibodies by ELISA. Explanations for finding fewer participants with antibodies than had been vaccinated and infected include: one dose of vaccination may not be enough to induce the antibody response, the date of blood collection may have been too soon after vaccination for antibody development, or antibodies may have waned after initial exposure. These antibody profiles may help to explain the prolonged Omicron peak (January–May) Thailand experienced in 2022. When compare the antibodies to SARS-CoV-2 by ELISA between age group we found antibodies level was lowest in participants ages 5–18 years. Thailand started to provide the vaccine for children age above 5 years in January 2022.<sup>13</sup> Late vaccination in this age group may affect to antibody response.

Low prevalence through mid-2021 may be explained by widespread NPIs implemented by the Thai government, such as masking requirements, restrictions on gatherings and population movements, quarantine for international travelers, high local rates of adherence to these NPIs, and rapid identification and response to clusters of COVID-19 cases.<sup>14–17</sup> The low seroprevalence in Thailand, and some other countries of the Lower Mekong Delta during the first year of the pandemic, has also been attributed to ongoing investments in pandemic preparedness and outbreak response, and in the training of community responders.<sup>18</sup> As such, there may be more to learn from the first year of Thailand's pandemic response that may be applied to the future preparedness of both high- and low-income countries globally. All high seroprevalence among 4 provinces in the study at the end of 2022 showed the real situation in the Thailand when we consider by region.

We estimated VE of 72% to prevent hospitalization for two doses of all vaccine combinations against all SARS-CoV-2 variants circulating in Thailand during the study period, and 98% for three doses. VE tended to increase with increasing doses of vaccine and with vaccination plus infection. These results are similar to those reported elsewhere.<sup>19,20</sup> VE of these vaccines against Omicron and Omicron subvariants may be less than against other variants.<sup>21</sup> The Omicron wave occurred in Thailand during January–May 2022 and our data likely do not reflect VE against Omicron.

Groups with lower vaccine coverage included men, people aged 5–18 years, and people reporting low-income status. Low coverage in the young (5–18 years) age group may have been due to later implementation of vaccination programs due to delays in regulatory approval.

## Limitations

There were 23% of participants could not be contacted. Many people were not available because they had returned to their home villages, especially from Phuket and Chiang Mai because they had lost their jobs due to the depressed tourist economy. We did not have sufficient sample size to assess VE for each combination of vaccine or for SAR-CoV-2 variants. Early in the pandemic, national policy required that all people testing positive for COVID-19 be hospitalized regardless of severity of severity of infection; this may account for the high rate of hospitalization reported, although it is not likely that this biased VE estimates because vaccines were not available during this period this period. Participants in this survey were randomly selected from four provinces, and although we weighted for gender, age and population structure, results may only approximate prevalence in the national population of Thailand. This may be especially true when comparing data between urban and rural areas. Other limitations for VE estimation are 1) the VE could decline over time due to immunity waning, and 2) the calendar period of follow-up time between comparison groups may not be the same.

## Recommendations

Next study should assess T-cell responses to measure longer-term immunity and estimates of longer-term protection against severe disease. An exploration of antibody of antibody waning over time and factors associated with this would be useful to inform continuing pandemic response policy.

## Conclusion

A high proportion of study participants had SARS-CoV-2 antibodies, and VE for three doses of vaccine was 98%. As Thailand shifts from a pandemic to endemic model of response, ensuring high coverage of third booster doses of vaccine will be important.

## Suggested Citation

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