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Outbreak, Surveillance, Investigation & Response (OSIR) Journal

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Editorial

Preventing Reoccurrence of Outbreaks: Medical Anthropologists' Contribution to Identifying the Root Cause of an Outbreak and the Community's Adoption of Culturally and Context Appropriate Interventions

Alden Henderson, Senior Editor

In the complex and interconnected world of responding and controlling infectious diseases, understanding the what, when, where and how of an outbreak is no longer enough. To effectively halt transmission and prevent future resurgence, we must also understand the why—why people behave as they do during outbreaks, why certain interventions succeed or fail, and why disease spreads differently across seemingly similar communities. These questions lie at the intersection of epidemiology and medical anthropology.

Disease epidemiologists bring the critical technical expertise to identify the proximal causes of outbreaks: the etiologic agent, modes of transmission, and whether the outbreak is spreading. However, medical anthropologists aide epidemiologists in uncovering the root causes—social, cultural, economic, and behavioral factors that create the conditions for disease emergence and spread. These include housing and sanitation practices, health-seeking behaviors, local interpretations of symptoms, stigma, gender roles, culture, political structure and more.[1,2]

This integrated approach is not hypothetical. The Institute of Epidemiology, Disease Control and Research (IEDCR) in Bangladesh routinely includes medical anthropologists as part of their field outbreak investigation teams. These interdisciplinary teams use a mixed methods approach to investigate outbreaks of Nipah virus, dengue, chikungunya, anthrax, and other diseases. The epidemiologists search for cases, generate hypotheses, and conduct studies to test their hypotheses. The anthropologists conduct community interviews and focus groups, observe behaviors, and explore local health beliefs and culture to complement the epidemiologic findings. Their contributions have helped reveal not only the routes of transmission but also the underlying factors that sustain or interrupt those routes—leading to more precise and accepted recommendations.[3,4]

The benefits of this collaboration are clear:

- Appropriate, culturally sensitive questions that yield responses which help identify the root cause of the outbreak.
- Faster identification of transmission drivers, especially when they are socially, behaviorally, culturally or politically mediated and faster adaptation of interventions that control the spread of the outbreak.
- Improved community engagement and trust, which is essential for surveillance, contact tracing, isolation, vaccination, and other interventions.[5]
- Tailored recommendations that account for cultural norms and resource constraints, increasing the likelihood of compliance and long-term behavior change.
- Stronger insight into health system dynamics, such as why people delay seeking care or turn to informal providers or reluctant to adopt recommendations.

- Deeper understanding of context, identifying root causes like marginalization, misinformation, or historical trauma that fuel outbreaks and complicate response.[6,7]

To fully realize the potential of this interdisciplinary model, efforts should be made to recruit, train, and retain anthropologists as integrated members of outbreak investigation teams. While anthropologists are experts in cultural interpretation and human behavior, they typically receive little to no training in outbreak response. Introducing foundational public health and epidemiology principles—such as transmission dynamics, case definitions, and study design—into anthropological training programs, and conversely, incorporating social science concepts into epidemiology curricula, would build a shared language and operational understanding of not only the contribution of each discipline to resolving the outbreak but also the synergy when both collaborate to describe and solve a problem.[2,6] Trained anthropologists can play key roles in developing culturally relevant questionnaires, identifying behavioral patterns that contribute to disease spread, and crafting locally appropriate, actionable recommendations. Just as epidemiologists refine their ability to interpret laboratory and surveillance data, anthropologists can be equipped to navigate the field realities of public health emergencies. Building this workforce will enhance not only outbreak investigations but also overall community engagement and resilience.[5,7]

Recent outbreaks of Ebola, COVID-19, and mpox have further demonstrated the importance of integrating social science expertise into public health. Behavioral drivers, misinformation, and community mistrust have repeatedly emerged as major factors influencing the effectiveness of outbreak response. Addressing these factors early and systematically through anthropologic methods can make the difference between containment and escalation.

In conclusion, including medical anthropologists on outbreak investigation teams strengthens public health practice by ensuring that interventions are not only scientifically sound but also socially informed and culturally grounded. As the IEDCR model in Bangladesh shows, this interdisciplinary collaboration is both practical and impactful. I encourage other countries and institutions to embrace the IEDCR model and include anthropologists as their partner in an outbreak response.

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Comparison of Data and Performance Indicators: Before and After the Transition of Thailand's National Disease Surveillance System, 2023–2024

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Abstract

In 2024, Thailand modernized its national disease surveillance system, transitioning from Report 506 (R506) to the Digital Disease Surveillance (DDS) system, replacing batch file reporting with an application programming interface (API). To compare the data characteristics and performance indicators between the DDS and R506 systems, a descriptive study was conducted using data from January to September 2023 for R506 and 2024 for DDS, obtained from the Department of Disease Control. The DDS system contained 1,567,885 records, while R506 had 980,934. The number of hospitals and health centers reporting to the DDS system was 3,402, while 5,319 reported to R506. Due to the ongoing transfer of health centers to the Ministry of Interior, fewer reports were sent from health centers to the DDS system (14,374) compared to R506 (44,298). Timeliness (median interval from diagnosis to report) was 1 days (interquartile range (IQR) 0–2 days) in R506 and 1 days (IQR 0–4 days) in DDS. The DDS system achieved 99.99% completeness for citizen identification numbers and 100% for diagnostic codes, while R506 achieved 49.75% and 41.59%, respectively. The DDS system had a larger contribution from Bangkok than R506 (25.45% vs 10.70%). In conclusion, the data characteristics of the DDS system remained similar to R506. However, the DDS system is less than one year old, and the ongoing transfer of health centers might affect the reporting coverage. Therefore, follow-up surveillance evaluation with an emphasis on qualitative attributes is recommended.

Keywords: digital disease surveillance system, DDS, R506, surveillance, epidemiology

Introduction

A disease outbreak is defined as an occurrence of more than the expected number of people with a disease. Outbreaks often occur suddenly and can severely cause damage to society and public health. Therefore, public health surveillance is often initiated, which involves the ongoing systematic collection, analysis, and timely dissemination of information for identifying, preventing, and controlling outbreaks.

In 1967, Thailand established a national disease surveillance system, called Report 506 (R506), to provide timely information for disease control action and remained the centerpiece of Thailand's public health and epidemiology for many years.[1] The system started as a paper-based mail reporting system and was modernized in 2006 into an electronic batch file system using Microsoft Access® database. Since then, R506 used an offline batch file system that required personnel to manually extract records of specific diagnoses, and process and submit the data in batches to the Division of Epidemiology (DOE), Department of Disease Control (DDC), to analyze and provide response and policy recommendations.[2]

However, with the emergence of new technology and social media platforms, which have changed the speed and nature of information flow, R506 could not keep up with the virtually real-time nature of the information flow of the current era. Moreover, the manual process was prone to human error and caused a burden on staff workloads.[3]

The DOE realized the challenges of the R506 system and initiated further enhancements in 2010 to improve the system from the manual batch-file process into an automated application programming interface (API) system. However, several initiatives, e.g., the Electronic Integrated Disease Surveillance System, were not successful at being able to address the changes in the need for the surveillance system in a

timely manner and did not achieve nationwide adoption.[4]

During the coronavirus disease 2019 (COVID-19) pandemic in 2020–2022, Thailand established a national vaccine registry platform called "MOHPROMPT". The system was successfully integrated into the electronic health records of most hospitals in Thailand through an API interface. The DOE recognized the opportunity to modernize the system and created the COVID-19 recovery certificate that incorporates laboratories and diagnosis as a module of the chatbot that functions as the national COVID-19 disease surveillance system, COVID-19 case report (CCR). The CCR became the proof-of-concept of the electronic surveillance system for the R506 modernization initiative. At the end of the COVID-19 pandemic in 2022, the DOE decided to incorporate the R506 surveillance system into the CCR and renamed it the Digital 506 (D506) and later to the Digital Disease Surveillance (DDS) system.

The transition from R506 to DDS was initiated nationwide on 1 Oct 2023, and successfully upscaled nationwide on 1 Jan 2024. The DDS data was utilized as part of the routine surveillance system of R506 as of 2024. While a feasibility study of using the DDS as a replacement for R506 was conducted, there has been no operational comparison of data characteristics and performance indicators between the R506 and the DDS systems.[5] Therefore, we aim to compare the data characteristics and performance indicators between the DDS and R506 systems to guide the planning, and implementation of the DDS in the future.

Methods

Data Sources

The data flow of both R506 and DDS were presented and a descriptive study was conducted. For R506, we obtained all anonymized records available from 1 Jan to 30 Sep 2023 based on the date of reporting. For the DDS, all anonymized records from 1 Jan to 30 Sep 2024 based on the date of reporting were obtained.

The period from January to September (9 months) was used to compare the two systems instead of the full year because the transition period from R506 to DDS was initiated from 1 Oct to 31 Dec 2023.

Variables included in the analysis were demographic characteristics of the cases (age and gender), diagnosis, date of diagnosis, date of reporting, and reporting hospital. Timeliness was calculated from the case detection date to the reporting date. Completeness was defined separately for citizen ID (the number of records having a complete 13-digit citizen identification number divided by the total number of records) and for diagnosis (the number of records having a valid diagnosis code, based on the International Classification of Diseases, 10th revision (ICD-10), divided by the total number of records). The numbers of health facilities reporting to the R506 and DDS systems were used to represent the coverage of each system.

ICD-10 codes related to COVID-19 were excluded from both R506 and DDS as there were several other COVID-19 reports during and after the pandemic.

Statistics Analysis

A descriptive analysis was conducted to describe count and distribution of characteristics of the demographic data, diagnosis, and trend of the reporting and reporting hospital. Median with interquartile range (IQR), count and percentage were presented. A choropleth map was constructed to describe the distribution of case reports by province. Data management and analysis were conducted using Microsoft Excel 365® and Anaconda Packages version 2.6.3.[6,7]

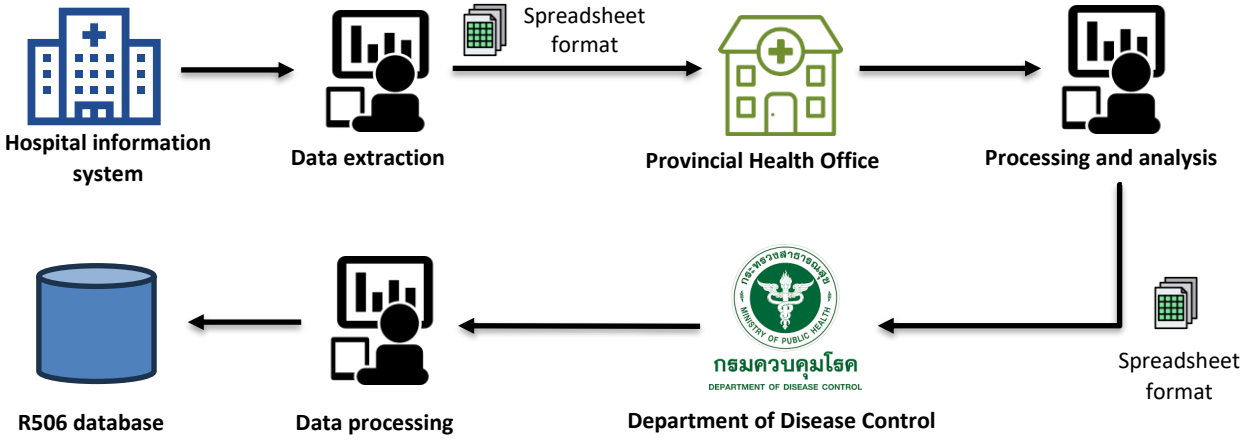
Results

System Description

Report 506 (R506)

The R506 system, established in 1967, was modeled after the U.S. Centers for Disease Control and Prevention's national surveillance system for priority diseases.[1] It was operated nationwide by the DOE, DDC, Ministry of Public Health, Thailand. In 2023, the system covered 57 priority disease groups, and more than one ICD-10 code was allowed for each disease group.[8] Briefly, hospital personnel would extract the database variables relevant to the requirement by Extract-Transform-Load process from their database and conduct the preliminary data cleansing and analysis. Data would then be submitted to the DOE in batches by e-mail or file-transfer protocol. For paper-based reports, DOE personnel manually keyed data into the R506 database.

DOE personnel retrieved the data and regularly conducted data cleansing and routine analysis. Due to the nature of the batch file approach, data summaries were only available weekly at best. The database was stored in a conventional relational database system at the DOE (Figure 1).[2]

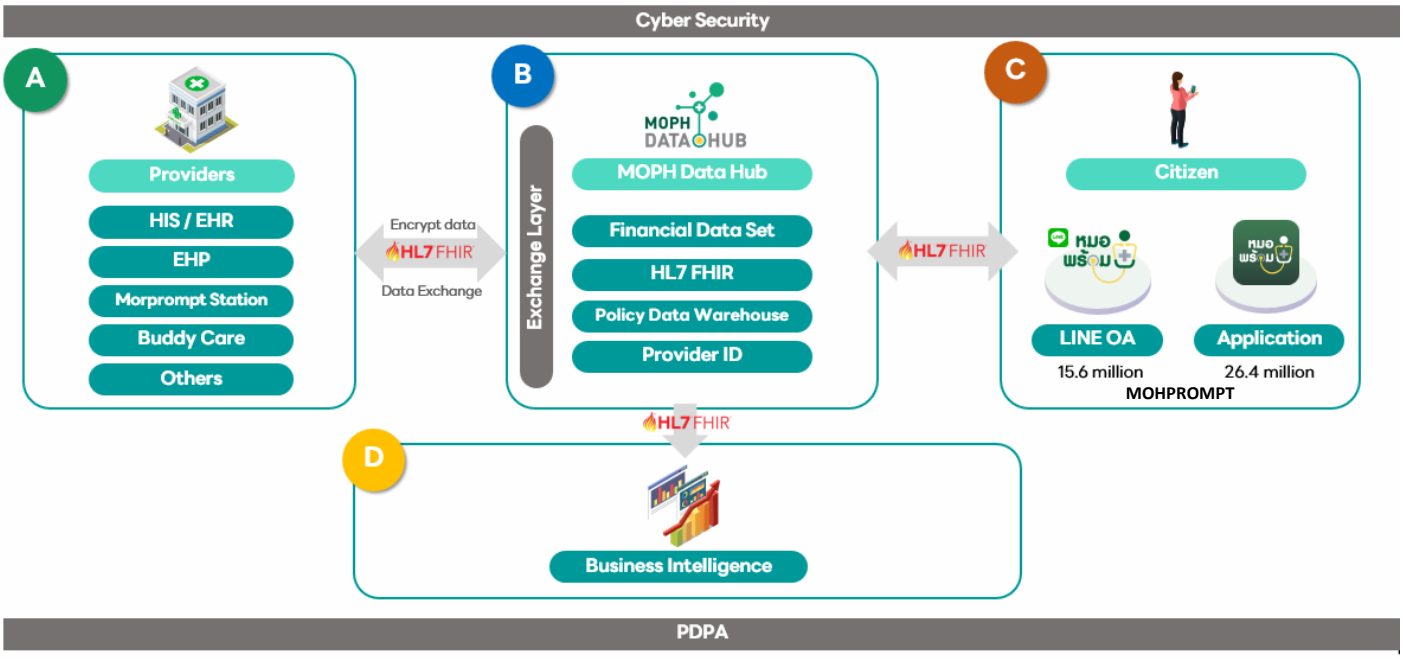


Hospital personnel extract data from the hospital information system (HIS) into a spreadsheet file format and then transfer it manually to the Provincial Health Office (PHO). PHO personnel process the data and then submit the processed data to the Department of Disease Control (DDC) in a spreadsheet format, which is then processed by the DDC personnel and then integrated into the R506 database.

Figure 1. R506 Dataflow diagram, 2023

Digital Disease Surveillance (DDS)

The DDS system was established as a central API and was connected to the electronic health record from each hospital. To reduce the cost of implementation, the DDS utilized existing authentication and authorization from the MOHPROMPT chatbot. Developers and electronic health record vendors can leverage the existing connection application already utilized for the MOHPROMPT system as described in Figure 2. This approach reduces the cost and simplifies the implementation of the system.



There are four components available for utilization by other systems: A) The hospital database, electronic health record, B) The central database overseen by the Ministry of Public Health (MOPH). All data transferred between the hospitals travel through this component. Several services on the database including authentication and authorization are available, C) The point of contact to Thai citizens including the LINE application and smartphone application, D) The dashboard displaying data to the stakeholders as needed. HL7 FHIR: Health Level 7 Fast Healthcare Interoperability Resources. EHR: Electronic Health Record. EHP: Excellent Health Platform.

Figure 2. Ministry of Public Health Digital Health Platform (MOHPROMPT), 2021–2024

The DDS system adapted the R506 variables into the JavaScript Object Notation format, a well-known data structure for many API services. The database utilized the "not only structured query language" (no-SQL) concept to allow the flexible nature of the surveillance system where specific variables are required in some circumstances while allowing better timeliness of data reporting than the batch-file approach. The overall process is described in Figure 3. The database is hosted centrally.

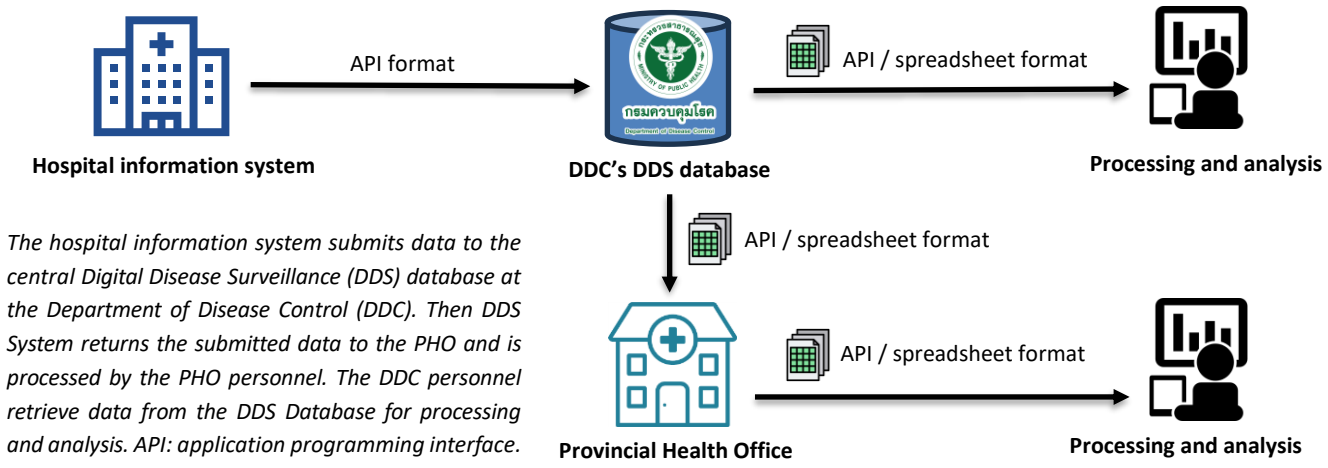


Figure 3. Digital Disease Surveillance system diagram, 2024

Four disease groups: Legionnaires' disease, filariasis, leishmaniasis, and leprosy, were added to the DDS while seven disease groups: influenza-like illness, viral exanthema, fever of unknown origin, adverse events following immunization, acute flaccid paralysis, viral conjunctivitis and acute diarrhea, were removed per the Communicable Diseases Act B.E. 2558 (2015), updated in 2024.[9] Therefore, the system covers 54 priority diseases. Provincial Health Office personnel can retrieve the data from the database in batch spreadsheet format.

Descriptive Study

From 1 Jan–30 Sep 2024 the DDS system contained 1,567,785 records, and from 1 Jan–30 Sep 2023 R506 contained 980,934 records. The number of hospitals and health centers reported to the DDS (3,402) was less than those reporting to R506 (5,319). This was reflected in the reports from health centers of both systems. There were 14,374 records from health centers sent to the DDS system compared to 44,298 for R506.

The 10 most common diagnoses from both systems are shown in Table 1. The top five highest diagnoses in the R506 were: fever, unspecified; pneumonia, unspecified organism; influenza with other respiratory manifestations; dengue fever (classical dengue); and influenza with other manifestations, virus not identified. The top five highest diagnoses in the DDS system were pneumonia, unspecified organism; influenza with other respiratory manifestations, seasonal influenza virus identified; influenza due to other identified influenza virus with other manifestations, influenza with other respiratory manifestations, virus not identified; and bacterial foodborne intoxication, unspecified.

Table 1. Top 10 ICD-10 diagnosis codes by frequency in R506 (January–September 2023) and DDS (January–September 2024)

	R506			DDS	
	ICD-10 code	n		ICD-10 code	n
1.	**R509** Fever, unspecified	103,815	**J189**	Pneumonia, unspecified organism	239,579
2.	**J189** Pneumonia, unspecified organism	45,446	**J101**	Influenza with other respiratory manifestations, seasonal influenza virus identified	173,524
3.	**J111** Influenza with other respiratory manifestations	26,642	**J108**	Influenza due to other identified influenza virus with other manifestations	161,114
4.	**A90** Dengue fever (classical dengue)	20,678	**J111**	Influenza with other respiratory manifestations, virus not identified	99,559
5.	**J118** Influenza with other manifestations, virus not identified	20,532	**A059**	Bacterial foodborne intoxication, unspecified	83,619
6.	**A059** Bacterial foodborne intoxication, unspecified	20,421	**J118**	Influenza with other manifestations, virus not identified	70,036
7.	**J101** Influenza with other respiratory manifestations, seasonal influenza virus identified	15,722	**J159**	Bacterial pneumonia, unspecified	69,376
8.	**J108** Influenza due to other identified influenza virus with other manifestations	11,558	**J10**	Influenza due to identified seasonal influenza virus	54,013
9.	**B084** Enteroviral vesicular stomatitis with exanthem	10,819	**J11**	Influenza due to unidentified influenza virus with pneumonia	53,504
10.	**H109** Unspecified conjunctivitis	9,399	**B084**	Enteroviral vesicular stomatitis with exanthem	51,452

R506: Report 506. DDS: Digital Disease Surveillance. ICD-10: the international classification of diseases, 10th revision.

Although the ranks by frequency of diagnoses differed, most of the diagnoses in the top ten were similar between the two systems, except for "fever, unspecified," which was removed from the DDS system as it was not listed in the Communicable Diseases Act B.E. 2558 (2015), updated in 2024.[9]

Table 2 compares the distributions of age group and gender between the two systems. The 1–6 year age group had the highest proportion in both systems (24.78% for R506 and 27.58% for DDS). The proportion of males was 51.66% for R506 and 50.19% for DDS.

Table 2. Demographic characteristics of cases reported in R506 (January–September 2023) and DDS (January–September 2024)

Characteristics	R506 (%) (n=980,934)	DDS (%) (n=1,567,785)
Gender		
Male	506,752 (51.66)	786,892 (50.19)
Female	474,182 (48.34)	780,893 (49.81)
Age group (years)		
<1	37,108 (3.78)	50,948 (3.25)
1–6	243,055 (24.78)	432,375 (27.58)
7–9	81,160 (8.27)	31,216 (1.99)
10–14	98,495 (10.04)	137,030 (8.74)
15–24	102,585 (10.46)	131,638 (8.40)
25–34	81,432 (8.30)	157,746 (10.06)
35–44	67,600 (6.89)	125,754 (8.02)
45–64	137,922 (14.06)	242,206 (15.45)
≥65	131,577 (13.41)	258,527 (16.49)

R506: Report 506. DDS: Digital Disease Surveillance.

The weekly case report count is shown in Figure 4. For each week, the DDS count was slightly higher than R506, except for two spikes in weeks 29 and 34 for the DDS.

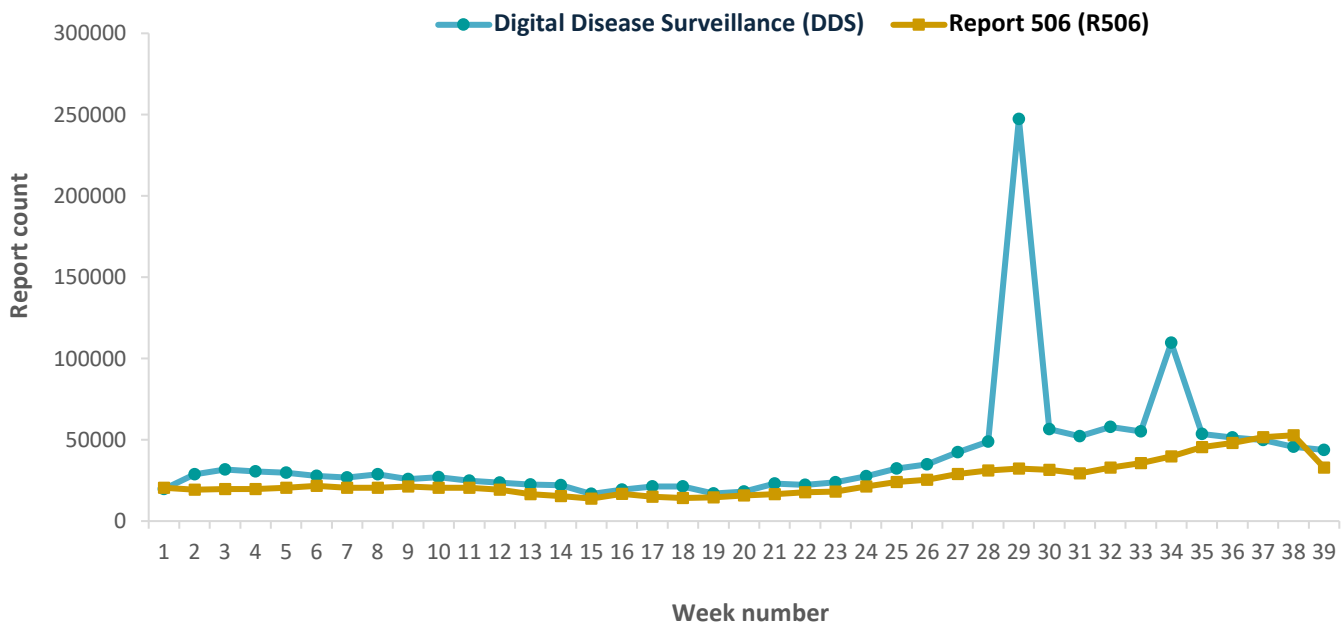
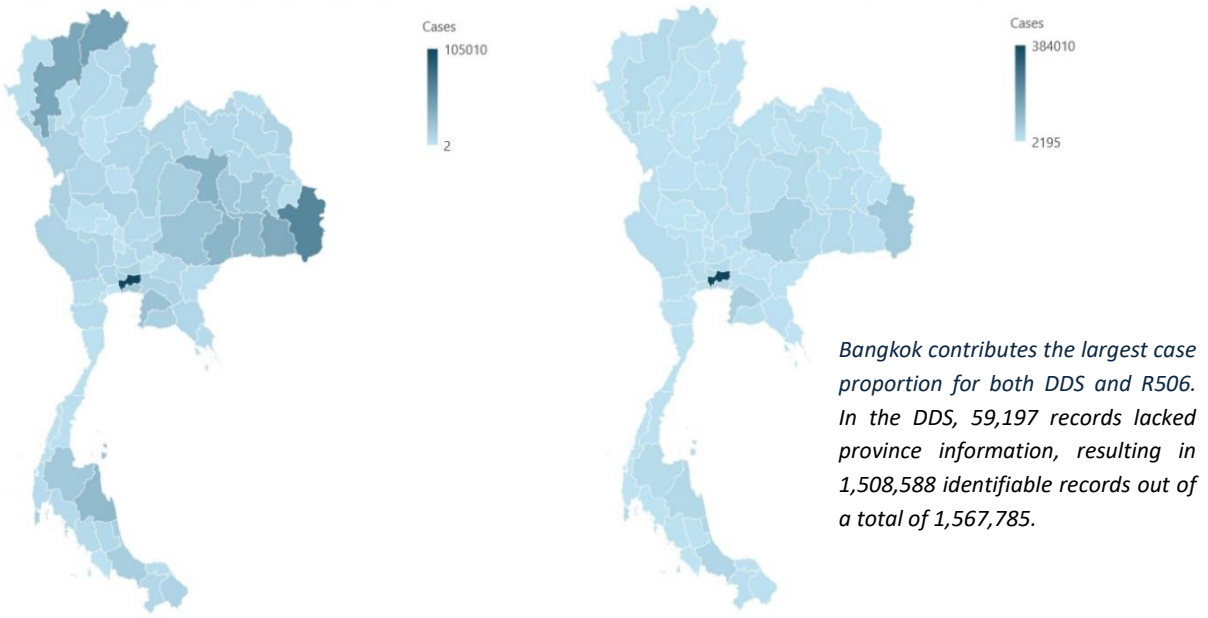


Figure 4. Number of reported cases in R506 (January–September 2023) and DDS (January–September 2024)

Figure 5 compares the distribution of case reports by province. Reports were concentrated in Bangkok for both systems (10.70% for R506 and 25.45% for DDS). However, the proportion of reports from provinces outside Bangkok, especially Ubon Ratchathani Province, in R506 was higher compared to DDS.



(a) Report 506 (R506) (n=980,934) **(b) Digital Disease Surveillance (DDS) (n=1,508,588)**

Figure 5. Distribution of case counts by province in R506 (January–September 2023) and DDS (January–September 2024)

Timeliness and Completeness

R506 had a median timeliness of 1 day (IQR 0–2 days) and there were no changes with the removal of fever, unspecified, while the DDS also had a median timeliness of 1 day (IQR 0–4 days).

DDS achieved 99.99% completeness for the citizen ID with only one record missing and achieved 100% completeness for ICD-10 codes. For R506, completeness for citizen ID was 49.75% and 41.59% for ICD-10 codes.

Discussion

The implementation of the DDS system has led to a 59.83% increase in case reports by the DDC, with minimal change in demographic characteristics. This increase cannot be primarily attributed to the inclusion of additional disease groups, as these accounted for only an extra 186 cases (<0.01%). A key achievement of the DDS system was the significant improvement in data quality, particularly the completeness of reports compared to the previous R506 system. This enhancement is likely due to the shift to an API-based reporting mechanism, which automates data extraction and direct submission to the Ministry of Public Health, thereby reducing manual data entry, workload, and human error at the facility level.

Despite the DDS system having fewer reporting health centers than R506, the number of reported facilities remains high. This reduction is primarily due to the transfer of 3,263 health centers to the Ministry of Interior.[10] These facilities are unable to participate in the DDS system because of differences in governance, policies, and regulations within their new organizational structure. This transition is an ongoing annual process that will continue to affect system coverage. Addressing this challenge will require a formal agreement between the Ministry of Public Health and the Ministry of Interior. The continued high number of reporting facilities, even with the one-time switching cost associated with the API approach for hospitals, is attributed to the DDS offering a dedicated portal as an alternative solution to minimize this cost.[11] This approach, developed with stakeholder feedback, has successfully facilitated the transition for hospitals from R506 to the DDS system.

As the R506 system was completely phased out in 2024 and replaced by the DDS system, the representativeness of R506 data, obtained from 2023, may not fully reflect the situation in 2024, from which DDS system data sources were obtained. A significant difference between the two systems lies in their hospital coding: R506 used the Health Service Code system, maintained by the DOE, DDC, specifically for its purposes, while the DDS system utilizes the standard hospital code system, maintained by the Office of the Permanent Secretary, Ministry of Public Health. The lack of a maintained mapping table between these two coding systems could lead to mismatches in identifying several hospitals, making a direct head-to-head comparison between the two systems at the hospital level unfeasible. These findings underscore the DDS system's more standardized approach, which, by using the widely adopted hospital code, potentially enhances system utilization and interoperability, allowing for integration with various electronic health records.

Despite the change from batch reporting to an API-based process, which was expected to improve reporting timeliness, the time from diagnosis to report remained consistent between the two systems. A plausible explanation is that hospital personnel may delay data submission to the DDS system until their local data analysis is complete, as the DDS system does not alter existing hospital workflows.

Furthermore, the timeliness indicator does not fully capture the benefit of reduced data processing time at the Provincial Health Office and the central unit, the Division of Epidemiology. The API approach enables a more efficient data analysis process at these levels, a benefit that could not be quantified in this study. Future comprehensive surveillance evaluations are needed to explore this aspect. This limitation arises because data processing for analysis, such as addressing policy concerns regarding outbreaks, is conducted externally after retrieving data from either the R506 or the DDS databases. Additionally, we could not assess man-hour savings or other timeliness benefits related to data processing when using the DDS system compared to R506 as this would require a more intensive qualitative study as part of a complete surveillance evaluation.

At the time of this study, the DDS system was less than one year old, meaning the available data may not fully represent its long-term success. We focused on coverage, completeness, and timeliness, but did not compare other surveillance evaluation attributes such as validity, accuracy, or sensitivity. In summary, the DDS system has demonstrated its ability to maintain data volume comparable to the previous reporting system, despite the complexities involved in a large-scale transition process. These findings align with previous study that suggested the DDS system could effectively replace R506.[5] While earlier research focused solely on COVID-19 comparisons, this study encompassed all diseases within the reporting system, supporting the potential for leveraging the success of the DDS system to enhance overall national disease surveillance.[5]

Recommendations

A comprehensive surveillance evaluation, encompassing both qualitative and quantitative attributes, should be conducted. This evaluation should involve both hospital staff and the central unit at the Department of Disease Control to thoroughly assess the impact of the Digital Disease Surveillance system. Future studies should consider the impact of health centers transferring to the Ministry of Interior on the reporting system and propose solutions to maintain the report coverage in these facilities.

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Author Contributions

Supharerk Thawillarp: Conceptualization, methodology, data curation, formal analysis, writing—original draft, writing—review & editing, and visualization.

Ethical Approval

This study used anonymized secondary surveillance data collected routinely by the Department of Disease Control, Ministry of Public Health, Thailand. Ethical approval was not required, as the study did not involve identifiable human subjects or direct contact with individuals.

Informed Consent

Informed consent was not required because the study used de-identified data collected for routine public health purposes, with no direct interaction with individuals.

Data Availability

The datasets used in this study are not publicly available due to legal and privacy restrictions. Data access may be granted upon reasonable request and with permission from the Department of Disease Control, Ministry of Public Health, Thailand.

Conflicts of Interest

The author declares no conflicts of interest.

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Declaration of Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the author used Gemini® to enhance clarity of the manuscript. The content produced by this tool was reviewed and edited by the author, who accept full responsibility for the final text.

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Barriers to Vaccine Uptake and Proactive Strategies: A Mixed-method Study of MMR2 Coverage in Narathiwat Province, 2023

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Abstract

Measles remains a public health concern in Thailand's southern border provinces due to persistent vaccine hesitancy despite national elimination efforts. Narathiwat Province continues to report a high incidence of measles, reflecting challenges in vaccine accessibility, cultural acceptance, and operational barriers. This study aimed to identify factors associated with the uptake of the second dose of measles-mumps-rubella (MMR2) vaccine and to explore parental vaccine hesitancy in Narathiwat Province using a mixed-methods approach. The quantitative study utilized secondary data from a 2023 performance survey of 114 childhood state vaccination service units, assessing key operational factors such as target area identification, vaccine uptake rechecks, and supervisor encouragement. Logistic regression identified factors associated with achieving ≥95% MMR2 coverage. The qualitative study explored vaccine hesitancy among 19 mothers in low-coverage districts, identifying concerns about post-vaccination side effects, religious permissibility, and trust in vaccination services. Results indicated that service units with >60 target children had significantly higher odds of failing to achieve ≥95% MMR2 coverage (adjusted OR 6.98, 95% CI 1.46–33.23). Vaccine uptake rechecks and target area clearance were associated with improved coverage but did not reach statistical significance. Common reasons for vaccine hesitancy included fear of side effects, particularly fever, and religious concerns. To enhance coverage, mobile vaccination clinics and door-to-door strategies should be expanded, alongside strengthened public health communication addressing parental concerns. Collaboration with local religious authorities is crucial in fostering trust. Addressing both logistical and cultural barriers is essential for improving vaccine acceptance in high-burden areas like Narathiwat Province.

Keywords: measles, MMR, vaccine hesitancy, barriers to vaccination, mobile vaccination clinics, Narathiwat

Introduction

An estimated 107,500 measles-related deaths occurred worldwide in 2023, despite the availability of effective vaccines.[1] Between 2000 and 2023, the World Health Organization and its partners prevented an estimated 60 million measles-related deaths globally through routine immunization programs, supplementary immunization activities, and targeted outbreak response strategies.[2] In 2010, Thailand committed to eliminating measles, adopting a strategic plan (2020–2024) that aimed for over 95% coverage of the first dose of the measles–mumps–rubella (MMR) vaccine (MMR1) and the second dose (MMR2) by ages 1 and 3, respectively.[3] These vaccines are freely provided through Thailand's universal healthcare system, contributing to increase coverage and reduce measles cases nationwide.[4,5] However, the southern border provinces (Pattani, Yala, Narathiwat) continue to report higher measles incidence and mortality than the national average, reflecting persistent barriers to acceptance.[6] Unique cultural contexts, including a predominantly Muslim population adhering to "halal" principles, contribute to vaccine hesitancy.[7–10] Despite endorsements from

Islamic authorities, concerns about vaccine side effects and service quality further hinder vaccine uptake.[11–14] Additionally, some operational barriers that may affect poor vaccine coverage, such as excessive target children per service unit which can overwhelm staff capacity, and the process of entering vaccination data into the Health Data Center (HDC) system (a national platform providing vaccine uptake statistics updated regularly) which requires digital literacy and regular data entry. These factors may compromise the accuracy and timeliness of vaccine coverage reporting. Narathiwat, with the highest measles incidence rate in Thailand (97.5 per 100,000 population), faces significant challenges in MMR vaccine uptake, particularly in districts such as Rueso and Bacho, which report the lowest coverage in the province.[6,15,16] This study aimed to identify factors affecting MMR vaccine uptake rates in Narathiwat Province through two approaches: describing the practices of childhood state vaccination service units in a quantitative study, and interviewing parents whose children have not completed the MMR vaccine series in a qualitative study. Findings will inform recommendations to enhance immunization programs in the region.

Methods

We used a mixed-method approach, integrating both quantitative and qualitative studies.

Quantitative Study

We conducted a cross-sectional analytic study using secondary data from the 2023 performance survey of all 114 childhood state vaccination service units in Narathiwat Province, spanning every subdistrict in 13 districts. Most units were based in Sub-district Health Promotion Hospitals (SHPHs). The survey, conducted by the Narathiwat Provincial Public Health Office, assessed operational performance using structured questionnaires completed by primary vaccination staff. Key variables included target child numbers, confidence in identifying target areas via the HDC Program, frequency of area clearance and uptake rechecks, supervisor encouragement, reasons for vaccine hesitancy, and proactive vaccination strategies.

Descriptive statistics included median, interquartile range (IQR), frequency, and percentage. Univariable and multivariable logistic regression models identified factors associated with failing to achieve ≥95% MMR2 coverage, defined as children aged 3 years in fiscal year 2022 receiving their second MMR dose. Vaccine coverage data were obtained from the HDC program. Variables with a p-value <0.2 in univariable analysis were included in the multivariable model. Logistic regression results were reported as adjusted odds ratios (ORs) with 95% confidence interval (CI). The minimum sample size was calculated at 54 per group using the formula for comparing two proportions (significance level 0.05, power 0.85)[17], based on vaccination rates during the intervention (51%) and non-intervention (28%) seasons.[18] However, sampling was unnecessary as all 114 units were included.

Data were reviewed for completeness, cleaned, and analyzed using R version 4.2.1.[19] Personal data were excluded, per the Personal Data Protection Act 2019.

Qualitative Study

We gathered insights from mothers of children who turned three in fiscal year 2023 but had not completed MMR2. We focused on maternal beliefs, trust in the health system, and vaccination decisions. We interviewed mothers residing in Bacho and Rueso districts.

Purposive sampling selected five service units with the lowest MMR2 coverage in each district (five SHPHs in Bacho, four SHPHs and one hospital in Rueso). Two mothers per unit were randomly chosen from local registries, yielding 20 participants. However, one could not be reached, resulting in 19 completed interviews.

Semi-structured, in-depth interviews were conducted in private settings for 30–60 minutes. When participants were more comfortable communicating in Malay, the interviews were conducted in the Malay language. All responses were recorded with consent. All interviews were conducted by trained village health volunteers (VHVs) from the Narathiwat Provincial Health Office. These VHVs had prior experience from the DRIVE Demand Thailand project and received additional training in interview techniques and ethics.[20] A pilot was conducted before data collection. Given their strong community ties and established trust, VHVs were well-positioned to elicit honest, low-bias responses on this sensitive topic. Thematic analysis was performed, and key quotes for each theme were collated and reviewed.

Result

Quantitative Results

Factors affecting MMR2 vaccine uptake in Narathiwat Province were identified by comparing units with at least coverage 95% (n=16) to those with coverage less than 95% (n=98). As shown in Table 1, service units with more than 60 target children had significantly higher odds of failing to achieve ≥95% MMR2 coverage compared to those with fewer than 60 children (adjusted OR 6.98, 95% CI 1.46–33.23, p <0.05).

Although not statistically significant, some factors showed trends related to higher MMR2 coverage. These included the use of mobile clinics or door-to-door services compared to vaccination events. In contrast, lower coverage trends were observed in units that lacked confidence in identifying target areas within the HDC program, performed less frequent clearance of target areas, or conducted HDC vaccine uptake status rechecks less frequently after administering vaccines. Compared to time constraints, distrust in vaccines, religious concerns, and fear of side effects, particularly fever, were more likely to be the primary reasons for vaccine hesitancy.

As shown in Figure 1, fear of side effects was the most frequently reported reason for vaccine hesitancy across all districts. In Rueso District, distrust in vaccines was also a notable concern, while Si Sakhon District showed time constraints as a secondary barrier, followed by religious (non-halal) concerns. Bacho District showed a more balanced mix of concerns, including distrust in vaccines and religious (non-halal) issues. Cho-airong District (55% coverage) reported almost exclusively fear of side effects, without notable concern for other barriers. Conversely, districts with the highest MMR2 coverage reported fewer barriers, with time constraints being the only moderate issue.

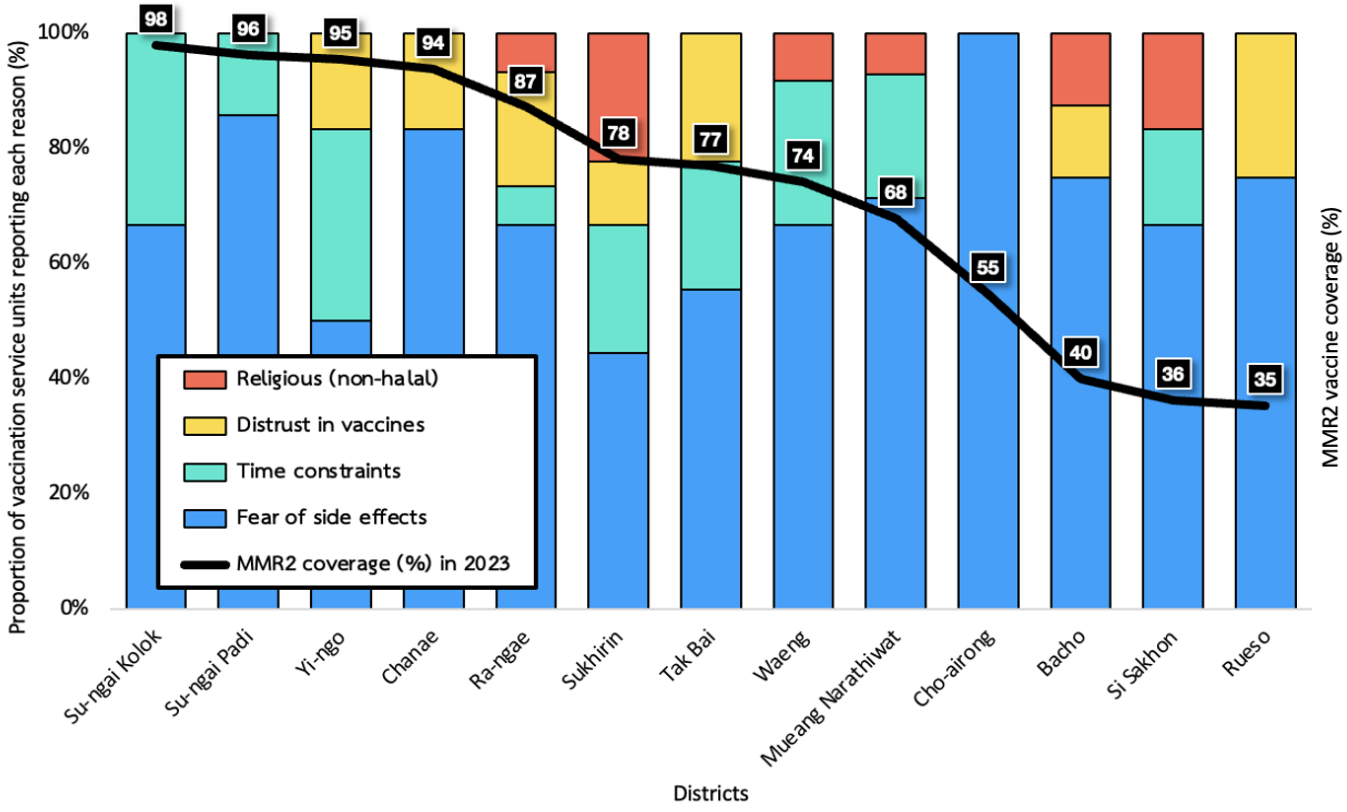

Figure 1. Reasons for MMR2 vaccine hesitancy reported by childhood state vaccination service units and corresponding MMR2 coverage by district, Narathiwat Province, 2023 (n=114)

From Table 1, each of the 114 childhood state vaccination service units reported their most commonly used proactive strategy to enhance vaccine uptake. The three main approaches were: mobile vaccination clinics (55/114, 48.2%), door-to-door visits (25/114, 21.9%), and vaccination events at health facilities (18/114, 15.8%).

Qualitative Results

All 19 mothers of children who turned three years old in Rueso and Bacho districts and had not completed the MMR2 in fiscal year 2023 were interviewed. The number of mothers in Rueso District was seven, with a median age of 33 years (IQR 27.5–37.5), while in Bacho District, the number was 12, and the median age was 32.5 years, with an IQR of 27.8–39.3. The overall median age of the 19 participating mothers across both districts was 33 years (IQR 27.5–39.5). These characteristics provide a foundation for understanding the perspectives and challenges faced by mothers in these districts regarding MMR2 vaccination. We identified six main themes from the interviews.

Table 1. Factors associated with failing to achieve ≥95% MMR2 coverage by childhood state vaccination service units in Narathiwat Province, 2023 (n=114)

Variable	MMR2 coverage <95% (n=98)	MMR2 coverage ≥95% (n=16)	Univariable	Multivariable
			Crude OR (95% CI)	Adjusted OR (95% CI)
Child target per unit				
>60	51	2	7.60 (1.64–35.20)*	6.98 (1.46–33.23)
≤60	47	14	Ref	
Confidence in the accuracy of target area identification within the HDC program				
No	42	3	3.25 (0.87–12.13)*	2.47 (0.60–10.20)
Yes	56	13	Ref	
Frequency of clearing target area type				
Monthly	34	8	Ref	
Quarterly	35	7	1.18 (0.38–3.60)	1.01 (0.31–3.32)
Yearly	29	1	6.82 (0.81–57.83)*	3.52 (0.38–32.87)
HDC vaccine uptake status rechecks				
Others	7	1	1.15 (0.13–10.06)	
Self	91	15	Ref	
Frequency of HDC vaccine uptake status rechecks				
Weekly	50	11	Ref	
Monthly	32	4	1.76 (0.52–6.01)	
Every 3 months	16	1	3.52 (0.42–29.42)	
Supervisor encouragement for vaccination efforts				
No	5	1	0.81 (0.09–7.38)	
Yes	93	15	Ref	
Main reason for vaccine hesitancy				
Time constraints	7	2	Ref	
Fear of side effects	74	12	1.76 (0.33–9.51)	
Distrust in vaccines	10	1	2.86 (0.21–38.00)	
Religious (non-halal)	7	1	2.00 (0.15–27.45)	
Proactive vaccination strategy most commonly used by childhood state vaccination service units to enhance uptake†				
Vaccination events at health facilities	18	1	Ref	
Door-to-door visits	25	7	0.38 (0.04–3.27)	
Mobile vaccination clinics	55	8	0.20 (0.02–1.76)	

**Variables with p-value <0.2 in univariable analysis were selected for inclusion in the multivariable model. †Vaccination events at health facilities targeted larger groups through special drives; Door-to-door visits reached households in areas with limited mobility; Mobile vaccination clinics were arranged within communities to improve access. HDC: Health Data Center. OR: odds ratio. CI: confidence interval. Ref: reference.*

Perceptions of Measles

Most participants recognized measles as a contagious viral illness marked by distinct symptoms such as red rashes and fever. However, their depth of understanding regarding the severity, progression, and other associated symptoms of the disease varied widely. While some participants provided detailed descriptions of the rash and the extent of spread, others perceived the condition as mild or were unfamiliar with it.

"Red rash with low fever." ...A1–3, A5, B1–4, B10, B12

"Red patches on the body spreading to the legs when having a fever." ...A4, A7, B7–8

"My child had small itchy red spots; it didn't seem too severe." ...B5

"I don't know it because this disease isn't common in my area." ...B11

Effectiveness of Vaccine

Participants recognized the benefits of vaccination in preventing disease and reducing severity. Most participants emphasized the vaccine's role in minimizing severe symptoms and preventing disease progression, demonstrating confidence in its effectiveness. Several participants also acknowledged its life-saving potential, noting that it can reduce the risk of death and increase immunity. However, some participants expressed more cautious views, acknowledging that while the vaccine offers protection, it may not fully prevent severe outcomes or infection.

"It helps prevent the disease and reduce severe symptoms." ...A1–3, A5–7, B1, B2, B5, B7–10

"It prevents death and provides immunity." ...A4, B4, B11

"It provides some protection." ...B6, B12

Support for Vaccination Campaigns

Participants highlighted the importance of vaccination campaigns in preventing diseases, especially measles. Most described the campaigns as effective in promoting awareness and increasing acceptance of measles vaccination within the community. One participant noted that while the campaigns were beneficial, some children might still become infected, suggesting a residual concern about vaccine effectiveness. However, overall feedback reflected strong support for the campaigns themselves rather than doubts about the vaccines.

"Vaccination campaigns are important because they encourage parents to vaccinate their children." ...A1–7, B1–3, B5–8, B10, B11

"the campaigns are good, but some children might still get infected." ...B12

Barriers to Vaccination Uptake

Participants highlighted various concerns regarding vaccination, reflecting a mix of fears, logistical challenges, and personal beliefs. A common worry was the potential for post-vaccination fever or more severe side effects such as paralysis, which some feared as being a disruption to their work or daily responsibilities. Time constraints due to work were also frequently mentioned. Additionally, personal beliefs, such as reliance on hygiene and diet for disease prevention or doubts about the halal status of vaccines, influenced vaccine hesitancy for some.

"I fear my child will get a fever afterward." ...A1–3, A5, A7, B1, B2, B8, B9

"If my child gets sick, it disrupts my work." ...A4, B3, B7

"I'm afraid of side effects, like paralysis, which would make our life harder." ...A6, B12

"I'm waiting until my child is a bit older." ...B11

"I don't have time because of working Monday to Friday." ...B4, B10

"I think maintaining hygiene and eating fresh food can prevent diseases, so vaccination isn't necessary." ...B6

Perceptions of Halal Status of Vaccines

Participants expressed a range of perspectives regarding the halal status of vaccines, emphasizing the importance of trusted sources and clear communication. Many participants highlighted the need for confirmation from health authorities to ensure the vaccine complies with religious principles. While some participants were confident that the vaccine was halal, others expressed hesitancy due to rumors or uncertainty.

"I need confirmation from health authorities." ...A1, A3, A5–7, B1, B4, B6, B8

"It is halal." ...A2, B2, B3, B7, B9–12

"I'm hesitant because people have mentioned it might not be halal." ...B5

Trust in Local Vaccination Services

Participants expressed varying levels of trust in vaccination services, with the majority indicating strong confidence in the system. However, some raised concerns about specific issues, such as side effects, staff behavior, or perceived inexperience among healthcare providers. While most participants trusted the services, frustrations arose from experiences of being reprimanded for missed appointments.

"I trust them." ... A4, A6, B1, B2, B4, B7, B8, B10, B12

"I trust them somewhat but worry about side effects." ...A7, B3, B5

"There are many inexperienced nurses." ...A5

"They complain if I miss appointments." ...A1–3, B6

Discussion

This study identified both service and demand-side factors influencing MMR2 coverage in Narathiwat. Units with more than 60 target children were significantly less likely to reach ≥95% coverage, suggesting that heavy workloads reduce performance. Trends also pointed to higher coverage in units using mobile clinics, door-to-door visits, and more consistent data practices, particularly by regularly clearing target area data and performing self-rechecks of vaccine uptake status using the HDC system. On the demand side, fear of side effects, concerns about vaccine content, and halal status remained key barriers, underscoring the need for both operational and cultural solutions. Hesitancy was largely driven by prior experiences of illness after vaccination, consistent with previous findings.[21,22] Although the MMR vaccine significantly lowers the incidence of post-vaccination fever compared to other vaccines such as Diphtheria, Tetanus, and whole-cell Pertussis and Japanese Encephalitis in Thailand's Expanded Program on Immunization schedule,[23,24] many mothers generalized their concerns to all vaccines. However,

this alone does not account for the high level of vaccine hesitancy in Narathiwat, as similar vaccines are used in other regions without similar resistance, indicating other sociocultural and economic factors. Economic barriers emerged as a critical concern, with mothers expressing fear of side effects—such as fever after vaccination—that could disrupt their work and lead to financial instability. This aligns with studies indicating that socio-economic challenges, such as poverty and limited access to economic resources, significantly impact vaccine uptake.[9,10,12] These challenges are intensified in Narathiwat, which faces long-standing economic hardship.[25] Similar challenges have been reported in other countries, where economic constraints exacerbate vaccine hesitancy.[26–28]

In Narathiwat, where most parents are Muslim, concerns about the halal status of vaccines and beliefs that vaccination may contradict Islamic teachings contribute significantly to hesitancy. Similarly, in other Muslim-majority countries, misconceptions about the religious permissibility of vaccines often foster distrust and influence parental decisions regarding immunization.[29] Islam prohibits the consumption of pork, and some vaccines use gelatin derived from pork products as a stabilizing agent.[30] However, Islamic jurisprudence prioritizes the preservation of life and permits vaccines derived from non-halal sources when no halal alternatives are available.[31] Jurisprudence councils generally deem vaccines permissible if they undergo transformation and purification processes.[32] Additionally, most Islamic scholars support vaccination as a public health necessity, based on the principle that necessities override prohibitions.[33] In Thailand, measles vaccines do not contain pig-derived ingredients, including porcine gelatin, as confirmed by the Director of the Division of Communicable Diseases, Ministry of Public Health, Thailand.[34] Nonetheless, this study found that some mothers still seek confirmation from health authorities about the halal certification of vaccines, beyond endorsements from the Central Islamic Council of Thailand. To address this, health agencies must take the lead in collaborating with the Central Islamic Council of Thailand and global or national halal certification bodies to provide credible and unified certification.

Mobile vaccination clinics have effectively improved coverage, and expanding this strategy to underserved areas could further boost uptake by addressing logistical barriers.[35] This is supported by our qualitative findings, where some participants reported challenges such as a lack of time due to work schedules. Our quantitative study also suggested a trend toward higher MMR2 coverage in units using mobile vaccination clinics, although this association was not statistically significant. These factors underscore the need for more accessible service delivery models. However, challenges persist, especially for staff managing large child populations. High workloads can hinder the accuracy of vaccination records and reduce the quality of client counseling. This aligns with our finding that units with over 60 target children were less likely to achieve high MMR2 coverage, suggesting that heavy workloads may hinder performance. Consistent with international studies, limited workforce capacity undermines the efficiency of immunization programs.[36] Furthermore, communication barriers, particularly when engaging with mothers who refuse or delay vaccination, also persist.

Other operational barriers, such as lack of confidence in identifying target areas and infrequent clearance of target areas (i.e., updating and verifying target population data), showed trends toward lower MMR2 coverage but were not statistically significant. These findings align with studies highlighting the importance of timely follow-up checks of immunization data, the frequency of these reviews, and supervisor support for accurate coverage.[37,38] Clearing target areas and updating population records are also crucial for improving MMR2 coverage and overcoming barriers.[39,40]

Limitations

While the quantitative component included all state vaccination service units and provided broad representativeness, the qualitative component was limited to 19 mothers from only two districts. This may limit the generalizability of maternal perspectives. Future studies should consider including fathers or other caregivers to better capture parental decision-making.

Recommendations

To strengthen service delivery, mobile vaccination clinics and door-to-door outreach services should be expanded especially in underserved areas. As units with more than 60 target children were significantly less likely to achieve high MMR2 coverage, reducing workforce burden is crucial. Optimizing core practices such as more frequent area clearance and self-rechecks of vaccine uptake data may also lead to better outcomes.

To reduce vaccine hesitancy among parents, communication strategies should emphasize that mild side effects like fever are temporary and far less severe than complications from non-vaccination. Conducting studies comparing the burden of post-vaccination side effects with the risks of not vaccinating would strengthen these efforts. Although the halal status of vaccines is clarified nationally, local health authorities should collaborate with religious leaders to address

concerns while improving provider communication to build trust and confidence in the vaccine program.

Conclusion

This study highlights several factors affecting MMR2 coverage in Narathiwat Province, particularly challenges related to service delivery. Mobile vaccination clinics and door-to-door outreach were key strategies for improving access, especially in areas with high target populations. Operational issues such as limited workforce capacity, infrequent clearance of target areas, and self-rechecks of vaccine uptake status also affected MMR2 coverage. On the demand side, the main barrier was concern over post-vaccination fever, while cultural concerns like the halal status of vaccines played a lesser but persistent role. Improving MMR2 coverage requires strengthening local service systems, optimizing operational practices, and addressing parental concerns through culturally appropriate engagement.

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Author Contributions

Farooq Phiriyasart: Conceptualization, methodology, formal analysis, writing—original draft, writing—review & editing, supervision, and project administration. **Arisman Kariya:** Investigation, data curation, and validation. **Nungrutai Ninlakan:** Resources, data curation, and writing—review & editing. **Saowanee Mueankhaw:** Investigation, resources, and writing—review & editing. **Sasikarn Nihok:** Data curation and visualization. **Adul Binyusoh:** Supervision, resources, and writing—review & editing.

Ethical Approval

This study was approved by the Human Research Ethics Committee of the Narathiwat Provincial Health Office, Narathiwat Province, Thailand, under research code 29/66. The research protocol strictly adhered to international standards. All participants provided informed consent to participate in the study and were given an information sheet detailing the study.

Informed Consent

Informed consent was obtained from all participants involved in the study. Written informed consent was obtained from all participants prior to the interviews.

Data Availability

The data that support the findings of this study are available from the Narathiwat Provincial Public Health Office. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from the corresponding author with the permission of the Narathiwat Provincial Public Health Office.

Conflicts of Interest

The author declares no conflicts of interest related to this work.

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Declaration of Generative AI and AI-assisted Technologies in the Writing Process

During the preparation of this work, the authors used ChatGPT (OpenAI) to enhance clarity and correct grammatical errors. The content produced by this tool was reviewed and edited by the authors, who accept full responsibility for the final text.

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Analysis of the Situation and Factors Associated with Dengue Incidence at the Provincial Level during 2019–2023, Lao PDR

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Abstract

We described the incidence of dengue infection in the Lao People's Democratic Republic (Lao PDR) from 2019 to 2023, presenting seasonal trends, geographic distribution, and socio-environmental factors. We used data from the National Surveillance Database to fit the time-series and random-effects Poisson regression model. In five years, over 111,000 cases were reported, with an annual incidence exceeding 450 cases per 100,000 in 2019 before declining during the COVID-19 pandemic in 2020 and 2021. Most cases were aged less than 30 years. The monthly incidences peaked during the rainy season (July-September). Rainfall, lagged rainfall, house index, and lagged house index were significant positive factors. A higher density of health facilities was also associated with a higher incidence. These findings underscore the importance of targeted public health interventions during peak transmission periods and suggest that additional factors, such as urbanization and economic status, should be addressed to enhance dengue control efforts in Lao PDR.

Keywords: dengue, Poisson regression, seasons, Lao PDR

Introduction

Dengue infection, transmitted by mosquitoes, usually causes mild symptoms such as fever and other influenza-like illnesses. However, severe infections can lead to bleeding, shock, and death. The disease has spread rapidly due to population growth, urbanization, and increased availability and access to air travel, affecting billions of people in endemic areas.[1]

Dengue is endemic in 48 countries in the Western Pacific and Southeast Asia regions. Each year, over 14 million cases and 10,000 deaths are reported globally.[2] Dengue virus (DENV) has four serotypes (DENV-1, DENV-2, DENV-3, and DENV-4), causing a wide range of illnesses from mild symptoms to severe shock. Children aged under 15 years are most affected by dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[3]

Dengue infection remains a significant public health concern in the Lao People's Democratic Republic (Lao PDR). Over 30,000 cases were reported in 2023, and the incidence rate was 480 cases per 100,000 population with 12 out of 18 provinces experiencing outbreaks.[4] The most prevalent serotypes in 2023 were DENV-1 and DENV-2.

While temperature and humidity are key factors in dengue transmission, these factors may not be relevant to Lao PDR due to its unique geographic and climatic conditions, economic factors, cultural practices, healthcare systems, and the prevalence of specific dengue serotypes.[5,6] Studies on factors related

to dengue incidence in Lao PDR are scarce, especially after the COVID-19 era. These distinctions emphasize the need for localized studies to better understand the socio-environmental determinants of dengue.

Therefore, the objectives of this study were to (1) describe the magnitude, severity, and characteristics of dengue cases in Lao PDR, (2) determine the trends, seasonality, and geographical patterns of dengue incidence, and (3) identify socio-environmental factors of dengue at the provincial level.

Methods

Study Design

A retrospective analysis was conducted using monthly data at the provincial level and cross-sectional data on individual dengue cases from 2019 to 2023. A descriptive study was conducted to address objective 1 while analytic studies were conducted to address objectives 2 and 3.

Data Source

We obtained data from the National Surveillance Database, National Centre of Laboratory and Epidemiology, Ministry of Health (MOH), Lao PDR, which collected data from public health facilities. We included all 18 provinces: Attapeu, Bokeo, Bolikhamxay, Champassak, Houaphanh, Khammouane, Luang Namtha, Luang Prabang, Oudomxay, Phongsaly, Salavan, Savannakhet, Sekong, Vientiane Capital, Vientiane Province, Xayaburi, Xaysomboun, and Xiangkhouang, which are endemic for dengue.

Operational Definition and Variables of Interest

Table 1 presents the operational definitions of the variables of interest together with the research team's working hypothesis for the outcome.[7]

Table 1. Operational definitions

Variable	Definition	Working hypothesis
Dengue incidence	Number of dengue cases (either dengue fever or dengue hemorrhagic fever or dengue shock syndrome) per 100,000 population	-
Temperature	Mean temperature in Celsius in a province in that month	Higher temperatures, higher incidence
Lagged temperature	Mean temperature in Celsius in a province in prior month	Higher lagged temperatures, higher incidence
Rainfall	Mean rainfall in mm. in a province in that month	Higher rainfall, higher incidence
Lagged rainfall	Mean rainfall in mm. in a province in prior month	Higher lagged rainfall, higher incidence
House index (HI)	Mean HI in a province in that month, from the field survey	Higher index, higher incidence
Lagged house index	Mean HI in a province in prior month from the field survey	Higher lagged index, higher incidence
Provincial population	Population volume in each province	Higher population density, higher incidence
Health facility density	Number of health facilities per 100,000 population	Higher health facilities density, higher incidence

Source: National Surveillance Database, National Centre of Laboratory and Epidemiology, Ministry of Health, Lao PDR.
We imputed missing values with the mean monthly temperature (and its lag), monthly rainfall (and its lag), and monthly house index for each province. Mean temperature was calculated by averaging daily temperatures across all days in a month. Mean monthly rainfall was calculated by summing the daily rainfall and dividing by the number of days in the month. Mean house index was measured by summing the index in all surveyed areas in the province and dividing by all surveyed areas (on average, 68 areas per province).

Data Analysis

For objective 1, we present descriptive statistics including percentage and frequency of dengue cases at the individual level stratified by age and gender. Population morbidity rates and case fatality rates were calculated. Choropleth maps were constructed to visualize and compare the geographical distribution of dengue incidence at the provincial level each year.

For objective 2, we employed time-series regression (Prais-Winsten regression) to decompose trends and seasonal patterns of monthly dengue incidence over time. The unit of analysis was the monthly number of

cases. Independent variables were the number of months since 1 Jan 2019 (month index) and the month of the year.

For objective 3, we utilized univariable and multivariable random-effects Poisson regression model where province was considered a higher-level variable. The monthly dengue incidence was the dependent variable. The natural logarithm of the provincial population was used as an offset. Independent variables were monthly temperature and its lag, monthly house index (the number of houses where mosquito larvae presented divided by the total number of houses inspected and expressed in percentage) and its lag, monthly rainfall and its lag, health facility density, the reporting year, month index, and month of the year. The lag period was set at one month. We included lagged variables because previous literature suggested that dengue cases and climatic factors such as the El Nino effect were positively correlated with a lag of 3 to 6 months.[8] Note that the specific duration of monthly lags varies across studies.[9]

We imputed missing data for monthly rainfall, house index, and temperature (about 14% of records) by mean substitution using data in each province in a year. Results were presented in the form of an incidence rate ratio (IRR) and 95% confidence interval (CI). We also assessed the robustness of the final model by excluding variables that exhibited multicollinearity based on the variance inflation factor (VIF). Variables with a VIF value of 10 or higher were excluded and the model was re-analyzed accordingly. We then assessed if and to what extent the findings from the final model would change if variables with potential multicollinearity were dropped from the analysis. Stata version 16 (serial number: 301506215585) and Microsoft Excel were used for the analysis.

Results

There were 111,826 dengue cases reported in Lao PDR from 2019 to 2023. The annual dengue incidence is presented in Table 2. The yearly incidence (cases per 100,000 population) varied from 21.6 in 2021 to 495.6 in 2019. The case fatality rate ranged from 0.04 to 0.14%. The male-to-female ratio remained constant at about 1:1 across all years.

Most cases were identified in younger populations, with more than 70% of the cases involving individuals aged under 30 years. Only 3% of the cases were reported in people aged over 60 years. In 2023, the incidence was highest among people aged 20–29 years (764.48) and lowest among those aged 50–59 years (290.71). Students constituted approximately 30% of the total cases while farmers approximately to about one-fifth of the cases.

Table 2. Key dengue indicators in Lao PDR, 2019–2023

Dengue indicators	Year				
	2019	2020	2021	2022	2023
New cases (n)	**32,334**	**8,215**	**1,585**	**33,163**	**36,529**
By occupations—n (%)					
Students	10,696 (33)	2,086 (25)	315 (20)	8,032 (24)	9,214 (25)
Farmers	4,419 (14)	2,340 (29)	247 (16)	6,457 (20)	9,229 (25)
Government staff	427 (1)	290 (4)	101 (6)	1,821 (5)	2,105 (6)
Others	16,792 (52)	3,499 (42)	922 (58)	16,853 (51)	15,981 (44)
New cases (per 100,000 population)					
Overall	495.93	113.61	21.60	445.58	48.11
By age group (years)					
0–9	1,105.41	129.96	23.22	456.78	512.00
10–19	659.94	172.33	31.12	640.99	699.60
20–29	637.51	212.67	43.32	860.58	764.48
30–39	376.92	140.36	27.19	585.68	656.53
40–49	234.81	92.86	15.15	330.03	397.63
50–59	157.66	74.66	13.82	237.41	290.71
60+	107.87	54.20	10.45	222.68	255.17
Case fatality rate (%)	0.14	0.04	0.06	0.07	0.05
Male to female ratio	1: 1.06	1: 0.99	1: 0.97	1: 1.01	1: 1.03

Dengue fever (DF) constituted approximately 80% of all dengue cases. The incidence in 2022–2023 exceeded the five-year median. As shown in Figure 1, the incidence was highest between May and September, with July and August being the most prominent months.

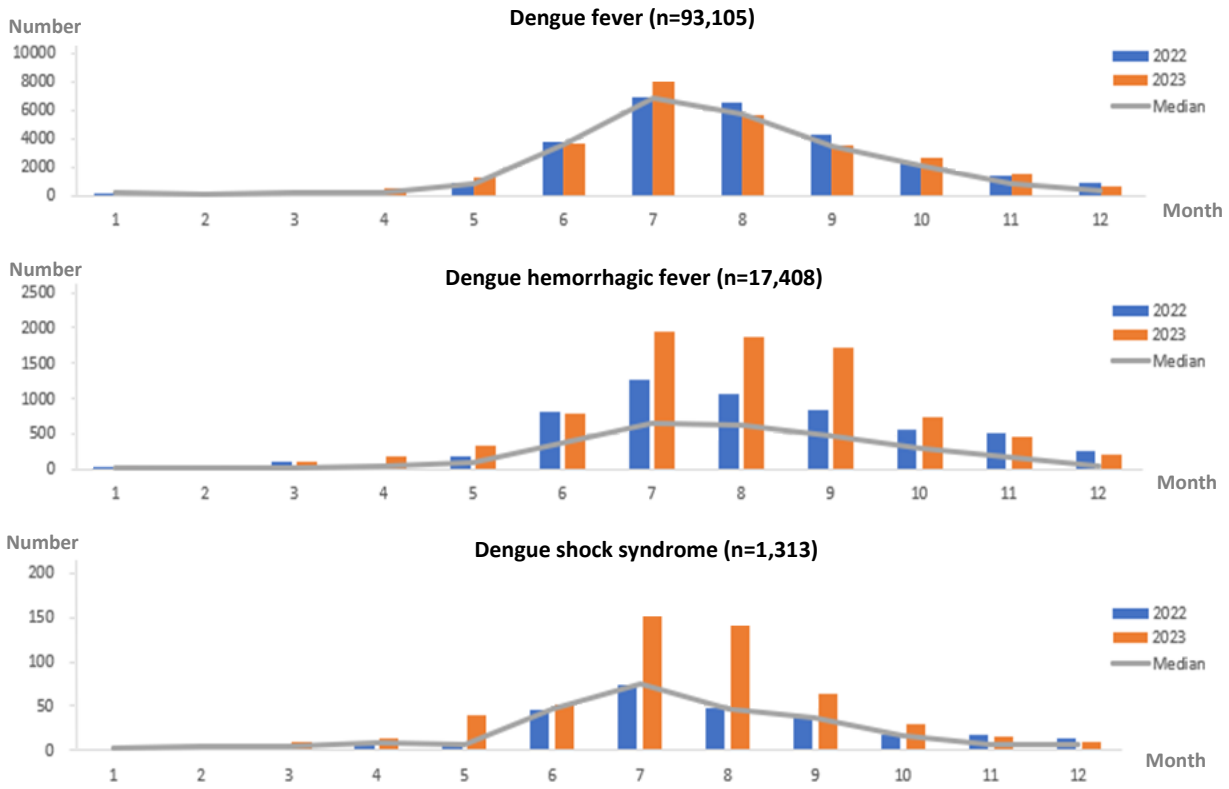

Figure 1. Number of dengue cases by months and disease classifications in Lao PDR, 2022–2023, with the five-year median

As shown in Figure 2, dengue cases were concentrated in the southern and northwestern parts of the country, notably in Khammouane and Luang Namtha, and especially in years 2019, 2022, and 2023.

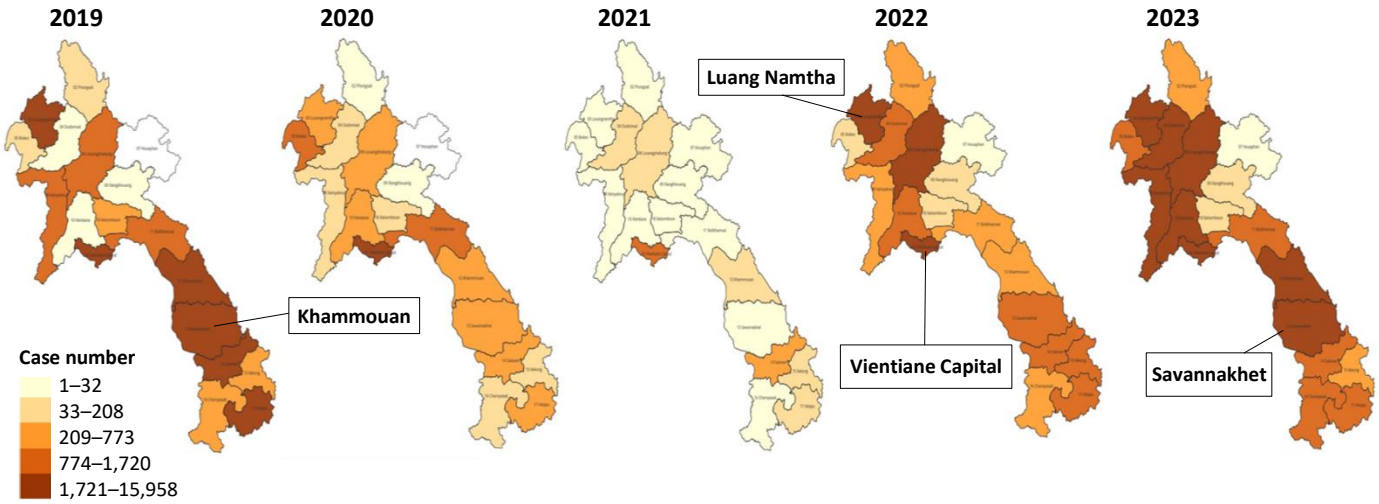

Figure 2. Geographical distribution of dengue cases in Lao PDR, 2019–2023

Table 3 shows the results of the trend and seasonal analysis using the Prais-Winsten regression model. The month index had a coefficient of 7.31, indicating a slight increase in dengue incidence over time, though without statistical significance. However, the seasonal effect was highly significant. Compared to January, the incidence rates during June–October were significantly higher, with a peak observed in July (coefficient 4,775.2, 95% CI 3,399.6–6,150.8). Table 4 displays the results from univariable and multivariable random-effects Poisson regression models. Entomological and environmental factors, such as house index and its lag, rainfall, and lagged rainfall, had significant positive associations with dengue incidence in both univariable and multivariable analyses, although their effect sizes were small. An increase in one unit of health facility density per 100,000 population was associated with an increase in dengue incidence by approximately 69% in the multivariable model, though exhibiting negative association in univariable model. The opposite was found in lagged temperature, where an increase in one degree Celsius was linked to a 2.2%-decline of dengue incidence in multivariable analysis despite presenting a positive association in univariable analysis.

The rainy season (July–September) was associated with an increase in dengue incidence of approximately 10–20 cases relative to January. The incidence in 2023 was roughly 1.66 times larger than the incidence in 2019. A marked decline in the incidence was observed in 2020–2021 (IRR for 2020=0.307, 95% CI 0.298–0.316).

Temperature, lagged temperature, and health facility density, were found to be linearly dependent in VIF analysis. After excluding those variables, the IRR estimates of most of the other variables in the model remained robust (for instance, IRR for house index decreased from 1.029 to 1.025 while remaining statistically significant).

Table 3. Trend and seasonality from time-series regression (Prais-Winsten) of dengue incidence in Lao PDR, 2019–2023

Factors	Coefficient	*P*-value	95% CI	
			Lower limit	Upper limit
Month index*	**7.31**	**0.84**	**-65.80**	**80.43**
Month of the year (ref=January)				
February	-66.18	0.86	-839.25	706.90
March	-16.27	0.98	-1,049.70	1,017.17
April	142.16	0.81	-1,051.28	1,335.60
May	678.34	0.30	-616.43	1,973.12
June	2,335.94	<0.01	982.74	3,689.14
July	4,775.22	<0.01	3,399.63	6,150.81
August	3,964.88	<0.01	2,600.77	5,328.98
September	2,541.41	<0.01	1,224.21	3,858.62
October	1,427.56	0.02	198.56	2,656.57
November	704.67	0.20	-381.37	1,790.72
December	179.33	0.68	-675.82	1,034.48

**Number of months since 1 Jan 2019. CI: confidence interval.*

Table 4. Factors associated with dengue incidence in Lao PDR, 2019–2023, by random-effects Poisson regression model*

Factors	Univariable analysis				Multivariable analysis			
	IRR	*P*-value	95% CI		IRR	*P*-value	95% CI	
			Lower limit	Upper limit			Lower limit	Upper limit
Month (ref=January)								
February	0.721	<0.001	0.657	0.791	0.943	0.286	0.846	1.051
March	0.982	0.680	0.902	1.070	1.320	<0.001	1.187	1.467
April	1.748	<0.001	1.621	1.885	2.489	<0.001	2.245	2.758
May	4.279	<0.001	4.003	4.574	5.491	<0.001	4.974	6.062
June	12.056	<0.001	11.327	12.833	12.935	<0.001	11.743	14.247
July	23.489	<0.001	22.094	24.972	21.757	<0.001	19.762	23.955
August	19.703	<0.001	18.528	20.952	15.653	<0.001	14.196	17.260
September	13.042	<0.001	12.255	13.880	11.513	<0.001	10.457	12.675
October	7.825	<0.001	7.342	8.339	9.196	<0.001	8.386	10.085
November	4.432	<0.001	4.147	4.736	5.988	<0.001	5.473	6.551
December	1.956	<0.001	1.817	2.106	2.696	<0.001	2.450	2.967
Year (ref=2019)								
2020	0.222	<0.001	0.216	0.228	0.307	<0.001	0.298	0.316
2021	0.044	<0.001	0.041	0.046	0.072	<0.001	0.068	0.076
2022	0.893	<0.001	0.878	0.907	1.558	<0.001	1.500	1.618
2023	0.868	<0.001	0.855	0.882	1.660	<0.001	1.585	1.739
House index	1.104	<0.001	1.103	1.105	1.029	<0.001	1.028	1.031
Lagged house index	1.090	<0.001	1.089	1.091	1.006	<0.001	1.004	1.007
Rainfall	1.003†	<0.001	1.003†	1.003†	1.001‡	<0.001	1.001‡	1.001‡
Lagged rainfall	1.003§	<0.001	1.003§	1.003§	1.000¶	<0.001	1.000¶	1.000¶
Temperature	1.173	<0.001	1.170	1.176	1.004	0.426	0.995	1.012
Lagged temperature	1.298	<0.001	1.294	1.302	0.978	<0.001	0.970	0.986
Health facility density	0.851	<0.001	0.837	0.865	1.693	<0.001	1.627	1.761

**n=660 (12 months × 5 years × 11 provinces). However, in multivariable analysis, as lag variables were used, the number of remaining records was 649 (dropping records in year 2019). †Full expression of the rainfall variable in univariable analysis is 1.00342 (95% CI 1.00337–1.00343). ‡Full expression of the rainfall variable in multivariable analysis is 1.00069 (95% CI 1.00064–1.00074). §Full expression of the lagged rainfall variable in univariable analysis is 1.00250 (95% CI 1.00246–1.00252). ¶Full expression of the lagged rainfall variable in multivariable analysis is 1.00023 (95% CI 1.00017–1.00028). IRR: incidence rate ratio. CI: confidence interval.*

Discussion

Our findings confirm that Lao PDR has faced a significant burden from dengue infections between 2019 and 2023. A total of 111,826 dengue cases were reported, with incidence rates varying across the years. The highest incidence occurred in 2019 with over 450 cases per 100,000 population, while 2021 had the lowest incidence. This fluctuation suggests that variations in dengue outbreaks are influenced by multiple factors such as seasonal climatic patterns, public health interventions, and environmental conditions.

The case fatality rate remained low at below 0.1% in most years, consistent with global trends of dengue, but the disease can have a high morbidity rate in some periods.[10,11]

The male-to-female ratio remained constant over the years, with a near-equal distribution between genders. We found that younger populations (age below 30 years) accounted for about three-quarters of dengue cases, while older populations (above 60 years) were less affected (3% of cases), a result consistent with other studies.[12]

Seasonal trends were evident, with peak infections typically occurring between July and September—a rainy season in the region. Findings from multivariable analysis confirmed this result. Studies in neighboring countries found relatively similar results.[13,14] Mean temperature, rainfall, and relative humidity were positively linked with DHF incidence near the Andaman Sea. Minimum temperature, rainy days and relative humidity were also associated with DHF incidence in areas near the Gulf of Thailand.[13] Choi et al reported that 2-to-3 monthly lagged rainfall affects dengue incidence in Cambodia.[14]

We found that house index and its one-month lag had a positive and significant association with dengue incidence, although the effect size was small. Similar findings were reported by Udanyanga et al, highlighting the association between house index, Breteau index, and the lagged values at one and two months, and dengue epidemics.[15]

The large decrease in incidence during 2020–2021 is likely due to the COVID-19 pandemic. In Thailand, the incidence of dengue cases decreased by over 6-fold in 2021 compared to 2019.[16] The reduction in dengue cases amid the COVID-19 era is likely due to an underreporting or the introduction of social distancing measures. Sharma et al suggested that the antigenic cross-reactivity between dengue and COVID-19 might result in false positives for COVID-19 among dengue patients.[17]

Health facility density was strongly associated with dengue incidence in both univariable and multivariable analyses. On the one hand, this may be attributed to the nature of our analysis, which relied solely on data from health facilities. On the other hand, it is possible that mild dengue cases—such as those who sought care at private facilities or those who were self-managed and did not visit any health facilities—were excluded from the analysis. Moreover, a high density of health facilities may partly reflect greater urbanization, where higher population density could contribute to increased dengue incidence.

Limitations

This study contains both strengths and limitations. A major strength lies in the inclusion of lagged variables to capture potential climatic effects on dengue incidence—a technique that, while used in some studies, has rarely been applied in other studies in Southeast Asia.[18,19] The use of data from all provinces in Lao PDR enhances the generalizability of the study. The assessment of multicollinearity adds robustness to the analysis and, although multicollinearity is not a strict violation of regression assumptions, addressing it strengthens the study's validity and academic value.[20] However, some limitations remain. First, the study relied on reported cases from health facilities, which may not fully represent the true disease burden in the population due to potential non-reporting from private facilities or misdiagnoses. Second, although environmental factors such as temperature and rainfall were considered, this study did not fully examine the potential contributions of other environmental influences, such as urbanization and land use changes. The absence of these unmeasured confounders in the model may partly explain the unexpected results that contradict established understanding in the field of dengue studies, such as the observed negative association between lagged temperature and dengue incidence. Moreover, potential measurement errors may have contributed to these findings. Third, since we collected data at the provincial level for objective 3, an ecological fallacy should be heeded. Finally, while the study covered a five-year period (2019–2023), we may not have sufficiently captured the long-term trends of dengue incidence. Thus, re-assessment of the dengue situation over a longer period is warranted

Recommendations

We recommend enhancing dengue surveillance in Lao PDR, particularly during peak transmission months (June–October). Public awareness campaigns should be intensified during periods of increased rainfall and higher temperatures. Regular monitoring of larval indices can provide early warnings of

potential outbreaks and aid in disease control efforts. Further studies incorporating other critical factors influencing dengue, such as health system capacity, urbanization levels, and provincial economic status, would greatly benefit public health initiatives against dengue in Lao PDR.

Conclusion

Lao PDR experienced a remarkable public health burden due to dengue infections between 2019 and 2023. Over 110 thousand cases were reported. Fluctuations in the incidence were observed, ranging from 20 to 500 cases per 100,000 population. A decrease in incidence was observed in the years 2020 and 2021. The case fatality rate remained below 0.1% after 2020. The incidence increased substantially during the rainy season. Rainfall, house index, and health facility density were positively correlated with dengue incidence. Further studies that incorporate key potential factors that contribute to dengue incidence, such as health system capacity and provincial economic level, are recommended.

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Author Contributions

Nouannipha Simmalavong: Conceptualization, data collection, formal analysis, methodology, project administration, validation, writing—original draft. **Rapeepong Suphanchaimat:** Conceptualization, formal analysis, methodology, project administration, supervision, validation, writing—original draft, writing—review & editing. **Waraluk Tangkanakul:** Conceptualization, project administration, supervision, writing—review & editing. All authors have read and agreed to the published version of the manuscript.

Ethical Approval

As this study was part of the routine monitoring by MOH, Lao PDR, ethics approval was not required. However, all results are presented anonymously. No individual information has been disclosed.

Informed Consent

Not applicable

Data Availability

The datasets analyzed in the current study are available from the corresponding author on reasonable request.

Conflicts of Interest

None declared.

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Declaration of Generative AI and AI-assisted Technologies in the Writing Process

During the preparation of this work, the authors used ChatGPT to enhance clarity in some parts of the text. The content produced by this tool was reviewed and re-edited by the authors, who accept full responsibility for the final text.

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A Novel Surveillance Evaluation Approach Using Clinical Text Extraction from the Hospital Information System: Case Study of Somdejpraboromrachineenart Natawee Hospital, Songkhla Province, Southern Thailand for Influenza in 2024

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Abstract

In 2024, Na Thawi District, Songkhla Province, reported the highest influenza cases in Southern Thailand. This cross-sectional study evaluated the influenza surveillance system (R506) at Somdejpraboromrachineenart Natawee Hospital in 2024 using both quantitative and qualitative methods. Stakeholders involved in the epidemiological surveillance system were interviewed to describe the system qualitatively. Quantitatively, 8,758 medical records from the hospital information system (HIS) and 358 R506 reports were reviewed to assess sensitivity, positive predictive value (PPV), completeness, accuracy, and timeliness. The female-to-male ratios were 1.17:1 in HIS meeting the R506 definition and 1.08:1 in R506. Most cases were in the 25–60-year age group in HIS and 5–9-year group in R506. The lowest proportions were among those aged 60 years or more. Cases peaked in July; HIS showed a gradual rise from May, while R506 surged from June. Most cases occurred in Na Thawi and Chana districts. Subdistrict-level data showed consistent hotspots in Na Thawi, Sathon, and surrounding areas. The overall incidence in the area was higher than in the reporting system. The sensitivity was 8.52% and the PPV was 84.92% with R506 showing 100% completeness and accuracy, except for onset date (21.79%). Timeliness was high: 98.88% within 3 days and 99.72% within 7 days. From the qualitative study, the stakeholders accepted the surveillance system, describing it as simple, flexible, stable, and useful for planning and resource allocation. Clinical text extraction enabled full review without the need for sampling.

Keywords: influenza, surveillance system, hospital information system, electronic medical record, clinical text extraction, report 506

Introduction

Influenza is an acute viral respiratory infection causing fever, headache, muscle aches, and fatigue.[1] Global outbreaks occur frequently and contribute significantly to morbidity and mortality.[2] The virus is classified into types A, B, and C, with type A being the most common.[3] Transmission occurs through respiratory droplets and contact with contaminated surfaces. The incubation period is 1–3 days and individuals are infectious from one day before symptom onset to 3–5 days afterward in adults and up to seven days in children.[1,4]

In 2024, Thailand reported over 645,000 influenza cases and 49 deaths, primarily caused by type A.[5] The Southern Health Region 12 reported 42,697 cases, with Songkhla Province reporting the highest incidence. In Na Thawi District, which has a population of about 60,000, 358 cases were reported through its district hospital, with frequent outbreaks occurring in prisons, schools, and hospitals.[6,7]

Thailand's traditional passive surveillance system faces several challenges such as limited coverage, delays, and resource constraints, which hinder timely outbreak detection.[8,9] Recent advancements in information technology and data science have enabled

improved data extraction from hospital information systems (HIS).[10–14] Manual record reviews remain time-consuming, while clinical text extraction enables faster and more accurate symptom identification from unstructured data.[15–17] Although this method has demonstrated high precision and recall (0.7–1.0), its use in surveillance evaluation is still limited—likely due to reliance on structured data, the complexity of natural language processing (NLP), and limited collaboration between informatics and public health professionals.[8,18–20] This study aimed to: 1) evaluate clinical text extraction for surveillance evaluation; 2) describe the influenza surveillance system qualitatively; and 3) assess quantitative characteristics using this method at Somdejpraboromrachineenart Natawee Hospital.

Methods

Study Overview

This mixed-methods study evaluated the influenza surveillance system at Somdejpraboromrachineenart Natawee Hospital using both quantitative and qualitative approaches. The quantitative component assessed system attributes—sensitivity, positive predictive value, data quality, timeliness, and representativeness—using data from the hospital information system (HIS) and Report 506 (R506) between 1 Jan 2024 and 31 Dec 2024. The qualitative component included semi-structured interviews with key stakeholders to explore system characteristics: acceptability, simplicity, flexibility, stability, and usefulness.[21]

Operational Definitions

We used two influenza case definitions to evaluate the surveillance system.

Influenza cases based on the R506 definition[22]

Any individual with fever (or a body temperature of 38°C or higher), cough, and one of the following symptoms: sore throat, runny nose, body aches, headache, or fatigue, who visited Somdejpraboromrachineenart Natawee Hospital, during 1 Jan to 31 Dec 2024.

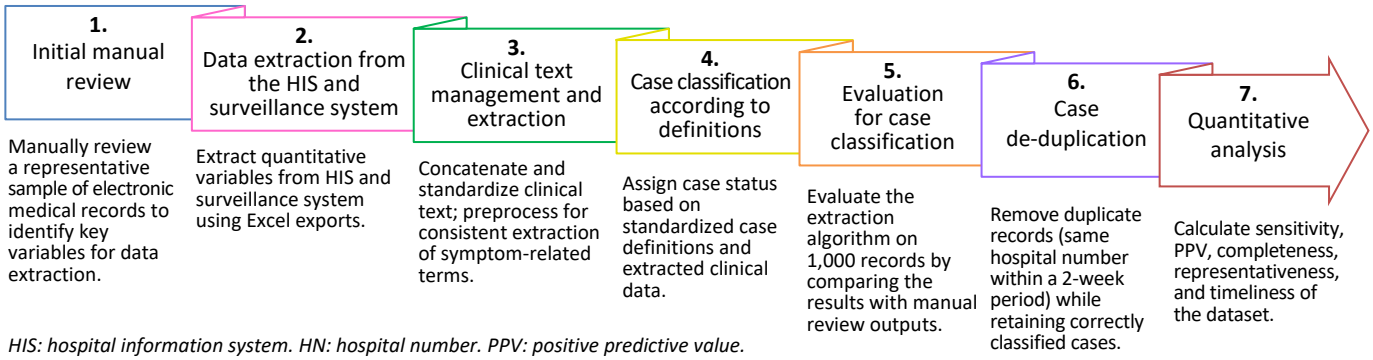
Influenza cases based on Somdejpraboromrachineenart Natawee Hospital (hospital definition)

Any individual who met the R506 definition or had a positive result on a rapid influenza diagnostic test (presumptive diagnosis based on a nasopharyngeal, throat, or nasal swab), who visited Somdejpraboromrachineenart Natawee Hospital from 1 Jan to 31 Dec 2024.

Data Collection

For system description and qualitative evaluation, 11 stakeholders across three levels—executives, department heads, and operators—were interviewed. These included the hospital director, public health officers, physicians, nurses, epidemiologists, and information technologists. The interview focused on disease reporting, case screening, diagnosis, coding, reporting frequency, data analysis, and system feedback.

For quantitative characteristics, an overview of the data analysis process is illustrated in Figure 1. An initial manual review of 30 medical records in the electronic medical record system was conducted to understand the traditional review process and identify relevant variables for HIS extraction, including text-based fields. Additional records were reviewed as needed when new variables of interest were identified. Next, data were extracted from the surveillance system and the HIS. The current capabilities of these systems allow reports to be exported in Excel format, facilitating subsequent data utilization. Cases included in the study were those diagnosed with influenza-related conditions based on the international classification of diseases, 10th revision (ICD-10) (Table 1). Primary ICD-10 (influenza diagnosis group) codes for influenza diagnoses include J09, J100, J101, J108, J110, J111, and J118, while secondary codes (related to influenza) include J00, J029, and J069. Variables collected included hospital number (HN), demographic characteristics, diagnosis codes, patient type, visit and diagnosis dates, laboratory results, report date, and clinical texts such as chief complaint, present illness, past history, and physical examination.



HIS: hospital information system. HN: hospital number. PPV: positive predictive value.

Figure 1. Quantitative data analysis process at Somdejpraboromrachineenart Natawee Hospital, 2024

Table 1. Characteristics of influenza cases by ICD-10 diagnosis at Somdejpraboromrachineenart Natawee Hospital, 2024

Diagnosis	ICD-10 code	Number of medical records	Medical records after deduplication	Met hospital definition n (%)	Met R506 definition n (%)	Reported in R506 (n)
Acute nasopharyngitis/ common cold	J00	6,366	4,374	2,432 (55.60)	2,281 (52.15)	25
Acute pharyngitis, unspecified	J029	391	309	137 (44.34)	127 (41.10)	-
Acute upper respiratory infection, unspecified	J069	297	724	499 (68.92)	484 (66.85)	-
Influenza due to identify avian flu virus	J09	8	6	2 (33.33)	2 (33.33)	-
Influenza due to other identified influenza virus with unspecified type of pneumonia	J100	57	45	40 (88.89)	39 (86.67)	-
Influenza with other respiratory manifestations, seasonal influenza virus identified	J101	194	143	124 (86.71)	124 (86.71)	87
Influenza with other manifestations, seasonal influenza virus identified	J108	272	203	171 (84.24)	169 (83.25)	123
Influenza with pneumonia, virus not identified	J110	18	13	12 (92.31)	12 (92.31)	4
Influenza with other respiratory manifestations, virus not identified	J111	113	91	74 (81.32)	73 (80.22)	27
Influenza with other manifestations, virus not identified	J118	413	358	266 (74.30)	256 (71.51)	92
Total		**8,758**	**6,266**	**3,757 (59.96)**	**3,567 (56.93)**	**358**

ICD-10: the international classification of diseases, 10th revision. R506: Report 506.

Data Management and Analysis

Stakeholder information was summarized to describe the system and create patient flow diagrams. Qualitative data were analyzed using thematic analysis based on acceptability, simplicity, flexibility, stability, and usefulness.

For quantitative analysis, clinical texts—including chief complaint, present illness, and physical exam—were concatenated using Excel's CONCAT() function. Text preprocessing addressed capitalization, spelling errors, and word choice inconsistencies (in Thai and English) for uniformity (Supplementary Table 1). Negation patterns (e.g., "no fever," "denied cough") were identified and standardized. Two doctors and one public health officer iteratively reviewed and refined the process on 500 records over five rounds to eliminate errors. Symptoms such as fever, cough, sore throat, runny nose, body aches, and fatigue were extracted using Excel's SEARCH() and ISNUMBER() functions and then compared against case definitions. For evaluation phase, we randomly selected 1,000 records (excluding 500 records in text pre-processing) to manually assess the accuracy of the clinical text extraction algorithm in identifying whether each record met or did not meet the case definition, compared against manual review of the raw clinical text.

After determining consistency with case definition, records with duplicate HN and visit date (i.e., the same diagnosis within a 2-week period) were identified. If the duplicates met the case definition, only the first occurrence was retained. Otherwise, the records were manually reviewed to determine the correct case classification, and the first matched case definition was retained. To calculate date of onset, duration of symptom was extracted from chief complaint and date of visit. The entire data set was managed and analyzed using Microsoft Excel version 16.78.3.

Sensitivity was defined as the percentage of cases who met the definition of influenza disease surveillance and were reported in the R506 system. It was calculated using the formula:

$$\text{Sensitivity} = \left(\frac{\text{Number of patients meeting the influenza surveillance definition and reported in the system}}{\text{Total number of patients meeting the influenza surveillance definition}} \right) \times 100$$

Positive predictive value (PPV) was defined as the percentage of cases reported in the R506 system who met the definition of influenza and was calculated using the formula:

$$PPV = \left(\frac{\text{Number of patients meeting the influenza definition in Report 506}}{\text{Total number of patients reported in the surveillance definition}} \right) \times 100$$

Completeness and accuracy of recorded variables in R506, including factors such as age (with an acceptable error margin of ±1 year), gender (male/female), and date of hospital admission (which should be on or before the reporting date) were evaluated. Timeliness was categorized into three levels: timely (within 0–3 days), moderately timely (within 4–7 days) and not timely (more than 7 days).

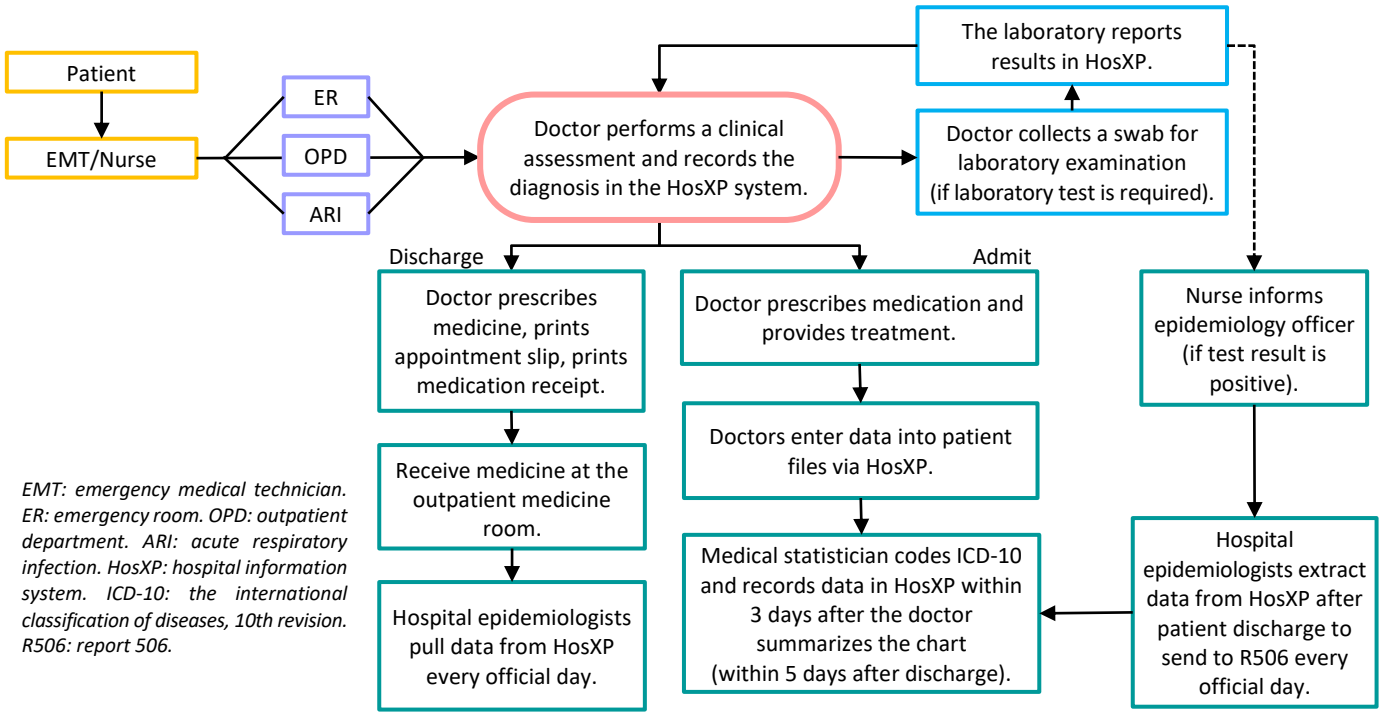
For representativeness, the characteristics of cases reported to R506 were compared with the characteristics of cases who met the R506 definition. The distribution were compared by person, time, and place, using variables such as gender, age, date of onset, place of onset including (province, district, and subdistrict).

Results

System Description

All cases were screened in the outpatient department during office hours and in the emergency room after hours. Nurses recorded symptoms and vital signs, and entered data into the HIS. Patients with influenza-like symptoms were directed to a separate area, instructed to wear masks, and sometimes underwent nasal swab testing. Physicians documented medical history, conducted physical examinations, and recorded diagnoses and ICD-10 codes in the HIS. Laboratory confirmation was not routinely performed. Most cases were treated as outpatients. Epidemiologists reviewed data and reported confirmed cases to the R506 system on working days, with retrospective reporting done after holiday periods. In the emergency room, similar procedures were followed. Laboratory-confirmed positive cases triggered alerts through the hospital's epidemic warning system, prompting verification and R506 reporting.

Hospitalized patients were isolated. Epidemiologists coordinated with local subdistrict hospitals for community control. ICD-10 codes were entered into the HIS within three days of discharge. Monthly data analysis was presented in hospital health meetings. The reporting process is shown in Figure 2.



EMT: emergency medical technician. ER: emergency room. OPD: outpatient department. ARI: acute respiratory infection. HosXP: hospital information system. ICD-10: the international classification of diseases, 10th revision. R506: report 506.

Figure 2. The process of reporting influenza disease at Somdejpraboromrachineenart Natawee Hospital, 2024

Clinical Text Management and Evaluation

We conducted five iterative rounds over three hours to refine negation handling and symptom search (Supplementary Table 1). From 8,258 HIS records based on ICD-10 codes (excluding 500 records in text pre-processing), 1,000 records were randomly selected for evaluation. Of these, 999 were classified as meeting (n=395) or not meeting (n=604) the R506 case definition

consistently between using the rule-based extraction algorithm and manual review, yielding an accuracy of 99.9%. The sole misclassification occurred because the keyword "fever" referred to a patient's relative, not the patient, highlighting challenges in contextual interpretation.

Quantitative Characteristics

From 8,758 HIS records, we excluded 2,492 duplicates, leaving 6,266 for analysis, of which 358 were reported to R506. As shown in Table 1, secondary ICD-10 disease groups had more diagnoses than primary disease groups.

Sensitivity

A total of 3,567 cases met the R506 definition with 304 reported to R506 (sensitivity 8.52%). Among unreported cases, 616 (18.89%) had COVID-19 infection, 220 (6.74%) had a negative rapid influenza diagnostic test, and 2,878 (88.21%) were diagnosed using an ICD-10 secondary disease group. After excluding these three groups of cases, the sensitivity values were 10.30%, 9.08%, and 11.13%, respectively. Similarly, 3,757 cases met the hospital definition, with 325 reported to R506 (sensitivity 8.65%). Among unreported cases, 365 (10.64%) were diagnosed with the ICD-10 primary disease group, of which 145 had COVID-19 infection and 220 had a negative rapid influenza diagnostic test. After excluding these two groups of cases, the sensitivity values were 9.00% and 9.19%, respectively and the overall sensitivity was 9.58% (Table 2).

Table 2. Number of influenza cases identified by medical record review according to R506 and hospital case definitions at Somdejpraboromrachineenart Natawee Hospital, 2024

	Number of cases by medical record review			
	R506 definition		Hospital definition	
	Met	Not met	Met	Not met
Reported in R506 system				
Yes	304	54	325	33
No	3,263		3,432	

R506: Report 506.

Positive predictive value

For the R506 definition, 304 cases met the criteria (PPV 84.92%). Among the 54 individuals who did not meet the criteria (21 cases had a positive laboratory test result), 10 had no symptoms recorded (one due to a relative collecting the medication, nine were prisoners brought by prison officers), 10 had no fever, and 25 had no cough (eight had a positive laboratory result). Nine cases tested positive for influenza despite not having influenza symptoms. For hospital criteria, 325 cases met the criteria (PPV 90.78%). Among the 33 individuals who did not meet the criteria, 18 had no cough, nine had no fever, five had no associated symptoms, and one had no symptoms recorded (Table 2).

Completeness, accuracy and timeliness

All variables were recorded completely (100% completeness). For accuracy, all variables except the date of onset were recorded correctly (100% accuracy). The accuracy of "date of onset" was 21.79%. The distribution of reporting timeliness is shown in Figure 3. Of the 354 cases (98.88%) were reported within 3 days and 357 (99.72%) within 7 days. One case was reported 14 days after the date of diagnosis.

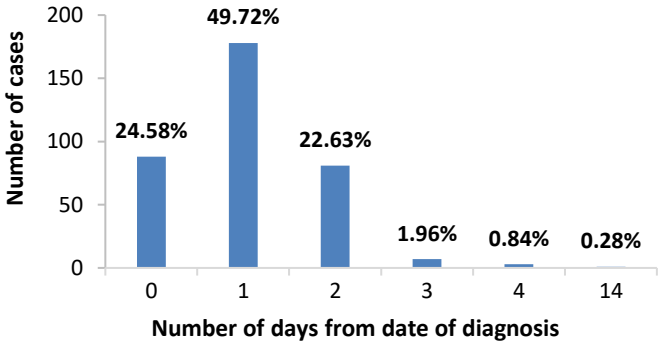


Figure 3. Distribution of time (days) between diagnosis and report among influenza cases reported to R506 at Somdejpraboromrachineenart Natawee Hospital, 2024

Representativeness

For R506 definition, the female to male ratios in HIS and R506 were 1.17:1 and 1.08:1, respectively. The 25–60-year age group had the highest proportion of cases (29.2% in HIS and 26.8% in R506). The age group of 60 years and older had the lowest proportion of cases (6.28% in HIS and 2.79% in R506) (Table 3).

Table 3. Characteristic of cases by R506 case definition and surveillance system at Somdejpraboromrachineenart Natawee Hospital, 2024

Characteristics	Met R506 definition (n=3,567) n (%)	R506 surveillance system (n=358) n (%)
Gender		
Female	1,915 (54.00)	185 (52.00)
Male	1,652 (46.00)	173 (48.00)
Age (years)		
0–4	727 (20.38)	70 (19.55)
5–9	678 (19.01)	89 (24.86)
10–14	447 (12.53)	56 (15.64)
15–24	449 (12.59)	37 (10.34)
25–60	1,042 (29.21)	96 (26.82)
60+	224 (6.29)	10 (2.79)

R506: Report 506.

Influenza cases peaked in July in both groups, with a high in January followed by a steady decline and then an increase from May to July. The number of cases reported to R506 increased sharply from June to July. Reporting was lower in May, June, and February, with no R506 cases in April, although some cases were recorded in HIS during that month (Figure 4).

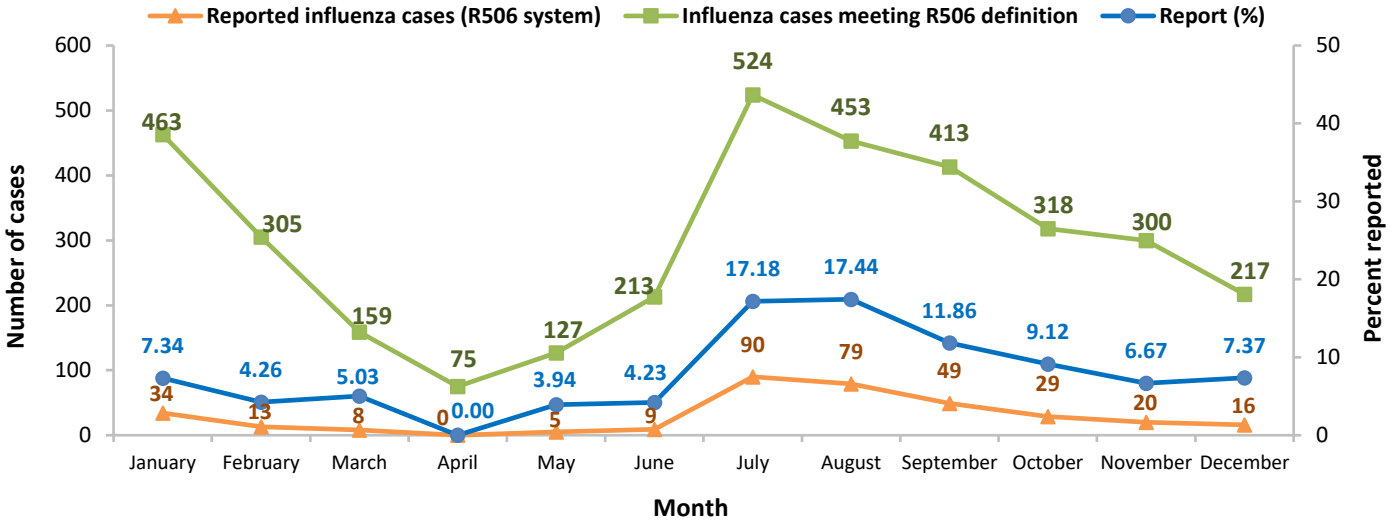


Figure 4. Number of cases per month and the proportion reported to the surveillance system at Somdejpraboromrachineenart Natawee Hospital, 2024

Figure 5 shows the distribution of reported influenza cases and cases meeting the R506 definition by subdistrict. Most cases were reported from Songkhla Province (99.72% for R506 and 98.07% for cases meeting the R506 definition). At the district level, reported R506 cases were concentrated in Na Thawi (72.1%), Chana (19.6%), and Thepha (3.91%), while cases meeting the R506 definition were concentrated in Na Thawi (69.5%), Chana (20.2%), and Saba Yoi (3.03%). Within Na Thawi District, the highest number of cases meeting the R506 definition were from Na Thawi (21.8%), Sathon (11.7%), and Khlong Sai (10.85%) subdistricts. The highest number of reported cases were from Na Thawi (22.1%), Thap Chang (13.9%), and Sathon (12.8%) subdistricts.

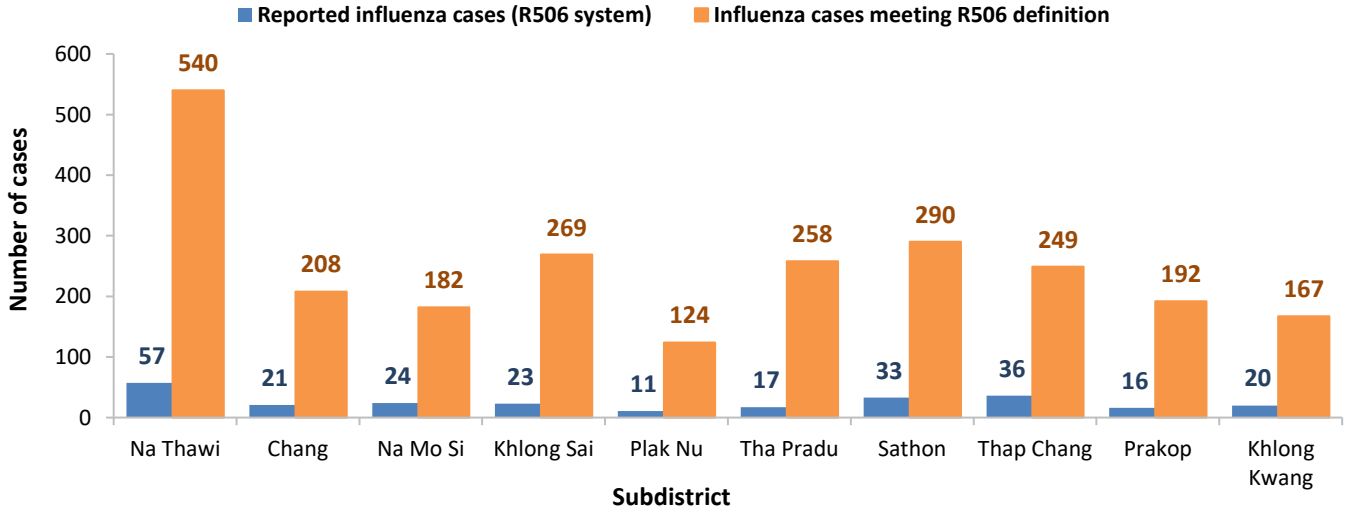


Figure 5. Distribution of reported influenza cases and cases meeting the R506 definition by subdistrict, Somdejpraboromrachineenart Natawee Hospital, 2024

Qualitative Characteristics

Simplicity

Stakeholders can efficiently use the HIS to retrieve influenza data quickly via ICD-10 codes, which are imported into the R506 surveillance system. Multiple reporting channels such as LINE and phone calls exist, though epidemiologists require time to screen and confirm cases.

Flexibility

Stakeholders can promptly update the system for ICD-10 changes or new diseases without requiring extra budget, allowing the system to adapt to similar diseases.

Acceptability

Executives and staff valued the system for outbreak detection and can cooperate in reporting. However, influenza reporting is only triggered by physician diagnosis, laboratory confirmation, or identified clusters, as influenza is not a high-priority policy disease.

Stability

The system benefits from strong leadership support and trained staff. Epidemiologists follow guidelines; however, backup coverage by subordinate staff is limited.

Usefulness

Data informs policy and budgeting and is shared externally for surveillance and outbreak alerts. However, feedback to hospital staff on outbreak status is lacking.

Discussion

A rule-based, iterative text extraction process, combining concatenation, spelling/negation handling, and symptom searches, achieved 99.9% accuracy in classifying records against R506 definitions. In other studies, this method enabled rapid review of over 8,000 records in one day, automating extraction of clinical symptoms and onset dates while improving processing speed and accuracy.[18,19] Despite its effectiveness, challenges remain, including variations in capitalization, spelling, word choice, time expressions, and negation in both Thai and English.[23] Addressing these issues requires advanced natural language processing, spelling correction, and support for medical terminology.[24,8]

The sensitivity of R506 and hospital definitions was 8.65% and 8.52%, respectively, which was lower than reported in prior studies (12.39–27.5%).[15–17] This may be due to the following reasons. First, physician diagnosis relies on clinical judgment, which may miss cases without positive results or correct ICD-10 coding. Second, epidemiologists determine which cases to report, often selecting the hospital definition when case numbers are high. This flexible interpretation can deviate from standardized surveillance criteria meant to guide outbreak detection and public health response.

The positive predictive values for R506 and hospital definitions were 84.92% and 90.87%, respectively, higher than reported in other studies (17.25–30.68%).[15–17] Our high values resulted from epidemiologists selecting cases based on ICD-10 codes and confirming symptoms and laboratory results prior to reporting. Among 54 reported cases that did not meet the R506 definition, 21 had positive laboratory results but lacked clinical symptoms. The hospital definition allows inclusion of asymptomatic, laboratory-confirmed cases. Laboratory confirmation was performed using the CiTEST influenza A+B rapid test, which has high sensitivity and specificity (99.0%/98.9% for influenza A and 98.8%/99.0% for influenza B).[25]

Data completeness was 100% for mandatory fields. Most variables were recorded accurately, except for the onset date, which was accurate in only 21.79% of records, although this value was within the reported range of 10.9–79.1% from other studies.[15,16] The inaccuracy was often due to staff recording the visit date instead. Previous research indicates higher accuracy in larger hospitals with more support from epidemiologists and information technologists.[15]

Timeliness was high. 98.88% and 99.72% of cases were reported within 3 and 7 days, respectively, due to daily reporting by epidemiologists. Delays occurred mainly during holidays, with only one case reported after 14 days.

For representativeness, the male-to-female ratio, date of onset, and place of onset aligned with their respective variables in the subset who met the definition. Although the magnitude does not reflect the real situation due to low sensitivity, the data remained representative in terms of gender, time trend, and location. The reporting proportion was lower in May, June, and February, as epidemic officers could choose to report based on the hospital or R506 definition. Case numbers were also low during this period, and no cases were reported in April, likely due to public holidays affecting reporting. The trend in case numbers did not show significant changes.

Our qualitative study findings showed strong system acceptability among executives and staff. The system was perceived as simple, flexible, and adaptable—ICD-10 codes could be updated without additional funding or external approval. Stability was supported by backup epidemiologists. However, some staff lacked awareness of reporting criteria. Surveillance data were actively used for policy planning and shared with external partners for outbreak detection.

Limitations

While the iterative rule-based process improved consistency in extracting clinical data, internal accuracy estimates do not substitute for external validation. No independent validation study comparing our algorithm to full traditional methods was conducted. Secondary data sources (HIS, medical records) may contain missing or misclassified information. During interviews, stakeholder responses might have been biased by the presence of department heads; however, confidentiality assurances and

separate interviews partly mitigated this potential bias. Random sampling across departments and levels was conducted to represent a wide range of perspectives but we did not include all staff.

Recommendations

Epidemiologists can effectively evaluate influenza surveillance using clinical text extraction with predefined search terms, adapted to local documentation styles. Training healthcare staff on surveillance definitions and improving symptom onset documentation are essential. Continued disease reporting with timely feedback and random strain testing will strengthen preparedness. Automating laboratory-based reporting ensures accuracy and reduces discrepancies. Collaboration among national and local health agencies is critical to establish a rapid test–based alert system, enhancing verification, reducing workload, and ensuring consistent reporting to R506.

The Division of Epidemiology should develop tools to extract symptoms and onset dates from clinical texts, including chief complaints and physical exams. Clinical criteria should be refined—such as reassessing the requirement for cough alongside fever—since 6% of RIDTs-positive cases lacked cough.[26] Reporting asymptomatic but laboratory-confirmed influenza cases is also critical, given the potential for transmission before and after symptoms, especially in children where viral shedding may last over seven days.[27,28]

Conclusion

The 2024 evaluation of the influenza surveillance system at Somdejpraboromrachineenart Natawee Hospital showed that actual influenza incidence exceeded reported figures. Case identification by epidemiologists using selective criteria may have introduced bias. Despite low sensitivity, the system demonstrated high positive predictive value, accuracy, and data completeness. It was adequately representative across person, place, and time, with timely reporting. Stakeholders described the system as simple, flexible and stable. Clinical text extraction via Microsoft Excel allowed complete medical record review without sampling, supporting effective surveillance evaluation and health planning.

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Author Contributions

Suralai Jongrakwong: Conceptualization, methodology, data curation, formal analysis, writing—original draft, writing—review, & editing. **Suphanat Wongsanupat:** Methodology, writing—review & editing, validation, supervision.

Ethical Approval

This study was approved by the Provincial Human Research Ethics Committee of Songkhla Province (approval no. 57/2568), dated 24 Mar 2025.

Informed Consent

Data from the HIS were used with strict confidentiality and without disclosure of personal details. For interviews, the study objectives were explained to participants, and informed consent was obtained prior to participation.

Data Availability

The data used in this study were obtained from the Hospital Information System (HIS) and Report 506 (R506) database at Somdejpraboromrachineenart Natawee Hospital. These data contain sensitive patient information and are not publicly available to protect patient confidentiality. Requests for access to the data may be considered on a case-by-case basis and require approval from the hospital's ethics committee and relevant authorities.

Conflicts of Interest

The authors declare no conflict of interest.

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Declaration of Generative AI and AI-assisted Technologies in the Writing Process

During the preparation of this work, the authors used ChatGPT to enhance clarity and correct grammatical errors, and used Napkin to create graphics. The content produced by this tool was reviewed and edited by the authors, who accept full responsibility for the final text.

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Obstetric Service Utilization in Public Health Facilities during COVID-19 Pandemic among Cross-border Migrants in Thailand, 2019–2022

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Abstract

The COVID-19 pandemic caused changes in obstetric care for the general population in Thailand. This study aimed to determine changes in obstetric admissions among migrants and assess potential factors influencing obstetric inpatient visits during the COVID-19 pandemic. An ecological time-series cross-sectional study was conducted using nationwide data between 2019 and 2022. Descriptive statistics were used to investigate outcome variables, including incidence number for obstetric inpatient care among insured migrants and uninsured migrants, and admission rate for obstetric inpatients among insured migrants. Independent variables included the cumulative incidence number of COVID-19 cases in a particular quarter, the number of hospital beds, geographical regions and time periods. This study then used random-effects negative binomial regression to explore the relationships between the outcome and independent variables. The incidence of all outcome variables during the COVID-19 pandemic (2020–2022) was higher than in 2019. The incidence of COVID-19 cases did not show a strong effect towards the change in obstetric admissions. For every 1,000-bed increase in hospital capacity, the admission rate decreased by approximately 8% (IRR 0.92, 95% CI 0.89–0.95) when adjusted for yearly periods, and by 9% (IRR 0.91, 95% CI 0.89–0.94) when adjusted for 6-monthly interval periods. Compared to Greater Bangkok, other regions exhibited lower numbers of hospital admissions for both insured and uninsured migrants. Conversely, the admission rate among insured migrants was higher in these regions. Continuous monitoring of the utilization of obstetric services by migrants offers benefits for proper policy design to ensure universal healthcare access for all.

Keywords: migrants, obstetrics, COVID-19, Thailand, cross-sectional study

Introduction

The coronavirus disease 2019 (COVID-19) pandemic caused changes in the landscape of healthcare delivery in Thailand, including obstetric care. In some areas, patients with non-urgent health conditions might have minimized their hospital visits to avoid contact with the virus.[1] Healthcare personnel were also occupied with caring for COVID-19 patients, leading to a shortage of staff to provide care for patients with other diseases.

Obstetric care, a fundamental pillar of maternal and child health, faced challenges during the pandemic. Evidence from other countries suggested a significant reduction in access to maternal and child health interventions, including antepartum care, immunizations, and institutional deliveries. Moreover, a substantial decline in the number of emergency visits by women with obstetric and gynecologic severe conditions were reported at the beginning of the pandemic.[2–5]

Although the Thai Government has health security measures in place, pregnant migrants have faced challenges in accessing maternal health care. This has been due to lack of knowledge of existing resources, language barriers, discrimination and stigmatization, and poor living conditions.

Migrants can be categorized into two groups: documented and undocumented migrants. Documented migrants are non-Thais who are legally admitted to Thailand, whereas undocumented migrants are non-Thais who enter or remain in Thailand without legal authorization. Documented migrants are, in theory, enrolled in public insurance schemes, while undocumented migrants are not. In this context, this study used the term insured migrants as a proxy for documented migrants, and uninsured migrants for undocumented migrants.

Little was known about the state of obstetric care for insured and uninsured migrants during the COVID-19 pandemic in Thailand. This study hypothesized that the burden of COVID-19, as reflected by the incidence of confirmed cases, might have strained the healthcare system and impacted the volume and utilization of obstetric services among migrants. The findings from this study were expected to inform health policy and evaluate whether the current system effectively ensures access to quality obstetric care for migrant populations, particularly in times of public health crisis.

To promote equitable access to obstetric care for all pregnant women in Thailand, regardless of nationality, this study aimed to determine changes in obstetric admissions among migrants and assess potential factors influencing obstetric inpatient visits during the COVID-19 pandemic.

Methods

Study Design and Site

This study was an ecological time-series cross-sectional data analysis using secondary data relating to obstetric admission numbers from five regions including Greater Bangkok, North, Northeast, Central, and South. Greater Bangkok included six provinces: Bangkok, Nakhon Pathom, Nonthaburi, Pathum Thani, Samut Prakan, and Samut Sakhon.

Study Population

This study's population included migrants from Cambodia, Laos, Myanmar, and Vietnam, who are often referred to as CLMV migrants. These migrants are often employed in construction, agriculture, and fisheries sectors. The Thai government public insurance policy primarily targets CLMV migrants.[6]

Operational Definitions

This study defined the pre-COVID-19 period as the year 2019 and the COVID-19 period as 2020–2022. To handle the time variable during the COVID-19 period, this study employed two distinct approaches in its analyses: 1) managing the time variable at yearly intervals, and 2) managing it at six-monthly intervals. Then this study assessed if the results were still robust given this change.

Variable and Measurements

Outcome variables included: 1) incidence number of obstetric inpatient care among insured female migrants; 2) incidence number of obstetric inpatient care among uninsured female immigrants; and 3) admission rate of obstetric inpatients among insured migrants (number of obstetric admissions by insured inpatient migrants divided by all insured migrants in a province). Independent variables were: 1) the cumulative incidence number of COVID-19 cases in a particular quarter (per 1,000 persons); 2) the cumulative incidence number of COVID-19 cases in the previous quarter (per 1,000 persons); 3) the number of hospital beds in a province (per 1,000 beds); 4) regions; and 5) yearly or six-monthly time-periods.

Data Collection

The data were collected between August and September 2023 from 1) Health Data Centre, Office of Permanent Secretary, Ministry of Public Health (MOPH); 2) Foreign Workers Administration Office, Department of Employment, Ministry of Labor (MOL); 3) Division of Epidemiology, Department of Disease Control, MOPH; 4) Health Administration Division, Office of Permanent Secretary, MOPH; and 5) Office of the National Economic and Social Development Council, Office of the Prime Minister. All relevant data from these sources were transferred to an Excel format, checked for completeness, and then imported into Stata.

Statistical Analysis

The analysis unit of this study was provincial-quarter record. Each row of the record in the Excel format contained the number of visits and value of the relevant independent variables in each province in a particular quarter. This study applied two statistical analysis techniques. First, descriptive analysis was used to explore: 1) the number of insured migrants; 2) the number of visits made by insured migrants; and 3) the number of visits made by uninsured migrants. Second, this study used random-effects negative binomial regression to account for the over-dispersion nature of the outcome variables. Since there was no

official information on the number of existing uninsured immigrants, this study omitted the admission rate for uninsured immigrants, but focused on the admission number instead. The main findings were demonstrated in the form of incidence rate ratio (IRR) and 95% confidence interval (CI). Stata 17 (serial number: 401709350741) was used for all statistical analyses.[7] Also, RStudio 2024.9.0.375 and QGIS 3.32.0, were used to visualize the data.

Results

A total of 296,344 migrant inpatient admissions for obstetric practices occurred during 2019–2022. Migrants who were obstetric inpatients before the pandemic made 55,248 admission visits in 2019. Inpatient visits during the pandemic era fluctuated, decreasing from 82,892 in 2020 to 77,232 in 2021 and then rising to 80,972 in 2022.

Table 1 provides a regional perspective where Central and Greater Bangkok saw the largest migrant inpatient visits for obstetric care in Thailand, and the Northeast encountered the fewest visits. In Greater Bangkok, the percentage of migrant inpatient visits in obstetric units decreased from approximately 22.7% in 2019 to approximately 21% in 2020 and 2021, then increased to approximately 23.0% in 2022. The percentage of migrants in obstetric inpatient units in the Central and the South increased from 31.4% and 16.7% in 2019 to 35.0% and 17.6% in 2022, respectively. The percentage of visits in the Northeast showed a downward trend, decreasing from 12.6% in 2019 to approximately 8.0% in 2022.

In Greater Bangkok, the proportion of visits made by insured migrants decreased from 23.3% in 2019 to 20.6% in 2020 and then increased to 21.2% in 2021 and 24.2% in 2022. Similarly, the percentage of visits among uninsured migrants in Greater Bangkok declined from 22.4% in 2019 to approximately 21% in 2020 and 2021 before rising to 22.1% in 2022.

The percentage of visits of insured migrants in the North fell from 13.7% in 2019 to 12.6% in 2021, before climbing to 14.2% in 2022. Meanwhile, the proportion of visits made by uninsured migrants remained at 17–18% throughout the study.

In the South, the percentage of visits to obstetric care by insured migrants showed a gradual decline from 2019 to 2022, decreasing from 26.8% in 2019 to 22.4% in 2022. In contrast, the percentage of visits made by uninsured migrants increased from 12.6% in 2019 to 14.7% in 2022. The percentage of obstetric care visits made by insured immigrants in the Northeast rose from 8.3% in 2019 to 8.8% in 2020. After that, it decreased to 5.7% in 2022. Meanwhile, the percentage of visits made by uninsured migrants decreased from 14.2% in 2019 to 9.4% in 2022.

Table 1. Percentage of visits of migrant obstetric inpatients (all migrants, insured migrants, and uninsured migrants) by five regions in Thailand, between 2019 and 2022)

Year	Type of migrant	Quarter	%				
			GB	N	NE	C	S
2019	**All migrants**	1	21.71	16.53	13.07	31.84	16.86
		2	23.36	15.89	12.19	31.62	16.93
		3	22.62	17.08	13.06	30.98	16.26
		4	22.96	17.30	11.95	31.16	16.63
		Total	**22.67**	**16.72**	**12.56**	**31.39**	**16.66**
	Insured migrants	1	24.24	14.00	8.14	25.89	27.73
		2	23.10	13.51	8.65	27.52	27.23
		3	22.61	14.10	8.23	27.94	27.13
		4	23.31	13.20	8.25	29.71	25.53
		Total	**23.30**	**13.68**	**8.32**	**27.86**	**26.85**
	Uninsured migrants	1	20.77	17.46	14.89	34.05	12.82
		2	23.47	16.87	13.65	33.32	12.69
		3	22.62	18.24	14.93	32.15	12.06
		4	22.81	19.02	13.51	31.77	12.89
		Total	**22.41**	**17.93**	**14.24**	**32.79**	**12.62**

GB: Greater Bangkok. N: North. NE: Northeast. C: Central. S: South.

Table 1. Percentage of visits of migrant obstetric inpatients (all migrants, insured migrants, and uninsured migrants) by five regions in Thailand, between 2019 and 2022) (cont.)

Year	Type of migrant	Quarter	%				
			GB	N	NE	C	S
2020	**All migrants**	1	18.55	17.00	12.01	34.14	18.30
		2	20.88	15.84	8.21	36.75	18.32
		3	22.94	16.12	8.34	34.89	17.71
		4	21.23	15.60	9.39	35.27	18.51
		Total	**20.98**	**16.11**	**9.44**	**35.26**	**18.21**
	Insured migrants	1	18.87	13.06	10.29	30.74	27.04
		2	21.57	12.43	7.28	31.41	27.32
		3	23.44	13.27	8.57	30.33	24.38
		4	18.61	11.93	9.29	35.06	25.12
		Total	**20.60**	**12.65**	**8.85**	**31.98**	**25.92**
	Uninsured migrants	1	18.37	19.18	12.97	36.01	13.47
		2	20.50	17.75	8.73	39.74	13.28
		3	22.68	17.55	8.22	37.17	14.37
		4	22.64	17.58	9.44	35.39	14.94
		Total	**21.18**	**17.98**	**9.75**	**37.03**	**14.07**
2021	**All migrants**	1	20.85	15.81	8.25	36.99	18.09
		2	22.33	14.10	7.88	37.73	17.96
		3	20.55	15.43	9.23	35.73	19.06
		4	20.18	16.67	8.44	37.08	17.63
		Total	**21.00**	**15.54**	**8.38**	**37.00**	**18.09**
	Insured migrants	1	17.71	14.52	7.15	35.22	25.40
		2	20.51	12.37	7.26	36.19	23.66
		3	23.97	12.80	6.73	33.70	22.81
		4	22.96	11.10	7.25	33.98	24.72
		Total	**21.20**	**12.57**	**7.14**	**34.82**	**24.27**
	Uninsured migrants	1	22.67	16.56	8.89	38.02	13.85
		2	23.37	15.08	8.23	38.61	14.71
		3	18.57	16.96	10.67	36.91	16.89
		4	18.47	20.09	9.17	38.99	13.28
		Total	**20.88**	**17.28**	**9.11**	**38.28**	**14.45**
2022	**All migrants**	1	21.26	16.90	8.15	35.84	17.84
		2	22.13	17.32	7.60	35.10	17.85
		3	24.26	15.17	8.04	35.05	17.48
		4	23.82	16.80	8.13	33.96	17.30
		Total	**22.91**	**16.52**	**7.98**	**34.98**	**17.61**
	Insured migrants	1	22.57	13.52	6.19	33.26	24.45
		2	22.19	14.02	5.88	34.06	23.85
		3	26.93	12.30	5.55	34.58	20.65
		4	24.85	16.82	5.07	32.20	21.07
		Total	**24.23**	**14.18**	**5.66**	**33.51**	**22.42**
	Uninsured migrants	1	20.47	18.97	9.34	37.42	13.81
		2	22.09	19.22	8.59	35.70	14.40
		3	22.62	16.94	9.58	35.34	15.52
		4	23.17	16.78	10.04	35.07	14.93
		Total	**22.11**	**17.94**	**9.40**	**35.87**	**14.68**

GB: Greater Bangkok. N: North. NE: Northeast. C: Central. S: South.

Figure 1 and Figure 2 present the number of admissions of insured and uninsured migrants, respectively between 2019 and 2022. In 2019, the number of insured and uninsured migrants admitted in obstetric units ranged approximately between 2,000 and 3,000, which was lower than during the COVID-19 pandemic period.

The highest number of admissions of insured migrants receiving obstetric care was in Samut Sakhon—a province in Greater Bangkok—both pre-COVID-19 and during COVID-19. In contrast, in 2019, the highest number of admissions of uninsured migrants was found in Chiang Mai—a province known for tourism and industry in the North. Chonburi, which is situated in Central, and Samut Prakan, a province in Greater Bangkok, had the highest admission number of uninsured migrants in 2020–2021 and 2022, respectively.

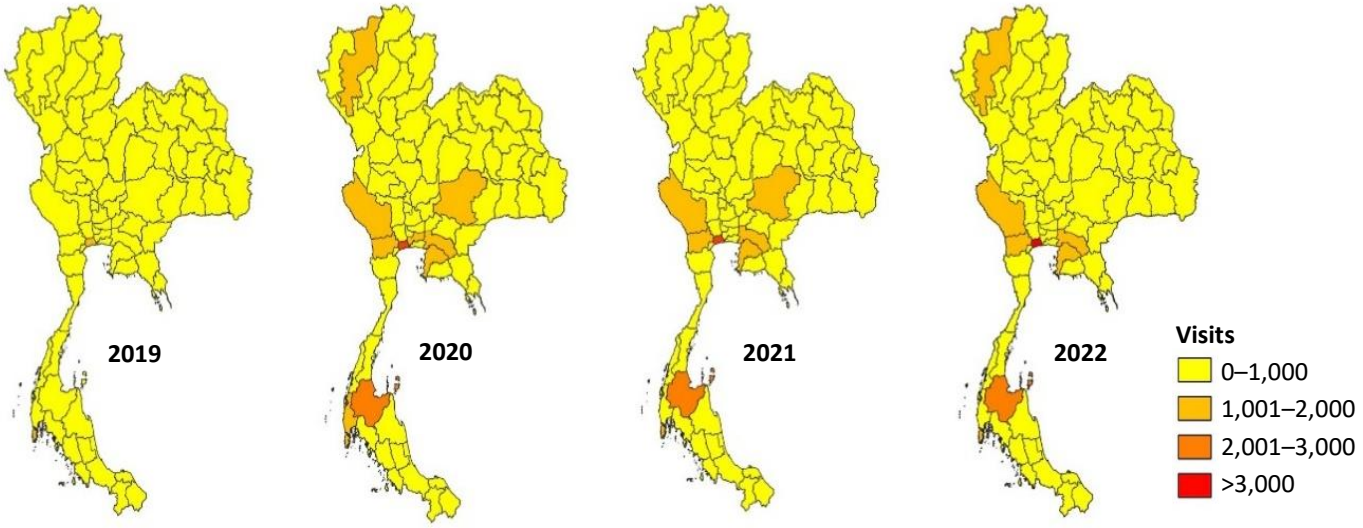

Figure 1. Number of obstetric visits made by insured migrants in Thailand, 2019–2022

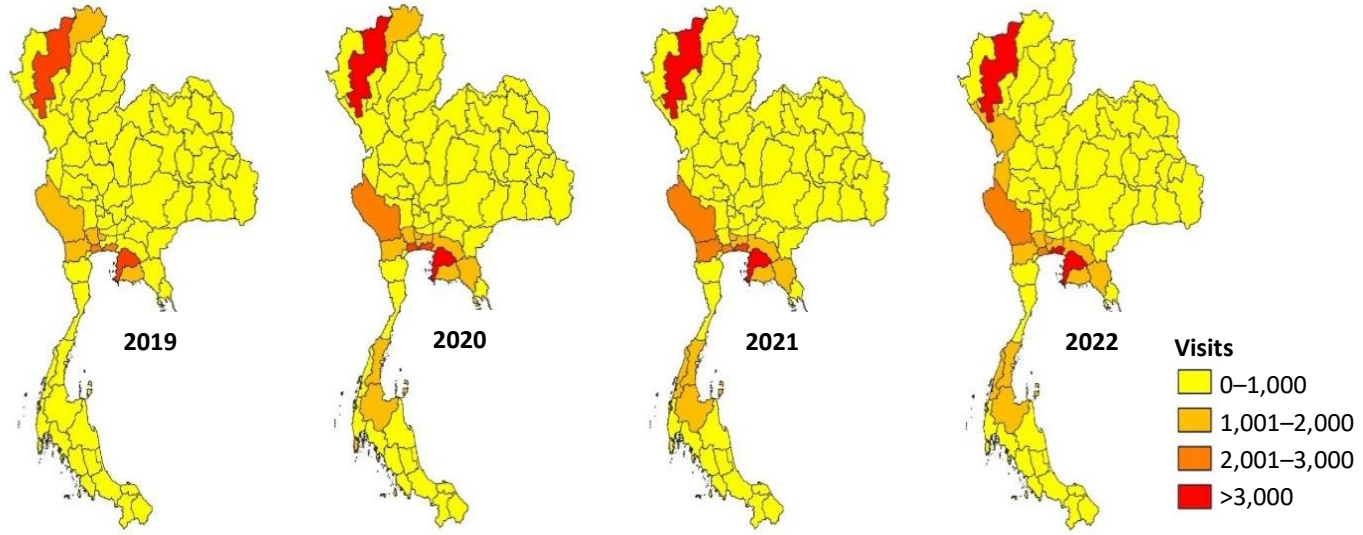

Figure 2. Number of obstetric visits made by uninsured migrants in Thailand, 2019–2022

Table 2 presents the IRR of the admission volume of insured and uninsured migrants, and the IRR of the admission rate of insured migrants at yearly intervals. In the Northeast, the number of obstetric care visits made by insured migrants was significantly lower than in Greater Bangkok (IRR 0.46, 95% CI 0.31–0.69). During the COVID-19 pandemic (2020–2022) the incidence of visits made by insured migrants was higher than before the pandemic: in 2022 IRR 1.80, 95% CI 1.66–1.95.

Regarding the number of admissions of uninsured migrants, with every 1,000-hospital-bed increase, a slight decrease in the incidence of the number of visits was observed (IRR 0.94, 95% CI 0.91–0.96). Geography-wise, the number of visits in the North and Northeast were fewer than in Greater Bangkok. In contrast, the incidence number of admissions of uninsured migrants in 2022 was approximately 24% higher than in 2019 (IRR 1.24, 95% CI 1.16–1.31).

For the obstetric admission rate of insured migrants, with every 1,000-hospital-bed increase, the admission rate decreased by approximately 8% (IRR 0.92, 95% CI 0.89–0.95). The rate in the Northeast was approximately 12.5 times the rate in Greater Bangkok (95% CI 8.79–17.89). Greater Bangkok saw the lowest admission rate compared with other regions. The rate during the COVID-19 pandemic was double the rate in the pre-COVID-19 era. For instance, the year 2022 showed an IRR of 2.17 (95% CI 2.03–2.32), considering year 2019 as a baseline. The lagged incidence of COVID-19 cases in the preceding quarter did not show a clear associational direction with the admission rate in the following quarter.

Table 2. Factors associated with obstetric admission numbers and admission rates in 2019–2022 in Thailand using time periods at yearly intervals

Predictor variables	Outcomes variables								
	Number of obstetric inpatient admissions by insured migrants			Number of obstetric inpatient admissions by uninsured migrants			Admission rate of obstetric inpatients by insured migrants		
	IRR	*P*-value	95% CI	IRR	*P*-value	95% CI	IRR	*P*-value	95% CI
Increased incidence number of COVID-19 in the present quarter (1,000 persons)	1.00	≤0.001	0.99–1.00	1.00	0.02	0.99–1.00	1.00	≤0.001	0.99–1.00
Increased incidence number of COVID-19 in the previous quarter (1,000 persons)	1.00	0.09	1.00–1.00	1.00	0.01	1.00–1.00	1.00	≤0.001	1.00–1.01
Number of hospital beds (1,000 beds)	1.02	0.09	1.00–1.05	0.94	≤0.001	0.91–0.96	0.92	≤0.001	0.89–0.95
Region (vs Greater Bangkok)									
North	0.80	0.27	0.53–1.20	0.37	≤0.001	0.25–0.55	8.47	≤0.001	5.98–12.00
Northeast	0.46	≤0.001	0.31–0.69	0.51	≤0.001	0.34–0.75	12.54	≤0.001	8.79–17.89
Central	0.95	0.80	0.64–1.41	0.75	0.17	0.50–1.13	5.11	≤0.001	3.60–7.24
South	1.44	0.11	0.93–2.23	0.67	0.06	0.44–1.02	7.95	≤0.001	5.54–11.41
Time-periods (vs 2019)									
2020	1.76	≤0.001	1.63–1.90	1.38	≤0.001	1.30–1.46	1.95	≤0.001	1.83–2.09
2021	1.66	≤0.001	1.52–1.80	1.22	≤0.001	1.15–1.30	2.05	≤0.001	1.91–2.20
2022	1.80	≤0.001	1.66–1.95	1.24	≤0.001	1.16–1.31	2.17	≤0.001	2.03–2.32

IRR: incidence rate ratio. CI: confidence interval. vs: versus.

Table 3 presents the IRR of the admission volume of insured and uninsured migrants, and the IRR of admission rate of insured migrants using time periods of a six-month interval. After replacing the semi-annual periods with an annual period, this study found that IRR for incidence number of COVID-19 in the present quarter, incidence number of COVID-19 in the previous quarter, number of hospital beds, and geographical regions, were similar to the findings in Table 2. For example, a unit increase of 1,000 hospital beds was associated with a slight decrease in the incidence of visits for insured migrants (IRR 0.91, 95% CI 0.88–0.94). Regarding regional variables, the Northeast showed a significantly lower IRR of admission number of insured migrants (IRR 0.45, 95% CI 0.30–0.67) and uninsured migrants (IRR 0.47, 95% CI 0.32–0.69) compared to the Great Bangkok. The North also showed a significantly lower IRR of admission number of uninsured migrants (IRR 0.35, 95% CI 0.23–0.52). Regarding the admission rate of insured migrants, Greater Bangkok saw the lowest admission rate compared with other regions. The IRRs of the admission numbers of insured migrants in the first and second quarters of 2019 were significantly lower than in other periods, except for the third and fourth quarters of 2019. The IRR for other independent variables remained the same as that presented in the prior analysis using annual time period.

Table 3. Factors associated with obstetric admission numbers and admission rates in 2019–2022 in Thailand using time periods at six-month intervals

Predictor variables	Outcomes variables								
	Number of obstetric inpatient admissions by insured migrants			Number of obstetric inpatient admissions by uninsured migrants			Admission rate of obstetric inpatients by insured migrants		
	IRR	*P*-value	95% CI	IRR	*P*-value	95% CI	IRR	*P*-value	95% CI
Increased incidence number of COVID-19 in the present quarter (1,000 persons)	1.00	≤0.001	0.99–1.00	1.00	0.17	1.00–1.00	1.00	0.01	0.99–1.00
Increased incidence number of COVID-19 in the previous quarter (1,000 persons)	1.00	0.04	1.00–1.00	1.00	≤0.001	1.00–1.00	1.00	≤0.001	1.00–1.01
Number of hospital beds (1,000 beds)	1.02	0.22	0.99–1.04	0.93	≤0.001	0.91–0.96	0.91	≤0.001	0.88–0.94
Region (vs Greater Bangkok)									
North	0.79	0.26	0.53–1.19	0.35	≤0.001	0.23–0.52	8.48	≤0.001	5.98–12.03
Northeast	0.45	≤0.001	0.30–0.67	0.47	≤0.001	0.32–0.69	12.59	≤0.001	8.81–17.98
Central	0.93	0.73	0.62–1.39	0.70	0.09	0.47–1.06	5.22	≤0.001	3.67–7.41
South	1.39	0.14	0.90–2.16	0.66	0.06	0.43–1.01	7.82	≤0.001	5.44–11.23
Time-periods (vs 2019 (quarters 1–2))									
2019 (quarters 3–4)	1.05	0.41	0.93–1.19	1.06	0.15	0.98–1.16	0.95	0.28	0.85–1.05
2020 (quarters 1–2)	1.72	≤0.001	1.54–1.92	1.34	≤0.001	1.24–1.46	1.77	≤0.001	1.61–1.94
2020 (quarters 3–4)	1.90	≤0.001	1.70–2.11	1.51	≤0.001	1.40–1.63	2.05	≤0.001	1.87–2.25
2021 (quarters 1–2)	1.81	≤0.001	1.62–2.02	1.31	≤0.001	1.20–1.42	2.16	≤0.001	1.97–2.37
2021 (quarters 3–4)	1.57	≤0.001	1.39–1.76	1.18	≤0.001	1.08–1.29	1.79	≤0.001	1.62–1.99
2022 (quarters 1–2)	1.77	≤0.001	1.58–1.99	1.20	≤0.001	1.10–1.31	2.08	≤0.001	1.87–2.31
2022 (quarters 3–4)	1.89	≤0.001	1.70–2.11	1.31	≤0.001	1.21–1.42	2.07	≤0.001	1.89–2.27

IRR: incidence rate ratio. CI: confidence interval. vs: versus.

Discussion

Overall, this study found that the hospital admission patterns for obstetric care for insured and uninsured migrants were not affected by COVID-19 in Thailand. This is unlike other global areas where certain types of care declined.[8,9] This study found a significant increase in the number of obstetric admissions of insured and uninsured migrants during the COVID-19 pandemic. This could reflect the resilience of Thailand's public health and social service initiatives that enabled it to accommodate obstetric care regardless of the severity of the pandemic.[10] On the other hand, it could also be due to the nature of obstetric conditions that always need urgent care.

During the COVID-19 pandemic, the Thai Government implemented prevention and control measures that affected travelling or migration, such as city lockdowns and travel bans.[11] There was also a strict travelling ban on land transport along the border. This might be a reason why the number of migrants' obstetric visits increased during the pandemic, as they could not return to their home country for obstetric care. Another possible explanation is that private care facilities might have limited obstetric services to create space for a surge in COVID-19 cases. This was in response to the classification of COVID-19 as a 'dangerous communicable disease', which allowed people to access healthcare for COVID-19 in both public and private facilities.[12]

In terms of geography, Central and Greater Bangkok saw the largest migrant inpatient visits for obstetric care in Thailand, while the Northeast encountered the fewest visits. Samut Sakhon, a province in Greater Bangkok, had the highest number of insured migrants admitted to the obstetric unit compared to other provinces nationwide. It is a major industrial area where both Thai and migrant workers are concentrated. In 2022, there were 259,567 migrant workers in Samut Sakhon, with approximately 90% (237,195) who were from Myanmar.[13] In contrast, in the South of Thailand, the percentage of visits of migrant obstetric inpatients decreased gradually between 2019 and 2022. This could be because the South was not the main area where CLMV migrants lived and worked.

Before the pandemic, the highest number of uninsured migrants was found in Chiang Mai, a tourist and industrialized city near Myanmar (approximately 130 kilometers from Muang Chiang Mai District to the closest border). However, during the pandemic, the highest admission numbers of uninsured migrants were in Chonburi and Samut Prakan. A possible reason for this is that many industries closed during the pandemic, and the number of employees who lost their jobs increased sharply.[14,15] Therefore, many migrant employees lost their health benefits and became uninsured migrants. According to a survey during the pandemic, almost one-fifth of respondents lost their jobs.[16] Although that survey collected data from Thais, inevitably, migrants were also affected by this.

Additionally, a large number of private healthcare facilities were not effectively connected to MOPH healthcare facilities, particularly super-tertiary hospitals which are health facilities ≥500-bed capacity.[10] This means it was also possible that some insured migrants in Greater Bangkok utilized services at private facilities, but whose records were not included in our data.

The number of hospital beds reflects healthcare resources. For every 1,000-bed increase in hospital capacity, the admission rate decreased by approximately 8%. This finding might be because hospital bed numbers likely reflect health resources in a province. Provinces with large cities usually have super-tertiary hospitals. During the COVID-19 period, these provinces had more availability of resources (both from public and private sectors) to accommodate the surge of COVID-19 cases. Thus, public hospital admission was not the only option for migrants, leading to a below-one IRR in the admission rate.

This study has both strengths and limitations. One of the study's strengths was the use of nationwide routine service data that spans from the pre-COVID-19 period across the entire COVID-19 period. The use of random-effects negative binomial regression, which helped account for spatiotemporal variance, was another key strength. The first limitation was the use of an ecological study design, which entailed ecological fallacy, i.e., the natural relationship explored at an individual level may not necessarily reflect the relationship at the group level to which those individuals belong. Secondly, this study lacked data on access to private healthcare facilities. This made it difficult to determine the true magnitude of hospitalization among migrants, especially in large cities where private institutions play a major role. However, as the objective of this study was to examine changes in obstetric admissions over time linked to specific variables, this limitation might not compromise the validity of this study's findings. Third, the insurance status of migrants is not always static. Theoretically, all immigrants who have applied for work permits are required to enroll with public insurance. However, there is no perfect alignment between documented status (e.g., possession of a work permit) and insurance coverage in real-world settings, and the validity date of the work permit and the insurance expiration date in practice do not always match together. Conversely, some migrants who held legitimate work permits might have let their insurance lapse. This measurement error can be viewed as a misclassification bias that potentially caused our estimates to be more conservative (moving towards the null), but at the same time, it can be also seen as a potential area for improvement for the nation's health information system.

Conclusion

The number of obstetric care visits among insured and uninsured migrants increased during the COVID-19 pandemic relative to the pre-COVID-19 era. Greater Bangkok saw the least increase of obstetric admissions of insured migrants compared with other regions. The severity of the outbreak, as reflected by the incidence of COVID-19 cases, as well as its lagged value, showed a small degree of association with obstetric admission amongst both insured and uninsured migrants. Further studies focusing on the health-seeking behavior of migrant individuals could address the limitation of ecological fallacy. Research that compares obstetric care behavior between Thai nationals and migrants would be of value. Government policies to ensure access to obstetric services in both normal and pandemic situations should be maintained.

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Author Contributions

Nisachol Cetthakrikul: Formal analysis, supervision, writing—original draft, writing—review & editing. **Boonyasit Ngamvirojcharoen:** Formal analysis and writing—original draft, **Natnicha Manaboriboon:** Formal analysis, writing—original draft. **Saruttaya Wongsuwanphon:** Conceptualization, formal analysis, writing—original draft. **Rapeepong Suphanchaimat:** Conceptualization, writing—review & editing, supervision. All authors have read and agreed to the published version of the manuscript.

Ethical Approval

This study was conducted as part of the function of the International Health Policy Program, Ministry of Public Health (MOPH), which aims to monitor the performance of the Thai healthcare system. Therefore, ethics clearance was not necessary. However, personal information in the datasets was kept anonymous. The findings were presented only for academic purposes. No personal information was disclosed.

Informed Consent

Not applicable.

Data Availability

Not applicable.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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As the study utilized only secondary data, no funding was allocated for the fieldwork. Additionally, no publication fee was required in accordance with the journal's regulations.

Declaration of Generative AI and AI-assisted Technologies in the Writing Process

None was used.

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Susceptibility to Diphtheria among Vaccinated Children Aged 1–14 Years: A Serosurvey in a Rural Subdistrict, Bangladesh, 2019

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Abstract

In Bangladesh, diphtheria vaccine is administered to children at six, ten and fourteen weeks of age, with no booster dose given up to 14 years. As antibody levels decrease over time, over five years may become susceptible to diphtheria. We conducted a serosurvey in a rural subdistrict among children aged 1–14 years to estimate the proportion of protected children, to determine the mean anti-diphtheria antibody concentration, and to identify factors associated with being unprotected in vaccinated children. We enrolled children who had completed their primary diphtheria vaccination and selected three age groups: 1–4 (n=422), 5–9 (n=518), and 10–14 years (n=402), using cluster sampling across 96 locations in a selected rural subdistrict. We collected information on socio-demographic, environmental, maternal and birth-related characteristics, and vaccination history. Serum diphtheria antibody levels were measured by ELISA, with ≥0.1 IU/mL considered protective. We used chi-squared test and odds ratio to identify associated factors and applied multiple logistic regression to adjust for confounding. The proportion of protected children in the three age groups was 76% (1–4), 48% (5–9) and 36% (10–14). The geometric mean titer (GMT) of diphtheria antibody was highest in 1–4 years (0.18 IU/mL) and lowest 10–14 years (0.08 IU/mL). Being in older age groups were significantly associated with being unprotected. Over half of children aged 5–9 years and two-thirds of children aged 10–14 years were unprotected. We recommend introducing a booster dose of diphtheria vaccine for children over five years.

Keywords: diphtheria, immunity, serosurvey, vaccine, booster

Introduction

Diphtheria, an acute infection caused by the exotoxin producing bacteria *Corynebacterium diphtheria*, spreads from person to person via respiratory route or direct contact.[1] The crude case-fatality is 5–10% and increases to 20% for children <5 years of age.[2] In the pre-vaccine era, diphtheria was a major cause of childhood death. With vaccination, global incidence of diphtheria decreased rapidly. However, spikes in incidence show diphtheria's potential for outbreaks in under vaccinated populations with no or waning immunity.[3] Vaccination is the most effective prevention strategy with 87% effectiveness after three doses.[4] Diphtheria immunity depends on presence of Immunoglobulin G (IgG) antibodies against diphtheria toxoid, known as anti-diphtheria toxoid antibodies (IgG-DTAb) or diphtheria antitoxin. Antitoxin levels

≥0.1 international units per milliliter (IU/mL) confer full protection and ≥1.0 IU/mL indicate long-term protection.[5]

Bangladesh initiated a weekly passive hospital-based surveillance for diphtheria and other vaccine preventable diseases in 1995. The surveillance case definition for diphtheria is a person with a respiratory tract illness characterized by sore throat, fever, adherent membrane of tonsils, pharynx or nose without other apparent cause determined by the physician. This is a clinical diagnosis and reported to the National Expanded Programme on Immunization (EPI).

No diphtheria outbreak was reported from 2012–2016 in Bangladesh.[6,7] In 2017, an outbreak of >7,000 cases occurred when Forcibly Displaced Myanmar Nationals entered Bangladesh from Myanmar, a diphtheria endemic neighboring country.[6] Median age of cases was 10 years.[6] However, their vaccination status remains unknown due to unavailability of vaccination cards.[8] From 2018–2023, the Institute of Epidemiology, Disease Control and Research (IEDCR) investigated 16 diphtheria notifications from different parts of Bangladesh. Reports from these investigations show that, among 25 clinically confirmed cases with a typical pseudo-membrane, 65% were between 5–14 years of age. Of cases with known vaccination status, 79% were fully vaccinated as per EPI schedule. Case fatality rate was 8% (2/25). Although only sporadic cases have been reported, diphtheria remains a threat to children with low sero-protection.

Bangladesh EPI vaccinates children with diphtheria toxoid in combination with pertussis, tetanus, hepatitis-B and Haemophilus influenza-B as DPT-HepB-Hib (pentavalent) vaccine at ages 6, 10 and 14 weeks.[9,10] The third dose of DTP-Hep B-Hib vaccine has 98% coverage.[11] Since 2019, EPI recommends tetanus-diphtheria (Td) vaccine only for women aged 15–49 years.[12] However, no diphtheria booster is recommended in Bangladesh for children aged 1–14 years.

Immunity to diphtheria following 3-dose primary schedule wanes over time without a boosting effect from natural exposure in the environment.[13] At 5–6 years after vaccination, antibody titers drop to pre-vaccination level.[14] World Health Organization recommends three diphtheria booster after completing 3-dose primary schedule, to be administered at 12–23 months, 4–7 years and 9–15 years of age.[15]

However, the number and timing of boosters vary in different countries, depending on local epidemiologic patterns linked to regional diphtheria endemicity (endemic, low-endemic or non-endemic), local incidence of respiratory diphtheria, prevalence of cutaneous diphtheria as a source of natural immunity, herd immunity, and seroprevalence of antitoxin in different age groups.[1] In India, two boosters are administered at 16–24 months and 5–6 years.[2] In Indonesia, four boosters are administered at 18 months of age and at 1st, 2nd and 5th grade of elementary school.[16] However, socioeconomic changes, especially migration and sociocultural changes, may change local epidemiologic patterns of diphtheria.[1]

The objectives of our study were to estimate the proportion of vaccinated children having a protective level of anti-diphtheria antibody in different age groups, determine the mean anti-diphtheria antibody concentration in vaccinated children of different age groups, and determine factors associated with being unprotected against diphtheria in vaccinated children.

Methods

Study Design and Site

A cross-sectional serosurvey was conducted from July–September 2019 in Belabo Subdistrict of Narshingdi District, Bangladesh. We selected Narshingdi District due to high coverage of pentavalent vaccine (94.1%) and high vaccination card retention rate (98.3%).[17] Belabo is a rural subdistrict of Narshingdi District with 190,086 population.[18] According to EPI (internal report, 2019), Belabo Subdistrict had an administrative coverage of the third dose of pentavalent vaccine of 96.4% in 2018.

Study Population

We included children from three age groups: 1–4; 5–9; and 10–14 years, who had completed all three doses of pentavalent vaccine. Age was determined by the date of birth on the EPI vaccination card. We excluded children who had received the third dose of pentavalent vaccine within one month of data collection, children with known bleeding disorder or with a clinical diagnosis of diphtheria, and children without a vaccination card.

Sample Size and Assumptions

The sample size for this study was 483 participants per age group, totaling 1,449 individuals. This estimation was based on an assumed 70% protection rate among children, drawn from findings in a similar study, with a 5% margin of error and a design effect of 1.5.[19,20]

Recruitment

We recruited children by household cluster sampling. Belabo Subdistrict has eight administrative unions, each has three wards with four blocks. Each block has

two vaccination centers. We conveniently selected one of two vaccination sites in each block (total 96 vaccination centers) as the starting point of a location. Thus, total 96 locations were selected across Belabo. From the selected starting point (vaccination center) in each location, the survey sampling direction was randomly determined by spinning a pen. In that direction, the nearest house was visited first and then the next house, until a sample of five eligible children were recruited from each age group. If there were more than one child in the same age group in a house, one of them was randomly selected by lottery.

Collection of Socio-demographic Information

Eight teams conducted face-to-face interviews of parents of eligible children using a pretested semi-structured questionnaire. Data were collected on socio-demographic, socio-economic and environmental conditions, gestation and birth related history, clinical information and vaccination history of the children.

Collection and Transportation of Biological Samples

Recruited medical technologists aseptically collected two milliliters (mL) of venus blood from eligible children. Serum was daily transported under cold-chain to the IEDCR laboratory, where it was stored at -20 °C.

Determination of Diphtheria Toxoid IgG Antibody

Diphtheria antitoxin (IgG type) was measured in IU/mL of serum by enzyme linked immuno-sorbent assay (ELISA) kit (diphtheria toxoid IgG ELISA, Demeditec Diagnostics GmbH, Lise-Meitner, Kiel, Germany).[21] The ELISA kit is calibrated using international standards (WHO reference preparation 00/496). This assay has been shown to correlate well with other ELISAs (coefficient of correlation of 0.94 with Immunolab diphtheria IgG test, Virotech, Germany [Cat No. EC129.00]).[22] There is good correlation between clinical protection and serum antitoxin level; a level of 0.1 IU/mL is considered protective.[23] For this analysis, we considered children with titers ≥0.1 IU/mL as protected and children with titers <0.1 IU/mL as unprotected.[19,24,25]

Data Analysis

We calculated the proportion of protected children in each age group by dividing the number of protected children by the number of all children in that age group. To examine association between antibody titer and age, log antibody titers were compared with age using correlation and linear regression and by calculating the correlation coefficient. Geometric mean titer (GMT) of diphtheria antitoxin with corresponding 95% confidence interval (CI) was calculated for each age group and for both genders. Differences in GMT among three age groups were assessed by one-way ANOVA. Differences in GMT between males and females were assessed using a t-test. A p-value of <0.05 was considered significant.

We compared unprotected to protected children to analyze the association of socio-demographic characteristics, environmental conditions, gestational and birth-related characteristics. We calculated odds ratio (OR) and chi-square to determine statistical significance. To adjust for confounding effects, multiple logistic regression was performed.

The following independent variables were tested for a 15% change in odds ratio of the main variable age group to form a model: age group, gender, maternal diabetes during pregnancy, birthplace, mode of delivery, completion of pneumococcal conjugate vaccine (PCV) and color-marking of tube-wells representing the arsenic content in water.[26] Completion of PCV was excluded, as it was applicable to only age group 1–4 years. During model formation, the following variables were excluded by forward selection: gender, maternal diabetes during pregnancy, birthplace and mode of delivery. Finally, the final model comprised of two variables: age group and colour of tube-wells. Adjusted odds ratio with 95% confidence intervals (CI) were calculated.

Results

We interviewed and collected samples from children in three age groups: 1–4 years (422), 5–9 years (518) and 10–14 years (402), totaling 1,342 children. Among participants, 674 (50.22%) were male and 668 (49.78%) were female (Table 1).

Mean maternal age at birth was 22.65±5.52 years, and the median was 22.14 years. Among different age groups, the mean maternal age at birth was highest in youngest age group and lowest in oldest age group. Only 262 (19.52%) mothers of the participating children attended at least four antenatal visits while pregnant with that child (Table 2).

Immunity Status of Study Participants and Associated Factors

Of 1,342 children, 713 (53.13%) children were protected, and 629 (46.87%) children were unprotected. Overall GMT of diphtheria antitoxin was 0.11 IU/mL (95% CI 0.11–0.12) in all 1,342 children (Table 3).

Table 1. Participant characteristics of vaccinated children aged 1–14 years in Belabo Subdistrict, Narshingdi District, Bangladesh, 2019

Characteristics	n (%)
Age distribution, years (n=1,342)	
1–4	422 (31.45)
5–9	518 (38.60)
10–14	402 (29.96)
Gender distribution (n=1,342)	
Male	674 (50.22)
Female	668 (49.78)
Educational status (n=915)	
Attending educational institute	839 (91.70)
Not attending educational institute	76 (08.30)
Family size of the participant children (n=1,342)	
Up to five family members	887 (66.10)
More than five family members	455 (33.90)
Monthly family expenditure in BDT (n=1,342)	
Up to 12,000 BDT	739 (55.07)
More than 12,000 BDT	603 (44.93)
House-hold floor structure (n=1,337)	
Clay made	934 (69.85)
Cemented	387 (28.95)
Other materials (woods, tiles etc.)	16 (01.20)
Use of tube well water for drinking (n=1,323)	
Yes	1,284 (97.05)
No	39 (02.95)
High arsenic content in tube well water (n=1,265)	
Yes	14 (01.11)
No	355 (28.06)
Unknown	896 (70.83)
PCV vaccination in 1–4 years age group (n=422)	
PCV-1	277 (65.64)
PCV-2	268 (63.51)
PCV-3	247 (58.53)

Based on 1 US dollar (USD) was equivalent to 82.91 Bangladesh Taka (BDT). PCV: pneumococcal conjugate vaccine.

Table 2. Maternal and birth related characteristics of vaccinated children aged 1–14 years in Belabo Subdistrict, Narshingdi District, Bangladesh, 2019

Characteristics	n (%)
Maternal age at birth	
Mean±SD (years)	22.65±5.52
Median	22.14
Number of antenatal visits	
At least four visits	262 (19.52)
Less than four visits	1,080 (80.48)
Gestational period (n=1,329)	
Pre-term	103 (07.75)
Term completed	1,226 (92.25)
Known diabetes mellitus during pregnancy (n=1,273)	
Absent	1,257 (98.74)
Present	16 (01.26)
History of hypertension during pregnancy (n=1,208)	
Absent	1,148 (95.03)
Present	60 (04.97)
Active smoking during pregnancy (n=1333)	
Smoked	18 (01.35)
Did not smoke	1,315 (98.65)
History of passive smoking during pregnancy (n=1,256)	
Present	506 (40.29)
Absent	750 (59.71)
Place of birth (n=1,330)	
Health Facility	447 (33.61)
Home	883 (66.39)
Mode of delivery (n=1,320)	
Vaginal	1,040 (78.79)
Caesarian	280 (21.21)
Reported birth weight (kilograms)(n=980)	
Less than 2.5	205 (20.92)
More than 2.5	775 (79.08)

SD: standard deviation.

Table 3. Immunity status against diphtheria among participant vaccinated children aged 1–14 years in Belabo Subdistrict, Narshingdi District, Bangladesh, 2019

Immunity status	Do not have protected level of diphtheria IgG n (%)	Have protected level of diphtheria IgG n (%)	*P*-value	GMT in IU/mL (95% CI)
Overall (n=1,342)	713 (53.13)	629 (46.87)		0.11 (0.11–0.12)
Age (years)				
1–4 (n=422)	100 (23.65)	322 (76.35)	<0.0001	0.18 (0.16–0.19)
5–9 (n=518)	270 (52.12)	248 (47.88)		0.10 (0.09–0.11)
10–14 (n=402)	259 (64.48)	143 (35.52)		0.08 (0.08–0.09)
Gender				
Male	300 (44.51)	374 (55.49)	0.08	0.12 (0.11–0.13)
Female	329 (49.25)	339 (50.75)		0.11 (0.10–0.12)

GMT: geometric mean titer. IgG: Immunoglobulin G. IU/mL: international units per milliliter. CI: confidence interval.

The proportion of unprotected children gradually increased with age and was lowest in children aged one year and highest in children aged 11 years. At age four years, more than 30% of children were unprotected (Figure 1).

The correlation coefficient between age (x) and ELISA titer (y) was -0.362 (p 0.01) and the regression equation was: y=-0.65–0.04x (Figure 2).

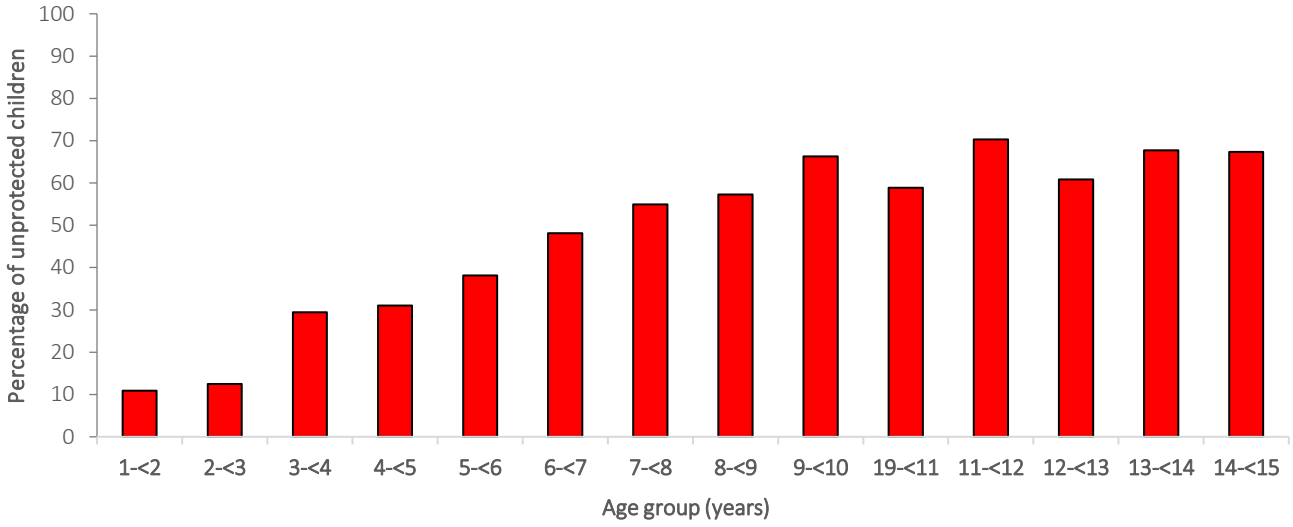

Figure 1. Proportion of unprotected children in different age groups among participant vaccinated children of 1-14 years in Belabo Subdistrict, Narshingdi District, Bangladesh, 2019

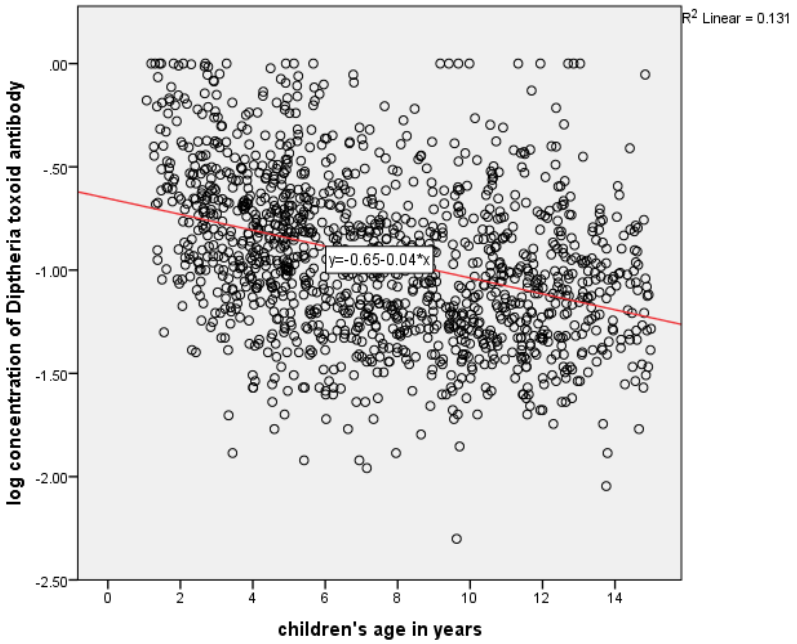

Figure 2. Log diphtheria toxoid antibody concentration and age of participant vaccinated children aged 1–14 years in Belabo Subdistrict, Narshingdi District, Bangladesh, 2019

The proportion of protected children was 76.35% in age group 1–4 years, 47.88% in age group 5–9 years, and 35.52% in age group 10–14 years, which was highly significant (p <0.0001) (Table 3).

GMT varied in three age groups and was highest in age group 1–4 years and lowest in age group 10–14 years. GMT of anti-diphtheria in age group 1–4 years was 0.18 IU/mL (95% CI 0.16–0.19), in age group 5–9 years was 0.10 IU/mL (95% CI 0.09–0.11) and in age group 10–14 years was 0.08 IU/mL (95% CI 0.08–0.09). GMT was significantly lower in older age groups, compared to 1–4 years (Table 3).

Among males, 55.49% (374/674) and among females 50.75% (339/668) were protected against diphtheria, which did not vary significantly (p 0.08). GMT of anti-diphtheria toxin antibody in males and females were 0.12 IU/mL (95% CI 0.11–0.13 IU/mL) and 0.11 IU/mL (95% CI 0.10–0.12 IU/mL) respectively (Table 3).

Among children who drank water from tube-wells marked arsenic-free by green paint, 47.59% were unprotected. However, only 7.14% of children drinking water from tube-wells containing arsenic marked by red paint were unprotected. Drinking water from tube-wells marked green (arsenic-free) was found to be a risk factor for being unprotected both in univariate (OR 11.80, 95% CI 1.52–90.99) (Table 4) and multivariate analysis (OR 17.42, 95% CI 2.17–139.90) (Table 5).

Table 4. Univariate analysis for factors associated with not having protective level of diphtheria antibody (IgG) in participant vaccinated children aged 1–14 years in Belabo Subdistrict, Narshingdi District, Bangladesh, 2019

Immunity status	Do not have protected level of diphtheria IgG n (%)	Have protected level of diphtheria IgG n (%)	OR (95% CI)
Age (years)			
1–4 (n=422)	100 (23.65)	322 (76.35)	Reference
5–9 (n=518)	270 (52.12)	248 (47.88)	3.51 (2.65–4.66)
10–14 (n=402)	259 (64.48)	143 (35.52)	5.83 (4.30–7.88)
Gender			
Female	329 (49.25)	339 (50.75)	1.21 (0.98–1.50)
Male	300 (44.51)	374 (55.49)	
Colour of tube-well used for drinking water			
Green	167 (47.59)	184 (52.41)	11.80 (1.52–90.99)
Red	1 (07.14)	13 (92.86)	
Maternal diabetes			
Absent	588 (46.77)	669 (53.23)	3.81 (1.08–13.41)
Present	3 (18.75)	13 (81.25)	
Maternal hypertension			
Absent	542 (47.19)	606 (52.81)	1.25 (0.74–2.11)
Present	25 (41.67)	35 (58.33)	
Birthplace			
Home	445 (50.34)	438 (49.66)	1.55 (1.23–1.95)
Hospital	177 (39.60)	270 (60.40)	
Mode of delivery			
Vaginal	523 (50.27)	517(49.73)	2.00 (1.52–2.64)
C-section	94 (33.60)	186 (66.40)	
Gestational period			
Pre-term	54 (52.38)	49 (47.62)	1.28 (0.86–1.91)
Term completed	568 (46.34)	658 (53.66)	
Birth weight (kilograms)			
<2.5	98 (47.83)	107 (52.17)	1.10 (0.82–1.48)
≥2.5	353 (45.54)	422 (54.46)	

IgG: Immunoglobulin G. OR: odds ratio. CI: confidence interval.

Table 5. Multivariate analysis of characteristics associated with not having protective level of diphtheria antibody (IgG) in participant vaccinated children aged 1–14 years in Belabo Subdistrict, Narshingdi District, Bangladesh, 2019

Characteristics	Crude OR	Adjusted OR	95% CI
Age 1–4 years			Reference group
Age 5–9 years	3.51	4.17	2.38–7.14
Age 10–14 years	5.83	7.69	4.00–14.29
Drinking water from arsenic-free tube-well	11.80	17.42	2.17–139.90

Multivariate model included all variables presented in the table. IgG: Immunoglobulin G. OR: odds ratio. CI: confidence interval.

Protection against diphtheria was not associated with known maternal diabetes mellitus during pregnancy, known maternal hypertension during pregnancy, gestational period, child's birthplace, mode of delivery and interviewee-reported birthweight of participant children. Among children aged 1–4 years, not completing of three doses of PCV was found to be associated with being unprotected (OR 2.06, 95% CI 1.31–2.40). However, in the same age group, when the effect of age was adjusted, this was not found to be associated with being unprotected (OR 1.50, 95% CI 0.90–2.50) (Table 6).

Using multivariate analysis, age group was significantly associated with immunity status. Children of age group 5–9 years were 4 times more likely to be unprotected than children of age group 1–4 years (OR 4.17, 95% CI 2.38–7.14). Also, children of age group 10–14 years were seven times more likely to be unprotected than children of 1–4 years (OR 7.69, 95% CI 4.00–14.29) (Table 5).

Table 6. Association between incomplete PCV vaccination and being unprotected among children aged 1–4 years in Belabo Subdistrict, Narshingdi District, Bangladesh, 2019

Completion of PCV	Do not have protected level of diphtheria IgG n (%)	Have protected level of diphtheria IgG n (%)	Crude OR (95% CI)	Adjusted OR* (95% CI)
Incomplete PCV	55 (31.43)	120 (68.57)	2.06 (1.31–2.40)	1.5 (0.9–2.5)
Completed PCV	45 (18.22)	202 (82.78)		

**Adjusted for age. PCV: pneumococcal conjugate vaccine. IgG: Immunoglobulin G. OR: odds ratio.*

Discussion

In this study, we found that immunity decreased with increasing age in children who completed primary vaccination against diphtheria. Proportion of protection was highest in age group 1–4 years, and lowest in age group 10–14 years. The GMT of diphtheria antibody also varied significantly in three age groups, being highest in age group 1–4 years and lowest in age group 10–14 years. Being in an older age group was significantly associated with being unprotected.

Studies show that although antibody titer gradually decreased with increasing age, when there was a booster dose, titer increased.[19] Protective levels of antibody were found in 70% of Indian children of 4–6 years of age who had completed a total of four doses of diphtheria vaccine, including one booster by age 2 years. After a second booster was administered at age 4–6 years, 98% of these children had protective antibody levels after 28 days.[27] In our study, 60–70% of children aged 4–6 years were protected with just the 3-dose primary schedule, similar to Indian children before the second booster.

A prospective study conducted in Bangladesh between 2008–2017 examined association between drinking water arsenic concentrations and serum diphtheria antitoxin concentrations (IgG antibodies). Among vaccinated children, water arsenic concentrations measured during toddlerhood and early childhood were not associated with antibody levels.[28] In contrast, another study in Bangladesh, found significantly higher (p <0.001) diphtheria specific IgG in serum of vaccinated children from a high arsenic area compared to a low arsenic area.[29] According to the authors, arsenic metabolites may upregulate factors that are responsible for isotype switching and immunoglobulin production boosting both total IgG and protein specific isotype antibody responses. In our study, drinking water from tube-wells with a high arsenic content was also found to be positively associated with protection. However, this association was not strongly established in multivariate analysis, as the range of 95% confidence interval was very wide. This result needs careful interpretation.

Our study did not show any association between children's immunity status and gender, maternal characteristics during pregnancy, or receiving three doses of PCV. PCV contains carrier protein cross-reacting material 197 (CRM-197) for conjugation. CRM-197 is an ideal carrier protein that is globally used in conjugated vaccines including vaccines for Haemophilus influenzae, pneumococcus and meningococcus. CRM-197 is structurally identical to diphtheria toxoid and is an enzymatically inactive and non-toxic form of diphtheria toxoid.[30] As a result it has immunogenic properties similar to diphtheria toxoid and is immunologically indistinguishable from diphtheria toxoid.[31] Bangladesh EPI routinely administers PCV (containing CRM-197) along with pentavalent vaccine (containing diphtheria toxoid) simultaneously, since 2015. Whether this simultaneous administration of diphtheria toxoid and structurally similar CRM-197 has any boosting effect or interfering effect on inducing immunity needs further study. Completion of three PCV doses was excluded from multivariate analysis, as this variable was applicable to only a single age group 1–4 years. In age group 1–4 years, completion of three PCV doses was not found significantly associated with protection, when the effect of age was adjusted within the single age group.

Studies including systematic reviews and meta-analyses show post-vaccination diphtheria antibody titer was persistently higher than pre-vaccination levels up to five years, then declined toward pre-vaccination levels. At 5–6 years post-vaccination, antibody titers were not significantly different from pre-vaccination level and dropped to pre-vaccination level.[10,14] Therefore, boosters are needed to ensure long-term protection in older children.

Limitations

We only performed ELISA test for estimating diphtheria antibody titers. We did not perform the "gold standard" in vitro toxin neutralization assay. Though there is a good correlation between ELISA and neutralization assay, ELISA may overestimate some sera below 0.1 IU/mL.[32] Misclassification of history of maternal diabetes mellitus, maternal hypertension, gestational period, and birthweight may have occurred as this was self-reported. Only color-marking of tube-well was used to indicate Arsenic content; current Arsenic content was not measured. Thus, examination for an association between immunity and these factors may not have been adequately assessed. We also did not apply weighting for age-specific population size per site, as age-group stratified population size by site was not available.

Recommendations

Our findings suggest that the Bangladesh national EPI should introduce and routinely administer a booster vaccine for diphtheria to children <5 years old to ensure sufficient level of protection among the high-risk children. This could be implemented by introducing a routine booster at the age of school entry. A campaign for booster vaccination against diphtheria should be conducted for children 10–14 years old to avert any potential outbreak of diphtheria. A similar study should be conducted to assess the persistence of immunity after booster vaccination and to decide if another booster should be introduced for older age groups. Also, vaccination programs with only primary schedule should evaluate the need and optimal timing for a booster.

Conclusion

In Bangladesh, about half of children aged 5–9 years, and two-thirds of children aged 10–14 years were unprotected against diphtheria. GMT of diphtheria antibody also varied in three age groups and was highest in age group 1–4 years and lowest in age group 10–14 years. Being unprotected was significantly associated with age group of the vaccinated children.

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Author Contributions

Farzana Islam Khan: Conceptualization, methodology, investigation, project administration, data curation, formal analysis, visualization, writing—original draft, writing—review & editing. **Mallick Masum Billah:** Methodology, visualization, writing—review & editing. **Alden Keith Henderson:** Validation, visualization, writing—review & editing. **Sharifuddin Hasnat:** Data curation, formal analysis, software, visualization. **Arifa Akram:** Validation. **Ashek Ahammed Shahid Reza:** Methodology. **Mohammad Rashidul Alam:** Conceptualization. **Tahmina Shirin:** Resources. **Meerjady Sabrina Flora:** Conceptualization, funding acquisition, resources, supervision.

Ethical Approval

The study was approved by the Institutional Review Board of IEDCR before commencement of the study (protocol number: IEDCR/IRB/2019/09; date of approval: 20 Jun 2019). Participant identities and results of the serum sample tests remained confidential and were anonymously used solely for analysis purpose.

Informed Consent

We obtained written consent from parents and assent from children >5 years.

Data Availability

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

Conflicts of Interest

No conflicts of interest by all authors.

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Declaration of Generative AI and AI-assisted Technologies in the Writing Process

No generative AI or AI assisted technologies were used in writing.

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The Grammar of Science: How "Robust" Are Your Study Results?

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All statistical estimates have some degree of uncertainty due to sampling variability. The process of statistical modelling and interpretation typically requires implicit assumptions about random sampling and data distribution.[1–3] But as we know in real life that data were quite often deviated from these model assumptions.

The standard error (SE) quantifies the uncertainty around a sample estimate.[4] When the underlying assumptions are violated, the calculated SE may be incorrect. Instead of using classic SE, some researchers may decide to use "robust" SE which are robust to violations of certain assumptions.[2–4] You may run into clinical and epidemiological papers that used robust SEs. Robust options can be applied in various statistical context including: estimating descriptive statistics (e.g., mean, proportion), hypothesis testing (e.g., t-test, ANOVA), regression model fitting (i.e., linear, logistic, Poisson, Cox), and repeated measures or clustered data analysis (e.g., generalized estimating equation, multilevel mixed model).

This paper examines the concept of robust standard errors—what they are, how they are calculated, and the reasons for using or avoiding them.

Definition of "Robust"

The term "robust" in statistics refers to the resilience of an estimator or statistical model under conditions that deviate from ideal assumptions.[5] A robust model maintains its accuracy and reliability even when assumptions are only partially met while the results can still yield meaningful insights despite such imperfections.[6] In essence, a robust statistic resists provides trustworthy results even in less-than-ideal analytical conditions.[5]

Certain statistical methods are considered robust under specific conditions. For example, t-test and ANOVA assume normally distributed data; however, they still perform reliably when this assumption is violated—so long as each group includes a sufficiently large sample size. This robustness is supported by the central limit theorem, which assumes the statistics remain unbiased in a wide variety of probability distributions.[2,5] Similarly, nonparametric methods are robust by nature, offering resistance to both distributional deviations and the presence of outliers.[2,3] In regression analysis, issues like outliers and heteroscedasticity (non-constant variance of residuals) can undermine model validity. (Heteroscedasticity can be detected through formal tests such as the Breusch-Pagan test or simple residual plots as illustrated in Figure 1.[7,8] Robust regression techniques, however, are designed to accommodate such violations, offering more dependable results when standard assumptions fail.

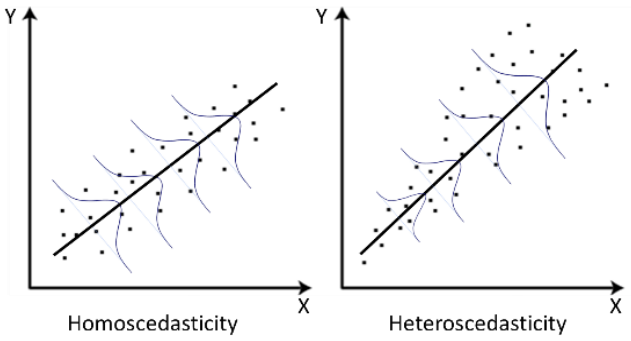


Figure 1. Homoscedasticity vs. heteroscedasticity in regression residuals

From a data-analytic perspective, robust statistics represent an extension of traditional parametric methods. These techniques acknowledge that statistical models are, at best, approximations of reality.[6] Rather than requiring the stochastic (random) component of a model to be precisely specified, robust procedures aim to capture the main structure of the data while flagging anomalous points or substructures for further investigation. In case of the dataset containing outliers, the goal of the analysis is not to eliminate outliers, but to model the majority of the data effectively.[1,5]

Review of Standard Error

SE is a fundamental concept of inferential statistics, measuring how accurately a sample statistic represents the corresponding population parameter. To review the concept of SE, let's go back to some basic statistics—SE of mean (SEM). Mean ($\bar{X}$) is a measure of central tendency that represents the average value within a dataset. The standard deviation (SD) quantifies the spread or variability of data points around the mean. While SD describes the dispersion of individual data points within a sample, SE measures the precision of the sample mean—or other statistics—relative to the true population value.[9,10] Suppose the average value in population is known (μ) and we collect a sample data drawn from that population and calculate the sample mean ($\bar{X}$) and its standard deviation (SD). In theory, if we repeat sampling the data from the same population, we will obtain several sample means and SDs, so-called sampling distribution. The average of sample means ($\bar{\bar{X}}$) is approximately the population mean (μ) and the distribution of sample means is the SE. (Figure 2) In practice, SEM can be estimated by dividing the sample's standard deviation (s) by the square root of the sample size (n). This value reflects how much the sample mean is expected to vary from the true population mean.

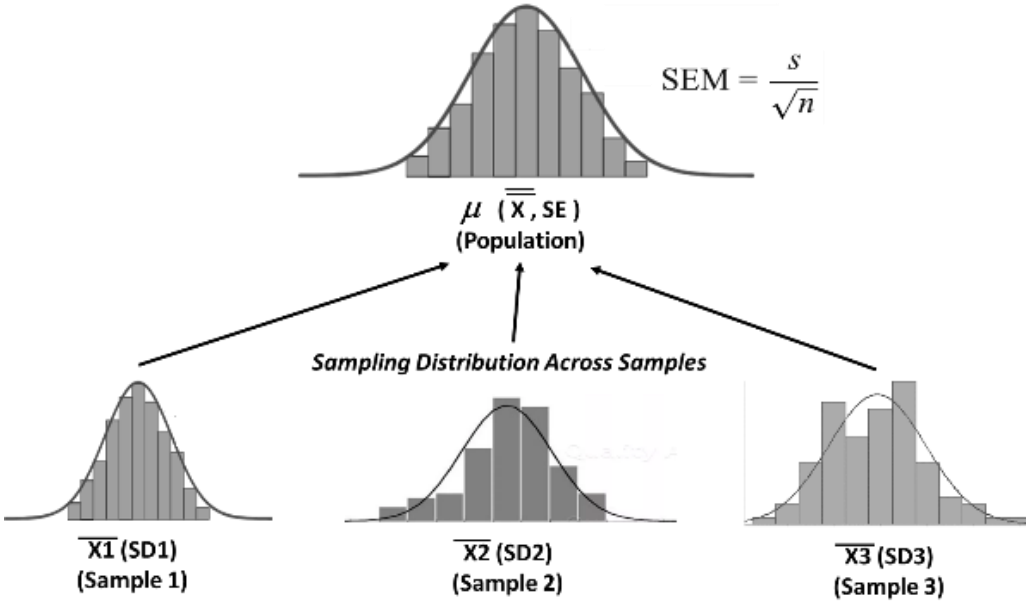


Figure 2. Sampling distribution and SEM

SE can be calculated not just for means, but for a wide variety of statistics and models. Here are some common examples:[9–12]

Simple SE for the Proportion

Calculated from the sample proportion (p) and the sample size (n). It is used to estimate the variability of a sample proportion from the true population proportion.

$$SE_p = \sqrt{\frac{p(1-p)}{n}}$$

SE of the Difference between Means

Used in comparing two means in independent t-test is calculated from the SE of the two samples being compared.

$$SE = \sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}$$

SE of the Regression Coefficient

Derived from variance-covariance matrix of the estimated coefficient in a regression model (β). It is used to test the significance of the estimate of the regression coefficient.

$$SE(\hat{\beta}) = \sqrt{Var(\hat{\beta})}$$

SE of the Regression Estimate

Calculated from the deviation of the observed values and predicted values divided by the sample size (n) and the numbers of predictors in the regression model (k). It Indicates how well the regression model fits the data.

$$SE = \sqrt{\frac{\sum(y_i - \hat{y}_i{}^2}{n-k-1}}$$

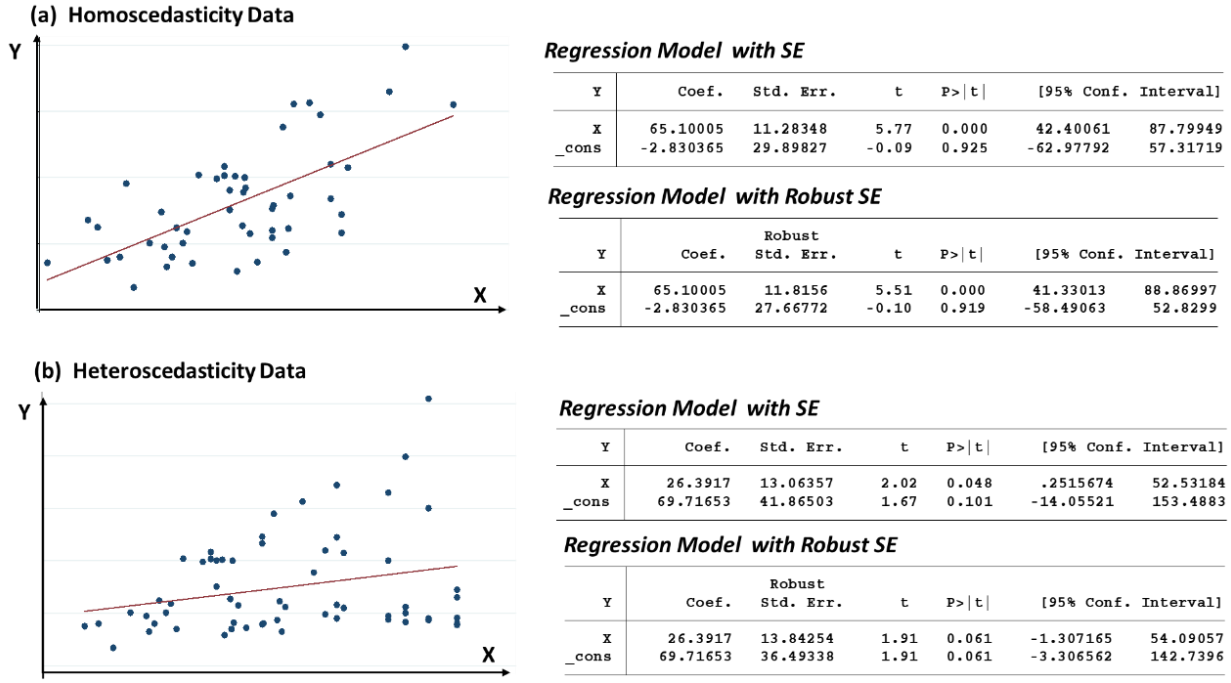
In general, SE quantifies the variability of an estimated statistic around the true, but often unknown, population parameter.[13] Since we rarely know the actual population value, we rely on sample

statistics to make educated guesses. These estimates are usually reported with confidence intervals (CIs) that incorporate the SE. A common approach is to construct a 95% CI using the formula: Estimate ±1.96 × SE. A narrow CI suggests high precision and greater confidence in the estimate, while a wide CI may indicate insufficient data or poor sampling methods.[1,10,13] In addition to describing precision, SE plays an essential role in hypothesis testing and statistical modeling, as outlined above.

Robust Standard Errors

You can see that SE calculations rely on the assumption that the sample is both random and representative. When a sample is biased, collected improperly, or too small, the SE might be underestimate or not accurately capture the true level of uncertainty. Thus, it will distort confidence intervals and lead to incorrect conclusions in hypothesis testing. SE calculations also assume that the underlying data follows a specific distribution. If the data is skewed or contains outliers, the SE may not reliably reflect the actual variability in the estimate.[1,13] On the other hand, robust SEs can still yield meaningful insights even when data don't perfectly meet ideal assumptions. They tend to hold up under varied distributions and can accommodate atypical values, making them a practical choice for analyzing real-world data.[2]

As an example, in a linear regression analysis of homoscedasticity and heteroscedasticity datasets running by Stata 14 with and without the robust SE option (Figure 3). While both methods produce identical coefficient estimates, the standard errors differ. This variation affects the width of the 95% confidence intervals and the *p*-values. In heteroscedasticity data, applying robust SEs leads to wider confidence intervals and higher *p*-values that are not statistically significant (0.061). Without the robust option, the *p*-values may appear close to marginal significance (0.048), potentially giving a misleading impression of the results. However, it's important to recognize that using the robust option doesn't always produce different outcomes or ensure the "correct" conclusion. When discrepancies do appear, we should further explore the data and assess model fit indicators to better understand the source of the variation.



Y	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
X	65.10005	11.28348	5.77	0.000	42.40061	87.79949
_cons	-2.830365	29.89827	-0.09	0.925	-62.97792	57.31719

Y	Coef.	Robust Std. Err.	t	P>|t|	[95% Conf.	Interval]
X	65.10005	11.8156	5.51	0.000	41.33013	88.86997
_cons	-2.830365	27.66772	-0.10	0.919	-58.49063	52.8299

Y	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
X	26.3917	13.06357	2.02	0.048	.2515674	52.53184
_cons	69.71653	41.86503	1.67	0.101	-14.05521	153.4883

Y	Coef.	Robust Std. Err.	t	P>|t|	[95% Conf.	Interval]
X	26.3917	13.84254	1.91	0.061	-1.307165	54.09057
_cons	69.71653	36.49338	1.91	0.061	-3.306562	142.7396

Figure 3. Linear regression models with and without robust options

Types of Robust SE in Statistical Modelling

Robust SEs are often referred to as heteroscedasticity-consistent standard errors when used to address violations of the homoscedasticity assumption.[14] Beyond addressing heteroscedasticity, robust SEs can also help correct for certain forms of model misspecification in regression analysis. Various techniques have been developed to adjust standard errors, as suggested in the literature. Below are some commonly used methods:

Robust SE Options

The methods account for varying variances of the residuals in the model instead of assuming homoscedasticity. Two common methods are: (1)

Huber-White Sandwich Estimator (i.e., also known as sandwich estimator, adjusted for the covariance matrix and some forms of model misspecification) and (2) Newey-West Standard Errors (i.e., robust SE adjusted for both heteroscedasticity and autocorrelation in time-series data).[14–16]

Clustered SE

This method is appropriate when observations are collected within clusters (e.g., students within schools, patients within hospitals, or people within regions) or from the same subjects over time periods. Such data are, in theory, correlated; thus, the adjustment allows for intra-cluster correlation while assuming independence between clusters.[17]

Weighted Least Squares (WLS)

This technique adjusts by weighting each observation inversely to its error variance, thereby reducing the bias of heteroscedasticity.[18]

Bootstrapped SE

This is a resampling technique that is often used when the data do not meet the assumptions of traditional statistical methods (e.g., normality, homoscedasticity). By repeatedly resampling the data with replacement, the SE is derived from the variability in the estimates across the "bootstrapped samples".[19]

Finite Sample Adjustments

This method is commonly used with small sample sizes, so-called "small-sample correction" technique. It adjusts the covariance matrix of regression models.[20]

Generalized Least Squares (GLS) and Feasible GLS (FGLS)

The methods adjust for both heteroscedastic or autocorrelated among residuals in regression model. GLS accounts for the known residual structure while FGLS is used when the exact covariance structure is unknown.[21]

Delta Method

The method is approximate the standard error of a nonlinear transformation of estimated coefficients. It's useful in cases involving ratios, exponentials, or other nonlinear functions.[22]

Sampling-Weighted SE

This method is common in survey analysis. It is a design-based SE, accounted for sampling weights, levels of sampling strata, and clustering of observations.[23–24]

So—When to Use Robust SE?

There are various methods available for calculating robust SEs, each designed to handle different issues such as non-constant variance, outliers, autocorrelation, and other model irregularities. In the linear regression example discussed earlier, we saw how extreme data values combined with heteroscedasticity can influence statistical significance and ultimately affect study conclusions. This often raises the question: which model is truly the "best fit" or even "correct"—with or without the robust SE option? So–when should we use robust SEs?

There are diagnostic tools available for evaluating regression models, though a detailed discussion of these methods is beyond the scope of this paper. For interested readers, please refer to Zellner's papers and other references.[8,21,25,26] One key indicator that robust SE may be appropriate is the presence of large residuals or high-leverage points. We can say that if your model is approximately correct, conventional SEs are generally sufficient, and using robust SE is unlikely to add much value. However, if the model is seriously in error, robust adjustments may improve the estimation of variance, but the parameters being estimated are still controversial and require caution in interpretation. Even with robust SEs, the model might be overfitting or underfitting the data, especially when assumptions are clearly violated.[27,28]

Robust SE should not be used as a superficial safeguard against reviewer criticism or assumed to correct all problems.[29] Simply choosing to report only classical or only robust SEs can be misleading. We should take a closer look when the classical SE and robust SE differ substantially. A larger discrepancy between the two types of SEs means that you are potentially have a misspecification model.[29]

A Word of Caution

Robust statistics are not a replacement for classical methods.[6] Misunderstanding this can lead to misuse. While robust SEs are valuable for addressing certain issues in traditional models, their use should be justified, not automatic. You should carefully consider whether it is necessary or not.

Choosing the right approach to SEs depends not only on your data and sampling method but also on your broader research goals—how you intend to generalize the results across units and over time, and how you will use the model estimates. You should pick a method to adjust or not adjust your SE when you carefully consider your model's purpose and how the study

would be replicated.[10,30] As emphasized in the literature, robust SEs do not substitute for careful model specification.[14,29] Use all available diagnostic tools, ensure your model fits the data well, test its predictions, and refine it based on those insights. When a model is well-specified, both classical and robust SEs are expected to converge.[29]

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