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Editorial

Is It Already Too Late for Measles Elimination in Thailand?

Wiwat Rojanapithayakorn, Senior Editor

In the field of disease control, the ability or possibility to control or even eliminate a communicable disease depends on the availability of technologies or innovations for manipulating the three epidemiological determinants of disease occurrence: host, agent and environment. A perfect example is the positive outcomes of controlling coronavirus disease 2019 (COVID-19), which were achieved through host adaptation (by mask wearing and hand washing), environmental arrangement (by social distancing), and targeting the causative agent—SARS-CoV-2 virus (by COVID-19 vaccines). Some diseases can be controlled even without the need to address all three determinants; just one is enough. There are many successful pieces of evidence in global history. The success of smallpox eradication relied mainly on the use of smallpox vaccines, and that for yaws elimination was due to the availability of effective antimicrobials (mass treatment by penicillin and azithromycin). The low prevalence of yaws has led to an aim for global eradication. The key message here is that once the efficacious control measures are available, it is always possible to control, eliminate or even eradicate the target diseases. Thus, it is difficult to accept that many countries around the world are still unable to eliminate measles, a disease that can be ended simply by mass immunization.

Measles is a contagious disease that mainly affect children, and the health outcomes include high fever, respiratory tract symptoms, dermatological manifestations, internal organ damage (particularly to the lungs and the brain) or even death. Fortunately, the disease is preventable by immunization. Successful elimination was observed over 40 years ago in Finland, a country that began providing a 2-dose measles vaccine to children at the national level. As a result, the disease was eliminated. All new cases identified were mostly imported. Subsequently, 2-dose measles immunization has been widely accepted and become a global norm. The positive outcomes of measles immunization were so well documented that the World Health Assembly in 2012 agreed to set a global policy of measles elimination. Since then, efforts have been made around the world to eliminate the disease. The main principle is that if all countries can achieve over 95% of 2-dose measles immunization, the global elimination can then be successful. Many countries around the world had already declared the state of elimination. In the Southeast Asia region, the World Health Organization had verified measles elimination in Sri Lanka, Maldives, Bhutan, Timor-Leste and North Korea.

In Thailand, the 2-dose measles immunization was approved in 1996. The immunization scheme has long been included in the national expanded program on immunization (EPI) through the use of measles, mumps, and rubella (MMR) vaccine at the ages of 9 and 18 months. The question is, "Why were measles outbreaks still observed?" The answer is obvious: the country is still unable to attain a high level of immunization coverage. The overall coverage of MMR2 (the second dose) for 2024 was only 87.5%, and the coverage for some provinces was even much lower: 42.8% for Pattani Province, 55.9% for Narathiwat Province and 65.5% for Yala Province. Failure to attain over 95% immunization coverage of measles vaccines had resulted in several outbreaks of the disease. For 2024, the number of reported cases of measles in Thailand was 5,372, and many more suspected cases were reported.

Reasons for immunization failure may be many; one of which may be due to the epidemic of COVID-19 in the past few years, which had caused interruption of routine health services in most health care facilities. Since the COVID-19 epidemic is now over, it is time to catch up. The most important driving force that exists is the understanding of health personnel on the need for high vaccination coverage and to create herd immunity, as well as the willingness to protect the lives of children. We used to hear that in Mongolia, a health worker carried vaccines in a freeze-prevention container traveling by horse in the freezing land just to vaccinate a child living in a ger (traditional tent in the country) very far away, who was at the age for diphtheria, tetanus, pertussis and polio vaccination. Responsibility to immunize all children relies on local health workers, and the monitoring efforts belong to provincial and central health leaders. To eliminate measles successfully, over 95% coverage of the measles vaccine has to be ensured.

Currently, the Ministry of Public Health of Thailand is planning to strengthen the immunization program for measles. Unfortunately, the plan is only for some selected provinces with the lowest coverage. Since no health region in the country had MMR2 coverage reaching over 95%, the strengthening efforts should be made nationwide. It is quite slow to target only a small number of provinces, as it is probably already too late for the country to achieve the goal for national measles elimination.

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Turning the Tide on Measles: EOC-Led Response and School-Based Vaccination in Narathiwat Province's Outbreak, 2024–2025

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Abstract

This study aimed to describe the epidemiological characteristics of the 2024–2025 measles outbreak in Narathiwat Province, identify factors associated with severe illness, and evaluate the effectiveness of outbreak control measures. A suspected case was defined as fever with maculopapular rash plus cough, coryza, conjunctivitis, or Koplik's spots. Confirmed cases had laboratory evidence of infection, detected either by measles-specific immunoglobulin M antibodies using enzyme-linked immunosorbent assay or viral RNA via reverse transcription polymerase chain reaction. Epidemiologically linked cases met clinical criteria without laboratory confirmation but had documented exposure to a confirmed case. Between February 2024 and January 2025, 2,710 cases were reported: 47.0% suspected, 13.4% epidemiologically linked, and 39.6% confirmed. Most cases occurred in children aged 9 months to 4 years, and 9.3% of confirmed cases were severe. Risk factors included female gender (adjusted odds ratio (OR) 1.81, 95% confidence interval (CI) 1.18–2.79), age under 9 months (adjusted OR 7.84, 95% CI 1.77–34.70), and diarrhea (AOR 2.29, 95% CI 1.47–3.60). Following Emergency Operations Center activation, school-based surveillance, ring vaccination, vitamin A supplementation, and a phased vaccination campaign were implemented. School-based clusters declined from 19 to 1 within 42 days post-intervention. Ring vaccination coverage reached 65% and reduced secondary infections from 2.0% to 1.3% (p-value <0.01). The vitamin A uptake rate rose rapidly, reaching 100% by October 2024. The measles vaccine coverage increased from 47.9% to 65.0% among children aged under 12 years. These results highlight the outbreak burden in low-coverage areas and support integrated interventions.

Keywords: measles outbreak, measles vaccine, school-based vaccination, vitamin A, Emergency Operations Center, Narathiwat

Introduction

Measles is a highly contagious viral disease with high mortality. The disease caused an estimated 107,500 deaths globally in 2023, mainly among unvaccinated children under five years of age.[1] Thailand committed to measles elimination at the 63rd World Health Assembly in 2010 and implemented a strategic plan (2020–2024) under the National Expanded Program on Immunization (EPI), aiming for 95% coverage with the first dose of the measles, mumps, and rubella (MMR) vaccine (MMR1) at 9 months and the second dose of MMR (MMR2) at 18 months.[2] In Narathiwat Province, MMR1 coverage remained below 50%, contributing to an outbreak in 2024.[3] The province has historically faced challenges in vaccine coverage due to cultural and trust-related barriers. Persistent vaccine refusal, primarily due to parental concerns about halal content and vaccine side effects, remains a barrier.[4,5]

Measles transmission begins four days before rash onset and continues for a further four days. Symptoms include fever, cough, coryza, conjunctivitis, and rash.[6] Pneumonia is a common complication and the main cause of death.[7] Maternal measles infection increases the risk of adverse pregnancy outcomes, including fetal loss and neonatal death. Intravenous immunoglobulin (IVIG) is recommended for susceptible newborns.[8]

The MMR vaccine provides 93% protection after one dose and 97% after two doses.[9] Due to low routine MMR vaccine coverage, outbreak control measures such as ring vaccination are used to prevent further spread. However, as a live vaccine, it is contraindicated during pregnancy.[10] Vitamin A supplementation is also essential, particularly for malnourished children, to reduce disease severity.[11] In response to the outbreak, the Narathiwat Emergency Operations Center (EOC) was activated on 3 Sep 2024, to coordinate surveillance, isolation, and control measures. This study aims to describe the epidemiology of the outbreak, identify factors associated with severe illness, and evaluate the effectiveness of control measures.

Methods

To describe the magnitude and characteristics of measles cases between February 2024 and January 2025, the Narathiwat EOC applied a modified clinical case definition based on Thailand's national measles surveillance guideline.[12]

A clinical case was defined as a patient with fever and maculopapular rash plus at least one of the following: cough, coryza, conjunctivitis, or Koplik's spots.

Case classification comprised three groups. A suspected case was defined as an individual meeting the clinical criteria or clinically diagnosed by a physician. An epidemiologically linked case was defined as a suspected case without laboratory confirmation but with a documented link to a confirmed case through investigation. A confirmed case was a suspected case with laboratory confirmation, including a positive or equivocal immunoglobulin M (IgM) result or a positive reverse transcription polymerase chain reaction (RT-PCR) test.

High-risk contacts (HRCs) included individuals with close contact to suspected, epidemiologically linked, or confirmed measles cases, including household members, close contacts without masks, and healthcare workers without proper protective equipment.

Severe cases were those with complications such as pneumonia or respiratory distress, while non-severe cases had no complications.

Measles confirmation was done by IgM in blood (4–28 days after rash onset) and RT-PCR for viral RNA in throat or nasal swabs (5–14 days after rash onset), according to the Thailand national measles surveillance guideline.[12] Specimens were stored at −10 °C for up to 48 hours and transported within two hours to the Regional Medical Sciences Center 12, Songkhla.

Data on measles cases were collected through daily updates entered into the online patient registry by district health personnel. The collected data included demographics (age, gender, district of residence), clinical features (symptoms, pneumonia, hospitalization, mechanical ventilation, fatality), and vitamin A supplementation. Categorical variables were summarized using frequencies and percentages and continuous variables using medians with interquartile range (IQR).

A cross-sectional study was conducted to identify factors associated with severe cases among laboratory-confirmed measles patients as compared to non-severe cases. Variables included gender, age group, and occupational exposure risk (high: healthcare workers, students, teachers; intermediate: laborers, vendors, farmers; low: unemployed, dependents). Clinical factors included symptom-to-visit interval and symptoms. Univariable and multivariable logistic regression models were used to estimate an odds ratio (OR) with 95% confidence intervals (CI) for each variable in the model. Variables with p-value <0.2 were included in the multivariable model. Significance in the multivariable analysis was determined using the 95% CI. Analyses used R version 4.2.1.[13]

The effectiveness of outbreak response and control measures implemented by the Narathiwat EOC was assessed, focusing on school-based surveillance, vitamin A supplementation, ring vaccination, and the measles vaccination catch-up campaign.

School-based surveillance was implemented through symptom screening in kindergartens and primary school for early detection and isolation. Effectiveness was evaluated by comparing the number of schools reporting measles clusters, defined as two or more measles cases in the same class or with evidence of an epidemiological link in the same school within 14 days, before and after EOC activation.

Vitamin A supplementation was assessed by comparing the uptake rates, defined as the proportion of all cases receiving vitamin A, before and after EOC activation.

Ring vaccination targeted HRCs identified through contact tracing. The measles and rubella vaccine (MR) was administered to all HRCs, except that children aged under seven years received the MMR vaccine instead. Effectiveness was measured by the measles vaccine uptake rate within the MR or MMR vaccine among HRCs and the secondary infection rate, defined as the number of secondary cases divided by the total number of HRCs. A chi-square test compared proportions before and after EOC activation. Statistical significance was set at p-value <0.05.

The measles catch-up vaccination campaign was conducted in three phases to progressively increase cumulative vaccine coverage among approximately 63,519 unvaccinated children aged ≤12 years. Effectiveness was assessed using two indicators. First, phase-specific catch-up rates were calculated as the proportion of previously unvaccinated children receiving any measles vaccine in each phase of the campaign. Secondly, province-wide measles vaccination coverage was calculated by summing the number of children who received at least one dose of the measles vaccine before EOC activation (including routine MMR) and after EOC activation, including ring vaccination and the measles catch-up vaccination campaign (MMR or MR), then dividing by the total child population in Narathiwat Province.

Results

Outbreak Description in Narathiwat Province

The outbreak resulted in 2,710 measles cases: 1,273 suspected (47.0%), 364 epidemiologically linked (13.4%), and 1,073 confirmed (39.6%). The annual attack rate for measles in Narathiwat was 0.33%. The male-to-female ratio was 1.1:1. Children aged 9 months to 4 years accounted for the highest proportion (50.8%), followed by 5–9 years (22.7%), ≥10 years (17.4%), and <9 months (9.2%) (Table 1). Common symptoms included rash and fever (100%), cough (92.0%), coryza (83.2%), conjunctivitis (52.0%), diarrhea (50.4%), and Koplik's spots (7.5%). The median time from fever to rash was 3 days (IQR 1–4). Overall, 82.7% of cases were hospitalized, and 8.8% developed pneumonia. Pneumonia was most common in children aged 9 months–4 years (59.4%), followed by 5–9 years (18.4%) and <9 months (17.2%). Seven cases (0.3%) required mechanical ventilation. One neonatal death occurred despite IVIG administration (case fatality rate 0.04%). The mother had not received measles vaccination and was infected shortly before delivery.

Cases were distributed across multiple districts, highest in Rueso (420), Ra-ngae (371), and Bacho (360). Twenty school-based outbreaks were identified in kindergartens and primary schools. The epidemic curve peaked in September–October and declined by December. The EOC was activated on 3 Sep 2024, when weekly cases exceeded 162, and closed on 21 Jan 2025 (Figure 1). Laboratory testing confirmed the diagnoses. The IgM positive rate was 82.0% (998/1,217) and the RT-PCR positive rate was 83.2% (124/149).

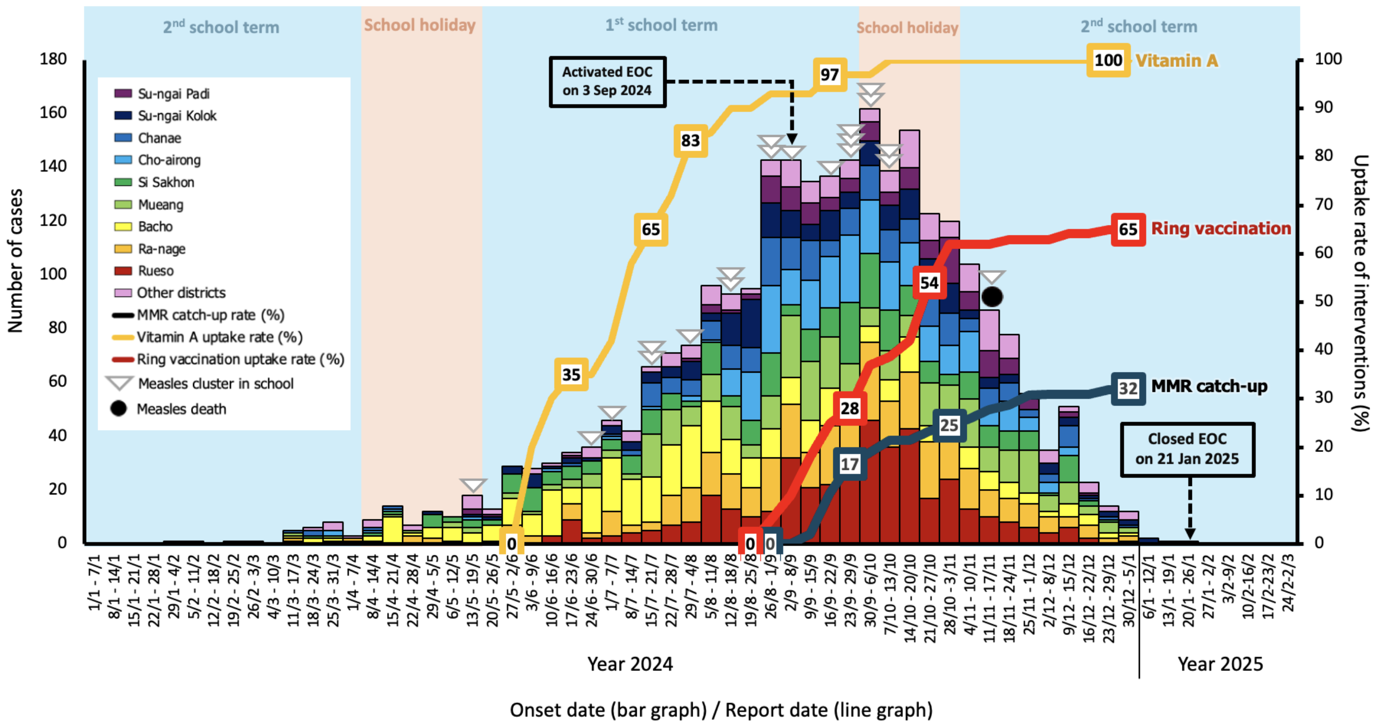

Figure 1. Weekly measles cases by district, school-based clusters, and uptake of key outbreak interventions in Narathiwat Province, Thailand, 2024–2025 (n=2,710)

Factors Associated with Measles Severity (Analytical Perspective)

Multivariable analysis showed female (adjusted OR 1.81; 95% CI 1.18–2.79), aged <9 months (adjusted OR 7.84; 95% CI 1.77–34.70), and having diarrhea (adjusted OR 2.29; 95% CI 1.47–3.60) were significantly associated with severe disease. Runny nose was not statistically significant (adjusted OR 1.25; 95% CI

0.64–2.44). Although the MMR vaccination status was not significant on multivariable analysis, individuals who were never vaccinated had a higher crude odds of severe disease (crude OR 1.82; 95% CI 0.97–3.40) compared to those with uncertain vaccination status (Table 1).

Table 1. Factors Associated with severe measles in Narathiwat Province, 2024–2025 (N=1,073)

Variables	Severe cases (n=100)	Non-severe cases (n=973)	Crude OR (95% CI)	Adjusted OR (95% CI)
Demographics				
Gender				
Female	58	456	1.56 (1.03–2.37)*	1.81 (1.18–2.79)
Male	42	517	Ref	
Age group				
<9 months	16	66	6.48 (2.10–20.23)*	7.84 (1.77–34.70)
9 months–4 years	55	497	2.96 (1.05–8.34)*	3.31 (0.83–13.25)
5–9 years	23	228	2.70 (0.91–8.00)*	2.93 (0.70–12.28)
10–14 years	2	75	0.71 (0.13–4.00)	0.84 (0.12–5.81)
≥15 years	4	107	Ref	
Risk factors				
Occupational exposure risk				
High	47	488	2.37 (0.73–7.83)*	1.10 (0.23–5.19)
Low	50	411	3.00 (0.91–9.88)*	4.28 (0.20–4.36)
Intermediate	3	74	Ref	
MMR vaccination status				
Never vaccinated	86	756	1.82 (0.97–3.40)*	1.01 (0.23–5.19)
MMR1 only	2	25	1.28 (0.27–6.05)	0.93 (0.20–4.36)
Uncertain	12	192	Ref	
Symptom onset to healthcare visit				
More than three days	75	676	1.32 (0.82–2.11)	
Within the first three days	25	297	Ref	
Associated signs and symptoms				
Cough				
Yes	97	922	1.79 (0.55–5.84)	
No	3	51	Ref	
Runny nose				
Yes	89	818	1.53 (0.81–2.94)*	1.25 (0.64–2.44)
No	11	155	Ref	
Conjunctivitis				
Yes	56	519	1.11 (0.74–1.69)	
No	44	454	Ref	
Diarrhea				
Yes	68	461	2.36 (1.52–3.66)*	2.29 (1.47–3.60)
No	32	512	Ref	

**Meeting selection criteria for multivariable analysis (p-value <0.2). OR: odds ratio. CI: confidence interval. MMR1: first dose of the measles, mumps, and rubella (MMR) vaccine.*

Outbreak Response and Control Measures

Following the activation of the Narathiwat EOC on 3 Sep 2024, targeted control measures were implemented to enhance surveillance, vaccination coverage, and outbreak containment.

School-based surveillance and control

School-based surveillance and isolation protocols were enhanced to enable early detection and containment of measles cases. Upon identification of a suspected case, teachers actively screened other symptomatic students through in-person checks or online surveys. Symptomatic students were hospitalized and isolated. Close contacts, including classmates and household members, were identified for ring vaccination. Students with fever or upper respiratory symptoms without rash were advised to remain at home for at least four days. Teachers conducted symptom screening in class for 42 days. This intervention reduced school-based transmission, with measles clusters decreasing from 19 to 1 school within 42 days post-intervention, covering two incubation periods (Figure 1).

Vitamin A supplementation

Vitamin A supplementation was provided to all cases regardless of laboratory confirmation, with priority given to children under five years of age, malnourished individuals, and those with signs of vitamin A deficiency. The dosage was based on age: 50,000 IU for infants under 6 months, 100,000 IU for those 6–12 months, and 200,000 IU for children aged 12 months or more. Two doses were given, one day apart. Daily monitoring ensured proper administration. The uptake rate increased rapidly from 0% to 90% within one month and reached 100% by October 2024 (Figure 1).

Ring vaccination

Ring vaccination was implemented for high-risk contacts of suspected measles cases in schools, workplaces, and households, regardless of vaccination history. The target was to administer the MMR or MR vaccine within 72 hours of exposure. District EOCs coordinated with local health teams to ensure timely vaccine deployment during case investigations. Coverage increased from 0% to 10% in September, 54% in October, and 65% by January 2025 (Figure 1). Secondary infection rates declined significantly from 2.0% (199/10,079 contacts) before EOC activation to 1.3% (262/19,798 exposures) after activation (χ^2 = 18.63, p-value <0.01).

Measles vaccination catch-up campaign

During the campaign, 20,454 children were vaccinated, representing 32.2% of the 63,519 targeted. Of these, 1,572 (7.7%) were preschool children, achieving 40.0% coverage in their group, and 18,882 (92.3%) were school-aged children (31.7% coverage). The campaign was conducted in three phases as shown in Figure 2.

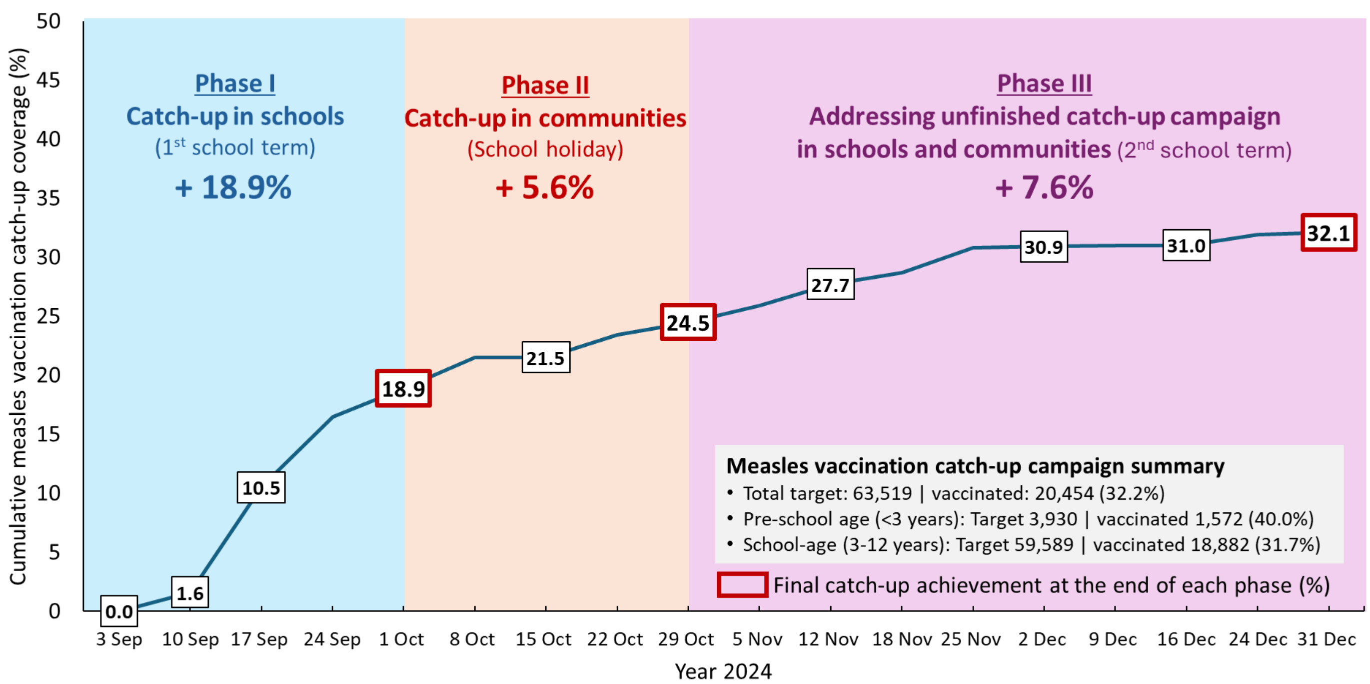

Figure 2. Phase-specific coverage during the measles vaccination catch-up campaign in the 2024 measles outbreak in Narathiwat Province

Phase I focused on school-based vaccination before the school break. A four-week plan began with communication via the LINE messaging application, which was already established in nearly all schools across Narathiwat. All pre-kindergarten and first-grade classes across the province had access to the application. Homeroom teachers played a key role by delivering all communication materials directly to parents. The materials were adapted from locally tested graphics developed under the Digital Results Improve Vaccine Equity and Demand (DRIVE Demand) project, piloted with caregivers in Rueso and Bacho districts. Messages, also translated into Malay, featured photo-based designs to build trust.[14] The Narathiwat EOC also released an official LINE message emphasizing measles severity and the importance of vaccination (Figure 3). Consent forms were then collected, and MMR or MR vaccines were administered based on the children's ages. Records were updated in health books and digital systems. By 1 October, coverage had increased by 18.9%.

Figure 3. LINE-based communication materials, adapted from locally tested graphics developed under the DRIVE Demand project, promoting during the measles vaccination catch-up campaign in the 2024–2025 measles outbreak response in Narathiwat Province

Phase II extended to communities during school holidays, prioritizing districts according to case burden. High-risk areas, such as Sri Sakhon and Rueso districts, aimed for 10% weekly increases, moderate-risk areas for 7%, and low-risk districts maintained one session per week. Sri Sakhon and Tak Bai districts met their targets, while others required more engagement. By 29 October, coverage rose by 5.6%, reaching 24.5%.

Phase III closed the remaining gap, adding 7.6% coverage to reach 32.1% by 31 December.

The province-wide measles vaccination coverage (at least one dose) rose from 48% (n=58,525) to 65% (n=78,979) among children aged under 12 years (n=121,966).

Discussion

The 2024 measles outbreak in Narathiwat revealed important epidemiological patterns. Infants and young children were most affected, with severe outcomes, particularly in those aged under 9 months. Despite school-based surveillance, ring vaccination, vitamin A supplementation, and a vaccination catch-up campaign, vaccination gaps persisted. These findings highlight underlying vulnerabilities and inform strategies for immunological risks, intervention effectiveness, and strategies to strengthen outbreak preparedness.

Infants are initially protected by maternally derived anti-measles IgG antibodies; however, immunity wanes after 6–9 months, as seen in this outbreak, where the highest incidence occurred in children aged 9 months to 4 years.[15] However, the highest risk of severe disease was seen in infants aged under 9 months (adjusted OR 7.84, 95% CI 1.77–34.70). These findings align with prior studies reporting higher infection rates in children under five years and increased severity in those under one year of age.[16,17] Possible explanations include immune immaturity, smaller airways, and weaker cough reflexes.[18] Female gender may act as a proxy for other unmeasured factors, while diarrhea could reflect disease progression or contribute to severity through dehydration. These associations should be interpreted with caution.

The only fatality in this outbreak occurred in a newborn whose mother was infected shortly before delivery, highlighting the risk of insufficient transplacental antibody transfer and direct transmission from mother to child.[19] The infant did not survive despite IVIG, emphasizing the need for alternative treatments. MMR vaccination at 6 months during outbreaks may offer short-term protection, but a second dose after 12 months remains necessary.[15,20] Vaccinating women of reproductive age before pregnancy ensures maternal immunity and antibody transfer to infants. Postpartum vaccination of susceptible women is also recommended. However, infants born to mothers with vaccine-derived immunity tend to have lower antibody levels than those with natural infection.[8,21] For unvaccinated pregnant women exposed to measles, serologic testing and IVIG therapy within six days are advised.[8] However, given its high cost (30,000–40,000 THB per case),[22,23] the cost-effectiveness of IVIG therapy must be considered in outbreak preparedness policies.

Vitamin A deficiency increases measles severity and mortality, particularly among children under the age of five years.[11,24–26] In Narathiwat, the prevalence of vitamin A deficiency was 25.6% in 2019, exceeding the WHO threshold of 20%.[27,28] During the 2018–2019 outbreak, the case fatality rate was 0.92%, higher than the national average of 0.56%.[27,29,30] In response to the 2024 outbreak, vitamin A supplementation was provided to all suspected cases, prioritizing malnourished and vitamin A-deficient children.[31] The uptake rate reached 100% by October 2024. This contributed to a reduced mortality compared to the 2018 outbreak. However, at least two doses are needed to significantly reduce measles mortality.[32] While vitamin A is critical in case management, vaccination remains the most effective preventive strategy.

School-based catch-up vaccination is effective during measles outbreaks, especially in high-density classrooms. A four-week campaign in Narathiwat increased the coverage by 18.9%, with teachers playing a key role in communication and parental engagement, reducing school-based outbreaks within 35 days. These findings align with studies from Germany showing that vaccination within 6–14 days can prevent large outbreaks.[33] However, evidence suggests that school-entry vaccination verification remains the most effective preventive strategy, as reactive campaigns are costly and have limited benefits.[34,35] Teachers can contribute to vaccine acceptance by addressing hesitancy and delivering consistent messages.[36] Nonetheless, lack of knowledge among teachers regarding vaccine types, side effects, and preventable diseases limits their effectiveness.[37] Capacity-building for school nurses, parents, and teachers is essential for the long-term success of school-based vaccination programs.[38]

Limitations

Clinical information was collected only during the initial hospital visit or first contact with field investigators without any follow-up on symptom progression or later complications such as pneumonia or otitis media. The EOC online report lacked data on height, weight, and signs of vitamin A deficiency, limiting the assessment of baseline nutritional status and its association with severe illness. Finally, this was an observational study; therefore, causal inferences between interventions and outcomes cannot be established.

Recommendations

Prioritize Early MMR Vaccination

According to the national EPI, MMR1 is recommended at 9 months and MMR2 at 18 months. Based on our findings, we recommend administering an early first dose before 9 months for high-risk infants to ensure timely protection against measles.

Address Vaccine Hesitancy Through Trusted Community Engagement

Strengthen outreach efforts by involving respected local leaders, religious authorities, and healthcare professionals to promote vaccine acceptance, particularly in populations concerned about halal compliance and other cultural considerations.

Enhance School-based Surveillance and Vaccination

Empower teachers and school administrators as frontline advocates for immunization. Their active role in symptom screening, parent engagement, and health education has proven effective in reducing school-based outbreaks and improving vaccination coverage.

Maintain Vitamin A Supplementation during Outbreaks

Continue supplementation, especially in provinces with high deficiency rates, to mitigate complications and reduce mortality associated with measles.

Long-term Strategy

Implement catch-up vaccination campaigns as early as possible and develop communication tools to address parents' concerns and vaccine hesitancy. Focus on school-based vaccination, with teachers promoting immunization.

Conclusion

This study described the measles outbreak in Narathiwat Province from 2024 to 2025, identified factors associated with severe disease, and assessed the effectiveness of key control measures. Most cases occurred in children aged 9 months to 4 years, with infants under 9 months most affected by severe illness. Being female and having diarrhea were significant risk factors of severe illness, leading to longer hospital stays, increased need for medical resources, and higher mortality risk. The response, coordinated by the Emergency Operations Center (EOC), helped reduce transmission through early detection, ring vaccination, and vitamin A supplementation. The measles vaccination catch-up campaign increased coverage from 47.9 to 65.0%, highlighting the value of school and community-based strategies. Ongoing challenges such as vaccine hesitancy and operational gaps underscore the need for sustained, community-driven efforts to improve immunization in low-coverage areas.

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Author Contributions

Farooq Phiriyasart: Conceptualization, methodology, formal analysis, writing—original draft, writing—review & editing, supervision, project administration. **Ahamud Seerako:** Investigation, resources. **Tharathip Suksridaeng:** Resources, investigation. **Rusmanira Khwankerd:** Data curation, writing—review & editing. **Sasikarn Nihok:** Data curation, visualization. **Nungrutai Ninlakan:** Resources, data validation. **Peerawan Cheewaiya:** Investigation, writing—review & editing. **Noreeda Waeyusoh:** Resources, data support. **Ekawit Jindapet:** Supervision, writing—review & editing. **Adul Binyusoh:** Supervision, resources, writing—review & editing.

Ethical Approval

Ethical clearance was waived as this investigation was conducted under Narathiwat EOC outbreak management. Data collection was part of the investigation, with participants informed of the study objectives and benefits beforehand. Responses were recorded on forms without audio, ensuring anonymity by excluding full names and addresses. All documents are securely stored and accessible only to the principal investigator.

Informed Consent

Not applicable. This study used fully de-identified secondary data obtained from routine outbreak surveillance and reporting systems. No identifiable personal information was collected or used, and the data cannot be linked back to individual participants.

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 permission from the Narathiwat Provincial Public Health Office.

Conflicts of Interest

The authors declare 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 improve 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 version.

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Drunk Driving, Sleep Deprivation, Unsafe Vehicle, and Poor Road Design: Converging Hazards in a Road Traffic Crash in Sukhothai Province, Thailand, 2025

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Abstract

Road traffic injuries are a leading cause of death globally, with alcohol impairment increasing the risk of an accident. At 7:10 AM on 10 Feb 2025, a pickup truck rear-ended a passenger vehicle carrying students in Sukhothai, Thailand. This study aimed to identify factors associated with the crash and recommend preventive measures. Data were collected through medical record reviews, site surveys, interviews with witnesses and stakeholders, and a joint agency meeting. Haddon's Matrix guided the analysis. All 20 occupants (2 drivers, 18 students) sustained injuries, with one case requiring admission for eyelid laceration. The weather was clear, the road was dry, and both drivers were experienced. Pre-crash risks included driver intoxication (blood alcohol concentration of 133 mg/dL) and drowsiness, the use of a modified passenger vehicle with unsafe seating and no seatbelts, and an inadequate road design, specifically a sudden lane reduction and a sub-standard U-turn constructed at villagers' request. Crash-phase risks included speeding, an abrupt lane change, and a steep roadside with a narrow (30 cm) shoulder, which caused the passenger vehicle to overturn. Post-crash issues included a lack of initial scene management, resulting in poor crowd control. This incident illustrates how alcohol impairment, an unsafe passenger vehicle, poor road design, and emergency response gaps contributed to the crash severity. The investigation led to policy actions, including U-turn closures, school transport vehicle reforms, and improved emergency medical services training. The value of field investigations in turning real-world crashes into targeted, system-level prevention strategies is underscored.

Keywords: pickup truck, alcohol, microsleep, school truck, Thailand

Introduction

Road traffic injuries (RTIs) are the leading cause of death globally, with 1.2 million deaths annually.[1] In 2023, Thailand ranked first in ASEAN in RTI mortality.[1] In 2022, the disability-adjusted life years lost was 1.35 million among males and 0.49 million among females.[2] Although the national RTI mortality rate declined from 34.3 to 26.9 per 100,000 population between 2011 and 2023, it remains more than twice the national target of 12 per 100,000.[2,3]

Pickup trucks accounted for the highest proportion of RTIs by vehicle type in 2023, comprising 36.1% of reported cases with eight of the top ten causes of RTI are driver-related.[4] Drunk driving remains a major contributor to RTIs.[1] In Thailand, 2025 injury surveillance data indicated that 16.8% of RTIs were alcohol-related.[5] National surveys from 2007 to 2017 showed a rise in binge drinking among current drinkers from 17.3% to 42.8%.[6] Alcohol impairs reaction time and increases lane deviation and risk-taking behaviors such as speeding and heightened vulnerability to drowsy driving.[7–9]

On 10 Feb 2025, in Sukhothai Province, Thailand, a pickup truck rear-ended a modified passenger vehicle, resulting in one severe and 19 minor injuries. This event met Thailand's RTI investigation criteria according to the Ministry of Public Health (updated on 13 Sep 2024). Accordingly, a joint investigation team (JIT) investigated the event on 14 Feb 2025, aiming to describe the characteristics of the event, identify risk factors, and provide recommendations for future prevention.

Methods

Study Design

This descriptive study outlined the accident site and surrounding healthcare facilities, provided details of the event, characterized the injuries sustained, and described the rescue timeline and management. Additionally, road, environmental, and vehicle assessments were conducted.

Data on the number of accident victims and injury cases, driver behavior, blood alcohol levels, passenger seating arrangements, seatbelt availability and use, date of tax expiration and inspection of the vehicle, and driving licenses of the drivers, were obtained from a stakeholder meeting of the Road Safety Operations Center Committee, Sukhothai Province. Participating agencies included the Office of Disease Prevention and Control Region 2 Phitsanulok, the Sukhothai Provincial Public Health Office, Department of Disaster Prevention and Mitigation, Provincial Transport Office, Sukhothai Highway Department, the Primary and Secondary Educational Service Area Offices, Sukhothai Provincial Education Office, Ban Dan Lan Hoi Hospital, Ban Dan Lan Hoi Police Station, the Office of Insurance Commission, and an insurance agency in Pak Khwae Subdistrict. Additional insights into drivers' and passengers' behavior and barriers to rescue operations were obtained through interviews with drivers and nursing staff. A case was defined as an individual who sustained a physical injury during this event. The review of case triage was based on the Modified National Triage Algorithm.[10]

Medical records from Ban Dan Lan Hoi Hospital were reviewed to collect data on injury characteristics. Details of emergency medical management, including the type of rescue team, receiving hospitals, and timelines, were documented. The prehospital time frame provided by Thailand's National Institute for Emergency Medicine included: (1) dispatch time: time between emergency call receipt from the Emergency Medical Services Command and Control Center, also known as the 1669 hotline, to dispatch decision, (2) activation time: time from call receipt to Emergency Medical Services (EMS) being dispatched, (3) response time: time from call receipt to scene arrival, (4) on-scene time: time from arrival to departure, and (5) transfer time: time from scene departure to hospital arrival.[11,12]

The JIT surveyed the collision site for road type, number of lanes, structural features, traffic direction, roadside objects, surrounding terrain, and the presence of tire marks at the scene. Information on previous accidents was obtained from the stakeholder meeting, Thailand Road Accidents Data Centre for Road Safety Culture (ThaiRSC) database, and interviews with villagers. Environmental factors, such as weather conditions and lighting during the incident, were gathered through interviews with drivers and bystanders.

Haddon's matrix was used to classify risk factors across human, vehicle, road, and environment during pre-crash, crash, and post-crash periods.[13] The consensus of the JIT determined each factor.

Results

Accident Site and Surrounding Healthcare Facilities

The accident occurred at 7:10 AM on 10 Feb 2025, on Jarod Withee Thong Road (Highway No. 12, Tak–Sukhothai route) between km 132+250 and km 133. The pickup truck (index vehicle) had traveled 57 km from Tak toward Sukhothai (Figure 1A). The nearby facilities include Ban Dan Lan Hoi Hospital, a 30-bed community hospital, located approximately 15 km from the accident site and Sukhothai Hospital, a 300-bed general hospital 27 km away. According to ThaiRSC, two incidents were reported at the same general location in 2022 and three in 2023, involving a total of eight individuals (two deaths and six injuries).

Event Description and Drivers' Behaviors

The collision diagram illustrated a northeast-bound passenger vehicle was traveling at approximately 50–70 km/h in the left-hand lane (Figure 1B). As the vehicle approached a temple, the driver reduced speed, intending to turn into the temple's driveway to pick up more students. A pickup truck, travelling in the same direction but in the right-hand lane, at an estimated speed of 100–120 km/h, made a sudden lane change to avoid traffic poles and subsequently made a rear-end collision with the passenger vehicle. The passenger vehicle then overturned and rolled into a roadside ditch.

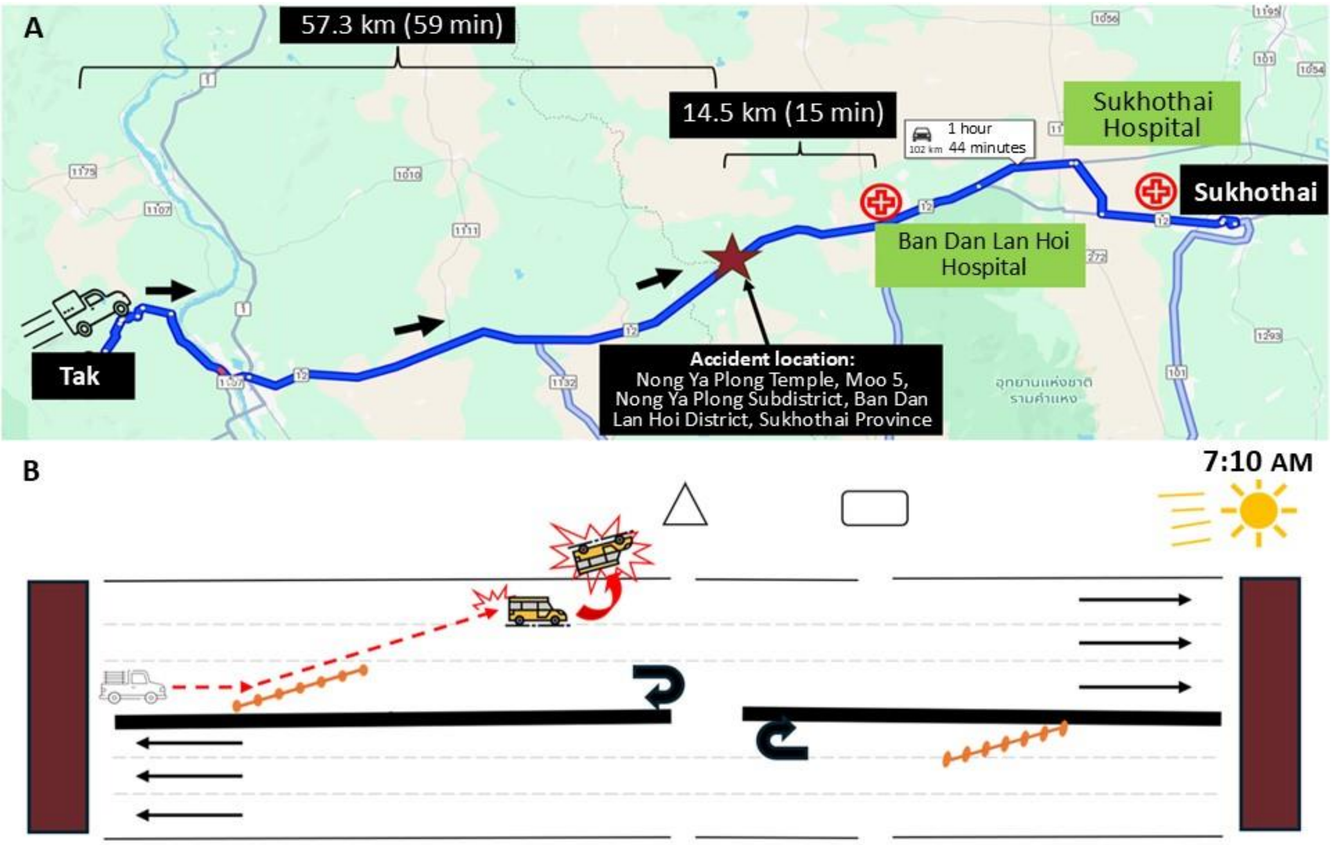

Figure 1. (A) Map showing the pickup truck's route from departure (Tak Province) to destination (Sukhothai Province), the accident location, and the nearest hospital for the road traffic accident in Sukhothai Province on 10 Feb 2025. (B) A collision diagram illustrating the pickup truck rear-ending the school transport vehicle. The red dashed arrow indicates the path of the pickup truck as it abruptly moved to the left lane to avoid traffic poles.

Both drivers held valid licenses, and were familiar with the route (Table 1). The pickup truck driver had been driving for about one hour without a break. A breathalyzer test revealed a blood alcohol level of 133 mg/dL. No alcohol was detected in the passenger vehicle driver.

The pickup driver is a social drinker and has no history of traffic accidents. Before the event, he attended a work dinner party in Tak province that began at around 7:00 PM. He consumed at least two large bottles of beer before midnight. He continued drinking beer with his colleagues until approximately 4:00 AM. He had only one to two hours of sleep before the incident.

Characteristics of Injuries

Twenty individuals sustained injuries from the crash. The pickup truck driver, a 31-year-old male, sustained a minor superficial thoracic injury. The passenger vehicle driver, a 39-year-old male, sustained a superficial injury to his right elbow. Among the 18 passengers, 6 were male and 12 were female, and the median age was 14.5 years (range 13–18 years). Nine (50%) were categorized as urgent. Of the nine urgent cases, two had puncture wounds, one had a laceration, and two had abrasions; the remaining four reported only pain. Among the non-urgent cases, four had abrasions, with no puncture wounds or lacerations reported. One was referred to Sukhothai Hospital due to a laceration wound to the right upper eyelid with suspected involvement of the lacrimal duct and levator muscle, with a closed nasal bone fracture, requiring ophthalmologist evaluation.

The passenger vehicle had been modified to include a third row of seats. This additional row lacked both seatbelts and handrails, features not permitted. The passenger who was admitted to hospital was seated in row 2, position 3 (Figure 2). The proportion of urgent cases was highest in rows 1 and 2 (67%; 2/3 and 4/6, respectively). The distribution of injury locations revealed the highest proportion of injuries to extremities (41%), followed by external body surface (26%), and head and neck (15%) (Supplementary Figure 1).

Table 1. Driver behavior and related factors in a road traffic accident in Sukhothai Province, Thailand, on 10 Feb 2025

Variable	Pickup driver	Passenger vehicle driver
Driver details	Male, 31 years old. No underlying diseases.	Male, 39 years old. No underlying diseases.
License & experience	• Held a Type 3 driver's license (issued in 2019) with over 5 years of driving experience. • Familiar with this route, due to his job.	• Held a Type 2 driver's license (issued in 2018) with over 5 years of driving experience. • Familiar with this route.
Occupation	Deliveryman for agricultural products	Driver and general employee at a school
Driving behavior	• Drove at approximately 100–120 km/h. • Wore a seatbelt.	• Drove at approximately 50–70 km/h. • Did not wear a seatbelt.
Incident details	• Drove for approximately one hour without a break, departing around 6:00 AM. • Changed lane suddenly before the accident and suspected drowsiness. • Attempted to avoid traffic poles, which were installed to narrow the lane and slow down vehicles before a U-turn area near Nong Ya Plong Temple. • Drank yogurt immediately after the crash.	• Departed home in Nong Ya Plong Subdistrict, Ban Dan Lan Hoi District around 6:00 AM. • Traveled from Nong Ya Plong Subdistrict to Ban Dan Lan Hoi Kindergarten and Ban Dan Lan Hoi Wittaya School. • Turning near the entrance of Nong Ya Plong Temple, approximately 500–700 meters from the crash site, to pick up more students from the village behind the temple. • At the time of the accident, 18 students were on board. The vehicle can carry up to 30 passengers.
Alcohol test	Post-accident breathalyzer test showed a blood alcohol content of 133 mg/dL (converted).	No alcohol detected on breathalyzer test.

Road and Surrounding Environment

The road at the incident site is a straight, asphalt-paved four-lane highway with a recently constructed (June 2024) concrete barrier median installed to prevent cross-lane collisions (Figure 3). Approximately one month after construction, villagers requested that a U-turn be created near the entrance to the temple. During the incident, road conditions were dry with clear lane markings and no visual obstructions. The roadside included a dry ditch situated below road level. Visibility was adequate in the morning. The pickup truck driver reported mild sun glare; however, it did not impair his visibility of other vehicles, traffic lane markers, or traffic poles. Warning signs and speed limit indicators were small and placed only after the U-turn, with none located within 100 meters before the U-turn. Specifically, four deviations from the GD-402 guideline specified by the Department of Highways, Thailand, for U-turns at a median barrier were identified: absence of a road shoulder, insufficient width (<3.5 meters) of yellow cross-hatchings, lack of post-U-turn cross-hatchings, and lack of pre-U-turn warning signs (Supplementary Figure 2).[14]

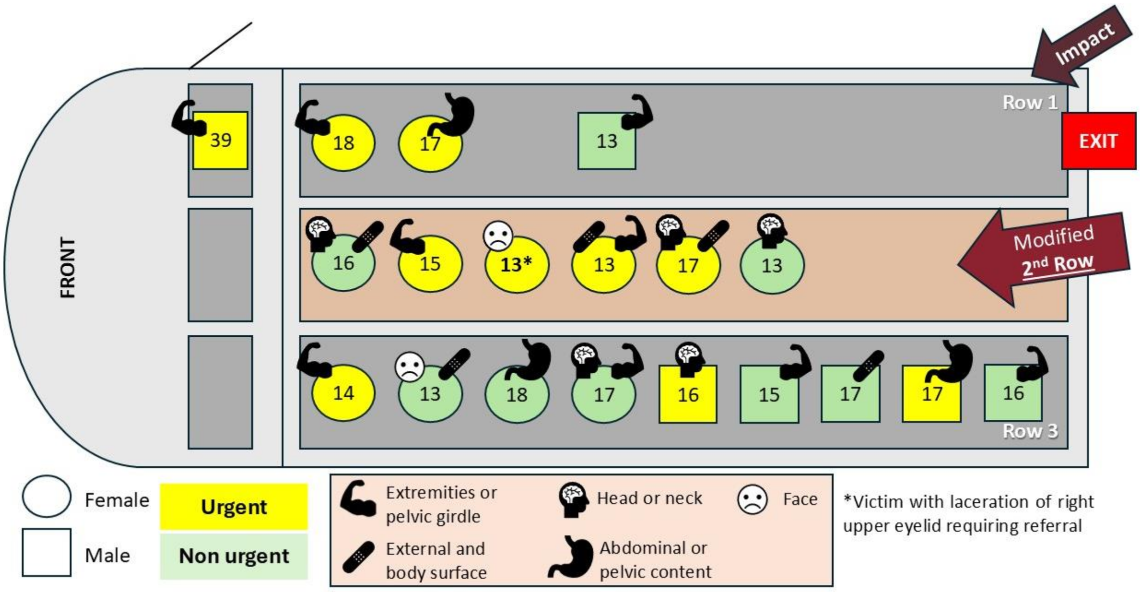

Figure 2. Seating arrangement in the passenger vehicle and corresponding injury characteristics of the road traffic accident in Sukhothai Province on 10 Feb 2025. The numbers within each shape denote the passenger's ages.

Figure 3. Images of the accident site on Jarod Withee Thong Road (Highway No. 12, Tak–Sukhothai route) between km 132+250 and km 133, in front of Nong Ya Plong Temple. (A) Google Earth image showing the previous road layout with no median barrier and only two lanes each way. (B) Photo taken on February 14, 2025, showing the newly constructed median barrier and approach containing orange traffic poles leading up to the U-turn bay, expanding the road to three lanes. (C) Image highlighting narrow yellow cross-hatching and unclear warning signs. (D, E) Photos taken on the day of the accident (10 Feb 2025) showing adequate visibility, visible tire marks from the passenger vehicle (upended), and a narrow road shoulder.

Vehicle Assessments

The pickup truck was a two-door truck with a modified metal cargo frame registered as a private passenger vehicle under the Motor Vehicle Act. It was covered by compulsory insurance through ERGO Insurance (18 Apr 2024–18 Apr 2025); no voluntary insurance was found with a recent inspection in April 2024. Post-crash inspection revealed front-end collapse on the passenger side, a detached grille, an open hood, and misaligned wheels, with greater damage on the passenger side (Figures 4A and 4B).

The modified passenger vehicle was a six-wheel vehicle registered for public transport use. It was covered by compulsory insurance from Viriyah Insurance (31 Dec 2024–31 Dec 2025), with no voluntary insurance. The vehicle featured reinforced steel framing, three rows of metal-framed bench seats fixed to the body, and no seat belts. Each row could accommodate approximately 10 passengers. The vehicle passed its most recent inspection in December 2024. However, the third row of seats had been removed prior to the inspection and was reinstalled afterward. Post-crash damage included a collapsed roof on the driver's side, a crushed driver's door, and a detached seat from the metal frame (Figures 4C and 4D).

Figure 4. Post-crash images of the pickup truck and passenger vehicle. (A) Front view of the pickup truck; (B) side view of the pickup truck; (C) side view of the passenger vehicle; and (D) rear view of the passenger vehicle.

Rescue Timeline, Management and Barriers

The incident occurred at approximately 7:10 AM and was reported to the police by a bystander. At 7:17 AM, the Emergency Room at Ban Dan Lan Hoi Hospital received notification from the EMS command center. An advanced life support vehicle was dispatched at 7:20 AM (activation time: 3 minutes). Concurrently, the EMS nurse requested support from the subdistrict administrative organization and coordinated traffic control with the police. Both EMS teams arrived at the scene by 7:28 AM. The first urgent case arrived at the hospital at 7:35 AM (Figure 5). Although the dispatch time was only one minute, an additional two minutes were required to collect complete incident details before deployment (Table 2).

Table 2. Time frame for Emergency medical services at a road traffic accident in Sukhothai Province on 10 Feb 2025

Time elements	Actual duration (minutes)	Standard time* (minutes)
Dispatch time	1	1
Activation time	3	2
Response time	11	8
Scene time	2	10
Transfer time	8	-
Total time	**24**	

**According to Provincial Emergency Medical Services Performance Scoring Index, 2023*

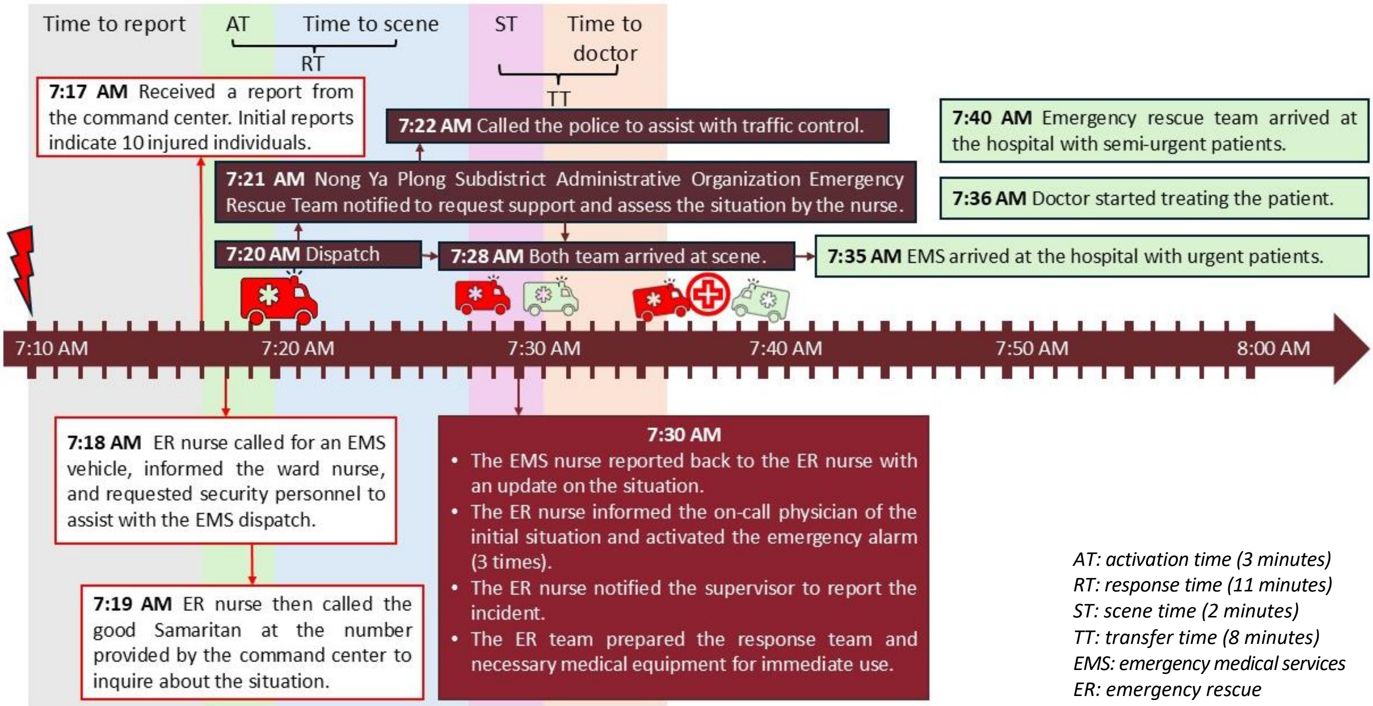

Figure 5. Emergency medical services (EMS) timeline, including notification, rescue process, and time frame, based on the 2023 Provincial EMS Performance Scoring Index (PEPSI), for the road traffic accident in Sukhothai Province on 10 Feb 2025

Pre-hospital care at the accident site faced several challenges, including the absence of initial scene management due to the EMS team's lack of confidence and an unclear command structure. This led to no formal scene safety assessment or traffic control, despite a recent rescue training workshop in January 2025. Crowd control was limited by an insufficient number of authorities at the scene, the large size of the crowd, and the restless behavior of bystanders. Additionally, some victims' relatives moved injured individuals before the EMS arrived. The lack of designated triage zones hindered accurate casualty assessment. Pre-arranged support from the Nong Ya Plong Subdistrict Administrative Organization EMS enabled the timely transfer of patients to the hospital.

Possible Risk Factors

Haddon's matrix is shown in Table 3. The primary pre-crash human factor was attributed to the pickup truck driver intoxication and a lack of sleep following a work-related social event, resulting in drowsiness, possible speeding, and a delayed response to road traffic poles. Road-related risks included inappropriate placement of warning and speed limit signs, narrow road shoulder, and narrow yellow cross-hatchings. The modified passenger vehicle also posed safety concerns due to non-standard seating configurations. Post-crash, the absence of a confident leader from the EMS team contributed to insufficient scene safety management and crowd control.

Table 3. Haddon's matrix model to assess risk in a road traffic accident in Sukhothai Province, Thailand, on 10 Feb 2025

Period	Human	Vehicle	Environment
Pre-crash	• Both drivers have adequate driving experience. • Pickup truck driver: ▪ Consumed alcohol (breathalyzer: 133 mg/dL). ▪ Drove at high speed. ▪ Experienced drowsiness or microsleep. ▪ Slept 1-2 hours before driving.	• Passenger vehicle: ▪ Did not meet school transport vehicle safety standards. ▪ Roof frame was modified from wood to metal.	• Downhill slope. • Modified U-turn near temple entrance for local access, causing lane narrowing. • Lane reduction from three to two lanes with markings and flexible traffic posts. • Absence of speed limit signs. • No road shoulder. • Insufficient width of yellow cross-hatching.
Crash	• Pickup truck driver: ▪ Changed lanes suddenly. ▪ Attempted to avoid traffic poles. • Passenger vehicle driver: ▪ Did not wear a seatbelt.	• Passenger vehicle: ▪ Lacked backrests and handholds in the second row. ▪ No fitted seatbelts.	• Passenger vehicle overturned into a 1-meter-deep roadside ditch (~60° incline). • Mild sun glare was present but did not impair the pickup truck driver's visibility.
Post-crash	• No formal scene safety assessment. • Delayed traffic control, increasing risk of secondary accidents. • Faced poor crowd control due to large number of bystanders and presence of concerned relatives. • Moved injured individuals before EMS arrived, limiting injury assessment. • Lacked knowledge of how to activate an EMS call. • No compensation due to lack of voluntary insurance.	• The roof of the passenger vehicle collapsed on the driver's side.	• The road surface was elevated by approximately 1 meter above the roadside with a 60-degree incline, hampering rescue efforts.

EMS: emergency medical services.

Action Taken

A stakeholders meeting was convened to assess risks, implement preventive measures, and guide further investigations. A centralized and standardized system for school transport vehicles was established through collaboration among the Primary and Secondary Educational Service Area Offices of Sukhothai, the Sukhothai Provincial Education Office, and the Provincial Transport Office. This system includes random inspections to identify unfit drivers and non-compliant vehicles, particularly those with unauthorized seat modifications. A social network-based communication platform was established to facilitate reporting of any misconduct, enabling direct communication between authorities and parents. Ban Dan Lan Hoi Hospital was recommended to strengthen emergency response training, emphasizing team leader roles and preparedness of all members.

As of 1 Apr 2025, the traffic in front of Nong Ya Plong Temple has been monitored. Two minor motorcycle accidents occurred, attributed solely to human factors. Recommended road changes—warning signs, speed limits, and median barrier closure—are under consideration by the Department of Highways and expected to be implemented in the next fiscal year.

Discussion

This event demonstrates how several risk factors converged and subsequently led to RTIs, resulting in numerous casualties. The combination of the risk factors makes this study unique compared to many previous studies on RTIs, which have typically identified only a single or a few risk factors.[11,15–17]

The pickup driver's intoxication and sleep deprivation were key contributing factors in this incident. Drunk driving is a leading cause of RTIs on Thai highways, with the risk of fatal crashes increasing notably at blood alcohol concentrations above 50 mg/dL.[4,18] A national survey reported that 40% of respondents had driven under the influence in the past year, particularly during special occasions, consistent with the present case.[6,19] However, evidence suggests that drunk driving is less prevalent in Bangkok, likely due to greater public awareness, stricter law enforcement, and better access to public transportation options.[6,20]

The passenger vehicle, registered as a public transport vehicle, violated several school transportation safety regulations. It lacked the required large orange "school vehicle" sticker and absence of handholds and seatbelts in the modified middle row. These omissions compromise passenger safety, as both handholds and seatbelts are proven to reduce injury severity.[21] In 2021, 51%–61% of U.S. crash fatalities among teens and adults involved unrestrained passengers.[22] Nevertheless, standard seatbelts may offer limited protection in non-conventional seating arrangements, such as rear- or side-facing seats.[23] A previous case in Khon Kaen Province linked modified seating in a passenger van with a side-facing position to increased injury risk.[15]

In this incident, although the modified passenger vehicle overturned, neither the driver nor the passengers sustained life-threatening injuries. This outcome may be attributed to several factors. First, the reported speed of the pickup truck by the bystanders may have been exaggerated.[24] Second, the passengers were primarily teenagers, a group generally at lower risk of severe injury compared to young children or the elderly.[25] Finally, the modified passenger vehicle had reinforced steel framing, which likely prevented the roof from collapsing.

At the request of local villagers, a new median barrier was installed at the section of road near Nong Ya Plong Temple, followed by a lane reduction. However, the abrupt lane reduction and absence of adequate warning signs or speed limits posed a significant safety risk. Abrupt lane changes have been linked to increased crash risk, contributing to 33% of all road collisions in the U.S.[26,27] Consistent with the present study, inadequate signage and speed control measures are well-documented environmental factors contributing to RTIs.[28]

The steep roadside and narrow shoulder likely contributed to the increased risk and severity of the incident. Although most of the affected could walk unaided, the terrain posed challenges for rescuers during their extraction from the damaged vehicle. Narrow shoulders limit vehicle recovery space, reduce lateral clearance, and increase the risk of run-off-road crashes and abrupt maneuvers.[29,30] Studies show that broader road shoulders, up to 2.7 meters, significantly reduce crash severity, while paved shoulders of 0.9–1.2 meters are cost-effective for rural roads.[30,31]

Post-crash challenges included the absence of an initial scene management. Although EMS personnel are trained to be incident commanders, the position was not effectively assumed in this event due to a lack of confidence by the team leader and an unclear command structure. The lack of scene control increases the risk of secondary crashes and interference by untrained bystanders, potentially worsening injuries.[32] Public education on road safety and appropriate bystander behavior can help mitigate such risks.[33] Moreover, while police often act as first responders, a survey in Northeastern Thailand found that only 56% of traffic police had comprehensive emergency medical training, potentially delaying effective care.[32]

Limitations

To avoid potential psychological distress, the injured students were not interviewed. Instead, their behavioral information was obtained from the driver of the passenger vehicle and two nursing staff. The scene survey occurred four days after the accident, which prevented an accurate assessment of real-time conditions, and no CCTV or dashcam footage was available. Although a stakeholder meeting provided helpful information, speed and collision analysis was limited by the absence of mechanical or traffic engineering expertise.

Recommendations

The Provincial Transport Office should enforce school vehicle registrations, seatbelt use, passenger limits, and driver licenses, and conduct random inspections in collaboration with schools and police. Inspections should specifically verify seat configurations, as the addition of a third row, found in this case, may violate regulations. The Department of Highways should review the U-turn area for compliance with GD-402. Ban Dan Lan Hoi Hospital should regularly conduct mass casualty drills focusing on the command structure. For a long-term plan, schools should formalize agreements with transportation operators to ensure that they use appropriately licensed vehicles and establish channels for parents to report any unsafe behavior. Public campaigns should raise awareness of appropriate bystander roles in trauma situations. Lastly, employers should end celebratory events before midnight, limit alcohol consumption, and screen drivers for fitness before duty. Moreover, this case also highlights the need for other jurisdictions to proactively assess their highways for hazardous road designs.

Conclusion

This investigation of a road traffic injury in Sukhothai, involving a pickup truck rear-ending a modified passenger vehicle, resulted in 20 injuries, one severe and 19 minor. The primary cause was driver intoxication and drowsiness following a celebratory event by a typically non-drinker. Contributing modifiable risks included an unsafe school transport vehicle, poor road infrastructure, and the absence of initial scene management. Preventing similar incidents requires coordinated efforts across sectors, including monitoring driver fitness, enforcing school vehicle regulations, improving road safety features, and enhancing RTI training for healthcare and law enforcement personnel.

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Author Contributions

Sethapong Lertsakulbunlue: Conceptualization, data curation, formal analysis, methodology, project administration, validation, visualization, writing—original draft, writing—review & editing. **Sirirat Tunsawai:** Conceptualization, data curation, validation. **Chatuphon Sanseela:** Conceptualization, data curation, validation. **Rungnapa Kamkhae:** Conceptualization, data curation, validation. **Rapeepong Suphanchaimat:** Methodology, resources, supervision, validation, writing—review & editing. **Peeriya Watakulsin:** Conceptualization, resources, supervision, validation. **Pitiphon Promduangsi:** Conceptualization, resources, supervision, validation, writing—review & editing.

Ethical Approval

This study was a part of routine investigation and response activities of the Thai Department of Disease Control, Ministry of Public Health. Ethics approval was not required.

Informed Consent

Not applicable. This study used fully de-identified secondary data obtained from routine outbreak surveillance and reporting systems. No identifiable personal information was collected or used, and the data cannot be linked back to individual participants.

Data Availability

The datasets used and/or analyzed in this study are available from the author on reasonable request (via Sethapong.ler@pcm.ac.th).

Conflicts of Interest

The authors declare no conflicts of interest.

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We utilized ChatGPT-4.0 to assist with grammar editing of the manuscript; however, the authors remain fully responsible for the accuracy and integrity of the content.

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Performance of the Severe Acute Respiratory Infection (SARI) Surveillance System: A Case Study of Chey Chumneas Hospital, Kandal Province, Cambodia, 2022

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Abstract

Cambodia's Severe Acute Respiratory Infection (SARI) surveillance system was established in 2012. The system monitors SARI cases, detects outbreaks, and identifies influenza trends. However, the system has not undergone evaluation since its inception. This evaluation aimed to assess surveillance attributes at Chey Chumneas Hospital, Kandal Province. A mixed-methods approach was utilized, following US-CDC guidelines. Medical records in 2022 were reviewed to assess sensitivity and positive predictive value (PPV). Case reporting forms were reviewed to determine completeness. The timeliness of weekly reports in the system and the release of laboratory results were evaluated. Semi-structured interviews with key stakeholders were used to assess qualitative attributes. Between 2018 and 2022, 576 SARI cases were reported. The sensitivity in detecting true SARI cases among admitted patients was 33%, and the PPV was 73%. In 2022, 54% (28/52 weeks) of weekly reports were submitted on time, and 59% (52/88) of SARI cases had laboratory results released within 24 hours. Of 88 case reporting forms, 91% of socio-demographic and date of onset variables were complete, and three SARI symptom variables had a completion of 95%. The system was positive in terms of usefulness, simplicity, acceptability, and flexibility, but stability was relatively weak due to dependence on external funding. The system was useful in estimating morbidity and mortality and monitoring influenza trends. Although its performance was good, gaps in sensitivity, timeliness, and stability remained. Targeted training, supervision for the hospital SARI focal point, and sustained financial support are needed to improve the surveillance system's performance.

Keywords: Cambodia, evaluation, SARI surveillance, attribute

Introduction

Public health surveillance involves the continuous collection, analysis, and interpretation of data to guide public health actions.[1] It is crucial for monitoring infectious diseases and informing prevention and control efforts.[2,3] Global influenza surveillance has been conducted through the World Health Organization (WHO) Global Influenza Surveillance and Response System (GISRS) since 1952.[4] Most countries have a well-established weekly near-real-time surveillance system for influenza-like illness (ILI) and acute respiratory infections (ARIs) in primary care, which are reported weekly.[2] In the past century, four pandemics emerged from new influenza strains: the 1918 Spanish flu, 1957 Asian flu, 1968 Hong Kong flu, and 2009 swine flu.[5] The WHO recommended establishing national severe acute respiratory infection (SARI) surveillance systems to assess epidemic severity and enable early detection of potential epidemics and pandemics.[2,6]

In 2009, the Department of Communicable Disease Control, Ministry of Health (CDC-MOH), Cambodia established sentinel SARI surveillance at nine hospitals: three sites in the national hospital in Phnom Penh and one site in each of the following provinces—Siem Reap, Takeo, Svay Rieng, Kampong Cham, Kampot, and Kandal. Once patients are identified as having SARI based on case definitions, nasopharyngeal samples are collected and transported to the National Institute of Public Health (NIPH) laboratory in Phnom Penh for influenza virus testing. The system's primary goal is to monitor influenza in humans and detect outbreaks of novel influenza strains.[7]

The SARI surveillance system in Chey Chumneas Hospital (CCH) has not undergone formal evaluation since its inception. We conducted a surveillance system evaluation of the SARI sentinel surveillance site at CCH in Kandal Province. The CCH is located 11 kilometers from Phnom Penh. The provincial population in 2023 was 1,820,505.[8] The CCH sentinel site had low data quality as a result of the surveillance data quality audit. Regular evaluation of the SARI surveillance system is essential to ensure its effectiveness in detecting abnormal increases in respiratory infections. The findings of this evaluation should help guide improvements in surveillance in other similar hospitals in Cambodia. Therefore, our evaluation aims to assess SARI surveillance attributes and recommended improvements to enhance its functioning.

Methods

Study Design and Setting

We conducted a descriptive cross-sectional study to assess both qualitative and quantitative attributes of the SARI surveillance system at the CCH sentinel site between June and July 2023, following the updated U.S. Centers for Disease Control and Prevention guidelines for evaluating public health surveillance systems.[9]

CCH is a provincial-level referral hospital with eight inpatient wards and 120 inpatient beds. The pediatrics, internal medicine, and intensive care unit (ICU) wards, with 40 beds, participate in SARI surveillance.

We analyzed weekly trends of reported SARI cases over a five-year period (2018–2022) as part of the stability assessment of the surveillance system.

Quantitative attributes assessed included timeliness, sensitivity, positive predictive value (PPV), and completeness. Timeliness was assessed for both laboratory processing and weekly reporting of SARI cases. Sensitivity was defined as the proportion of SARI cases in the hospital records that are reported by the surveillance system, while PPV was defined as the proportion of reported cases that are SARI cases. Completeness was defined as the proportion of variables in the SARI case reporting form that were fully recorded. To evaluate these attributes, 10 individual weeks out of 52 in 2022 were selected by simple random sampling, and full medical record reviews were conducted and compared with the corresponding reports in the system.

For qualitative attributes, we assessed simplicity, acceptability, flexibility, usefulness, and stability. Semi-structured interviews were conducted with national-level focal points, including SARI surveillance chiefs and officials selected through convenience sampling, and local-level focal points directly involved in implementing the system at the CCH.

Case Definition

A SARI case was defined as an individual who meets all of the following criteria: (1) a measured temperature of ≥38°C (fever) or a history of fever with onset within the past ten days; (2) cough or sore throat; (3) shortness of breath or difficulty breathing; and (4) hospitalization required.[10] A reported SARI case was defined as any case reported in the SARI surveillance system, regardless of whether it met the SARI case definition.

Data Source

Weekly aggregated data between 2018 and 2022 were collected from the CCH's SARI surveillance system database. For 2022, additional data were obtained on SARI cases, including demographic characteristics, admitted hospital, and patient disposition. Laboratory data in 2022—including time of sample collection and result availability—were obtained from the NIPH to assess timeliness. In 10 randomly selected weeks of 2022, all admitted patients' records were reviewed to identify SARI cases. Data on symptoms, onset date, and admission date were extracted. A single interviewer administered a semi-structured questionnaire to relevant stakeholders from national and provincial surveillance focal points.

Data Analysis

SARI case trends

We analyzed weekly trends of reported SARI cases from 2018 to 2022. Descriptive statistics were performed for the total SARI cases in 2022 and for the cases identified during the 10 randomly selected weeks.

Timeliness

We assessed the timeliness of the SARI surveillance in 2022 using two measures. First, timeliness of laboratory processing was defined as the proportion of nasopharyngeal samples with results released within 24 hours of collection. Second, timeliness of the weekly SARI report was defined as the proportion of weeks in which all SARI cases were entered into the surveillance system by Monday of the following week, calculated across all 52 weeks.

Completeness

Completeness was assessed by completing all variables in the 2022 SARI case report forms. It was calculated by dividing the number of completed variables by the total number of required variables for each form.

Sensitivity and positive predictive value

Among the admitted patients selected for medical record review during the 10 sampled weeks, we compared the number of patients who met the SARI case definition upon review of clinical information in the medical record "gold standard" with reported SARI cases. Sensitivity was calculated by dividing the number of SARI cases reported in the surveillance system that met the SARI case definition by the total number of SARI cases identified in the medical record review. PPV was defined as the percentage of SARI cases reported in the surveillance system. PPV was calculated by dividing the number of reported SARI cases that met the SARI case definition by the total number of reported SARI cases, both overall and stratified by ward.

All data analysis was performed by Microsoft Excel version 16.96.1 (25042021).

Simplicity, acceptability, flexibility, usefulness, and stability

We adapted a previous study's semi-structured questionnaire. Stakeholders were asked to evaluate specific indicators of the qualitative attributes via a 5-point Likert scale (1=strongly disagree, 2=disagree, 3=neutral, 4=agree, 5=strongly agree) for simplicity, acceptability, and flexibility.[11] For usefulness and stability, a binary format was used (1=yes, 0=no). Higher scores reflected better performance in the given attribute. The total scores for each attribute were calculated by summing the indicator scores and dividing by the maximum possible score to yield a percentage. The qualitative attributes were then ranked as follows: excellent (>80%), good (60%–80%), average (40%–60%), poor (20%–40%), and very poor (<20%). We analyzed key insights and quotations from interviews (paper-based questionnaires) with SARI focal points at the national and provincial levels to further assess the qualitative attributes of the surveillance system.

Results

Description of the SARI Surveillance System Flowchart

The SARI surveillance system involves identifying cases in clinical departments, reporting data, sending specimens to the sentinel site, and forwarding samples to the NIPH laboratory for testing. Test results and aggregated reports are submitted to the CDC-MOH, which then shares its findings with international partners (Figure 1).

Trend of SARI Cases over a 5-year Period

Between 2018 and 2022, 576 reported SARI cases were recorded in the SARI surveillance system, including two deaths. No reported SARI cases were documented during 103 weeks, including 65 consecutive weeks between week 10 of 2021 and week 27 of 2022 (Figure 2).

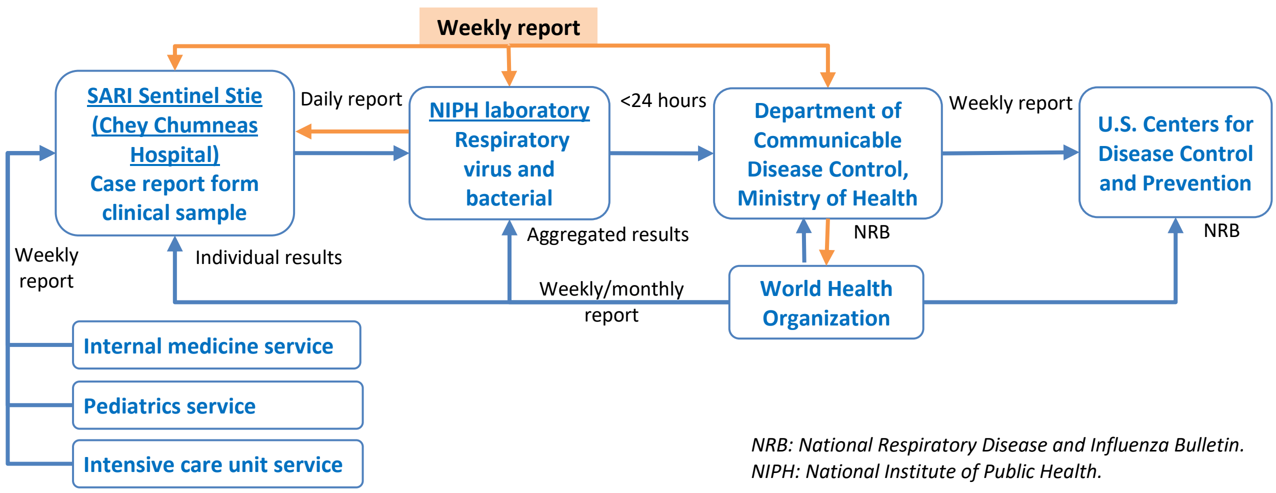

Figure 1. Flowchart for the severe acute respiratory illness (SARI) surveillance system in Chey Chumneas Hospital, Kandal Province, Cambodia, 2022

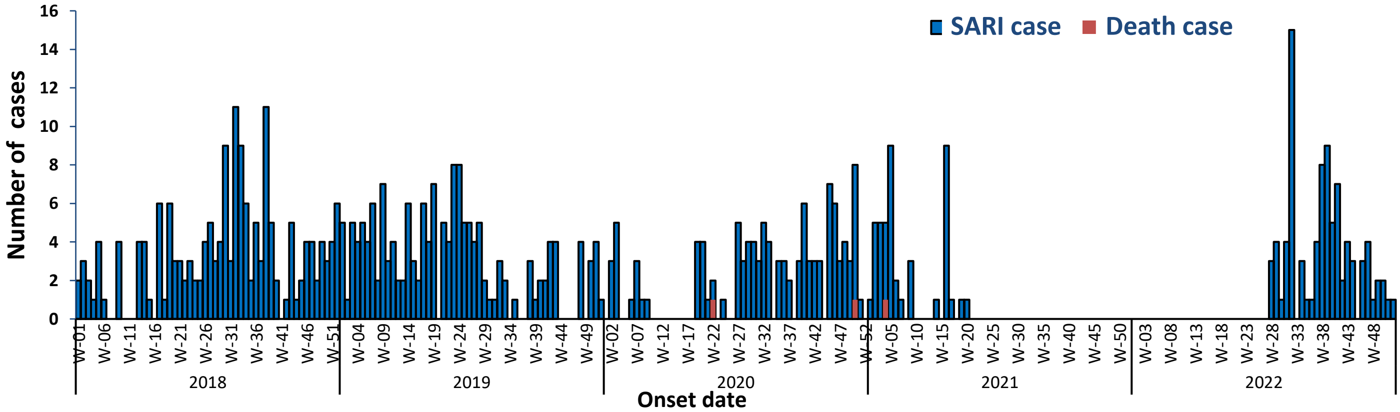

Figure 2. Distribution of SARI cases by week at Chey Chumneas Hospital, Kandal Province, Cambodia, 2018–2022 (n=576)

In 2022, 88 reported SARI cases were recorded in the SARI surveillance system at CCH. Among the cases tested for influenza, 9 (45%) were positive for A (H3N2), 4 (20%) were positive for influenza B/Victoria, and 7 (35%) were positive for COVID-19. Of the 88 reported SARI cases in 2022, 19 (22%) were selected from 10 weeks (weeks 3, 7, 16, 25, 27, 28, 31, 40, 44, and 47) for full medical record review. Among these, 57.9% were male, compared with 59.1% male among all reported SARI cases. The age group with the largest proportion was children aged 0–4 years (26.1%), compared to 36.8% of the reviewed group. Most were treated in the ICU ward (40.9%), followed by the pediatric ward (32.9%), and the internal medicine ward (26.1%) (Table 1).

Table 1. Patient characteristics under monitored the severe acute respiratory illness (SARI) surveillance system at Chey Chumneas Hospital, Kandal Province, Cambodia, 2022

Characteristics	Total reported cases in 2022 (N=88)		Cases in 10 randomly selected weeks in 2022 (n=19)	
	n	%	n	%
Gender				
Male	52	59.1	11	57.9
Female	36	40.9	8	42.1
Age group (years)				
0–4	23	26.1	7	36.8
5–14	6	6.8	2	10.5
15–24	7	7.9	0	0.0
25–49	17	19.3	3	15.8
50–64	19	21.6	5	26.3
65+	16	18.2	2	10.5
Wards				
ICU	36	40.9	6	31.6
Pediatrics	29	32.9	9	47.4
Internal medicine	23	26.1	4	21.0
Sample types				
NP/OP swab	88	100.0	19	100.0
Sputum	0	0.0	0	0.0
Province				
Kandal	59	67.1	12	63.2
Others*	29	32.9	7	36.8
Final outcome				
Discharged	85	96.6	19	100.0
Transferred	3	3.4	0	0.0
Lab result (Influenza)†				
H3N2	9/20	45.0	2/3	66.7
Influenza B/Victoria	4/20	20.0	1/3	33.3
COVID-19	7/20	35.0	0/3	0.0

**Phnom Penh, Kampong Cham, Takeo, and Kampong Speu Provinces. †We used only virus-positive cases as the denominator. NP: nasopharyngeal. OP: oropharyngeal. ICU: intensive care unit.*

Quantitative Attributes

Timeliness

In 2022, 54% (28/52 weeks) of surveillance reports were submitted on time, meeting the reporting requirements every Monday following the week under review. Among the 88 reported SARI cases, 59% (52/88) had laboratory results processed within 24 hours.

Completeness

Of the 88 reported SARI cases in 2022, 91% of the variables were complete, and three SARI symptom variables had a completeness of 95%.

Sensitivity and positive predictive value

In the 10 weeks selected for full medical record review, 289 patients were admitted to three medical wards where SARI surveillance was implemented. Among these, 42 met the SARI case definition; 14 SARI cases were reported into the SARI surveillance system, resulting in a sensitivity of 33% (14/42). Nineteen SARI cases were reported in the system, resulting in a PPV of 73% (14/19). In pediatric ward, the PPV was 100% (8/8) and the sensitivity was 47% (8/17). The internal medical ward had a PPV of 50% (2/2) and a sensitivity of 11% (2/17), while the ICU had a PPV of 57% (4/7) and a sensitivity of 50% (4/8) (Table 2).

Table 2. Performance of the severe acute respiratory illness (SARI) surveillance system at Chey Chumneas Hospital, comparing the number of reported cases with the number identified by manual medical record review of all admitted patients during the evaluation period

Ward	Reported SARI cases that met the case definition (true SARI)	Reported SARI cases that did not meet the case definition*	SARI cases not reported	Sensitivity[§]	PPV[†]
Pediatrics	8	0	9	47% (8/17)	100% (8/8)
Internal medicine	2	2	15	11% (2/17)	50% (2/4)
Intensive care unit	4	3	4	50% (4/8)	57% (4/7)
All wards combined	14	5	28	33% (14/42)	73% (14/19)

**Those reported into the surveillance system as a SARI case but did not meet the case definition upon manual medical record review. [†]Positive predictive value calculated as SARI cases/total reported SARI cases. [§]Sensitivity is calculated as SARI cases that reported in the system/SARI cases.*

Qualitative Attributes

We conducted semi-structured interviews with three persons at the national sites and eight persons at the hospital sites (three nurses, four medical doctors, two laboratory technicians, one data entry personnel or information technology staff, and a public health specialist) to evaluate the system.

Usefulness and stability

Three national-level focal points reported the system's usefulness and stability. The usefulness was rated as excellent, and the stability as good. All questions were ranked as excellent or good, except for stability without sponsor funding, which was rated poor (Table 3). Moreover, the unclear temporal pattern of reporting SARI cases might reflect a lack of system stability.

A national-level focal point stated: "*The SARI surveillance system played a critical role in detecting all avian influenza cases in Cambodia in 2022. Without this system in place, the outbreak could have spread much more widely.*"

Simplicity and acceptability

Eight local-level focal points highlighted the system's simplicity and acceptability; simplicity was excellent, and acceptability was good. With a score of 80%, the SARI system is well accepted by the focal points involved in its operation. The focal points' willingness to participate in the system, as well as their satisfaction with it, both received a score of 80% (Table 3).

Flexibility

All eleven national and local focal points were asked about the system's flexibility. The system demonstrated good flexibility, with a score of 69%. It adapts well to changes in the SARI case definition (76%) and integrates with other surveillance systems (71%). The system also accommodates new and additional information reasonably well (65%) and adapts to new health events with moderate efficiency (62%) (Table 3).

A national-level focal point stated the following: "*It is possible to add new variables or information as needed. For example, during the COVID-19 pandemic, we incorporated sample collection to monitor COVID-19.*"

Table 3. Qualitative attribute performance of the severe acute respiratory infection (SARI) surveillance system at Chey Chumneas Hospital, Kandal Province, Cambodia, 2022

Indicators	Score	Percent	Rank
Usefulness (n=3)*			
Estimates morbidity and mortality related to SARI	3	100	Excellent
Stimulates research for prevention and control of SARI	3	100	Excellent
Supports resource planning for SARI prevention, control, and interventions	2	67	Good
Informs updates to national SARI policy and strategy	3	100	Excellent
Detects trends and outbreaks of SARI	3	100	Excellent
Enables timely detection and diagnosis of SARI	2	67	Good
Total score	**16/18**	**89**	**Excellent**
Stability (n=3)*			
Adapts to resource changes	3	100	Excellent
Stable without sponsor funding	1	33	Poor
Supported by external or governmental funds	2	67	Good
Total score	**6/9**	**67**	**Good**
Simplicity (n=8)†			
SARI case definition available or staff remembers it	32	80	Good
SARI case definition is easy to use	35	88	Excellent
System is user-friendly and easy to fill out	34	85	Excellent
Staff received special training to update and use the system	29	72	Good
Total score	**130/160**	**81**	**Excellent**
Acceptability (n=8)§			
Focal point willing to participate in the SARI system	32	80	Good
Focal point satisfied with participating in the system	32	80	Good
Total score	**64/80**	**80**	**Good**
Flexibility (n=11)			
Easily adapts to changes in SARI case definition	42	76	Good
Integration with other surveillance systems	39	71	Good
Accommodates new, additional information.	36	65	Good
Adapts to new health events with minimal resources, time	34	62	Good
Total score	**151/220**	**69**	**Good**

**Usefulness and Stability: Interview with yes/no questions with 3 SARI focal points at the national level. †Simplicity and acceptability: Interview with a 5-point Likert scale with 8 SARI focal points at the provincial level, and the total score is the denominator. §Flexibility: Interview with a 5-point Likert scale with 3 SARI focal points at the national level and 8 SARI focal points at the provincial level; the total score is the denominator.*

Discussion

For a five-year period, there were several weeks with no reported SARI cases. The system exhibited low sensitivity and low PPV in medical wards and the intensive care unit; however, it had lower accuracy in correctly identifying SARI cases. The stability of the system was rated as good overall; however, it was found to be vulnerable due to a lack of external funding. Despite the challenges in terms of sensitivity, PPV, and stability, the SARI surveillance system, which is useful, simple, flexible, acceptable, timely, and complete, performs well.

We found low sensitivity, meaning that a large proportion of true SARI cases were missed. This poor result was largely due to the evaluation being conducted during the COVID-19 pandemic, when most staff were occupied with outbreak response efforts, lacked supervision, and were monitoring at a relatively high level. This finding was consistent with an evaluation in Ireland during the same period.[12] In addition, the lack of formal training for newly appointed SARI focal points likely contributed to this under-detection. Unsurprisingly, our sensitivity was lower than that of a previous SARI evaluation at Kirivong Hospital, Takeo Province, Cambodia, 2016.[13]

The PPV of the surveillance system varied across wards, with the pediatric ward performing excellently, whereas the medicine ward and the ICU had lower accuracy, probably because one of SARI's focal points in these two areas was a new staff member who had never received formal training. Another reason for the low accuracy may be due to inconsistent application of the case definition at sentinel sites or incomplete documentation of signs and symptoms in medical records. This variability highlights the need for targeted improvements in case identification, particularly in more complex clinical settings, such as ICUs, where the nature of patient conditions may make SARI diagnosis more challenging.

The timeliness of reporting and rapid laboratory results is critical for effective case management, early outbreak detection, and timely public health response. In CCH, the timeliness of laboratory processing is good because the hospital is near the national laboratory, facilitating faster sample transfers. We also discussed how delays in reporting could weaken the system's ability to detect emerging threats such as avian influenza, highlighting the need for continuous efforts to improve timeliness in surveillance operations.

The SARI surveillance system is invaluable for estimating morbidity and mortality related to SARI, promoting research aimed at its prevention and control. Most importantly, it plays a critical role in detecting avian influenza. In fact, the system was instrumental in identifying all avian influenza cases in Cambodia in 2022. Without this system, the outbreak could have spread far more extensively. Similarly, previous studies in Zambia and Yemen demonstrated the usefulness of their surveillance systems.[14,15]

The stability of the system was rated as good overall; however, it was found to be vulnerable due to a lack of external funding. This reflects the system's reliance on external resources, which may pose a risk to its long-term sustainability. Establishing a more robust and locally supported financial framework is crucial to ensuring that the system can continue to operate effectively, even during periods of funding shortages.

The system's simplicity was one of its strongest attributes. The SARI case definition is clear and easy to use, making it straightforward for healthcare workers to identify and report cases. Additionally, the system's user-friendly design facilitates efficient data entry and reporting, reducing the potential for errors and minimizing the time required for staff to learn and implement the system. This ease of use promotes consistent case identification and data collection, ensuring that the system operates effectively without placing an undue burden on healthcare workers.

The system demonstrated considerable flexibility, particularly during the COVID-19 pandemic. The ability to integrate COVID-19 testing alongside routine SARI surveillance without major system modifications reflects its capacity to adapt to new health threats. Furthermore, the system's ability to accommodate changes in the SARI case definition and the inclusion of additional information, such as new testing protocols, highlights its versatility in responding to evolving public health needs. This flexibility ensures that the system can remain relevant and useful even as new challenges arise.

The acceptability of the SARI surveillance system was also a key strength, with high levels of engagement and satisfaction reported among healthcare workers. Staff are willing to participate in the system, indicating a strong sense of ownership and commitment to its success. This high level of acceptability is critical for ensuring the system's sustainability, as it relies on the active participation of healthcare providers to function effectively. The system's design, which is both easy to use and adaptable, likely contributes to positive perceptions among those responsible for its implementation.

Limitations

This evaluation had several limitations. First, it was conducted at a single sentinel site and focused only on data from 2022, which had relatively few SARI cases, limiting the generalizability of the findings to other regions or SARI sites. Additionally, a small number of interviewees were for qualitative attributes, which may limit the depth and diversity of perspectives captured. Expanding the evaluation to include multiple years, more sites, and a larger sample size would provide a more comprehensive and representative assessment of the effectiveness of the SARI surveillance system.

Recommendations

To strengthen the severe acute respiratory infection (SARI) surveillance system, it is recommended that both provincial and national SARI focal points conduct regular supervision and provide refresher trainings to improve case detection, ensuring that all true SARI cases admitted to hospitals are accurately reported. Newly assigned focal points should also be provided with comprehensive training and continuous guidance to build their capacity and ensure consistency in implementation. In addition, detailed budget planning should be developed to secure the sustainability of the system over the long term. To further improve data quality, continuous monitoring of reporting practices should be implemented, coupled with timely and constructive feedback to reporting sites.

Conclusion

While the SARI surveillance system has strengths in terms of data completeness, timeliness, usefulness, flexibility, simplicity, and acceptability, the system did poorly in terms of sensitivity, PPV, and stability. Targeted training for health care workers involved in SARI reporting and regular supervision, particularly in medical wards and ICUs, is essential. Our evaluation contributes not only to improving the surveillance system at the CCH hospital but also provides evidence representative of the gaps that other health facilities should consider or lessons applicable to the SARI surveillance in the country. Future evaluations should continue to monitor these attributes, with particular attention given to improving case detection and system resilience.

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Author Contributions

Khemrin Pong: Conceptualization, formal analysis, methodology, project administration, writing—original draft, writing—reviewing & editing. **Sophanith Ung:** Supervision, resources. **Sengdoeurn Yi:** Supervision. **Piseth Keam:** Supervision, validation. **Sokly Mom:** Writing—review & editing. **Hayputhik Long:** Conceptualization, methodology, writing—reviewing & editing.

Ethical Approval

Approval from the National Ethical Review Board was not required. This evaluation utilized data from routine surveillance systems and various types of surveillance quality improvement.

Informed Consent

Verbal consent was obtained from key SARI stakeholders prior to the interviews. Written (paper-based) consent was not required, as this type of evaluation did not involve the collection of detailed personal information and posed no risk to participants.

Data Availability

The datasets supporting this study are available from the corresponding author upon reasonable request (via khemrinpong@gmail.com).

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this report.

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

No artificial intelligence (AI) tools were used to generate the content or findings of this evaluation. However, while the preparation of this manuscript, the author used AI–ChatGPT solely for grammar correction, language refinement, and formatting support. All content was reviewed, edited, and finalized by the author, who takes full responsible for the final text.

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High Sensitivity with Suboptimal Predictive Value and Delayed Reporting: Identifying Gaps in Congenital Zika Syndrome Surveillance at Saraburi Hospital, Thailand, 2022–2023

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Abstract

Zika virus is an arboviral infection primarily transmitted by Aedes mosquitoes, with severe complications in children, notably congenital Zika syndrome (CZS). This study evaluates the surveillance system of CZS based on the R506 reporting system, the nationwide reporting platform of the Department of Disease Control, at Saraburi Hospital, Thailand, during 2022–2023. We employed both quantitative and qualitative methods. A cross-sectional quantitative study was conducted through a review of hospital records and R506 surveillance data. Attributes such as sensitivity and positive predictive value (PPV) were calculated. For the qualitative study, attributes such as acceptability, simplicity, flexibility, and stability were assessed mainly through semi-structured interviews, and a framework analysis was conducted. The surveillance system demonstrated a sensitivity of 100.0% and a PPV of 44.4%. Completeness was high for demographic variables; however, timeliness was suboptimal, with 11.1% of reports submitted within a one-week window. The system was deemed useful and stable; however, challenges in interoperability between R506 and the hospital database were noted. Notably, the in-house hospital laboratory lacked the capacity to perform Zika polymerase chain reaction (PCR) tests, necessitating external processing and likely contributing to reporting delays. While the surveillance system could detect cases effectively, improvements in timeliness, coding consistency, and data integration are needed. Revising the case definition could increase the PPV. Enhancing the hospital's laboratory capacity, particularly for PCR testing, may reduce reporting time. Strengthening reporting practices and stakeholder collaboration could further improve system efficiency.

Keywords: Zika, surveillance evaluation, sensitivity, positive predictive value

Introduction

The Zika virus is primarily transmitted by *Aedes mosquitoes*, notably *Aedes aegypti* and *Aedes albopictus*. From the 1960s to the 1980s, sporadic human infections occurred across Africa and Asia. Major outbreaks emerged globally from 2007 onwards, with significant epidemics in the Pacific Islands and the Americas.[1]

Most Zika virus infections are asymptomatic. Symptoms typically appear between 2–12 days after infection, but are usually mild and include rash, fever, conjunctivitis, muscle and joint pain, malaise, and headache, and last for 2–7 days.[2] Due to similarities with other diseases, laboratory tests are required to confirm the diagnosis. Over the past decade, Zika virus outbreaks have been associated with increased cases of Guillain-Barré syndrome.[3] During the 2015 epidemic in Brazil, the link to microcephaly was first reported and later confirmed in French Polynesia. In 2016, the World Health Organization (WHO) declared Public Health Emergency of International Concern due to Zika-related neurological disorders, ultimately confirming its association with congenital malformations.[4]

Zika virus infection during pregnancy can cause congenital Zika syndrome (CZS), leading to microcephaly, parenchymal or cerebellar calcifications, ventriculomegaly, central nervous system hypoplasia or atrophy, arthrogryposis, abnormal visual function, and low birthweight for gestational age.[5] Additionally, the virus can be transmitted through sexual contact, blood transfusion, and organ transplantation.[6]

Diagnosis of Zika virus infection is confirmed through laboratory tests, including polymerase chain reaction (PCR) and IgG/IgM serology of blood, serum, plasma, or urine samples. There is no specific antiviral treatment. Preventive measures, such as avoiding mosquito bites and practicing safe sex, are essential to reduce the risk of infection.

According to the national notifiable disease surveillance system (R506) of the Department of Disease Control (DDC), the main reporting platform of key communicable diseases from all health facilities across Thailand, there has been an increase in reported cases of Zika virus disease during 2022–2023 compared to the previous five years. Saraburi Province was among the most affected areas, reporting 39 confirmed cases in 2023, and ranked among the top four provinces (after Bangkok, Chanthaburi, and Phetchabun). Saraburi Hospital, a provincial referral hospital, had reported only sporadic cases in earlier years; however, in 2023, it reported nine newborns with microcephaly. This rise in Zika cases and the occurrence of microcephaly highlight a potential risk of CZS in the province. Because CZS can cause lifelong disability and a significant public health burden, it is critical to assess the hospital's surveillance system to ensure effective detection, reporting, and response, and to identify areas for strengthening maternal and child health protection.

Therefore, this study aims to assess the usefulness and performance of the CZS surveillance system at Saraburi Hospital from 2022 to 2023 and provide recommendations for system improvement.

Methods

Study Design

This study used a mixed-methods approach. A cross-sectional quantitative study was conducted to assess attributes such as sensitivity, completeness, and timeliness, using the surveillance data during 2022–2023. A qualitative descriptive study was also conducted to describe the system and assess acceptability and simplicity of the surveillance system.

Study Site

The study was conducted at Saraburi Hospital and the Saraburi Provincial Public Health Office (PPHO) in Saraburi Province, Thailand.

Study Period

The study focused on individuals who visited or were born at Saraburi Hospital between 1 Jan 2022 and 31 Dec 2023.

Qualitative Study

Target population and samples

Stakeholders involved in the CZS surveillance system at Saraburi Hospital and Saraburi PPHO were the target respondents. We used purposive sampling to recruit potential interviewees, covering executive-level officers, frontline physicians, and data entry operators (n=18), focusing on those with at least one year of experience in the system (Table 1).

Table 1. List of interviewees for system description and qualitative attribute assessment

Organization	Stakeholders (n=18)			
	Policy makers or executives	Information technology (IT) administrator	Data entry operator	Healthcare provider
Saraburi Provincial Public Health Office	Chief medical officer (1) and head of disease control unit (1)		Epidemiologists (2)	
Saraburi Hospital	Hospital director (1) and deputy director (1)	IT staff (1) and coders (2)	Epidemiologists (3)	Labor-ward nurses (3), internist (1), obstetrician (1), and pediatrician (1)

Data collection and analysis

In-depth and group interviews took place at the respondents' workplaces, with interviews lasting 30 minutes on average. Direct observation of the CZS reporting workflow and document review of relevant reports and guidelines related to the hospital's CZS reporting mechanism were also conducted. A semi-structured questionnaire guided the interview topics. Framework analysis was applied throughout the process.

System description

This topic included the purpose of surveillance, an overview of data flow, operational resources used, and views on public health importance and system usefulness.

Qualitative attributes

We focused on the following attributes: acceptability—the willingness of stakeholders to engage with the system, reflecting user satisfaction and cooperation; flexibility—the system's adaptability to changes, such as modifications in data collection methods or case definitions; simplicity—the ease of use and reporting processes within the system, ensuring that operations are straightforward and user-friendly; and stability—the reliability of the system's functionality over time, ensuring consistent performance without frequent disruptions.

Public health importance and usefulness

Stakeholders' perspectives on the value of the surveillance system in disease monitoring and response, indicating its effectiveness in public health management.

Quantitative Study

Data sources and data collection

We reviewed the surveillance data from the following three sources: (i) R506, (ii) the hospital information system (HIS), and (iii) the hospital serology laboratory logbook. Medical records with the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10) diagnosis codes A92.5, A92.8, and P35.4. We also examined other ICD-10 codes that may mimic CZS, such as Q87.0 and Q87.1. Although our initial search focused on newborns suspected of CZS, we also expanded our search to include the mothers of these children (Table 2).

Table 2. List of the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10) codes retrieved for quantitative attribute assessment

Group	ICD-10	Diagnosis
Exact	A92.5	Zika virus disease
	A92.8	Other specified mosquito-borne viral fevers
	P35.4	Congenital Zika virus disease
	P35.8	Other congenital viral diseases
Mimic	Q00.0	Anencephaly
	Q02	Microcephaly
	Q87.0, Q87.1, Q872, Q87.4, Q87.8	Congenital anomalies (congenital malformation syndromes predominantly affecting facial appearance, congenital malformation syndromes predominantly associated with short stature, congenital malformation syndromes predominantly involving limbs, Marfan syndrome, other specified congenital malformation syndromes, not elsewhere classified)
	P05.0, P05.1, P05.9, P07.0, P07.1	Light for gestational age, small for gestational age, slow fetal growth, unspecified, extremely low birth weight, other low birth weight

Quantitative attributes

The following attributes were assessed: sensitivity—the proportion of true cases reported out of the total actual cases according to the case definition; positive predictive value (PPV)—the proportion of reported cases that meet the case definition; completeness—the proportion of records containing complete data for key variables, including age, sex, current address, and date of diagnosis; accuracy—the percentage of matched variables between cases reported in the R506 system and those recorded in the HIS; timeliness—the duration between diagnosis and reporting to the PPHO, with a seven-day window set as the threshold, indicating the promptness of the system's reporting mechanism; and representativeness—the comparison of the number of cases meeting the case definition with monthly trends and overall male-to-female ratio between the HIS and R506.

Sample size calculation to assess sensitivity and PPV

We applied the prevalence estimation formula for sample size calculation.[7] The expected sensitivity was 19%, adapted from a previous study in Thailand, with an acceptable error of 5%.[8] We assumed that the percentage of cases meeting the case definition out of the total reviewed cases was 100% for Zika-related ICD-10 codes and 35% for Zika-mimicking ICD-10 codes. We hypothesized that 80% of the information would be incomplete.

Due to the small number of medical charts with an exact diagnosis (based on ICD-10), we reviewed them all. However, we used stratified random sampling on the pool of Zika-mimicking ICD-10 codes with the overall sampling fraction of 44.5% (250/562) (Table 3). A total of 305 medical charts were reviewed. During sampling, a non-proportional to size approach was used to ensure that ICD-10 codes with very few charts (not more than five) were not omitted; all charts for those codes were examined.

Concerning PPV, we applied the same formula, using an expected PPV of 10%, adapted from the previous study with an acceptable error of 5%.[8] This resulted in a minimum sample size of 35. However, there were only nine Zika records in the R506, thus we reviewed all nine cases for PPV estimation.

Table 3. Sampling frame of the medical charts for sensitivity assessment

ICD-10 category	Total number in the pool	Number to be reviewed	Note
Exact	7	7	Review all
Mimic	562	250	Stratified sampling
Mothers of infants with microcephaly or Zika	48	48	Review all

ICD-10: International Statistical Classification of Diseases and Related Health Problems, 10th revision.

Case definition and data analysis

The case definitions for CZS (as well as mothers of CZS newborns) were adapted from the Centers for Disease Control and Prevention and the Division of Epidemiology guidelines, with minor adjustments to align with the evaluation process (Table 4).[9] An investigation into R506 commenced following the identification of a probable case. Descriptive statistics, including frequency and proportion, were used to analyze quantitative attributes. Weighted analysis was applied to account for the sampling design. For the qualitative study, key quotes from interviewees were extracted verbatim.

Table 4. Case definition for quantitative attribute assessment

Type	Criteria
Suspected	Newborn infant aged less than a month who received treatment at Saraburi Hospital during 2022–2023 with a head circumference less than the 3rd percentile according to sex and gestational age.
	Mother of newborns who were reported as Zika disease or diagnosed with microcephaly according to Zika-related ICD-10 at Saraburi Hospital during 2022–2023.
Probable	A suspected case with any of the following: • Maternal history of Zika disease with plasma or urine showing Zika PCR positive, or • History of staying in the subdistrict with a confirmed case found within the same month, or • Dengue Ns1Ag showing negative within 3 days of illness, or • Other laboratory tests for measles, rubella, dengue, and chikungunya negative within that month.
Confirmed	Suspected case with specific laboratory result for Zika positive: • Plasma and/or urine is/are Zika PCR positive, or • Zika IgM showing positive, or • Zika seroconversion IgG showing positive (more than 3 weeks).

ICD-10: International Statistical Classification of Diseases and Related Health Problems, 10th revision. PCR: polymerase chain reaction.

Results

System Description

Overall, the surveillance system for CZS at Saraburi Hospital is a hospital-based passive surveillance system. Its primary purpose is to detect, confirm, and report suspected CZS cases to the R506 system to allow early investigation. The system involves multiple stakeholders. Obstetricians and ultrasonographers provide routine pre-natal care and detect suspected fetal abnormalities. Pediatricians perform neonatal examinations and manage suspected cases; laboratory staff conduct Zika virus testing and hospital epidemiologists are responsible for case verification and notification to the R506.

Patient Flow

Pregnant women receive routine care by ultrasonography. If fetal microcephaly is suspected, blood and urine tests for Zika virus are performed. Positive cases are reported to obstetricians and epidemiologists. For newborns, head circumference is routinely measured against the 3rd percentile for gestational age and sex. Those with a head circumference less than the 3rd percentile receive additional tests to confirm CZS. Positive cases are then notified to the in-charge pediatrician and hospital epidemiologists (Figure 1).

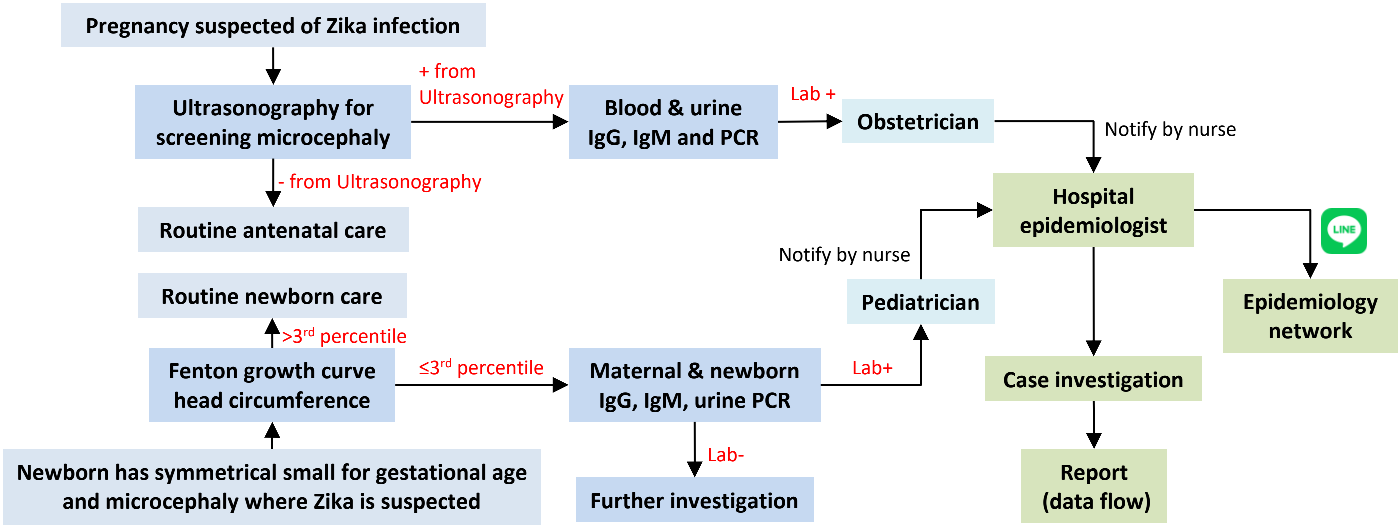

Figure 1. Patient flow of congenital Zika syndrome in Saraburi Hospital, 2023

Data Flow

Data on suspected Zika cases are collected from various sources, including antenatal care clinics, health screening units, obstetric and pediatric units, and outpatient departments. All records from these sources are transferred to the HIS. Laboratory results—primarily PCR in routine settings and IgG/IgM during Emergency Operating Center activation—are sent to the laboratory information system. Zika PCR testing is conducted by external laboratory units, either by the Department of Medical Sciences network or by the Bamrasnaradura Infectious Diseases Institute, DDC. HIS data should be submitted to the epidemiological unit within one day and to the PPHO within one week. HIS data were expected to be submitted to the epidemiological unit within a day. If a suspected case was identified but laboratory results were still pending, the epidemiological staff received phone notifications from ward nurses. Laboratory results are communicated via the LINE application. Once notified, hospital epidemiologists will investigate the event. The findings are then shared with public health officers in the hospital's epidemiological unit, who subsequently enter the data into the R506 system, while the Saraburi PPHO serves as the primary recipient. The PPHO's R506 data are then shared with the Office of Disease Prevention and Control Region 4 Saraburi (ODPC 4) and the DDC (Figure 2).

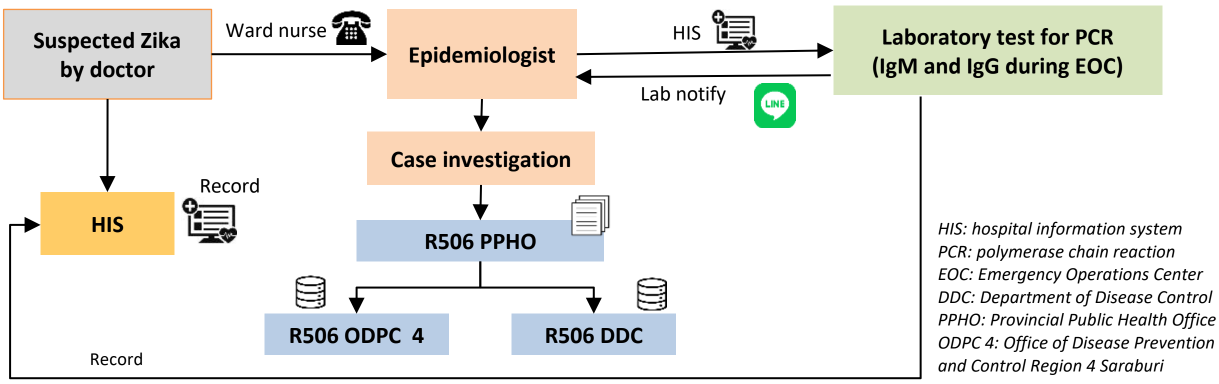

Figure 2. Data flow of congenital Zika syndrome based on R506, 2023

Saraburi Hospital had three full-time epidemiologists managing CZS cases through the R506 surveillance system. Funding primarily came from the hospital's routine budget, while local government units supported field disease control. Coordination between the health sector and these local units was essential. Laboratory costs were mainly covered by the hospital, with partial reimbursement from the National Health Security Office (NHSO).

Qualitative Attribute Assessment

Public health importance and usefulness

All interviewees, including executives from Saraburi Hospital and the PPHO, viewed R506 as an important tool for Zika disease control. However, operational-level staff were less aware of its significance. Compared with other informal reporting channels, such as the LINE application, R506 was perceived as less favorable by operational staff.

"Anyway, more or less, it (the R506) is always useful for disease monitoring." (Executive staff, PPHO)

Simplicity

Most interviewees stated that R506 was easy to operate and could be integrated with the HIS. However, some respondents reported difficulties in automatically linking R506 data with the HIS due to outdated HIS software.

Flexibility

While R506 was flexible to operate, its adaptability depended on the HIS, which served as the primary gateway for data entry. Maintaining flexibility required frequent HIS updates (e.g., ICD-10 list updates). Additionally, any modifications to the HIS required explicit directives from executives rather than being solely managed by information technology staff.

Stability

Overall, the Zika surveillance system based on R506 was stable in terms of human resources and materials. Additionally, R506 had a strong firewall to prevent system failures.

Acceptability

Interviewees generally accepted the system, as it provided a clear understanding of outbreak situations. However, its acceptability was limited to disease monitoring rather than prompting immediate action.

"Using a case investigation form is better (than R506) to initiate investigation" (Executive staff, Saraburi Hospital)

Other concerned points

A mismatch existed between the Zika ICD-10 code specified by the DDC guideline (A92.5) and the code in the WHO-2016 coding manual (A92.8). This discrepancy also affected the NHSO reimbursement process for inpatient records, as NHSO auditing typically followed the WHO-2016 coding manual. Additionally, stakeholders (ODPC, PPHO, and Saraburi Hospital) had varying interpretations of the reimbursement criteria for Zika laboratory testing. In some cases, doctors ordered Zika PCR tests to rule out other diseases on a case-by-case basis. However, the ODPC generally covered laboratory costs only for disease investigation purposes.

"We must follow ICD-10 of the coding manual. We are fine to change our coding practice if there are clear directives from the NHSO, like in the COVID era." (Coder, Saraburi Hospital)

"To tackle this problem, we negotiated with the hospital from time to time. And if the ODPC can relax the criteria, this will be helpful." (Executive staff, Saraburi PPHO)

Quantitative Attribute Assessment

Sensitivity and PPV

Of the 305 records reviewed, four met the case definition for reporting, all of which were reported, resulting in a 100% sensitivity. For PPV, nine records were reported in R506, of which four met the case definition, yielding a PPV of 44.4%. All nine cases involved newborns diagnosed with conditions related to microcephaly. No cases were classified under ICD-10 codes mimicking Zika. To this end, although weighted analysis was planned from the outset, the results (100% sensitivity and 44.4% PPV) were similar to those of the non-weighted analysis, as all cases included in the calculation had the same sampling fraction. Further exploration with the in-charge physicians suggested that the low PPV was likely attributable to discrepancies between the case definition and the providers' clinical perceptions in certain instances. For example, some newborns exhibited positive laboratory results, but their head circumference did not fall below the 3rd percentile, rendering them incompatible with the case definition, even though the physicians classified them as CZS. Table 3 provides a summary of the reviewed medical records at Saraburi Hospital.

Completeness

The completeness of key variables—age, sex, current address, and date of diagnosis—was 100%.

Timeliness

Timeliness was assessed based on the time between the date of diagnosis and the date of reporting to R506. The median lag time was 14 days (Q1–Q3: 9–54 days). Only one out of nine cases (11.1%) was reported to R506 within one week.

Accuracy

The accuracy of the sex variable was 100%, while the accuracy for the diagnosis date, age, and residential address was 55.6% (5/9), 22.2% (2/9), and 22.2% (2/9), respectively.

Representativeness

The male-to-female ratio of Zika cases in the HIS was 3:1, which was higher than the ratio recorded in the R506 of the PPHO and DDC (1.25:1). The fluctuation of cases in the HIS generally aligned with the trends observed in R506, except in August 2023, when cases were reported in R506 despite no corresponding cases meeting the case definition in the HIS (Figure 3).

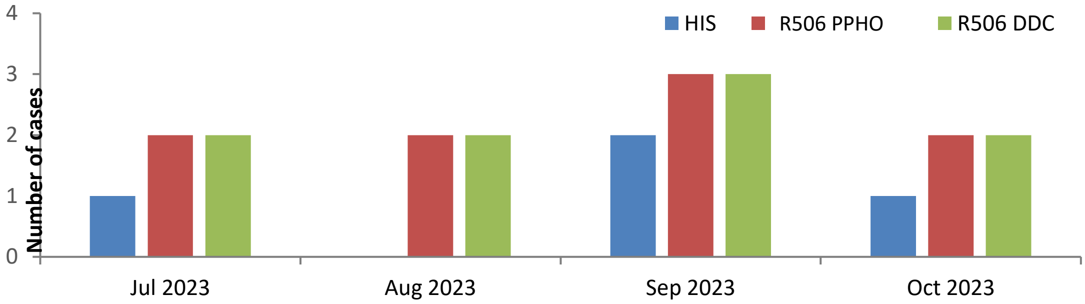

Figure 3. Number of congenital Zika syndrome cases by months in the hospital information system (HIS) and the R506 at Provincial Public Health Office (PPHO) and Department of Disease Control (DDC), 2023

Discussion

The CZS surveillance system at Saraburi Hospital plays a critical role in disease detection and response. Interviews with stakeholders confirmed its usefulness and public health importance. While stakeholders generally viewed the system positively, operational staff preferred alternative reporting channels over the R506 surveillance system for prompting disease investigation. Effective integration with the HIS system remains essential for accurate and timely reporting.

The sensitivity of R506 for Zika surveillance was high, though the PPV was relatively low. Unlike prior studies on other vector-borne diseases, where PPV was high and sensitivity was low, the opposite was observed here.[8] This is likely because all Zika cases reported in R506 at Saraburi Hospital were confirmed through laboratory testing, leading to high sensitivity. However, nearly half of the reported cases did not meet the case definition, primarily due to discrepancies in head circumference measurements. Some cases had head circumferences above the 3rd percentile despite laboratory confirmation. This situation occurred since the providers relied mainly on laboratory findings while focusing less on the circumference measures, as indicated in the clinical definition. Additionally, the reporting was broadened as a precautionary measure to avoid missing potential cases.

The findings of this study contrast with those of a study in Rayong Province, although that study focused on Zika disease more broadly rather than focusing specifically on CZS.[8] The study found low sensitivity but high PPV, which is not surprising since the case definition for Zika disease in adults does not always require laboratory confirmation. Clinical symptoms (e.g., rash) and a history of residence in endemic areas are often sufficient, increasing the denominator for calculation of sensitivity. Additionally, methodological differences—such as variations in including ICD-10 codes—may have contributed to differences in findings between studies.

Timeliness remains a major challenge, as only about one-tenth of cases were reported within a week. A key contributing factor is the lag time for laboratory results, which relied on external laboratory facilities. Similar challenges have been reported in Latin America, where limited laboratory capacity delayed Zika disease reporting, particularly in cases involving Guillain-Barré syndrome.[10]

Limitations

This study has several limitations. First, recall bias may have influenced responses, as data collection occurred more than a month after the Zika outbreak. Second, selection bias cannot be ruled out, as we examined only specific ICD-10 codes relevant to CZS rather than a comprehensive list of ICD-10 codes involved with Zika disease. Third, since this study focused on a single hospital, the generalizability of the findings is inherently limited. Additionally, at the time of the study, the introduction of the new national surveillance system, Digital Disease Surveillance (DDS), aimed at replacing R506, was imminent. As a result, our findings based on R506 may soon become less applicable. The DDS aims at synchronizing the HIS and the R506 data. The upcoming reporting platform is likely to improve data accuracy, especially for some key variables such as age and residential address through an application programming interface. Therefore, a re-evaluation of the surveillance system will be necessary to assess whether the new system functions as intended.

Despite these limitations, this study offers valuable lessons for other settings where CZS is of public health concern. Several practical lessons have emerged, including the importance of clear case definitions, effective integration of hospital information systems with central reporting mechanisms, and achieving an optimal balance between sensitivity and positive predictive power.

Conclusion

The sensitivity of the R506 surveillance system for congenital Zika syndrome at Saraburi Hospital during 2022–2023 was 100%, while the PPV was 44.4%. Only 11.1% of reported cases were submitted timely. The cases reported in R506 generally reflected the case trends in the hospital information system. Most stakeholders found the reporting system useful, acceptable, simple, and stable. However, inconsistencies in ICD-10 coding for Zika and challenges in reimbursement for laboratory testing remained key concerns.

Recommendations

Update the hospital information system: Saraburi Hospital should update its HIS to ensure compatibility with the national reporting system. Hospital executives should clearly communicate reporting roles to all relevant staff and address any misunderstandings, particularly regarding diagnosis coding. This will not only enhance R506 data reporting but also prepare the hospital for the transition to the new surveillance system.

Strengthen monitoring and coordination: The Saraburi PPHO should actively monitor and encourage hospitals to report cases in R506. Additionally, a series of consultative meetings should be organized with key stakeholders, including ODPC and Saraburi Hospital, to establish a common understanding of key issues such as optimal CZS reporting criteria and their implications for monetary reimbursement.

Enhance laboratory capacity: Saraburi Hospital should strengthen its laboratory capacity for Zika virus PCR testing. This improvement will enhance overall laboratory performance, reduce waiting time for test results, and ultimately improve the timeliness of case detection.

Re-evaluate Zika case definition: The DDC should consider revising the Zika case definition in the current guidelines. Newborns with a head circumference above the 3rd percentile but with positive laboratory results should be classified as meeting the case definition.

Certain lessons from this setting may be relevant for broader public health contexts. Streamlining the disease definitions established by central agencies with the practices of local providers is important for improving the sensitivity and predictive power of surveillance systems. Additionally, internal laboratory capacity is a fundamental component in enhancing surveillance system performance, particularly regarding timely diagnosis and more precise reporting. Other health facilities may consider using the surveillance evaluation process described in this study to assess their own surveillance system performance for CZS and other infectious diseases of concern.

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Author Contributions

Nouannipha Simmalavong: Conceptualization, data collection, methodology, writing—original draft, writing—review & editing. **Soutthongkham Sitthideth:** Data collection. **Wanchat Saowong:** Data collection, formal analysis. **Supanut Chotichavalrattanakul:** Data collection, formal analysis. **Chanakan Duanyai:** Data collection, formal analysis. **Ingkarat Somarungson:** Data collection, formal analysis. **Panupong Tantirat:** Data collection, formal analysis. **Sutham Jirapanakorn:** Data collection, formal analysis. **Thanaphon Yisankhun:** Data collection, formal analysis. **Thanit Rattanathamsakul:** Conceptualization, methodology, project administration, supervision, validation. **Rapeepong Suphanchaimat:** Conceptualization, supervision. All authors have read and agreed to the published version of the manuscript.

Ethical Approval

As the study is part of the routine monitoring of the Division of Epidemiology, Department of Disease Control, Ministry of Public Health, ethics approval was not required. However, all results are presented anonymously. No individual information has been disclosed.

Informed Consent

For the quantitative data, access was granted by Saraburi Hospital, utilizing routine service records; therefore, individual informed consent was not required. For the qualitative data, all interviewees were fully informed about the study and provided verbal consent to participate in the interviews.

Data Availability

The data that support the findings of this study are available from Saraburi Hospital. Access to these data is generally restricted, as they were used under license for this study. However, data may be available based on reasonable request from the corresponding author with permission from Saraburi Hospital.

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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Modeling the Potential Spread of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Evaluating Strategic Preparedness Measures in Thailand

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Abstract

Middle East respiratory syndrome (MERS) remains a public health threat due to its severity and potential for nosocomial and international transmission. Thailand remains at risk of a MERS outbreak due to ongoing travel, pilgrimage, and trade with the Middle East, despite having no confirmed case since 2016. This study aimed to assess the potential spread of MERS-CoV and evaluate national preparedness for MERS outbreaks by using a mixed-methods study. A quantitative study employed Susceptible-Exposed-Infectious-Recovered models to simulate the dynamics of MERS outbreaks under various scenarios in Yala, Pattani, and Narathiwat provinces. The qualitative component included documentary reviews and in-depth interviews with 21 key policymakers, experts, and relevant officers from provincial, sub-national, national, and international levels. The modeling revealed a low likelihood of widespread outbreaks, and combined interventions and early detection resulted in decreased peak and cumulative outcomes across various basic reproductive number values. Documentary reviews revealed that in Thailand, MERS surveillance was integrated into the national communicable disease surveillance, and its priority has diminished since 2016. In-depth interviews showed strengths in strategic plans, human resources, and cross-sector coordination, although gaps were identified in MERS-specific surveillance systems, laboratory surge capacity, insufficient community-level preparedness, and fragmented data systems. The results showed that Thailand has foundational capacity for MERS, supported by enhanced public health infrastructure following the COVID-19 pandemic. Recommendations include strengthening combined intervention and early detection measures, MERS-specific surveillance protocols, laboratory capacities, health literacy among high-risk groups such as pilgrims and caregivers, preparing sufficient resources, and enhancing digital health systems.

Keywords: spreading, preparedness, Middle East respiratory syndrome, MERS, MERS-CoV, Thailand, SEIR modeling

Introduction

Middle East respiratory syndrome (MERS), caused by the Middle East respiratory syndrome coronavirus (MERS-CoV), has been reported in 2,627 confirmed cases and 946 deaths across 27 countries in six global regions, reflecting a global case fatality rate of approximately 36%, as of 2025.[1] The highest number of cases has been documented in Saudi Arabia which has reported 2,218 cases, with 865 deaths as of 2025, with a 39% case fatality rate.[2] In 2015, South Korea experienced a major nosocomial outbreak, revealing the high potential for rapid human-to-human transmission in healthcare setting.[3] Since 2019, no confirmed cases have been reported outside the Middle East.

In 2023 and 2024, the number of pilgrims traveling to perform the Hajj from around the world was approximately 899,353 and 1,655,188, respectively. Thailand has been allocated a quota of roughly 13,000 pilgrims per year. In practice, the number of Thai pilgrims traveling was 3,738, 11,893, 7,738, and 6,603 persons in 2022, 2023, 2024, and 2025, respectively.[4–9]

In Thailand, the number of Muslims in Pattani, Yala, and Narathiwat provinces was 44% of the total Muslims in Thailand.[10] These provinces are considered high-risk due to their high Muslim population density. Moreover, Thailand, a regional travel hub and destination for Muslim pilgrims traveling to and from the Middle East, remains at risk for MERS importation. The reports from the Division of Epidemiology of the Thai Department of Disease Control showed that, from 2015 to the present, there were 1,007 imported suspected cases in Thailand, comprising 532 males and 475 females, including three confirmed cases. As of 2025, no new confirmed cases have been reported in Thailand since 2016.[4] Nevertheless, the risk persists due to the arrival of international travelers, particularly Hajj and Umrah pilgrims from high-risk regions, as well as tourists visiting high-risk areas before traveling to Thailand.

The International Health Regulations (IHR) 2005 and the Joint External Evaluation guide all member countries to emphasize the importance of strengthening surveillance, laboratory diagnostics, early detection at the point of entry, and risk communication to mitigate the threat of emerging infectious diseases, such as MERS.[5,6] Nationally, according to the Communicable Disease Act B.E. 2558 (2015), MERS is classified as one of fourteen dangerous communicable diseases. As such, it is mandatory to implement surveillance, prevention, and control measures for this disease under the legal framework.[7]

The objectives of this study were 1) to estimate the extent of a potential spread following importation of a MERS outbreak in Thailand using predictive modeling and 2) to assess Thailand's preparedness through qualitative analysis of policy, systems, and stakeholder opinions to provide evidence-based recommendations and policy guidance for the Department of Disease Control and the Ministry of Public Health to develop effective disease control strategies, and reduce the burden on improving people's quality of life and well-being.

Methods

Locations and Timeframe

This study was conducted at the Ministry of Public Health, Nonthaburi, Thailand, between October 2024 and May 2025. The preparatory activities, including problem identification, objective setting, literature review, study design, and questionnaire design and validation, were conducted between October and December 2024.

Study Design

The study employed a mixed-methods study, combining quantitative and qualitative studies. The data were collected from January to May 2025.

Quantitative study

The quantitative study was conducted between January and May 2025, utilizing a predictive modeling study based on the deterministic Susceptible-Exposed-Infectious-Recovered (SEIR) compartmental model. This study developed a modified SEIR model based on literature reviews to simulate MERS-CoV transmission in the three southern provinces of Thailand.[8–10] The model incorporated additional compartments to reflect quarantine and isolation measures and separately represented Muslim and non-Muslim populations to account for differences in contact patterns.

In the model, individuals transition from the susceptible (S) compartment to the exposed in the community (Ec). After exposure, individuals may either remain in the community or enter quarantine (Eq). Quarantined individuals who become infectious are transferred directly to isolation, either as symptomatic (Iisq) or asymptomatic (Iiaq). Other infectious individuals are categorized as symptomatic in the community (Ics), symptomatic in isolation after community exposure (Iisc), and asymptomatic in the community (Ica) or in isolation (Iiac). Symptomatic individuals may progress to hospitalization (H), with outcomes of either recovery (R) or death (D). All recovered individuals move to the R compartment, representing recovery and being immune (Figure 1).

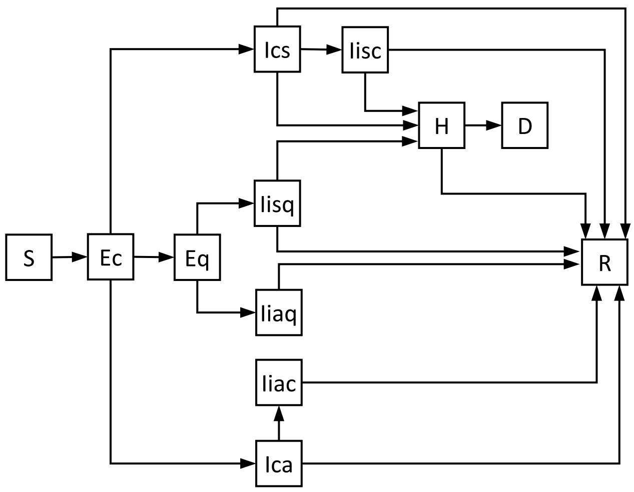

Figure 1. Model framework of MERS-CoV situation in three southern provinces of Thailand

The total modeled population was 2,111,820 individuals, comprising 1,567,756 Muslims and 544,064 non-Muslims. The model was initialized with

10 symptomatic and 10 asymptomatic MERS-CoV-infected Muslim individuals, while the rest of the population began as being susceptible. The simulation proceeded in daily time steps over a period of 120 days. The model assumed a closed population with no births, deaths unrelated to MERS-CoV, or migration. Mixing was considered homogeneous within Muslim and non-Muslim groups, with limited cross-group contacts. No model fitting was performed, as Thailand has not experienced a MERS-CoV outbreak to provide calibration data. Parameter values were taken directly from published literature and expert consensus and applied as fixed inputs for all simulations. Key parameters, system variables, and governing equations are detailed in Supplementary Tables 1–2.

The model was used to evaluate five intervention scenarios to explore the impact of different public health measures on MERS-CoV transmission (Supplementary Table 3). Scenario A served as the baseline with no interventions, reflecting the natural course of transmission without additional control measures. Scenario B examined the effect of increasing the proportion of severe cases admitted to high-resource hospitals, which have a lower case fatality rate compared with low-resource hospitals. Scenario C simulated increased quarantine coverage, increasing the proportion of exposed individuals identified and quarantined before becoming infectious in the community. Scenario D assessed the impact of earlier case detection by shortening the delay between infectiousness and isolation for both symptomatic and asymptomatic individuals, thus reducing onward transmission. Scenario E combined all major interventions—increased access to high-resource hospitals, increased quarantine coverage, and earlier detection—to reflect an integrated control strategies. The reproductive number (R) was classified into three scenarios (R=1, R=2, R=3) based on expert opinion and literature review.[11]

Qualitative study

The qualitative study was conducted between March and May 2025 as follows.

The documentary review part was conducted between March and May 2025 to assess Thailand's existing policies, plans, and operational frameworks related to MERS preparedness, as well as those of international organizations. The reviews included internal guidelines, national strategic plans, WHO technical reports, and MERS-specific plans and procedures, as well as original articles, totaling 29 online documents.[1,3,4,12–37]

Between April and June 2025, in-depth interviews were conducted using a semi-structured questionnaire to explore the views of participants, including policymakers, experts, and relevant officers. The interviews were informal, allowing participants to share their insights and experiences freely. This study collected data from 21 participants, including the director general of the Department of Disease Control, two deputy director generals of the Department of Medical Sciences and Health Service Support, eight directors of Department of Disease Control, three senior experts of Department of Medical Services and Disease Control, one deputy director of provincial health office, and four local public health officers of Department of Disease Control, and international organizations (one from the World Health Organization in Thailand and one from Thailand-MoPH-U.S. CDC Collaboration (TUC)).

Data Analysis

For Quantitative data, this study used predictive modeling based on the SEIR model, using the freeware of Vensim, which can be downloaded at URL <https://vensim.com/free-downloads/>.

Qualitative data were collected as part of the data triangulation process. A structured approach was applied to identify, select, and examine relevant documents, including national strategic plans, guidelines for MERS surveillance, World Health Organization (WHO) technical reports, and protocols.

This study analyzed documentary reviews by using a thematic analysis approach. According to the WHO International Health Regulations (IHR) core capacities, a deductive thematic analysis was conducted using pre-established themes.[33] Each extracted piece of content was coded into one or more IHR categories, and thematic analysis involved summarizing the content under each theme. Representative quotations from documents were used to illustrate key findings. Triangulation with qualitative data from in-depth interviews was used to enhance validity and provide a more comprehensive assessment.

This study employed thematic analysis for the in-depth interview data. It involved data preparation, coding, theme identification, including key themes and sub-themes, interpretation, and reporting of the results, which was supported by representative quotes. Additionally, this study employed data triangulation for verification purposes.

Results

Quantitative Study

The simulation of MERS-CoV outbreak in three southern provinces of Thailand showed that early case detection and combined interventions consistently reduced the epidemic burden across all reproductive number scenarios (R=1, 2, 3). Under baseline conditions, the peak number of daily new infectees reached 0.84, 1.80, and 3.00 for R=1, 2, and 3, respectively, with peaks occurring on day 7–11. Increasing quarantine coverage modestly reduced cumulative infections, whereas early detection and combined strategies had the greatest effect, lowering cumulative infections (including initial imported cases) from 37.67–241.65 in the baseline to 29.22–69.03 and 28.55–54.73, respectively. For severe cases, the baseline cumulative burden ranged from 13.66 to 79.92, but this was reduced to 8.70–16.22 with combined interventions. Mortality was also reduced with cumulative deaths decreased from 6.82–37.56 in the baseline to 3.76–7.00 under combined interventions. Peak timing of severe cases and deaths was delayed under higher R values, but occurred earlier when early detection was implemented (Table 1).

Table 1. Simulation results under different intervention scenarios, as indicated by the basic reproduction number (R)

Outcome	Scenario	R=1	R=2	R=3
Peak number of new daily infectees*	Baseline (A)	0.84	1.80	3.00
	High-resource hospital admission (B)	0.84	1.80	3.00
	Increased quarantine coverage (C)	0.84	1.75	2.77
	Early case detection (D)	0.62	1.30	2.05
	Combined interventions (E)	0.63	1.30	2.01
Cumulative number of infectees†	Baseline (A)	37.67	79.97	241.65
	High-resource hospital admission (B)	37.67	79.97	241.65
	Increased quarantine coverage (C)	35.37	60.12	105.90
	Early case detection (D)	29.22	43.61	69.03
	Combined interventions (E)	28.55	39.68	54.73
Incidence proportion (per 100,000 population)§	Baseline (A)	1.78	3.79	11.44
	High-resource hospital admission (B)	1.78	3.79	11.44
	Increased quarantine coverage (C)	1.67	2.85	5.01
	Early case detection (D)	1.38	2.07	3.27
	Combined interventions (E)	1.35	1.88	2.59
Peak number of new daily severe cases	Baseline (A)	0.82	0.86	0.95
	High-resource hospital admission (B)	0.82	0.86	0.95
	Increased quarantine coverage (C)	0.81	0.85	0.90
	Early case detection (D)	0.57	0.61	0.66
	Combined interventions (E)	0.57	0.60	0.66
Cumulative number of severe cases	Baseline (A)	13.66	27.86	79.92
	High-resource hospital admission (B)	13.66	27.86	79.92
	Increased quarantine coverage (C)	12.52	20.30	34.61
	Early case detection (D)	8.97	13.22	20.73
	Combined interventions (E)	8.70	11.90	16.22
Peak number of new daily deaths	Baseline (A)	0.20	0.26	0.44
	High-resource hospital admission (B)	0.17	0.23	0.37
	Increased quarantine coverage (C)	0.19	0.24	0.33
	Early case detection (D)	0.15	0.18	0.23
	Combined interventions (E)	0.12	0.15	0.19
Cumulative number of deaths	Baseline (A)	6.82	13.80	37.56
	High-resource hospital admission (B)	5.89	11.92	32.45
	Increased quarantine coverage (C)	6.26	10.13	17.16
	Early case detection (D)	4.48	6.61	10.33
	Combined interventions (E)	3.76	5.14	7.00

**The number of new daily severe cases did not include the initial 20 imported cases. †Cumulative number of infectees included the initial 20 imported cases (10 symptomatic and 10 asymptomatic). §Incidence proportion (per 100,000) was calculated as the cumulative number of infectees divided by total population (2,111,820) × 100,000.*

The epidemic curves (Figure 2) show distinct effects of interventions on transmission. Scenarios A (baseline) and B (high-resource hospital admission) produced identical infection trajectories, with cumulative cases rising steadily, especially when R=3. Scenario C (increased quarantine coverage) moderately flattened the curves, while Scenario D (early detection) and Scenario E (combined interventions) further suppressed transmission, with infections plateauing earlier.

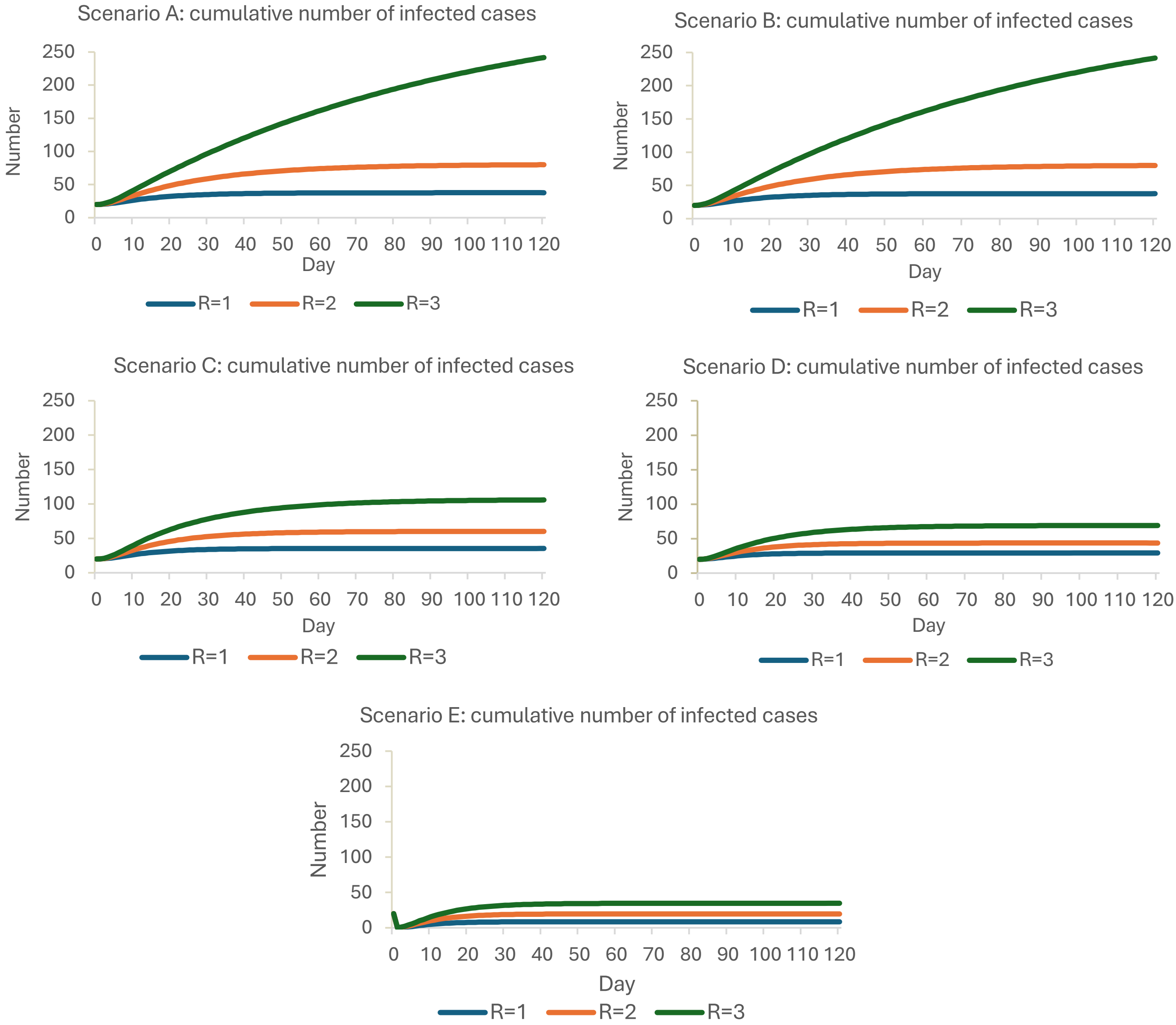

Figure 2. Scenario A: Baseline, Scenario B: High-resource hospital admission, Scenario C: Increased quarantine coverage, Scenario D: Early detection and Scenario E: Combined interventions

Qualitative Study

Documentary review

During March and April 2025, a review of 29 online documents was conducted based on the eight WHO IHR core capacities theme. These documents were categorized into the eight WHO IHR core capacity themes, including surveillance, response, preparedness, risk communication, human resources, laboratory, point of entry, and health information systems. These findings indicated that Thailand has established MERS preparedness relying on the eight WHO IHR core capacities; although MERS-specific updates have been limited since 2016. The challenges included resource allocation, developing appropriate risk communication strategies for the different risk groups, integrated exercise training, laboratory-based/ syndromic surveillance, and digital system integration.

In-depth interviews

The characteristics of participants showed that most participants were men (61.9%), with a median age of 50 years (range, 25–63 years). The majority of educators held a doctoral degree or its equivalent (n=16, 76.2%), followed by a bachelor's degree (n=4, 19.0%), and a master's degree (n=1, 4.8%). Most participants had more than 10 years of experience (n=16, 76.2%), followed by 5–10 years of experience (n=1, 4.8%), and less than 5 years (n=4, 19.0%). According to the workplace, most of them were affiliated with the Department of Disease Control (n=15, 71.43%), followed by the Office of the Permanent Secretary, Ministry of Public Health, (n=1, 4.76%), Department of Medical Science (n=1, 4.76%), Department of Medical Services (n=1, 4.76%), Department of Health Service Support (n=1, 4.76%), TUC (n=1, 4.76%), and WHO (n=1, 4.76%).

The results of interviews with 21 participants were described as six main themes and sub-themes, including policy, plans, and governance (national strategy, plans for MERS), operational and system gaps (surveillance systems, laboratory capacity, risk communication), human resources and capacity building (staff readiness, training systems, joint investigation team mechanisms), resource and medical supply management (personal protective equipment stockpiles, operational support), coordination and collaboration (domestic and international linkage, command structures), and technology and information systems (use of digital tools and technology, data fragmentation). It showed that operational gaps existed in strengthening specific MERS surveillance, laboratory capacity, MERS-specific training, and coordination mechanisms. Technology was underutilized due to siloed data systems. Stakeholders demonstrated the importance of integrated exercises, updated concept of operations, and enhanced local engagement at the community level.

Discussion

The results have also highlighted that Thailand has partial readiness in responding to the MERS outbreak, primarily related to improvements made during the COVID-19 pandemic and proactive preparedness, particularly in high-risk regions. However, gaps remain in operational aspects.

The SEIR models demonstrated the importance of early detection, quarantine, increased admission to high-resource hospitals, and integrated interventions in minimizing MERS-CoV transmission, particularly in high-risk provinces. The timely implementation of combined interventions (all major interventions) was more effective than isolated quarantine measures alone. The early case detection alone was a good measure to reduce the peak of infectees and severe cases compared to other measures alone. The model supported the use of targeted preparedness strategies and investment in surveillance, diagnosis, and community engagement for a timely public health response.

The modeling indicated the likelihood of MERS outbreak in three southern provinces, which demonstrated that MERS outbreak is less likely to be widely transmitted, especially nationwide. It is relevant to findings from the study of MERS in South Korea, where community transmission was limited and most widespread transmission occurred in healthcare settings.[3] Furthermore, the study has emphasized the importance of MERS context-specific preparedness, particularly in areas with high risk, such as the southern border provinces. According to literature reviews, the results indicated that tertiary or general hospitals were well-prepared for MERS, while primary and secondary hospitals were less prepared. The results showed that the parameters aligned with those from a study conducted in South Korea during the 2015 MERS outbreak and were relevant to the hypothesis of the SEIR modeling.[3] Modeling findings has emphasized the importance of timely isolation, particularly for both symptomatic and asymptomatic cases, in minimizing the size of the outbreak.

Lessons learned from the COVID-19 pandemic surveillance and disease control have indicated that suitable surveillance for emerging diseases is necessary. MERS showed a similar mode of transmission to COVID-19, it has a higher case fatality rate and is associated with high care costs, even though it is less likely to be widely transmitted. MERS preparedness remains a significant consideration. Additionally, it is one of fourteen dangerous communicable diseases listed under the Communicable Disease Act B.E. 2558 (2015). However, to date the restriction on surveillance has been low, which may have contributed to the system's limited sensitivity in detecting diseases effectively. This is also the case for MERS, for which there have been no outbreaks in Thailand since 2016. Its surveillance is included in the national communicable disease surveillance system, which currently covers 176 diseases.[13] To address this issue, a dedicated surveillance system for dangerous communicable diseases, including MERS, should be established to facilitate early and rapid detection of such diseases. This system could adapt and leverage the surveillance, prevention, and control measures that were strengthened during the COVID-19 pandemic. It will require a lesser increase in budgetary and resource burden compared to strengthening the entire notifiable disease surveillance, in addition to practical monitoring for those dangerous communicable diseases.

Qualitative findings have revealed gaps in MERS-specific surveillance systems, laboratory capacity, health literacy among high-risk groups, preparedness for resources, and data system fragmentation. Surveillance, particularly syndromic and laboratory-based, was identified as the most critical area requiring strengthening. Additionally, syndromic and laboratory-based screening at the points of entry should be considered for efficient measures, particularly in the early detection of international travelers and Hajj pilgrims, to reduce risk and lower the budget for tracing and quarantine. These findings aligned with the six building blocks for a health system, as recommended by the World Health Organization.[38]

The consistency of the coordination mechanisms indicated the challenge of coordination. The protocols within the Department of Disease Control have not been regularly updated. Therefore, this results in gaps in coordination and timely response. Additionally, health volunteers played a key role in the gap between policy and practice, thereby enhancing the surveillance system and risk communication. It is in consideration of supporting this community-level network to remain effective and integrate with the national preparedness strategy in disease control, as seen in the role of health volunteers in Thailand, who played a key role in surveillance and response to the pandemic.[31,34]

Another gap identified was the fragmentation of data across different units within the health system, leading to data delays, duplication, and incomplete information. Fragmentation of data was related to effective management in public health emergency management.[35–37]

Limitations

This study has some limitations. The SEIR modeling is based on hypothetical parameters regarding high-risk populations, MERS characteristics, and disease control measures, which were based on available data from literature reviews, may not accurately reflect real-world dynamics. This study primarily involved the perspectives of policymakers and experts, which may introduce information biases. Another limitation is that Thailand has never experienced indigenous transmission or a large-scale outbreak of MERS-CoV. Therefore, both the modeling component and the qualitative analysis were based on assumptions drawn from the experience of other countries or from previous respiratory outbreaks in Thailand. However, it can be reasonably defended that such knowledge and prior experience are relevant and applicable, given the similarities in transmission mechanisms and public health response requirements for emerging respiratory pathogens.

Recommendations

Recommendations include strengthening early detection, surveillance, laboratory capacity, and risk communication; regular preparedness plans, standard operating procedure, training, and coordination mechanisms; ensuring adequate resources and intersectoral collaboration and coordination; and advancing national data integration. Future studies should assess practical preparedness at regional levels and readiness for other emerging diseases.

Conclusion

The mixed-methods study assessed the potential spread and preparedness for the MERS outbreak in Thailand. SEIR modeling indicated that the baseline scenario resulted in the highest number of infections and deaths, while early detection and combined interventions reduced the outbreak size across all R values, with nationwide spread being unlikely. The qualitative findings revealed strengths in national strategies, experienced personnel, and coordination. However, gaps were in MERS-specific surveillance, laboratory capacity, health literacy among high-risk groups, resource preparedness, and fragmented data systems.

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Author Contributions

Rapeepan Phothong: Conceptualization, methodology, writing—original draft, writing—review & editing, supervision, validation, project administration. **Natthaprang Nittayasoot:** Conceptualization, methodology, writing—original draft (methodology), writing—review & editing. **Panithee Thammawijaya:** Conceptualization, methodology, validation.

Ethical Approval

This study was conducted as part of the Department of Disease Control's mandate in communicable disease surveillance, prevention, control, and public health preparedness. This was formally approved as routine public health activity and was therefore exempt from ethical review for research in humans.

Informed Consent

Data collection was conducted under an approved program with official permission letters obtained from legal authorities. Accordingly, individual informed consent from participants was not required.

Data Availability

The quantitative data supporting the findings of this study are available in the supplementary material of this article. The data from documentary reviews were derived from publicly available resources and cited in the references. The in-depth interview data are not publicly available due to privacy and ethical restrictions, but may be available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this article.

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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 generative AI tools (ChatGPT and Grammarly) to enhance clarity and correct grammatical errors. The content produced by these tools was reviewed and edited by the authors, who accept full responsibility for the final text.

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The Grammar of Science: Do Clusters Really Matter?

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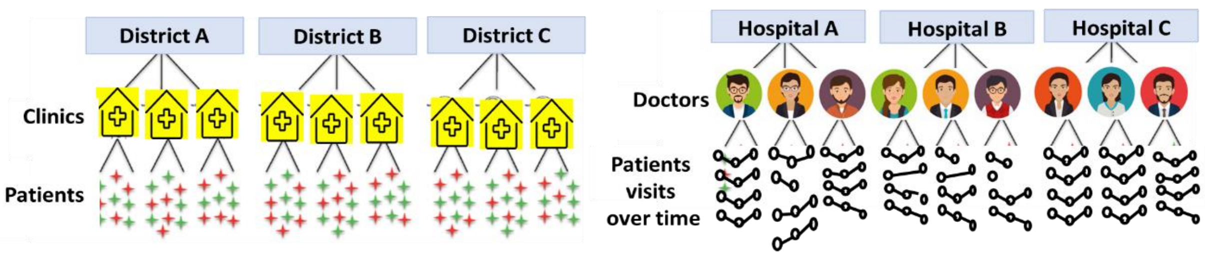
Clustering of observations is a frequent occurrence in epidemiological and clinical research.[1–3] When planning a study, it can be beneficial to consider whether clusters exist in the population and whether the sampling approach takes them into account. For instance, in two-stage sampling, where clusters (e.g., villages) are selected first and units (e.g., households) are sampled within them, clustering within such hierarchical structure may substantially impact statistical analysis results.[3] Individuals within the same group in a population may not be independent—for example, those who share health-related environments or affect each other's behaviors and exposures in a cohort study.[1] In complex surveys, where participants are drawn from the same setting (e.g., students in a classroom or family members in a household), recruitment may be planned to examine group membership effects.[2] In cluster-randomized trials where randomization occurs at the cluster level rather than the individual level, clustering can affect study conclusions, particularly when treatment effects vary across clusters.[3]

Even when clustering is present in the designs described, it is often not considered in statistical analyses. In this paper, we explore how clustering affects the analysis of clustered data using logistic regression.

Clustered Data: Concept and Implications

Several terms are commonly used to describe clustered data, including "clustering," "nesting," "grouping," and "hierarchies," which are often used interchangeably. All of these terms refer to the concept that observations that can be organized into several distinct groups at a lower, micro level within one or more higher-level, macro units. Each macro unit represents a "level," and datasets can include multiple levels (multilevel), such as in two-level or three-level sampling designs.[4,5] As shown in Figure 1, clustered data can occur at multiple levels. Patients are nested within doctors, and doctors are, in turn, grouped within hospitals. Similarly, repeated measurements on the same individual can be viewed as nested data, where the observations are nested within the person. The impact of clustering may differ across hierarchical levels. For example, patients (level-1 units) within a single hospital or community (level-2 units) may show minimal variation in background characteristics. By contrast, differences in infrastructure, preparedness, and patient backgrounds across hospitals or communities lead to greater heterogeneity among these units.[6]



Level 1: Patients are clustered within a clinic.
Level 2: Clinics are clustered within a district.

Level 1: Patient visits are repeated measures.
Level 2: Patients are clustered within a doctor.
Level 3: Doctors are clustered within a hospital.

Figure 1. Multilevel structure of clustered data

Clustered data are common and could be problematic. A fundamental assumption underlying most standard statistical methods is that individual observations are independent, meaning that the value of one observation does not affect another.[1,7,8] Clustering often causes observations within the same cluster to be more alike than measurements from different clusters.[9] When individuals are clustered, they are not fully independent of each other. Similarities, or homogeneity, between subjects in clusters reduces the variability of their responses, compared with that expected from a random sample.

Failing to account for clustering can lead to substantial increases in Type I error rates and reduce the statistical power to detect differences between groups.[10,11] Generally, analyzing clustered data requires a larger sample size than independent data to achieve comparable person-level power. Incorporating more clusters and allowing for varying cluster sizes can improve estimate accuracy and enhances the ability to detect differences between clusters.[4] It is important to note that, when the statistical model is correctly specified and the degree of clustering is moderate, coefficient estimates typically remain unbiased. However, if the correlation among observations within clusters is ignored, the estimation of standard errors can be substantially biased—either underestimated or overestimated—leading to incorrect inferences and potentially misleading conclusions.[7] Some researchers even suggest that, in cases where statistical analysis taking into account clustering effect may not be strictly necessary, applying it can still yield approximately correct standard errors.[3]

Clustering can influence statistical inference in regression analyses, especially when the outcome variable remains clustered even after accounting for all measured predictors.[2] It also matters when both residuals and predictor variables are correlated within clusters.[3] Ignoring clustering may lead to biased estimates or inaccurate standard errors in regression model. When observations vary more between clusters than within clusters, standard regression models tend to overestimate the precision of predictor effects. Conversely, when observations are less clustered, the precision may be slightly underestimated.[2]

Logistic Regression vs. Multilevel Mixed Logistic Regression

Logistic regression is a widely used statistical method, especially in epidemiology. In particular, binary logistic regression describes the relationship between one or more predictor variables (X) and a binary outcome (Y), where Y takes one of two possible values: 0 (no event) or 1 (event occurs).

Unlike linear regression, which assumes a continuous and normally distributed outcome, logistic regression applies a logit (log-odds) transformation to the outcome. The log-odds is the natural logarithm of the odds, where odds represent the ratio of the probability of the event occurring to the probability of it not occurring, ln(Py/1-Py) or ln(Py=1/Py=0). As illustrated in Figure 2(a), in a simple logistic regression model, a one-unit increase in predictor X changes the log-odds of the outcome by an amount equal to the coefficient β_1. When this coefficient (β_1) is exponentiated, it produces the odds ratio (OR), which represents the multiplicative change in odds associated with a one-unit increase in the predictor.[12,13]

The logistic function, also called the sigmoid function, produces an S-shaped curve (Figure 2(b)) that maps log-odds to probabilities. The resulting probability, P(Y=1), is referred to as a conditional probability because it is calculated given specific values of the predictors (X). In other words, the probability of the event occurring depends on the values of the variables included in the model—P(Y=1 | X).[14]

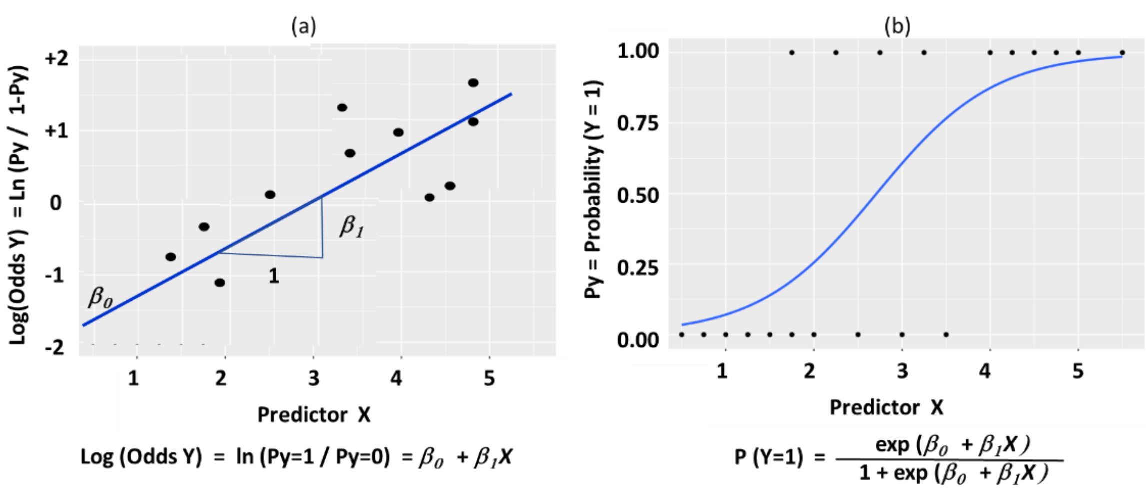


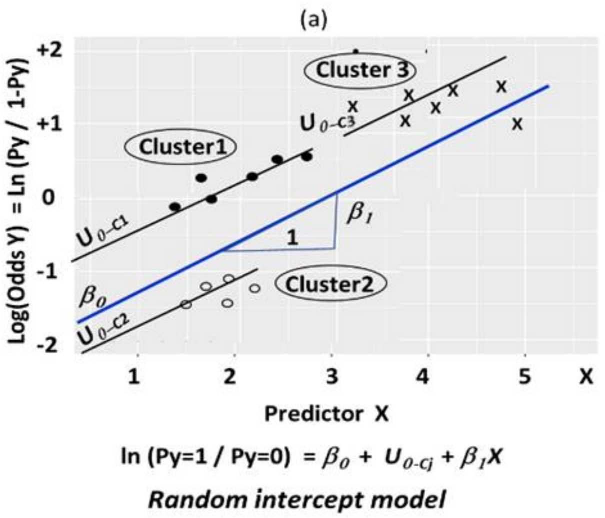
Figure 2. Logistic regression model

Multilevel mixed logistic regression extends the traditional logistic regression framework by incorporating the dependency among observations caused by clustering.[6,15] This method is frequently used in health research to properly handle clustered data when estimating the influence of both individual-level and group-level predictors on binary outcomes.[6] Ignoring clustering in a standard logistic regression, rather than addressing it with a multilevel mixed model, can result in substantial problems due to variability within clusters.[16] When a multilevel approach is not applied, an alternative is to include cluster indicators as dummy variables—though this is only practical when the number of clusters is relatively small. Nevertheless, this approach is often inefficient and less parsimonious.[17]

Notably, multilevel mixed models are extensions of the three most common regression approaches: linear, logistic, and Poisson. These models, also known as mixed-effects, hierarchical, or multilevel models, provide a statistical framework for analyzing data organized into multiple levels.[18] They are designed for situations where observations are clustered, enabling researchers to estimate both overall effects and cluster-specific differences.[19] Derived from the general linear mixed-effects model framework, they are termed "mixed" because they combine fixed effects—parameters that remain the same across clusters—with random effects, which vary between clusters.[4] Fixed effects capture consistent influences across all units, whereas random effects represent variability among them. When the units are individuals, random effects reveal individual-level differences. Common types include random intercepts, which account for differences in cluster means, and random slopes, which reflect variations in how predictors affect outcomes across clusters.[18]

The random intercept model includes a cluster-specific intercept that is estimated separately for each cluster. Its fixed component consists of the overall intercept (β_0) and slope (β_1), which apply to all observations, while the random component represents the unique intercept (U_0) for each cluster (Figure 3(a)). By incorporating random intercepts, the model accounts for unobserved group-level heterogeneity in the outcome, allowing baseline differences between groups to be properly reflected in the analysis.[20] This is especially useful for evaluating how much of the outcome's variation exists between clusters compared to within clusters. When clusters differ substantially, their intercepts deviate from the fixed component, resulting in a larger standard deviation of cluster-specific intercepts. Conversely, when observations within clusters are very similar, their outcomes tend to align closely with the fixed component.[1]

The random slope model allows the relationship between a predictor (or predictors) and the outcome to vary across clusters.[2,21] In contrast, the random intercept model allows intercepts to differ by group but assumes the slope (β_1) is the same across all groups. The random slope model relaxes this assumption by letting slopes vary randomly between groups.[1,20] As a result, both slopes and intercepts are treated as random effects, giving each cluster its own intercept (U_0) and slope (U_1). The model equation is adjusted accordingly to account for variability in both intercepts and slopes across clusters (Figure 3(b)). This flexibility is particularly useful for understanding how regression patterns differ across various group-level contexts.[20,22]



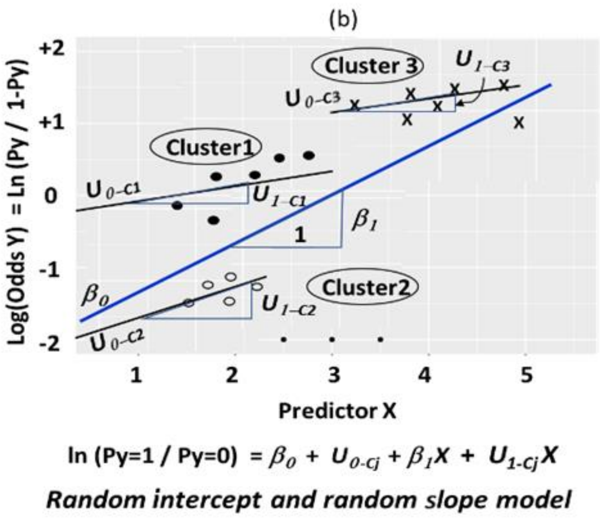


Figure 3. Multilevel mixed logistic regression models

In theory, the random slope model is appealing because it allows the relationship between predictor(s) and the outcome to vary across clusters. When the lower-level unit is at the individual level, it is even more plausible that individual characteristics will influence the outcome differently. There is considerable debate on this issue. If there are strong a priori reasons to believe that a fixed effect should vary across individuals or clusters, random slopes should be included, provided the data can support such a model.[23,24] This is particularly important when examining cross-level interactions, where the effect of a variable at one level (e.g., individual-level) on the outcome is influenced by a variable at a higher level (e.g., cluster-level). In such cases, the literature recommends using a random slope model. Ignoring these interactions can lead to seriously biased and anti-conservative inferences.[25]

Selecting a random slope model, however, comes with several challenges. Most studies using multilevel mixed models prefer a random intercept model, as it is simpler to assume that the relationship between predictors and the outcome is consistent across all groups. The rationale for including random slopes is less straightforward and should be guided by subject-matter knowledge. It is generally recommended to first identify variables for which a group-dependent effect (random slope) is plausible.[26] If the model converges without warnings, random slopes can generally be retained in the model. Inclusion decisions are usually driven by theoretical considerations rather than statistical significance in a particular sample. Nevertheless, likelihood ratio tests can be applied, and slopes that do not improve model fit should be removed to maintain model parsimony.[23]

There are several drawbacks associated with random slope models. They can sometimes encounter singular fits, either because the correlation between slopes and intercepts is estimated near ±1, or because the variance of the random slopes is estimated near zero. In the first case, a model without the correlation can be fitted; in the latter, the random slopes are typically removed.[23] In practice, including random slopes often leads to overfitting. Moreover, mixed models assume that random effects are multivariate normal—a condition that may not hold, particularly when random slopes are included.[24]

When choosing between a random intercept and a random slope model, researchers can fit both models and compare model fit metrics. Prioritize variables expected to have the strongest effects, then estimate the model including the selected fixed and random effects. Note that data generally contain less information about random effects than fixed effects, so including many random slopes can slow estimation or even prevent convergence. Importantly, not all predictors need random slopes; only those for which a group-dependent effect is theoretically justified should be considered. Evaluate the significance of random slopes and remove those that are not significant. Similarly, assess regression coefficients and exclude non-significant predictors and consider whether to include interaction effects between predictors in level-one variables. Random slopes for interaction terms are generally discouraged, as they are often difficult to interpret.[26]

Goodness of Fit of the Model

The concept of goodness of fit refers to how effectively a statistical model captures the patterns in observed data. It assesses the agreement between predicted results and actual outcomes, providing an indication of the model fit. Selecting an appropriate model often involves a trade-off between accurately explaining the data and avoiding overfitting or unnecessary complexity. Several metrics are available to guide this decision, with the most widely used being the Akaike Information Criterion (AIC) and the Bayesian Information Criterion (BIC). These criteria help balance model fit and simplicity, leading to models that explain the data well without adding excessive complexity.[27–30]

AIC evaluates models by considering both fit and complexity. It measures how well the model explains the data while applying a penalty for the inclusion of additional parameters to prevent overfitting. The formula is: $AIC = -2 \ln(\text{Likelihood}) + 2k$ where "Likelihood" reflects the model's fit to the data and k is the number of parameters. In essence, AIC combines the log-likelihood with a complexity penalty, ensuring a balance between model fit and parsimony. For example, in logistic regression, adding extra predictors will only improve AIC if they substantially enhance the model's fit, thereby reducing the risk of overfitting. In practice, goodness of fit is closely tied to model selection, especially in deciding how many significant predictors should be included in the model.

BIC is similar to AIC but imposes a stronger penalty for complexity, particularly in large datasets. Its formula is: $BIC = -2 \ln(\text{Likelihood}) + k \ln(n)$ where n represents the sample size. BIC is based on Bayesian probability principles and tends to favor simpler models when the evidence for added complexity is weak. Consequently, BIC is particularly useful in large-sample contexts where the risk of overfitting is high.

Both AIC and BIC estimates how much information is lost when a candidate model is used to approximate reality. Lower values indicate better models, but these metrics are meaningful only when comparing models estimated on the same dataset. In general, AIC tends to favor more complex models relative to BIC, making it a preferred criterion for smaller datasets where over-penalizing complexity could eliminate relevant predictors. Conversely, BIC is often preferred in large datasets because of its stricter penalty, which helps prevent overfitting. In practice, neither AIC nor BIC provides an absolute measure of model quality; rather, they are comparative tools that aid in selecting the most appropriate model among competing alternatives.[27–30]

Model Accuracy in Outcome Classification

Logistic regression is one of the most widely used algorithms for classification purposes. Its predictive performance is typically evaluated using the Receiver Operating Characteristic (ROC) curve and the Area Under the Curve (AUC).[17,30,31]

Initially developed in signal detection theory, ROC curves have become a widely used method for evaluating classification performance. Classification involves predicting the category an observation belongs to based on given features. To illustrate this classification concept, let us consider a diagnostic test evaluated against a 'gold standard' that determines the true disease status.[32] If the test predicts positive and the true condition is positive, it is a True Positive (TP). If the prediction is positive but the condition is negative, it is a False Positive (FP). Similarly, a negative prediction that matches a negative condition is a True Negative (TN), and a negative prediction for a positive condition is a False Negative (FN). From these, Sensitivity (or True Positive Rate, TPR) is calculated as TP/(TP+FN), representing the proportion of correctly identified positives. Specificity (or True Negative Rate, TNR) is TN/(TN+FP). The False Positive Rate (FPR) is FP/(FP+TN), which equals (1–Specificity), and the False Negative Rate (FNR) is FN/(FN+TP), or (1–Sensitivity). While some diagnostic tests produce binary results (positive or negative), others provide continuous scores. For such cases, a cutoff threshold is applied to determine the predicted class. Adjusting this threshold impacts sensitivity and specificity—improving one often reduces the other. ROC curves illustrate this trade-off by plotting FPR on the x-axis against TPR on the y-axis across various threshold values. Lower values on the x-axis correspond to fewer false positives, while higher values on the y-axis indicate more true positives. This visualization provides a comprehensive view of a classifier's performance under different threshold settings.[30,33,34]

So, how does logistic regression perform classification? The process starts by fitting a model and computing predicted conditional probabilities P(Y) for each observation. A threshold—commonly 0.5—is then used to assign class labels: predictions above 0.5 are classified as 1 (positive), and those below as 0 (negative). ROC analysis is then applied to assess the model's ability to discriminate between actual outcomes (Y = 0/1) across different thresholds using P(Y). Here, TPR is the proportion of actual positives correctly classified as positive, while FPR is the proportion of actual negatives incorrectly classified as positive.[17,30,31]

The Area Under the Curve (AUC) summarizes the ROC curve into a single value that reflects a model's overall capability to distinguish between positive and negative outcomes. It represents the likelihood that a randomly chosen positive case and a negative case are correctly ranked by the model. AUC values range from 0 to 1, where 0.5 indicates no discrimination (equivalent to random guessing), and 1 represents perfect classification performance (Figure 4).[17,30,31]

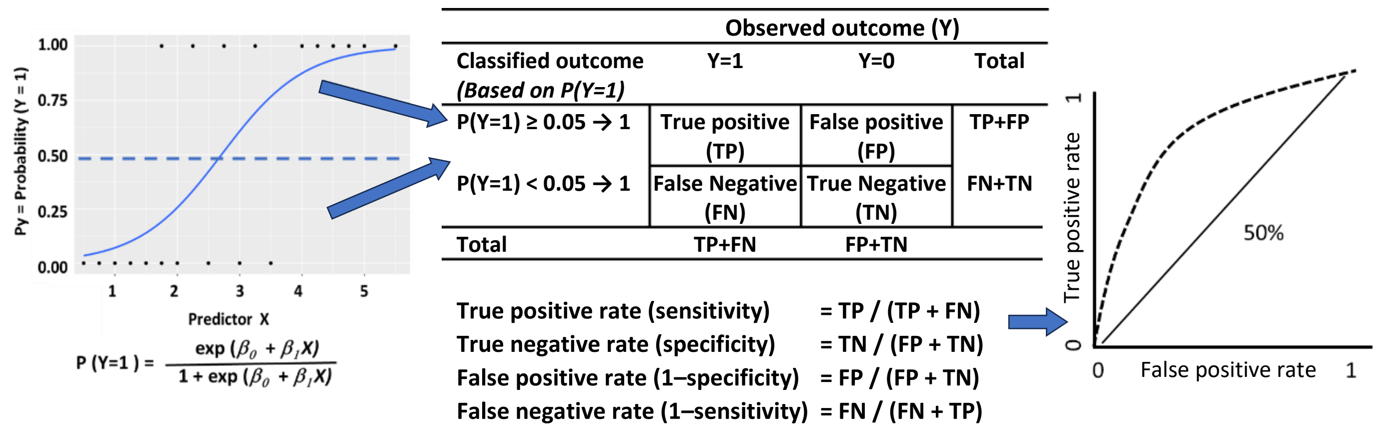


Figure 4. ROC curve & AUC for logistic regression classification

Relevancy of Clustering in the Model

One major challenge is that the degree of correlation among observations within a cluster can significantly impact study results. Even when this correlation is small or statistically insignificant, it can still affect the validity of the analysis.[16] Ignoring such correlation may lead to inaccurate *p*-values, overly narrow confidence intervals, and biased parameter estimates, ultimately resulting in misleading interpretations.[5]

Several metrics help quantify and interpret between-cluster heterogeneity and the influence of cluster-level variables. Examples include the median odds ratio (MOR), the 80% interval odds ratio (IOR-80), and the sorting out index (SOI).[6] Among these, the most commonly used measure is the intra-cluster correlation coefficient (ICC). The ICC, denoted by the Greek letter ρ (rho), indicates the similarity or relatedness of observations within the same cluster. It reflects the proportion of outcome variance explained by differences between clusters.[1,11] (ICC can also serve other purposes, such as evaluating measurement reliability/stability by assessing the correlation between two observations from the same group).[9]

There are multiple ways to compute the ICC, but the basic approach defines it as the ratio of variance between clusters to the total variance in the data. Like other correlation measures, ICC ranges from 0 to 1 and can be interpreted in both positive and negative directions. Its magnitude represents the degree of similarity within clusters: a higher ICC implies stronger clustering effects.[16] When all clusters have unique values, the ICC approaches 1; when clusters are identical, it approaches 0. In practical terms, an ICC near 0 suggests minimal contribution of clustering to the model, whereas an ICC close to 1 indicates strong clustering and significant relevance of clusters (Figure 5).[3,19]

$$ICC\ (\rho) = \frac{\sigma^2_{\text{between cluster}}}{\sigma^2_{\text{between cluster}} + \sigma^2_{\text{within cluster (residual)}}}$$

cluster	Y
1	10
1	10
1	10
2	15
2	15
2	15
3	21
3	21
3	21
4	34
4	34
4	34
5	45
5	45
5	45

Unique value in each cluster

ICC=1

cluster	Y
1	10
1	34
1	45
2	10
2	34
2	45
3	10
3	34
3	45
4	10
4	34
4	45
5	10
5	34
5	45

Similar values in all clusters

ICC=0

ICC: intra-cluster correlation coefficient

Figure 5. Intra-cluster correlation coefficients

Case Study

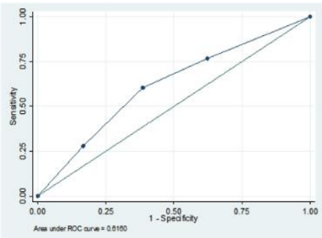
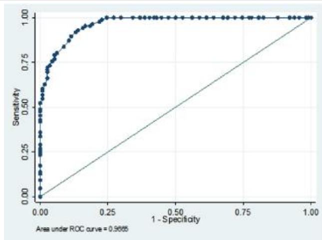
To illustrate the impact of clustering, consider two simulated datasets, each containing 200 observations divided into 20 clusters (10 observations per cluster). Both datasets include a binary outcome variable (Y=0/1) and two predictors (X1, X2). The primary distinction between them is the degree of clustering in the outcome: one dataset demonstrates a strong clustering effect, while the other shows a weak effect (Figure 6).

	Cluster																			
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Y	***High clustering effect***																			
0	10	4	10	9	10	1	3		7	10		3	10	10	5	6	5	1		10
1		6		1		9	7	10	3		10	7			5	4	5	9	10	
Y	***Low clustering effect***																			
0	4	5	5	5	5	7	4	4	6	4	8	3	5	3	2	5	7	2	3	9
1	6	5	5	5	5	3	6	6	4	6	2	7	5	7	8	5	3	8	7	1

Figure 6. Clustering effect in two hypothetical datasets

To evaluate model performance, two approaches were applied: standard logistic regression (which ignores clustering) and multilevel mixed-effects logistic regression with random intercepts (which accounts for clustering).

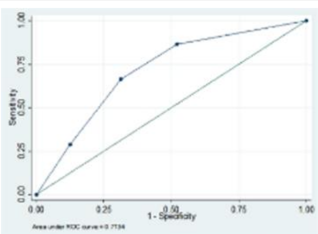
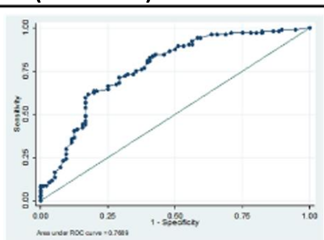
In the high-clustering dataset (Figure 7), the mixed-effects model substantially outperformed standard logistic regression in terms of fit. Classification accuracy showed a marked difference: the AUC for logistic regression was approximately 61%, compared to 97% for the mixed model. Here, the ICC was 0.89, underscoring the critical importance of accounting for clustering.

		Y=0	Y=1	Logistic regression Odds ratio (95% CI)	*p*-value	Mixed model–Logistic regression (with cluster effect) Odds ratio (95% CI)	*p*-value
X1	1	44	52	2.41 (1.36–4.29)	0.003	9.05 (2.74–29.81)	<0.001
	0	70	34	1		1	
X2	1	46	38	1.12 (0.63–2.00)	0.699	2.81 (0.93–8.47)	0.066
	0	68	48	1		1	
Model goodness of fit							
AIC				269.71		158.41	
BIC				279.61		171.61	
Relevancy of clustering							
ICC (95% CI)				-		0.89 (0.62–0.98)	
Accuracy of model classification							
AUC (95% CI)	0.61 (0.54–0.69)					0.97 (0.95–0.99)	

CI: confidence interval. AIC: Akaike information criterion. BIC: Bayesian information criterion. AUC: area under the curve. ICC: intra-cluster correlation coefficient.

Figure 7. Performance of models accounting for clustering versus ignoring clustering in a high-ICC dataset

In contrast, in the low-clustering scenario (Figure 8), both models produced similar fit statistics (AIC, BIC). Classification performance was also comparable: the AUC for logistic regression was about 71%, while the mixed model achieved 76%. The intraclass correlation coefficient (ICC) for the mixed model was 0.07, indicating that adjusting for clustering offered little advantage.

		Y=0	Y=1	Logistic regression Odds ratio (95% CI)	*p*-value	Mixed model–Logistic regression (with cluster effect) Odds ratio (95% CI)	*p*-value
X1	1	30	69	4.47 (2.44–8.18)	<0.001	4.90 (2.55–9.42)	<0.001
	0	66	35	1		1	
X2	1	32	51	2.05 (1.11–3.79)	0.022	2.12 (1.11–4.04)	0.022
	0	64	53	1		1	
Model goodness of fit							
AIC				252.44		252.70	
BIC				262.34		265.90	
Relevancy of clustering							
ICC (95% CI)				-		0.07 (0.01–0.37)	
Accuracy of model classification							
AUC (95% CI)	0.71 (0.64–0.78)					0.76 (0.70–0.83)	

CI: confidence interval. AIC: Akaike information criterion. BIC: Bayesian information criterion. AUC: area under the curve. ICC: intra-cluster correlation coefficient.

Figure 8. Performance of models accounting for clustering versus ignoring clustering in a low-ICC dataset

These examples show that the importance of clustering largely depends on the level of ICC. When ICC is low, using either a standard logistic regression or a mixed-effects model makes little difference. However, when ICC is high, ignoring clustering can result in poorer model fit, biased estimates, and reduced predictive accuracy.

Key Takeaways: Do Clusters Really Matter?

Clustering matters most when ICC is high—ignoring it can affect your results. When ICC is low, simpler models work fine, but with high ICC, mixed-effects models are recommended for more accurate and reliable predictions.

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