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Influenza virus circulation and vaccine effectiveness during June 2021–May 2023 in Thailand

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ABSTRACT

Thai Ministry of Public Health recommends influenza vaccination for certain risk groups. We evaluated 2023 Southern Hemisphere influenza vaccine effectiveness against medically attended influenza using surveillance data from nine Thai hospitals and a test-negative design. During June 2022–May 2023, influenza vaccine provided moderate protection against seeking care for influenza illness (adjusted vaccine effectiveness 51%; 95% confidence interval 28–67). Understanding vaccine effectiveness can help guide future antigen selection and support clinicians to make a strong influenza vaccine recommendation to patients.

Influenza contributes substantially to morbidity and mortality in Thailand and worldwide. [1] Thai Ministry of Public Health recommends influenza vaccination for pregnant people, health care workers, adults aged ≥65 years, children aged 6–35 months, and people with underlying medical conditions. Vaccination using a Southern Hemisphere composition is typically offered starting in May. Monitoring influenza activity can inform vaccination timing. Estimating vaccine effectiveness (VE) can help guide future antigen selection and support clinicians to make a strong influenza vaccine recommendation to patients. This report describes temporal trends of influenza virus detection during two seasons and influenza VE during one season in Thailand (see Table 1).

Influenza sentinel surveillance was established in Thailand in 2005. [2,3] Nine hospitals in eight provinces representing major regions of Thailand conducted influenza-like illness (ILI) surveillance in their clinics and severe acute respiratory infection (SARI) surveillance in their wards. We used WHO case definitions to define ILI as measured fever ≥38C and cough with onset within 10 days and SARI as fever history or measured fever ≥38C and cough with onset within 10 days requiring hospitalization. [4] Sites enrolled a convenience sample of two ILI patients (one age <5 and one ≥5 years) and two SARI patients (one age <5 and one ≥5 years) per working day for up to 20 patients total per week. Demographic, clinical, and self-reported influenza and COVID-19 vaccination data were collected on a standardized form. Among those who self-reported vaccination, vaccination date was verified by a national, digital, influenza vaccine database. Data were collected as routine public health surveillance, and written consent was not obtained. This project was reviewed by the Centers for Disease Control and Prevention (CDC) and was conducted consistent with applicable federal law and CDC policy (e.g., 45 CFR 46.102(l)(2)).

Nasopharyngeal or throat swab specimens were stored in viral transport media and tested at each site by QIAstat-Dx analyzer. This real-time reverse transcriptase polymerase chain reaction detected 19 viral and 3 bacterial pathogen targets, including influenza A, influenza A/H1N12009, influenza A H1, influenza A H3, and influenza B virus. The Thailand National Influenza Center in Bangkok conducted whole genome, next generation sequencing on influenza-positive samples with a CT value less than 25. The Nextera XT reagent kit was used to prepare

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Table 1
Influenza vaccine effectiveness during June 2022–May 2023 influenza season in Thailand.

	Influenza test-positive cases no.	Vaccinated casesno. (%)	Influenza test-negative controls no.	Vaccinated controlsno. (%)	Adjusted VE* (95 % CI)¶	Adjusted VE* (95 % CI)£
Overall medically attended illness						
Influenza (any)	781	30 (3.8)	5,960	490 (8.2)	47 (22, 64)	51 (28, 67)
Influenza A	633	26 (4.1)	5,960	490 (8.2)	44 (16, 63)	47 (20, 65)
A (H3N2)†	559	20 (3.6)	5,960	490 (8.2)	51 (23, 69)	53 (25, 70)
A (H1N1)pdm2009‡	74	6 (8.1)	5,960	490 (8.2)	−10 (−160, 53)	9 (−117, 61)
Influenza B§	148	4 (2.7)	5,960	490 (8.2)	60 (−10, 85)	68 (13, 88)
Secondary stratified analyses						
Outpatient visit						
Influenza (any)	560	21 (3.8)	3,336	326 (9.8)	54 (27, 71)	58 (33, 74)
Influenza A	465	18 (3.9)	3,336	326 (9.8)	52 (22, 71)	55 (36, 72)
A (H3N2)	421	14 (3.3)	3,336	326 (9.8)	59 (29, 76)	60 (30,77)
A (H1N1)pdm2009	44	4 (9.1)	3,336	326 (9.8)	−9 (−211, 62)	14 (−150, 71)
Influenza B	95	3 (3.2)	3,336	326 (9.8)	61 (–23, 88)	71 (7, 91)
Hospitalization						
Influenza (any)	221	9 (4.1)	2,624	164 (6.3)	32 (−37, 66)	29 (−44, 65)
Influenza A	168	8 (4.8)	2,624	164 (6.3)	25 (−58, 64)	21 (−68, 67)
A (H3N2)	138	6 (4.4)	2,624	164 (6.3)	20 (−91, 66)	26 (−78, 69)
A (H1N1)pdm2009	30	2 (6.7)	2,624	164 (6.3)	−11 (−390, 75)	−1 (−347, 73)
Influenza B	53	1 (1.9)	2,624	164 (6.3)	60 (−189, 95)	59 (−204, 94)
6–35 months						
Influenza (any)	95	4 (4.2)	1,857	78 (4.2)	3 (−172, 65)	−10 (−210, 61)
Influenza A	76	4 (5.3)	1,857	78 (4.2)	−21 (−241, 57)	−42 (−304, 50)
A (H3N2)	65	4 (6.2)	1,857	78 (4.2)	−46 (−312, 48)	−85 (−431, 36)
A (H1N1)pdm2009	11	0 (0)	1,857	78 (4.2)	NA	NA
Influenza B	19	0 (0)	1,857	78 (4.2)	NA	NA
3–17 years						
Influenza (any)	499	10 (2.0)	2,170	86 (4.0)	55 (11, 77)	41 (−17, 70)
Influenza A	406	9 (2.2)	2,170	86 (4.0)	50 (−2, 75)	33 (−38, 68)
A (H3N2)	363	7 (2.6)	2,170	86 (4.0)	57 (6, 81)	39 (−37, 73)
A (H1N1)pdm2009	43	2 (4.7)	2,170	86 (4.0)	−18 (−398, 72)	−7 (−361, 75)
Influenza B	93	1 (1.1)	2,170	86 (4.0)	74 (−86, 96)	69 (−130, 96)
18–64 years						
Influenza (any)	169	11 (6.5)	1,478	219 (14.8)	60 (24, 79)	56 (17, 73)
Influenza A	133	8 (6.0)	1,478	219 (14.8)	63 (23, 82)	57 (11, 80)
A (H3N2)	115	5 (4.4)	1,478	219 (14.8)	74 (35, 89)	68 (20, 87)
A (H1N1)pdm2009	18	3 (16.7)	1,478	219 (14.8)	−15 (−301, 67)	3 (−254, 73)
Influenza B	36	3 (8.3)	1,478	219 (14.8)	47 (−73, 84)	52 (−59, 86)
65 years and older						
Influenza (any)	18	5 (27.8)	455	107 (23.5)	−26 (−261, 56)	−45 (−335, 51)
Influenza A	18	5 (27.8)	455	107 (23.5)	−26 (−261, 56)	−45 (−335, 51)
A (H3N2)	16	4 (25.0)	455	107 (23.5)	−7 (−239, 66)	−21 (−303, 63)
A (H1N1)pdm2009	2	1 (50.0)	455	107 (23.5)	−279 (−6,099, 77)	−386 (−8,685, 70)
Influenza B	0	0	455	107 (23.5)	NA	NA
Underlying medical conditions						
Influenza (any)	96	11 (11.5)	1,237	213 (17.2)	33 (−29, 65)	36 (–23, 67)
Influenza A	75	9 (12.0)	1,237	213 (17.2)	31 (−41, 67)	32 (−40, 67)
A (H3N2)	65	7 (10.8)	1,237	213 (17.2)	42 (−29, 74)	39 (−38, 73)
A (H1N1)pdm2009	10	2 (20.0)	1,237	213 (17.2)	−20 (−470, 75)	−12 (−450, 77)
Influenza B	21	2 (9.5)	1,237	213 (17.2)	39 (−165, 86)	49 (−124, 88)
No underlying medical conditions						
Influenza (any)	685	19 (2.8)	4,723	277 (5.9)	49 (18, 67)	57 (30, 73)
Influenza A	558	17 (3.0)	4,723	277 (5.9)	45 (9, 67)	52 (20, 71)
A (H3N2)	494	13 (2.6)	4,723	277 (5.9)	52 (16, 73)	57 (24, 76)
A (H1N1)pdm2009	64	4 (6.4)	4,723	277 (5.9)	−10 (−208, 61)	18 (−134, 71)
Influenza B	127	2 (1.6)	4,723	277 (5.9)	69 (−24, 92)	77 (5, 94)

*Vaccine effectiveness was estimated using the test-negative design as 100% *(1 – adjusted odds ratio) in which the adjusted odds ratio represents the ratio of the odds of being vaccinated among influenza-positive cases to the odds of being vaccinated among influenza-negative controls.
¶Adjusted for age (continuous).
£Adjusted for age (continuous), sex, calendar week, self-reported presence of one or more underlying medical condition, and received 2 or more COVID-19 vaccinations.
†Predominantly A/Darwin/9/2021 (H3N2)-like virus, clade 3C.2a1b.2a.2.
‡A/Sydney/5/2021 (H1N1)pdm09-like virus, clade 6B.1A.5a.2a.
§Predominantly B/Austria/1359417/2021 (B/Victoria lineage)-like virus, subclade V1A.3a.2.

the influenza library. The library was sequenced using the Illumina MiSeq platform. Raw data in the FastQ file format were analyzed using Geneious Prime and deposited in GISAID.

We estimated influenza VE using a test-negative design, comparing the odds of vaccination between influenza test-positive cases and test-negative controls identified during June 2021 through May 2023. [5] Children ages 6 months to 8 years of age who needed two doses and had only received one dose were excluded from analysis. Influenza seasons in Thailand are defined as June through May of the following year. [2] We used a logistic regression model adjusted for age (continuous), sex, self-reported underlying medical condition, calendar week, and COVID-19 vaccination (2 or more doses). [6] VE was estimated as (1-adjusted odds ratio) * 100 %. To account potential confounding related to correlation of influenza and COVID-19 vaccinations, we adjusted for COVID-19 vaccination. [7] As an alternate approach, we ran a sensitivity analysis excluding COVID-19 cases. Secondary analyses were stratified by setting (outpatient and inpatient), age group, and presence of ≥1 underlying medical condition and were adjusted for age, sex, underlying medical condition (when not stratified), calendar week, and COVID-19 vaccination.

Overall, 11,312 patients had ILI or SARI during June 2021 through May 2023. After excluding 55 patients for receiving influenza vaccination < 14 days before symptom onset, there were 11,257 patients included—4,516 patients during 2021–2022 and 6,741 patients during 2022–2023.

After notably low influenza circulation during the 2021–2022 season (10 influenza test-positive cases), influenza cases increased at the beginning of the 2022–2023 season (Fig. 1). Cases peaked at the end of August 2022 (predominantly A/Darwin/9/2021(H3N2)-like virus, clade 3C.2a1b.2a.2) with a second, smaller peak in late January 2023 (predominantly B/Austria/1359417/2021 [B/Victoria lineage]-like virus, subclade V1A.3a.2). Vaccination coverage was 5.6 % of all included patients in 2021–2022 and 7.0 % in 2022–2023.

Influenza VE was not calculated for 2021–2022 because there were too few influenza cases. In 2022–2023, adjusted VE against any medically attended influenza illness (ILI or SARI) was 51 % (95 % confidence interval [CI] 28–67) (Table). Against influenza A, VE was 47 % (95 % CI 20–65) and against influenza B, VE was 68 % (95 % 13–88). Influenza VE against outpatient visits was 58 % (95 % CI 33–74), but we were unable to obtain a stable VE estimate against influenza hospitalization (VE 29 %, 95 % CI −44–65). The alternative approach of excluding COVID-19 cases yielded similar VE estimates with overlapping confidence intervals (supplemental table).

Influenza virus circulation resumed during the 2022–2023 season with a typical temporal pattern for Thailand. [2,8] Our estimate of 2023 Southern Hemisphere influenza vaccine effectiveness against any medically attended influenza was similar to estimates from South Africa and Peru. [9,10] Small differences in estimates could be related to differences in study sample size, health care seeking behavior, population characteristics, or circulating influenza strains. We had difficulty comparing our VE against hospitalization estimate with recent estimates from five South American countries because of wide uncertainty in our estimate due to very few vaccinated cases requiring hospitalization. [11] Although we verified vaccination status with a national registry, future studies to validate vaccination status and other test-negative design features are needed. Nevertheless, this analysis demonstrates that influenza vaccine provided moderate protection against influenza virus infection in Thailand.

Author attestation

All authors attest they meet the ICMJE criteria for authorship.

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CRediT authorship contribution statement

Kriengkrai Prasert: Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing. **Prabda Praphasiri:** Conceptualization, Writing – original draft, Writing – review & editing. **Sutthichai Nakphook:** Writing – review & editing. **Darunee Ditsungnoen:** Data curation, Writing – review & editing. **Patranuch Sapchookul:** Data curation, Writing – review & editing. **Kanlaya Sornwong:** Writing – review & editing. **Suriya Naosri:** Writing – review

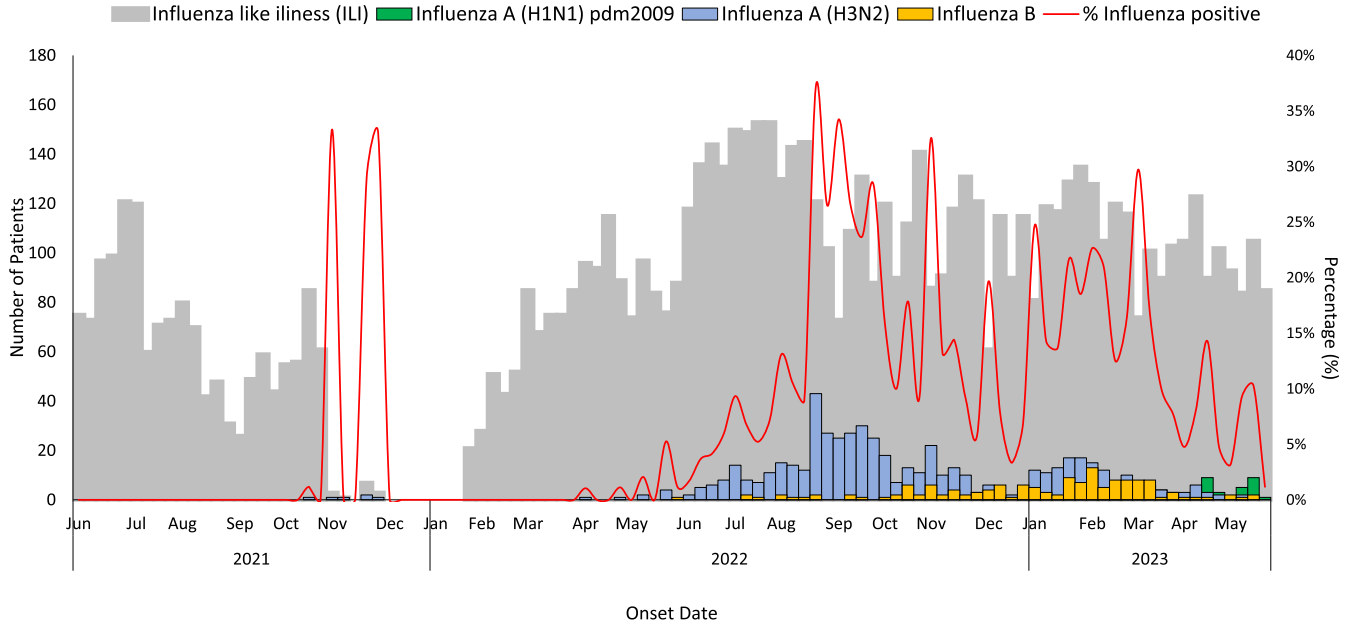

Fig. 1. Influenza virus circulation by subtype and lineage from influenza sentinel surveillance during 2021–2022 and 2022–2023 seasons in Thailand.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jvacx.2024.100517.

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