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Editorial

Mass Psychogenic Illness and Immunization Stress-related Responses: Rapid and Appropriate Management are Critical

J. D. Heffelfinger, Senior Editor

An article included in this issue of *Outbreak, Surveillance, Investigation & Response* describes the occurrence of mass psychogenic illness (MPI) during a human papillomavirus vaccine (HPV) campaign in a rural school in Bangladesh.[1] In 2020, cervical cancer was the fourth leading cause of cancer and cancer deaths among women, with approximately 600,000 new cases and more than 340000 deaths.[2] Almost all cervical cancer cases are caused by oncogenic or high-risk HPV types. WHO recommends that HPV vaccines be included in all national immunization programs to prevent cervical cancer, with the goal of reaching all girls by the age of 15 years and accelerate cervical cancer elimination by 2030.[2] HPV vaccines are very safe. Since the first HPV vaccine was licensed in 2006, more than 500 million doses have been administered and post-licensure surveillance has not detected any serious safety issues other than rare instances of anaphylaxis.[2] As of November 2023, 140 countries had introduced HPV vaccine.[3] Bangladesh introduced the HPV vaccine in a national campaign in October 2023. In October 2024, an event classified as MPI occurred among 19 students at an all-girls school in Bangladesh who developed symptoms shortly after receiving HPV vaccine. MPI has also been termed mass sociogenic illness, mass hysteria, epidemic hysteria, and anxiety-related reactions occurring in clusters, and it is defined as the collective occurrence of physical signs or symptoms (e.g., headache, dizziness, weakness) in persons with common beliefs about the cause of their symptoms.[4,5] MPI can occur in persons who are anxious, stressed, or emotionally vulnerable and may be associated with vaccinations and various exposures, such as to toxins, or rumors of exposures. The World Health Organization (WHO) uses the term "immunization stress-related responses" (ISRR) to describe symptoms and signs that develop following immunization that are related to anxiety and are not to the vaccine product or errors in the immunization program.[6] When ISRR occurs in clusters, it can be categorized as MPI. MPI can become epidemic, with spread of facts admixed with misinformation and rumors that are communicated rapidly and widely by word of mouth, phone, social media, and the press, and it can become increasingly difficult to contain. It is important to plan for ISRR, detect it early, manage it appropriately and communicate about it effectively before, during, and following vaccination campaigns to minimize chances it will spread.

MPI has occurred during HPV vaccination campaigns in multiple countries, frequently resulting in minimal impacts but occasionally leading to increased vaccine skepticism and vaccine hesitancy and dramatically reduced rates of vaccine coverage. Widely reported ISRR events with disastrous impacts occurred in Japan in 2013 and Columbia in 2014. In 2013, following extensive coverage of a widespread ISRR event in Japan, the country's national immunization program suspended its proactive recommendations for the HPV vaccination, and HPV vaccine coverage declined from approximately 70% in 2013 to less than 1% in 2019.[7] The decline in HPV vaccination in Japan between 2013–2019 is predicted to lead to approximately 25,000 excess cases and more than 5,000 additional cervical cancer deaths over cohort lifetimes than had HPV vaccine coverage remained at 70%.[7] In 2014, an ISRR event occurred during an HPV vaccine campaign in Carmen de Bolivar, Colombia, that initially involved 15 adolescent girls. However, with viral spread of reports and videos of affected girls fainting, twitching, and arriving unconscious at emergency rooms, the outbreak expanded to more than 600 cases across Colombia.[8] The events in Columbia shook public confidence in HPV immunization and by 2016, vaccine acceptance had declined to less than 15% from approximately 80% in 2014.[8]

WHO, in collaboration with the independent Global Advisory Committee on Vaccine Safety, developed a manual for program managers and health professionals on how to prevent and manage ISRR. The manual provides approaches to the prevention, diagnosis and management of ISRR; emphasizes that all healthcare professionals involved in immunization should be aware of and receive training about ISRR; discusses the importance of addressing prevention measures (including identifying individuals who may be at high risk for an ISRR, paying attention to precipitating factors during immunization, and taking measures to prevent or control ISRR); describes the role of WHO causality assessment classification; and outlines communication strategies before, during, and following immunization.[6]

The importance of the management of MPI and ISRR resonates with me personally. In 2019, as a technical officer with the WHO Regional Office for the Western Pacific's Expanded Program on Immunization, I provided technical assistance to the Solomon Islands' Ministry of Health and Medical Services (MHMS) in their national HPV roll out. A vaccination event was conducted at a school in a rural area. Girls in grades 5 and 6 (most of whom were 10–12 years old) were vaccinated in the school's gymnasium. Many of the girls had not eaten breakfast and it became hotter in the gymnasium as the day progressed. Several hours into the event, five girls became dizzy and weak in rapid succession. All five girls were given water and hard candy; four felt better after 30–40 minutes, but one girl was sent to the local emergency room because of persistent dizziness and weakness. There was concern about the reaction of students who saw the girls get dizzy and vaccination was called off for the day after the fifth girl's symptoms began. The vaccination team spoke to the headmistress, teachers, and concerned students and parents about the episodes to let them know that the episodes were likely due to a combination of heat, dehydration, lack of eating breakfast and observing the reactions of others. The team followed up with the five girls and they all were feeling well and attended school the following day. The team reconfigured the vaccination site on the second day so students could not watch others being vaccinated and provided water and candy to the students and the remaining girls in grades 5 and 6 were vaccinated; none complained of dizziness or weakness. The vaccination team credited the Solomon Islands' HPV vaccine crisis communication plan, which MHMS had developed in advance of the HPV vaccination campaign, with preventing the spread of ISRR to other girls at the school and beyond and with helping maintain public trust in HPV vaccination. The crisis communication plan described principles of appropriate response to rumors and steps that health officials and providers should take to respond to crises and rumors. The steps included ensuring proper sensitization and community mobilization in advance of vaccinations; understanding the content and source of rumors; providing key messages and facts to rumor sources via trusted partners; release of a statement about the safety of HPV vaccines; and notification of the provincial health authorities if crises or rumors escalate.

As with the ISRR event in the Solomon Islands, Jiti et al. reported that timely clinical care, appropriate and effective messaging, and coordinated response efforts were critical for preventing the spread of MPI and maintaining trust in the vaccination program.[1] When MPI occurs, it is essential to prevent and control its spread quickly and effectively. This is particularly true for ISRR following HPV vaccination at a time when vaccine skepticism and vaccine hesitancy are increasing in many areas, vaccine coverage rates are declining, and HPV-related morbidity and mortality may soon start to increase.

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A Typhus and Typhoid Fever Outbreak: A Diagnostic Dilemma in Joypurhat District, North-western Bangladesh, 2021

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Abstract

Typhoid (enteric) and typhus (*Rickettsia*) fevers are endemic in Bangladesh. This study describes an outbreak initially thought to be typhoid fever, but upon several patients' non-response to treatment, further evaluation discovered that these patients had typhus. One typhoid case did not respond to ceftriaxone (although sensitive in blood culture) and, due to empirical knowledge of the physician, was diagnosed as typhus by a significant Weil–Felix test and responded to doxycycline. A total of 241 cases were identified: 158 (65.6%) cases of typhoid fever, 44 (18.2%) with typhus, and 39 (16.2%) with typhoid and typhus co-infections. In this outbreak, cases in the spotted fever group rickettsia (SFGR) constituted the largest proportion, followed by the typhus group (TG), while the scrub typhus group (STG) had the smallest proportion. This finding was different from the typical subgroup pattern seen in Bangladesh of TG>STG>SFGR. Typhus may be misdiagnosed as typhoid fever due to similar clinical presentation, so it is essential for physicians to distinguish between the diseases because of different treatment and intervention modalities. Epidemiologists should be aware that both diseases can occur simultaneously in outbreaks. This study recommends enhanced training of physicians on the differential diagnosis of typhus and typhoid fever to reduce the misdiagnosis. In addition, laboratories need to upgrade their diagnostic protocols and capacity to use blood cultures to diagnose typhoid fever.

Keywords: typhoid fever, typhus, *Rickettsia*, typhus subgroups, Bangladesh

Introduction

Typhoid and typhus fever (*Rickettsia*) are endemic in tropical and subtropical countries worldwide, along with Bangladesh and neighbouring countries.[1–3] The three rickettsia subgroups are typhus group (TG), scrub typhus group (STG), and spotted fever group rickettsia (SFGR).[4] All typhus subgroups are evident throughout Bangladesh year-round, with the highest prevalence of SFGR in Rangpur and Rajshashi Divisions.[5,6] Rickettsial infections are a frequent, yet under-recognized cause of febrile illness in Bangladesh.[7]

Co-infection of typhoid fever with diseases such as dengue, malaria, leptospirosis, and hepatitis A or E has been documented.[7–10] There have been reports of typhoid and typhus co-infection in Bangladesh, other tropical and sub-tropical nations, and in South and East Asia. Both epidemic and endemic (murine) typhus can be misdiagnosed as typhoid fever due to overlapping clinical presentations and similar laboratory findings.[3,8–10]

A specific typhoid or typhus diagnosis is essential because the transmission and treatment is different. The mode of typhoid diseases transmission is mainly waterborne, followed by food-borne and direct contact. Multiple intervention strategies can be taken including provision of adequate chlorination and health education enhancement.[11–13] However, the mode of typhus transmission is mainly through vectors such as lice, fleas, or mites, or fecal droppings from rodents. Control and containment of typhus outbreak includes improving sanitation, controlling fleas, and reducing populations of rats, mice, and other animals.[11–14] Typhoid fever responds more effectively to fluoroquinolones or ceftriaxone; typhus with doxycycline treatment.[15]

On 17 Oct 2021, the pediatric consultant at Joypurhat Sadar Hospital (JSH) in Joypurhat District reported an increase in pediatric cases of suspected enteric fever to the Institute of Epidemiology, Disease Control and Research. The cases showed no improvement after two weeks of intravenous antibiotic treatment. The National Rapid Response team (NRRT), conducted an outbreak investigation to verify the outbreak, identify sources, determine the scope and magnitude, and described the misdiagnosis and mistreatment of a typhus fever case.

Methods

This study investigated the outbreak from 18 to 28 Oct 2021 at JSH, Joypurhat Municipality, Joypurhat Sadar Upazilla. A descriptive study following the One Health approach by describing the cases (by case definition, case finding) and field investigation (by case investigation with laboratory testing) followed by environmental sample testing.[15]

Operational Definitions

In this investigation, the term *typhus* was used to encompass all rickettsial infections detectable by the Weil–Felix test. Based on antigen reactivity, cases were categorized into typhus group (TG; OX19), spotted fever group rickettsiae (SFGR; OX2) scrub typhus group (STG; OXK), or mixed patterns involving more than one antigen.

This study defined suspected, probable and confirmed cases as follows:

- A suspected case (both for typhoid and typhus) was any person, irrespective of age and gender, in JSH presenting with fever associated with any of the following symptoms: headache, abdominal pain, nausea, vomiting, diarrhea/constipation for seven days from 4 Sep to 25 Oct 2021.
- A probable typhoid case was a suspected case with a fourfold or higher rise in Widal test titers. However, in this study, probable cases study were classified based on single high titers rather than a fourfold rise.
- A confirmed typhoid case had *Salmonella typhi* identified in a blood or stool culture.
- A probable typhus case was a suspected case with a fourfold or higher rise in Weil–Felix test.
- A confirmed case of typhus had a positive polymerase chain reaction (PCR) test for *Rickettsia*.

Data Collection

The NRRT reviewed medical records from the pediatrics and medicine departments at JSH and municipality health centers to compile a line list of cases, describing them by time and person. Clinical information and laboratory results (complete blood count, Widal test, Weil–Felix test, blood and stool cultures with drug sensitivity) were abstracted from these records.

Interviews were conducted with patients or their guardians using a semi-structured questionnaire (adapted from U.S. Centers for Disease Control and Prevention) to collect demographic information and symptoms.

Laboratory Investigation

The study team collected 5 mL whole blood and stool samples from patients with no prior history of antibiotic consumption. Serum was separated from blood cells, collected, stored refrigerated, and sent in a cold box to Rajshashi Medical College for serological testing. Stool samples were sent to Rajshashi Medical College microbiology laboratory for culture and antibiotic sensitivity test. Cold chain was maintained during storage and transfer of blood and stool samples within 72 hours.

The Widal test (Labkit, SPINREACT, S.A.U., Genoa, Spain) was used for typhoid and the Weil-Felix test for typhus (Tulip Diagnostics/PROGEN (India) and Sclavo Diagnostics (Italy), respectively. The Widal test measures agglutinating antibodies against the O and H antigens of *S. typhi* in sera of people with suspected typhoid. In Bangladesh, an antibody titer of greater than 1:160 and greater than 1:80 for anti-H antigen and anti-O antigen is the cutoff level to detect typhoid. However, the Weil–Felix test primarily checks for antibodies against certain Proteus bacteria strains (OX2, OX19, and OXK). High OX2 titer indicates “spotted fever group rickettsia”, high OX19 indicates “endemic/epidemic typhus group”, and high OXK titer suggests “scrub typhus”.

Environmental Investigation

This study collected surface and municipal water samples from seven sites where there were increased reported cases of typhoid fever and typhus and tested for salmonella and faecal coliforms. Samples were sent to the International Centre for Diarrhoeal Disease Research, Bangladesh laboratory, an international, non-profit health research organization based in Bangladesh, and the Public Health Engineering Department laboratory.

Data Analysis

The demographic characteristics of the study sample and detailed results were expressed as percentages. Descriptive statistics such as frequency, percentage, mean and standard deviation were used primarily to summarize and describe the data. Analyzed data were presented in the form of epidemic curve, and a Venn-diagram.

Case Study

After non-response to drug treatment was reported in a few cases in this typhoid outbreak, typhus was suspected because other cases had been diagnosed with typhus. Then key informants were interviewed, medical records were reviewed, and diagnostic laboratory tests for typhus were ordered. This study described two cases, one a misdiagnosis of typhus and another with concomitant typhoid fever and typhus.

Results

This study identified 241 probable cases in Joypurhat District; 158 (65.6%) were typhoid fever, 44 (18.2%) were typhus and 39 (16.2%) had typhoid and typhus co-infections. The epidemic curve represented a simultaneous outbreak of typhoid fever and typhus. The first case of typhoid fever started on 8 Sep 2021, peaked on 13 Oct 2021 and the last reported case was on 27 Oct 2021. The first typhus case was detected on 11 Sep 2021 which peaked on 21 Oct 2021, and the last case was on 31 Oct 2021 (Figure 1).

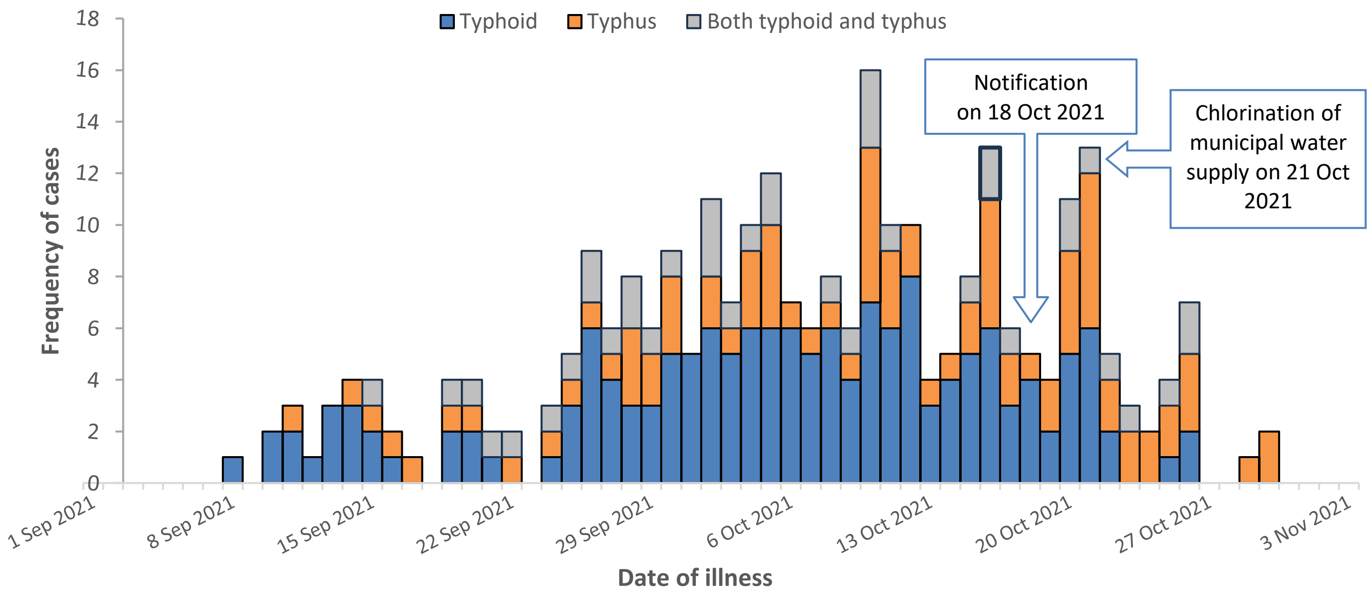


Figure 1. Frequency of cases by date of illness onset in the typhoid fever and typhus outbreak, Joypurhat District, Bangladesh 2021 (n=241)

Males accounted for 135 (56%) of the cases and children <15 years were mostly affected in the community. The most cases identified were in the 5–14 years age group. The fewest cases were in the ≥44 years age group (Figure 2). Clinical presentations of 241 typhoid and typhus fever cases were recorded as: fever (100%), headache (70%), nausea/vomiting (40%), abdominal cramps (36%), and hepatomegaly/hepatosplenomegaly (17%). Rash and lymphadenopathy were only reported in 5% of the cases. Thrombocytopenia occurred among 10% of the cases and mild to moderate anemia among 40% of the cases. The characteristic step-ladder rise in temperature in typhoid fever was reported in 38% of the patients. However, 9% of the cases developed pneumonitis, which is a common complication of typhus, but not common with typhoid fever. In addition, for all cases, the hospitalization rate was 54%, which was higher than 11–14% in previous months. The duration of hospital stay of 14 days, was longer than the 4–7 days duration in previous months.

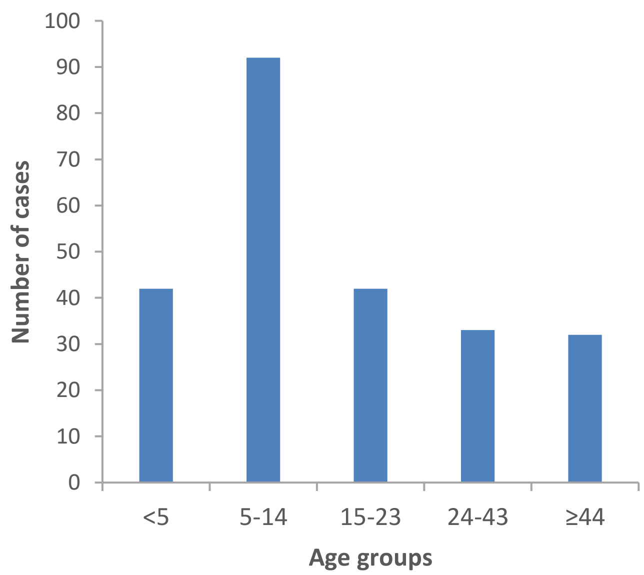


Figure 2. Distribution of cases by age groups in the typhoid fever and typhus outbreak, Joypurhat District, Bangladesh 2021 (n=241)

Case Study

The case study included information from case interviews conducted on 19–20 Oct 2021, when suspicion of typhus arose. A 7-month-old male with five days of fever, vomiting, abdominal pain, and nausea visited a doctor on 17 Oct 2021 and was admitted to JSH on 19 Oct 2021 with a diagnosis of typhoid fever, and a Widal test (average sensitivity 64–88%, average specificity 56–98%) was non-significant. The child was treated with ceftriaxone, but after four days, his fever did not subside. The physician suspected it could be typhus fever and a Weil–Felix test (average sensitivity 40–50%, average specificity 70–80%) was significant. The patient was given doxycycline and discharged on 27 Oct 2021 with complete recovery. Another case demonstrated co-infection with typhoid fever and typhus. On 6 Oct 2021, a 6-year-old male presented with three days of high fever, loss of appetite, no rash, and mild cough. He was given ciprofloxacin, paracetamol, and antihistamine and sent home. There was no response for ten days and the child returned to the doctor who advised a Widal test and blood culture, and both were positive for typhoid fever. The child was given ceftriaxone, but his fever did not subside after four days. The child returned to the doctor again and had a positive result for Weil–Felix test. The child was given doxycycline on 22 Oct 2021 and his fever subsided within three days.

Laboratory Investigation

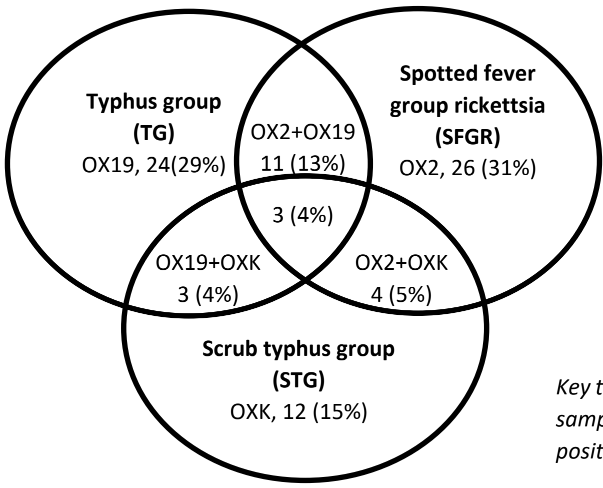
S. typhi was identified in four out of nine blood cultures and three out of seven stool cultures (Table 1). The Widal test was significant in 76% (158/241) cases, with 4% (12/241) anamnestic reaction based upon a fourfold increase of titers above standard. Among confirmed cases of typhoid fever, only one case was positive for both Widal test and Weil–Felix test. Culture sensitivity revealed that *Salmonella spp*. (antibiogram) showed resistance to cefuroxime, cefoxitin, cefixime, and ceftriaxone and intermediate to ciprofloxacin for most cases and sensitive to amoxicillin–clavulanate, meropenem, ofloxacin and 7–10 other antibiotics.

However, 83 cases had a positive reaction to antigens OX2, OX19, and OXK in the Weil–Felix test of typhus fever. No confirmation by PCR was feasible. Among 83 probable cases of typhus in this outbreak, the predominant subgroups were SFGR (31%) and TG (29%), followed by mixed subgroup (26%), and SFGR>TG>mixed>STG (15%). This study also observed the presence of multiple subgroups with OX2+OX19 (13%), OX19+OXK (4%), OX2+OXK (5%), and all three antigens at 4% (referred as mixed subgroup) (Figure 3).

Table 1. Distribution of cases by test: Widal test, Weil–Felix test, and confirmatory culture/PCR test for Typhoid and Typhus, Joypurhat District, Bangladesh 2021

Disease	Weil–Felix test positive	Widal test positive	Blood/stool culture positive for typhoid	PCR positive for typhus	Probable cases	Confirmed cases
Typhoid	39	158	7/16	NA	**151**	**7**
Typhus	44	39	NA	Nil	**44**	**-**
Typhoid and typhus	39	39	1/16	-	**38**	**1 (typhoid)**

Total number of people tested is unknown. NA: not applicable, Nil: not done, -: no cases in this cell.



Key to numbers: typhus subgroup, number of samples positive by Weil–Felix test, percent positive by Weil–Felix test.

Figure 3. Distribution of positive reaction with different antigens (OX2, OX19, OXK) in Weil–Felix test of Rickettsia fever, in typhoid and typhus fever outbreak, Joypurhat District, Bangladesh 2021 (n=83)

Environmental Investigation

Informal interviews of household members of the patients regarding their food habits, sanitation, water supply, hygiene and household environment revealed no specific clue, other than most of them consumed drinking water from the municipality water tank supply.

The source of the typhoid outbreak was suspected to be the municipal water supply because faecal coliform was detected in three out of seven municipal water samples. No *S. typhi* was recovered in these samples.

Actions Taken

On 21 Oct 2021, chlorination of the municipal water supply was done as immediate action. Moreover, awareness raising among community people and health workers was done for future prevention by providing information education and communication materials and training.

Discussion

Initially, this outbreak was classified as a typhoid fever outbreak, because patients presented with high fever, headache, vomiting/nausea, abdominal cramp and a positive Widal test for *S. typhi*. However, one physician suspected a rickettsial disease which was confirmed when a Weil–Felix test was positive, and patients had a rapid response to doxycycline. Thus, typhoid fever and typhus occurred simultaneously in this outbreak.

Typhus and typhoid fever have overlapping signs and symptoms. Diagnostic laboratory tests aid physicians to differentiate between the two. For typhoid fever, the diagnostic test is blood culture, but in Joypurhat District, the site of this outbreak, only the Weil–Felix and Widal tests were available. Physicians treated their patients for typhoid fever based on clinical suspicion. However, differentiation between typhoid fever and typhus is important because of different treatments and different public health responses.[16]

This outbreak did not have the typical distribution of typhus subgroups (TG>STG>SFGR) as previously seen in Bangladesh.[5,7] In this outbreak, the predominant subgroups were SFGR, followed by TG and STG. SFGR typhus is not common in Bangladesh due to vector unavailability. The *Rickettsia felis*, a variety of SFGR, is emerging in Bangladesh with a nationwide prevalence of 19.6%.[17,18] Higher detection rates of *R. felis* were observed in neighboring northwest regions of Rangpur and Rajshashi and central regions.[19]

Identifying the rickettsial subgroup is important because subgroups have different vectors and thus prevention strategies are different. The current typhus prevention strategy is based on control of ticks and mites. However, with the emergence of spotted fever group rickettsial, prevention needs to include control of cat fleas and mosquitoes, both regionally and nationally.

Reliance on clinical diagnosis of typhoid fever and typhus presents a diagnostic dilemma, because they have similar symptoms. Laboratory tests commonly used to test for typhoid fever and typhus, Widal and Weil–Felix tests, respectively, are widespread and inexpensive and need few sophisticated instruments. However, these tests are non-specific and have false negatives and positives.

In this study, spotted fever group rickettsioses were included within the broader *Rickettsia* group for analytical purposes, reflecting their shared epidemiologic and clinical characteristics with typhus group rickettsioses. However, cases identified through laboratory testing were reported separately as spotted fever where applicable. The case definitions used followed standard field epidemiology and surveillance practices suitable for resource-limited settings. Suspected cases were defined clinically by prolonged fever with associated systemic symptoms, while probable cases required a fourfold or higher rise in Widal or Weil–Felix test titers for typhoid and typhus, respectively. Confirmed cases were based on pathogen identification by culture for *S. Typhi* or by PCR for *Rickettsia*. This tiered diagnostic framework balances sensitivity for case detection with specificity for laboratory confirmation and enables meaningful interpretation of disease burden where diagnostic resources are limited.

In Bangladesh, other tropical infections such as dengue fever and malaria are also endemic and may present with overlapping clinical features, complicating the diagnosis of febrile illnesses. However, certain clinical distinctions can assist in differentiation. Dengue fever typically presents with very high fever, severe joint and muscle pain, and sometimes a rash. In contrast, typhoid fever and typhus generally cause continuous high fever with gastroenteritis and rash without joint pain. Malaria is characterized by intermittent fever and frequently leads to anemia due to hemolysis. Recognizing these characteristic fever patterns and associated symptoms, in combination with appropriate laboratory testing for malaria and dengue, is essential for accurate diagnosis and effective management in endemic settings.

Prevalence of typhoid fever in Bangladesh is high and Rajshashi with Rangpur are an endemic zone for typhoid. Therefore, a high-prevalence area, with a Widal test of moderate sensitivity and variable specificity, has very high positive predictive value (PPV) meaning a positive test strongly confirms disease. Bangladesh is considered endemic for several rickettsial infections, including scrub typhus and flea-borne spotted fever (especially *R. felis*). Using a Weil–Felix test of low sensitivity (many missed cases) and moderate specificity (many false positives) severely limits its reliability to confirm disease.

Limitations

All typhus cases were probable because confirmatory PCR test was not available. For confirmation of typhoid fever, only blood samples were collected from the 16 patients who did not start their antibiotic treatment. Despite universal health care in Bangladesh, people who have symptoms of fever may not seek health care and so selection bias might have been present in this study. The Widal and Weil–Felix tests have low specificity which weakens their diagnostic rigor. The low sensitivity (40–50%) and specificity (70–80%) of the Weil–Felix test can lead to misdiagnosis of patients.[21] In this outbreak, there were patients with a positive Weil–Felix test and diagnosed as typhus, but who had typhoid fever. The absence of paired sera resulted in probable cases being classified based upon single high titers rather than a four-fold rise. Reporting of demographic variables of the cases were limited to age and sex, because of the limited collection of demographic and clinical outcome data.

Conclusion and Recommendations

This was a unique outbreak of two different diseases with similar presentations: typhoid and typhus fever. The municipality water supply was the probable source of infection for typhoid fever, but the source of typhus remains unknown. These diseases must be differentiated because of different treatment and intervention modalities. Therefore, it is essential for physicians to recognize the importance of differentiating between typhoid and typhus fever, and for epidemiologists to be aware that both diseases can occur simultaneously in outbreaks.

Consequently, diagnostic accuracy should be improved for good patient outcomes. It is essential to screen patients diagnosed with typhoid fever for rickettsial diseases, especially when patients do not respond to standard typhoid treatment. Screening the patients with suspected typhoid fever by triple antigen test, so that concomitant/co-infection by typhus can be detected in earlier stage of disease progression, would mean that morbidity and mortality resulting from rickettsial fever could be prevented. Moreover, correct identification of the rickettsial subtypes could lead to effective prevention strategies. Initiating active rickettsial disease surveillance is recommended, using a One Health approach, incorporating vector assessments such as cat, dog and rat fleas to identify areas vulnerable to rickettsial transmission.

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Author Contributions

Sohel Rahman: Conceptualization, methodology, investigation, project administration, data curation, formal analysis, visualization, writing—original draft, writing—review & editing. **Alden Henderson:** Visualization, writing—review & editing. **Md. Yousuf Ali:** Investigation, writing—original draft. **Mallick Masum Billah:** Writing—review & editing. **Ishrat Jahan:** Investigation, conceptualization, project administration, visualization. **Nawsher Alam:** Formal analysis, writing—review & editing. **Zakir Hossain Habib:** Writing—review & editing. **Murshida Khanum:** Investigation, conceptualization, project administration, visualization. **Tahmina Shirin:** Project administration, resources, supervision.

Ethical Approval

This response was exempt from institutional review because it was a response to an emergency situation.

Informed Consent

Informed consent was obtained from all participants involved in the study.

Data Availability

The data that support the findings of this study are available on request from the corresponding author. The data is not publicly available due to privacy or ethical restrictions.

Conflicts of Interest

No conflicts of interest.

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Malaria Infection in Thapangthong District, Savannakhet Province, Lao PDR, 2025: Bed Net Use and Forest Visit

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Abstract

On 19 Mar 2025, four *Plasmodium vivax* cases were reported in Thapangthong District, Savannakhet Province—an area previously considered malaria-free in Lao People's Democratic Republic (Lao PDR). The investigation was conducted from 20–28 Apr 2025. We aimed to confirm the outbreak, describe characteristics of the cases, identify associated factors, and recommend containment measures. We reviewed District Health Information Software Version 2 (DHIS2)—a national surveillance system for public facilities of Lao PDR. An active case finding was conducted in three villages in Thapangthong District. Univariable and multivariable logistic regression models were performed. Qualitative phone interviews with key stakeholders were conducted. From January to April 2025, eight confirmed malaria cases were detected based on DHIS2. Of the 294 screened individuals, 20 *P. vivax* cases (12 suspected and 8 confirmed) were identified. Multivariable analysis showed that prior malaria infection and recent travel history to endemic areas were significantly associated with increased odds of infection. Use of long-lasting insecticide-treated nets (LLIN) was associated with a non-significant but lower odds of infection. All participants with a history of forest visits were cases. The interviews revealed that a malaria control barrier included low usage of LLIN by the villagers. Rapid interventions, including a mass drug campaign, were implemented. As of 31 May 2025, no new cases had been detected. To advance malaria elimination, we recommend strengthening campaigns that promote LLIN usage, particularly among forest-goers, providing refresher courses on malaria-related knowledge for villagers and health volunteers, and maintaining active vigilance for new cases.

Keywords: malaria, Lao PDR, long-lasting insecticide-treated net (LLIN), forest-related malaria

Introduction

Malaria transmission remains an important public health challenge in countries in the Greater Mekong Subregion, including Lao People's Democratic Republic (Lao PDR).[1,2,3] The Lao PDR National Strategic Plan 2021–2025 focused on universal access to long-lasting insecticide-treated nets (LLIN), early diagnosis and rapid diagnostic tests (RDT), and early provision of artemisinin-based combination therapy (ACT).[4] The strategy aimed to eliminate *Plasmodium falciparum (P. falciparum)* malaria by 2025.[5] The number of malaria cases declined from over 200,000 cases in 2018 to fewer than 700 cases in 2023.

However, outbreaks have continued to occur in low-burden areas, reflecting persistent challenges, such as importation of cases across provinces and *Plasmodium vivax (P. vivax)* relapse. Savannakhet is a province in the southern region of Lao PDR. Of 15 districts in the province, 13 are labeled as malaria elimination areas. However, in 2024, malaria cases were found in some districts.[6,7] Thapangthong District, located in Southern Savannakhet and predominantly covered by dry forests and highlands, is home to about 50,600 people living in 42 villages.

On 19 Mar 2025, four *P. vivax* cases were reported from two villages (Kengsakou and Naphanet) in Thapangthong District. This prompted a joint investigation from the Ministry of Health (MOH), Lao PDR, from 20–28 Apr 2025, aiming to (1) confirm the outbreak, (2) describe the characteristics of the cases, (3) explore factors associated with malaria infection, and (4) identify barriers to prevention and provide recommendations for further containment.

Methods

Study Design and Study Period

We conducted an analytical cross-sectional study, complemented by qualitative interviews from 20–28 Apr 2025.

Study Site

The study was conducted in three villages: Kengsakou and Naphanet—two villages where the initial cases were reported, and Lawang Yai—a nearby village in the elimination target area.

Operational Definitions

We defined LLIN usage as a reported history of sleeping under a bed net every night. A forest visit was defined as a history of staying overnight or spending at least eight consecutive hours in a forested area in the past two weeks. A forest-goer was defined as a person who earned a living by seeking goods from the forest.

Case Definitions

We defined a suspected case as a resident of Thapangthong District who developed fever within 14 days before the investigation; had at least two of the following symptoms: headache, chills, sweating, muscle aches, body aches, or diarrhea; and reported at least one risk factor: malaria infection within the past 28 days, travel to another malaria-endemic area, or forest-going. A confirmed case was any suspected case with malaria detected by RDT or microscopy.

Data Collection

Data collection involved three steps. First, we examined records from the district health information software version 2 (DHIS2), the national surveillance system for public hospitals in the Lao MOH, from January 2023 to April 2025, along with the 5-year median. Second, we implemented an active case finding (ACF) in the three villages using convenience sampling. Participants were recruited through public announcements. Structured paper-based questionnaires were administered via verbal interviews to gather information on demographics, symptoms, forest-going history, LLIN usage, travel history to endemic areas, and prior malaria infection. All suspected cases were confirmed by RDT or blood smear microscopy. RDT screening was also performed on family members of confirmed cases, symptomatic individuals, and forest-goers. Third, qualitative phone interviews were conducted with two respondents responsible for malaria elimination programs: the Deputy Director of Savannakhet Provincial Health Department and the Chief of the Epidemiology Division of Malaria Parasitology and Entomology. The interview questions focused on operational barriers and recommendations for malaria prevention and control.

Sample Size Calculation for Analytic Study

The two independent proportions formula was used. We assumed a 95% confidence interval, 80% power, with key parameters drawn from previous literature.[8] Noor et al. found malaria infection rates of 7% for bed net users and 17% for non-users.[9] By allowing for 10% rate of incomplete data, we needed approximately 200 participants per group.

Data Analysis

For quantitative data, we used descriptive statistics to determine the magnitude of the outbreak. Crude and specific attack rates were calculated. We fit univariable and multivariable logistic regression models in which the dependent variable was malaria infection (either a suspected case or a confirmed case). The independent variables were gender, age group (<5, 5–14, 15–49, and ≥50 years), occupation (forest-goer, farmer, student), reported LLIN usage, previous infection history, forest visit, and travel history to endemic areas. Variables with a p-value <0.1 in the univariable analysis were included in the multivariable analysis. To avoid model overfitting, multivariable analysis was conducted following standard events-per-variable (EPV) considerations, with priority given to LLIN use.[10] Crude odds ratios (COR), adjusted odds ratios (AOR), and 95% confidence intervals (CI) were presented. STATA version 16 was used. For qualitative data, thematic description was applied.

Results

Situation Review

From 1 Jan 2025 to 30 Apr 2025, data from the DHIS2 indicated that 4,137 individuals were tested for malaria in Thapangthong District. The number of cases in 2025 was higher than that in 2023 and 2024, and was close to the 5-year median. Eight cases were positive for *P.vivax*. All cases received outpatient care. There were neither reported deaths nor hospitalizations. The crude attack rate was 0.24 per 1,000 population. The median age of the cases was 24 years (range 22–39 years). All cases were male. *P. falciparum* infections presented in 2022, and since 2023, all cases were *P. vivax* infections (Figure 1).

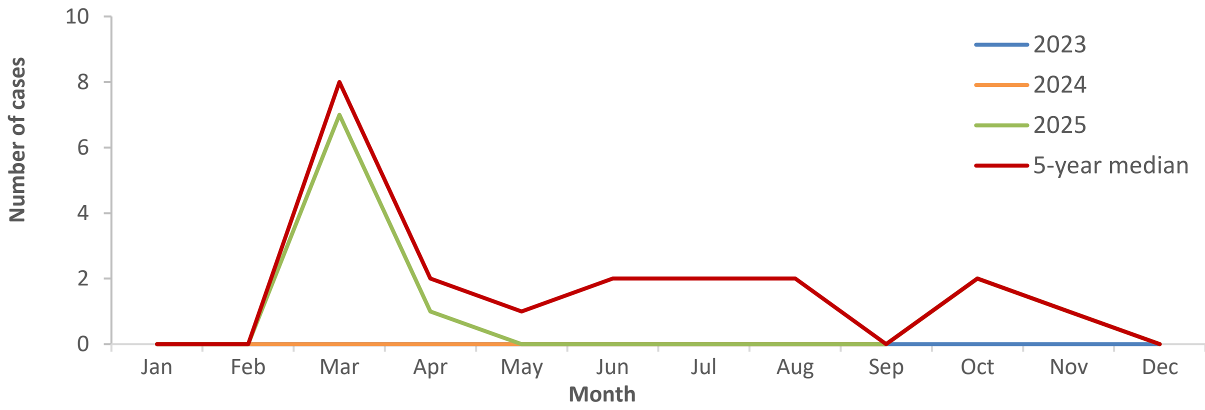

Figure 1. Malaria cases reported in the national surveillance system of Lao PDR, 2023–2025

Active Case Finding

A total of 294 individuals were screened across the three villages: Kengsakou (109, 37.1%), Naphanet (152, 51.7%), and Lawang Yai (33, 11.2%). Most participants were farmers (48.3%) and forest goers (46.6%). The samples were predominantly male (57.8%) and aged 15–49 years (79.9%).

Twenty individuals met the suspected case definition, and none developed severe symptoms. Subsequent blood testing confirmed *P. vivax* infection in eight individuals, who were then classified as confirmed cases, leaving 12 as suspected cases. All confirmed cases showed positive results for *P. vivax* and were treated by ACT. The male-to-female ratio was 4:1, and the median age was 26.5 years (range 14–65 years). We performed blood tests on 121 non-cases who were family members of the confirmed cases, or reported a history of visiting a forest, or being symptomatic during the investigation period. All of these individuals demonstrated negative results (Figure 2).

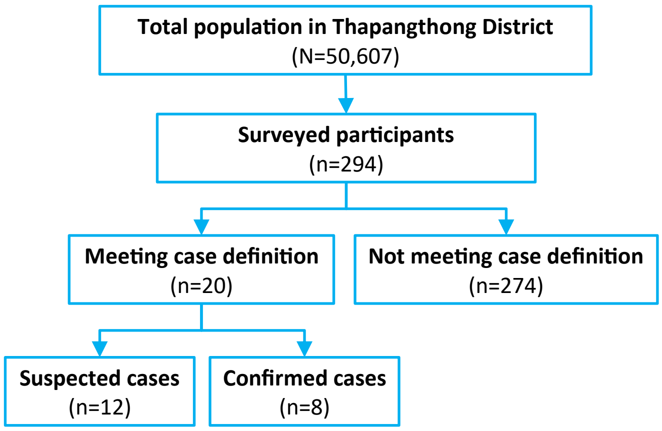

Figure 2. Active case finding in Thapangthong District, 20-28 Apr 2025

Regarding the specific attack rate by village, most (n=15) were residents of Kengsakou (specific attack rate 13.8% among screened samples), Naphanet recorded four cases, and Lawang Yai reported one case. Most (n=18) were aged 15–49 years, and males predominated (n=16) (Table 1).

Table 1. Specific attack rate by villages, age groups, and gender, Thapangthong District, 20–28 Apr 2025

Classification	Detail	Cases	Screened	Total population	Attack rate* (%)	Attack rate† (%)
Village	Kengsakou	15	109	663	13.76	2.26
	Naphanet	4	152	634	2.63	0.63
	Lawang Yai	1	33	1,264	3.03	0.08
Age group	<5	0	1	307	0.00	0.00
	5–14	1	22	666	4.55	0.15
	15–49	18	235	1,229	7.66	1.46
	≥50	1	36	359	2.78	0.28
Gender	Male	16	170	1,332	9.41	1.20
	Female	4	124	1,229	3.23	0.33

**Among screened. †Among total population.*

The first case occurred in mid-March, with sporadic cases continuing through late April. The cumulative case volume gradually increased until the end of April 2025. We further followed up on the situation in these three villages until May 31, 2025, by which time no additional cases were identified (Figure 3).

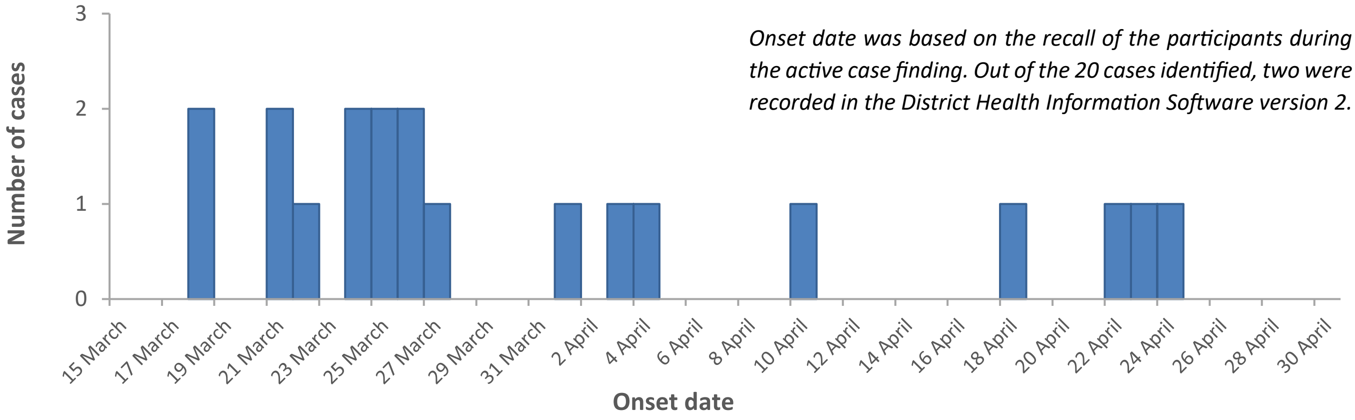

Figure 3. Cases identified by active case finding (n=20) in Thapangthong District, 15 Mar–30 Apr 2025

Fever occurred in all cases, with headaches (90%) and sweating (60%) the next most common symptoms.

Factors associated with malaria infection

Approximately two-thirds of the cases (14/20) reported using LLIN, compared to 86% (237/ 274) of non-cases. As shown in Table 2, LLIN usage exhibited borderline statistical significance, with a COR of 0.36 (p-value 0.052). All individuals with a history of forest visits were classified as cases. Both prior malaria infection (COR 22.2) and reported travel history to endemic areas (COR 12.3) demonstrated a strong association with malaria infection (p-value $\leq$0.001), while male gender (p-value 0.047) was moderately significant.

Table 2. Factors associated with malaria infection by univariable analysis, Thapangthong District, 20–28 Apr 2025

Factor	Case (n=20)	Non-case (n=274)	COR	95% CI	*P*-value
Gender					
Female	4	120	Ref.		
Male	16	154	3.12	1.01–9.56	0.047
Age group (years)					
<5	0	1	Ref.		
5–14	1	21	1.71	0.10–28.86	0.708
15–49	18	217	2.99	0.39–23.70	0.294
≥50	1	36	Omitted	Omitted	-
LLIN use					
No	6	37	Ref.		
Yes	14	237	0.36	0.13–1.01	0.052
Forest visit					
No	0	148	Ref.		
Yes	20	126	Omitted	Omitted	-
Prior malaria infection					
No	12	266	Ref.		
Yes	8	8	22.16	7.10–69.17	<0.001
Travel history to endemic areas					
No	7	238	Ref.		
Yes	13	36	12.27	4.59–38. 83	<0.001
Occupation					
Student	0	15	Ref.		
Farmer	0	142	Omitted	Omitted	-
Forest-goer	20	117	Omitted	Omitted	-

LLIN: long-lasting insecticide-treated net. COR: crude odds ratio. CI: confidence interval. Ref: reference.

As only 20 suspected cases were identified, we included only two independent variables in the multivariable models. Three candidate models were proposed for the multivariable analysis: (i) LLIN usage and gender, (ii) LLIN usage and prior malaria infection, and (iii) LLIN usage and travel history to endemic areas. In all three models, LLIN usage was non-significant but protective for malaria infection (AOR varying from 0.37 to 0.41). As shown in Table 3, prior malaria infection (AOR 21.3) and travel history to endemic areas (AOR 12.2) showed positive associations with malaria infection (*p*-value <0.001).

Table 3. Factors associated with malaria infection, Thapangthong District on multivariable analysis, 20–28 Apr 2025

	Model 1		Model 2		Model 3	
	AOR (95% CI)	*P*-value	AOR (95% CI)	*P*-value	AOR (95% CI)	*P*-value
LLIN use (Ref: no)	0.41 (0.51–1.14)	0.087	0.40 (0.13–1.27)	0.119	0.37 (0.12–1.15)	0.085
Male (Ref: female)	2.90 (0.94–8.95)	0.065				
Prior malaria infection (Ref: no)			21.29 (6.70–67.64)	<0.001		
Travel to a malaria risk area (Ref: no)					12.18 (4.51–32.89)	<0.001

LLIN: long-lasting insecticide-treated net. AOR: adjusted odds ratio.CI: confidence interval. Ref: reference.

Barriers to Malaria Control and Recommendations for Further Containment and Prevention

From the two respondents' perspectives, barriers of malaria control included: (i) importing of cases from neighboring provinces, (ii) low LLIN usage despite most villagers being provided with LLIN, (iii) presence of unregistered or hidden populations, such as migrants and mobile workers involved with forest working, and (iv) insufficient community engagement and support from local authorities.

To address these barriers, the respondents suggested targeting interventions toward hidden populations in the villages and identifying strategies to motivate the villagers to utilize LLIN. Community engagement and local authority involvement should also be strengthened.

Control and Prevention Response

A mass drug campaign (Pyramax®) was held for forest-goers and their families as preventive therapy to reduce the parasite reservoir and interrupt transmission. We also distributed LLIN to all forest-goers and encouraged them to use them during forest activities. Health education sessions were conducted to raise awareness and emphasize early care-seeking behaviors. In addition, the district malaria team carried out daily monitoring of new cases. No new cases were detected until the end of May 2025.

Discussion

Our situational review of the national surveillance system for public facilities of Lao PDR identified eight *P. vivax* cases (8/4,137, 0.2%) in Thapangthong District, with no deaths. From the active case finding, 20 cases were identified. The epidemic curve demonstrated continuous transmission from mid March 2025 until the investigation, indicating ongoing exposure rather than a single point-source outbreak.

Evidence in many countries suggests that forest work is strongly correlated with malaria transmission.[11,12] A scoping review suggested that rural and forested areas have been consistently identified as high-risk areas for malaria infection.[13]

Reported use of LLIN was associated with a 60% reduction in the odds of malaria infection. However, statistical significance was not established. Prior meta-analysis suggested that LLIN usage reduced the incidence of uncomplicated episodes of *P. vivax* by 39%.[14] Nevertheless, Kabeya et al. indicated that LLIN distribution briefly lowered malaria rates, but without statistical significance, suggesting the campaign alone was insufficient unless other prevention methods are in place.[15] This notion is supported by the interviewees' viewpoints, highlighting that while LLIN were widely distributed, their consistent usage could not be guaranteed.

Prior malaria infection is strongly associated with being a case as *P. vivax* parasites may relapse if not completely treated.[16,17] Reported symptoms—fever, headaches, and body aches—were consistent with those seen in typical malaria cases.[18,19]

Being male was significantly correlated with higher rates of infection. Numerous studies have documented this difference in case profiles across genders.[20,21] A survey in Tanzania found that being male was associated with a 32% increase in the odds of malaria infection.[22] In our context, males are typically the main breadwinners of the families and are more at risk of mosquito bites due to outdoor activities.

Limitations

There were certain limitations in our study. First, the small sample size limited the statistical power of the analysis. We were unable to obtain the number of participants required by the sample size calculation, which may explain why bed net use was not statistically significant. The small number of interviewees in the qualitative study may have undermined the validity of the findings. Second, the cross-sectional design and short investigation period restricted our ability to make causal inferences. Third, the convenience sampling in our study design may have underestimated the actual number of cases and reduced generalizability to other settings. Fourth, self-reported responses are subject to recall bias, where cases may be more likely than non-cases to report past risk factors, and to social desirability bias, as some participants may have been reluctant to disclose sensitive behaviors or circumstances (such as belonging to a hidden population) due to fear of social judgement. Fifth, the lack of information on key behaviors, such as medication use from prior malaria infection, and detailed bed net use, limited the comparability of our study with others.

Recommendations

Key strategies should be introduced. First, interventions should be specifically tailored for forest-goers. These interventions include providing comprehensive prevention packages, such as LLIN and repellents and ensuring proper net use in forest settings. Novel strategies, such as adding small incentives or launching short reminder messages via smartphones, have shown promise in encouraging LLIN usage and reinforcing protective behaviors.[23,24] Second, ensuring radical treatment for *P. vivax* infections is critical to prevent relapses, including strengthening treatment capacity at the district level. Third, intensive education programs to raise malaria awareness among villagers are essential and should be continued. A refresher course to update malaria-related knowledge among frontline health volunteers would also be beneficial. Fourth, efforts should be made to strengthen the registration and monitoring of hidden forest workers to ensure that no case is left untreated and remains a reservoir of malarial parasites.

Conclusion

This *P. vivax* outbreak in Thapangthong District shows that even in elimination areas, malaria transmission can re-emerge through forest-related exposure. Prior malaria infection and travel to malaria-risk areas were found to be strong risk factors, highlighting the importance of addressing relapses and cross-border exposure. The observed effect of LLIN on lowering the odds of infection supports their continued promotion. To achieve malaria elimination, collective efforts, including mass drug administration and tailored strategies targeting forest-goers, are warranted.

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Contribution of Authors

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

Ethical Approval

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

Informed Consent

Not applicable.

Data Availability

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

Conflicts of Interest

The authors have no conflicts of interest to declare.

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During the preparation of this work, the authors used Copilot and 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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High Usability but Limited Case Capture: Performance of Thailand's Digital Influenza Surveillance System in a Private Hospital Setting

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Abstract

The Digital Disease Surveillance (DDS) system was introduced in 2024 to enhance real-time monitoring of influenza. However, there has been no performance assessment among private hospitals that have adopted this system. This study assessed the performance of the DDS for influenza surveillance at a private hospital in Thailand. We conducted a mixed-methods study from January to December 2024. We analyzed data from the Hospital Information System, DDS and interviewed 23 stakeholders. We assessed system attributes, including sensitivity, positive predictive value (PPV), completeness, accuracy, timeliness, and representativeness. Qualitative findings indicated high system simplicity and usability, with data outputs utilized for hospital-level resource preparation and vaccination campaign planning. Quantitative attributes of 250 reported-cases showed a high PPV (82% for the Division of Epidemiology (DOE) case definition and 100% for physician diagnosis and laboratory-based definitions), 100% data completeness, and 89% timeliness (reporting within 7 days). A critical limitation in system automation was identified, notably incorrect data extraction via an application programming interface (API) necessitated a reliance on manual data entry. This contributed to a low sensitivity (535/5,751: 9%), particularly using the DOE definition, compared to physician diagnosis (622/1,776: 35%) and laboratory-based definitions (723/1,746: 41%). This low sensitivity was attributable to systematic exclusion of outpatients and non-local residents. While the DDS demonstrates high usability and data quality for reported-cases, its reliance on manual workflows due to API failure results in low sensitivity. These gaps limit its effectiveness for comprehensive surveillance. Enhancing API integration, revising case definitions, and standardizing reporting protocols are recommended.

Keywords: influenza, surveillance system, performance, Thailand, private hospital

Introduction

Influenza is an acute respiratory infection caused by influenza viruses.[1] The influenza burden is particularly high in regions with high human mobility.[2] The broader consequences of influenza are cardiovascular events, exacerbations of chronic underlying conditions and economic impact.[3]

Seasonal influenza affects approximately 1 billion people worldwide with 3 to 5 million severe cases and 290,000 to 650,000 deaths reported annually.[1] In 2024, Thailand reported 671,281 influenza cases with an incidence rate of 1,034 per 100,000 population leading to 51 fatalities (case fatality rate 0.008%). Nakhon Pathom Province experienced one of the highest incidence rates in the region at 1,256 per 100,000 population.[4]

Report 506 (R506), the traditional influenza surveillance system in Thailand, has relied on manual case reporting into an electronic surveillance system, which often suffered from delayed data transmission and underreporting. To address these limitations, the Digital Disease Surveillance (DDS) system was introduced in 2023 and fully implemented in 2024 to enhance real-time monitoring and data integration. The system utilizes a real-time application programming interface (API) connection with the hospital information system (HIS), automating case detection and improving reporting accuracy.[5]

In urban areas, private hospitals play a crucial role in influenza surveillance. Understanding the surveillance system's performance in such settings is essential. Hospital X, a private hospital in Nakhon Pathom, adopted the DDS system to replace R506 in 2024. This is the first study that assessed the surveillance system among DDS-adopted private hospitals in Thailand.

This study aims to describe and assess the performance of DDS-based influenza surveillance system at a single private hospital. It is hoped that the findings from this study will enhance the DDS-based influenza surveillance system in Thailand's private hospitals.

Methods

Study Design

A mixed qualitative and quantitative study based on the guidelines for evaluating public health surveillance systems was conducted at a single hospital (Hospital X).[6] The study period was from1 Jan 2024 to 31 Dec 2024. The evaluation included a system description and assessment using qualitative and quantitative attributes.

System Description

We used purposive sampling to enroll participants who were stakeholders and had been involved in influenza surveillance for more than six months. We included 23 participants from national (n=5), regional (n=3), provincial (n=4), and hospital (n=11) levels representing policymakers (n=4), information technology (IT) staff (n=4), data entry operators (n=8), and information users (n=7).

Data were collected through interviews using a semi-structured open-ended questionnaire, document reviews, and direct observation. Findings were presented using flowcharts aiming to describe the public health importance, objectives, usefulness, patients, data flow, and resources, including human resources, budget and equipment related to the DDS system.

Qualitative Assessment

Five key attributes were assessed: 1) simplicity—simpleness of the system structure and the ease of operation, 2) flexibility—ability of the system to adapt to changing information needs, 3) stability—reliability and stability of the system, 4) acceptability—willingness of stakeholders to participate in the surveillance system and 5) automation—application of technology or processes to achieve outcomes with minimal human involvement.

Participants and data collection were the same as the system description. Findings were analyzed using an attribute-based framework (framework analysis).

Quantitative Assessment

A cross-sectional study was conducted to assess sensitivity, positive predictive value (PPV), completeness, accuracy, timeliness, and representativeness.

Influenza cases were identified using three definitions according to the definition of the Division of Epidemiology (DOE), physician diagnosis and laboratory-based.[7] The DDS reporting criteria apply to any patient who meets the DOE definition.

Cases were retrieved from the HIS and classified into two groups based on the International Classification of Diseases 10^{th} revision (ICD-10) codes for influenza (J10–J11) and influenza-like illnesses (J00, J02–J04, J06, J09, J128–J129, J16–J18, J20, J21). There were 10,166 records in total. We extracted data from the HIS and the DDS system using a structured form. Stratified random sampling by ICD-10 code with 10% of the influenza group and 2% of the influenza-like illness group, was applied, with a minimum of 10 records per code.

Information from the pilot study was used for sample size estimation of sensitivity among HIS and PPV among DDS, we got 342 and 250 records respectively.

Sensitivity

Sensitivity was calculated as the percentage of HIS medical records meeting the case definition and were reported in the DDS system. To account for different sampling fractions across ICD-10 codes, weighted sensitivity was calculated.

Positive Predictive Value (PPV)

PPV was defined as the percentage of DDS-reported cases that met the influenza case definition.

Completeness

Completeness was defined as the percentage of complete reported cases out of the total number of observations in the DDS system by variable. We focused on five key variables: age, gender, onset date, patient type (outpatient or inpatient) and current address (subdistrict).

Accuracy

Accuracy was assessed by comparing data from the DDS system to HIS records by variable for the same five variables used in the assessment for completeness. Records were considered accurate if they met the following criteria: age within a one-year window, onset date within a one-day window, and exact matches for gender, patient type, and subdistrict of current address. Records with missing data were excluded from the analysis.

Timeliness

Timeliness was measured by the interval between the diagnosis date and the report date to the Department of Disease Control (DDC). A case was considered timely if it was reported within seven days. Additional time intervals (onset to visit and visit to diagnosis) were calculated. Median and interquartile ranges (IQR) were reported.

Representativeness

Representativeness was evaluated by comparing the characteristics between the HIS medical records meeting the case definition and those DDS reported-cases. The comparison focused on age, gender, week of onset and patient type. Distributions between groups were compared using bar charts and line graphs.

Results

General Information

Hospital X is a 210-bed tertiary hospital located in the urban area of Nakhon Pathom. The hospital adopted the DDS to replace R506 in 2024.

System Description

Public health importance

Influenza remains one of the top three notifiable diseases in Nakhon Pathom. Outbreaks have occurred in high-risk settings such as schools, prisons, and nursing homes, with many deaths. Influenza is preventable with vaccination, which is widely available and effective in reducing mortality.

Objectives and usefulness

The DDS was designed to monitor disease trends and detect outbreaks using automated workflow to improve timeliness and under-reporting. It supported mandatory disease reporting under the Communicable Disease Act B.E. 2558 (2015) and assisted in public health decision-making.[8] For private hospitals, the outputs were useful for situation analyses, vaccination marketing campaigns, and preparing resources such as medications and beds for influenza cases during outbreaks.

Resources

Three main types of resources support DDS operations: (1) personnel including infection control nurses (ICN), informatic staff, epidemiologists, and IT officers; (2) budget amounting to approximately 600,000 U.S. dollar per year for national system maintenance; and (3) equipment encompassing cloud servers, data storage systems, and software supported by both government and private sectors.

Patient and data flows

Influenza cases enter the hospital through the outpatient department (OPD) or emergency room (ER). Influenza diagnoses are based on physician judgement, especially in the OPD of the internal medicine unit, while cases in the ER and pediatric OPD cases are classified upon positive rapid influenza diagnostic test (RIDT) results. For admitted patients, R506 forms are completed in the wards, while non-admitted patients have R506 forms completed by the patients in the OPD or ER (Figure 1).

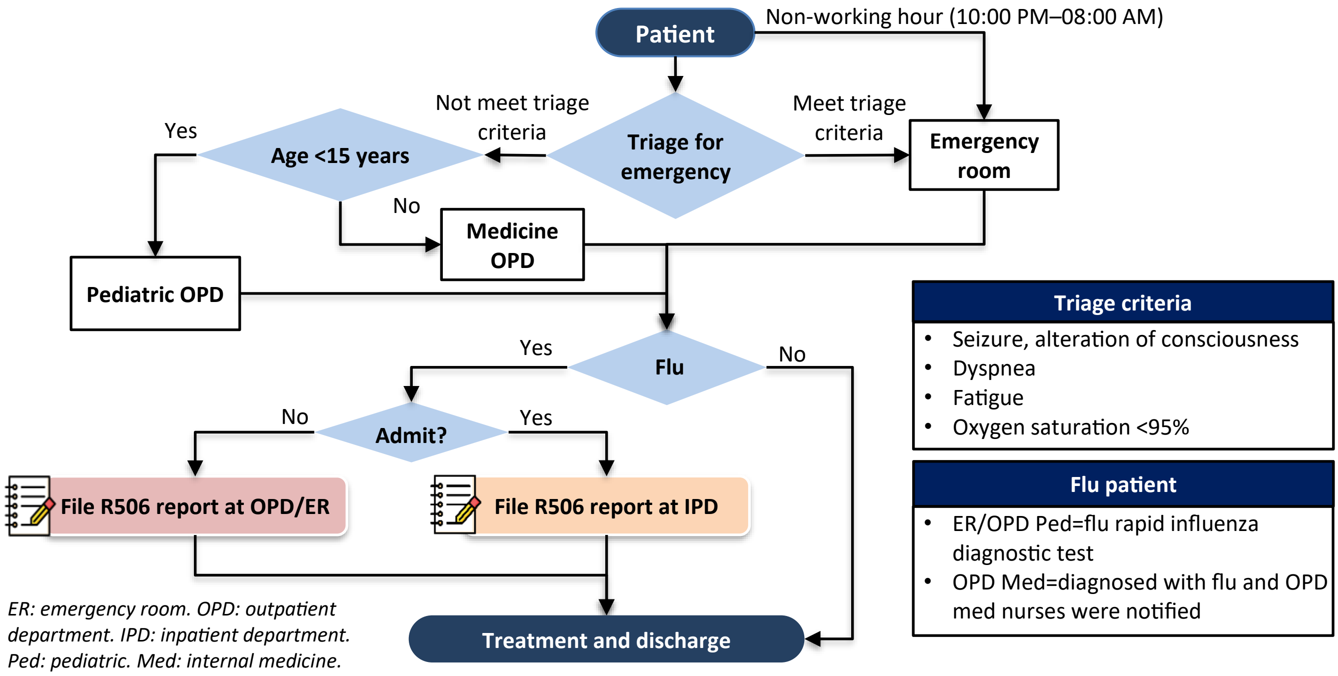


Figure 1. Patient flow in Hospital X in 2024 from entering hospital, capturing to surveillance system and discharge

R506 forms are submitted via the Line application or by clerks to the ICN, who manually enter the data into the DDS web portal for patients residing in Nakhon Pathom only (Figure 2). After validation for completeness and ICD-10 correctness, reports are sent for checking, cleaning and deduplication (if required). Verified data are processed hourly through a secure DDS server and made available for exporting through dashboards, datasets, or APIs (Figure 3).

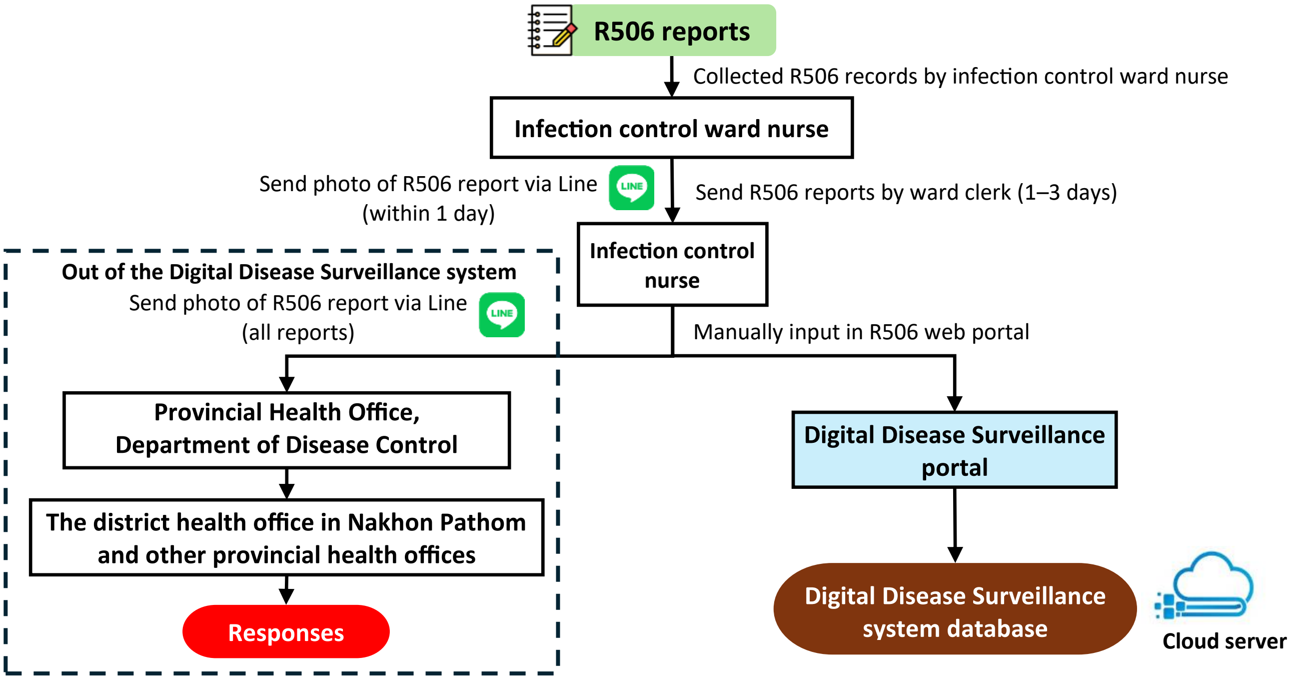
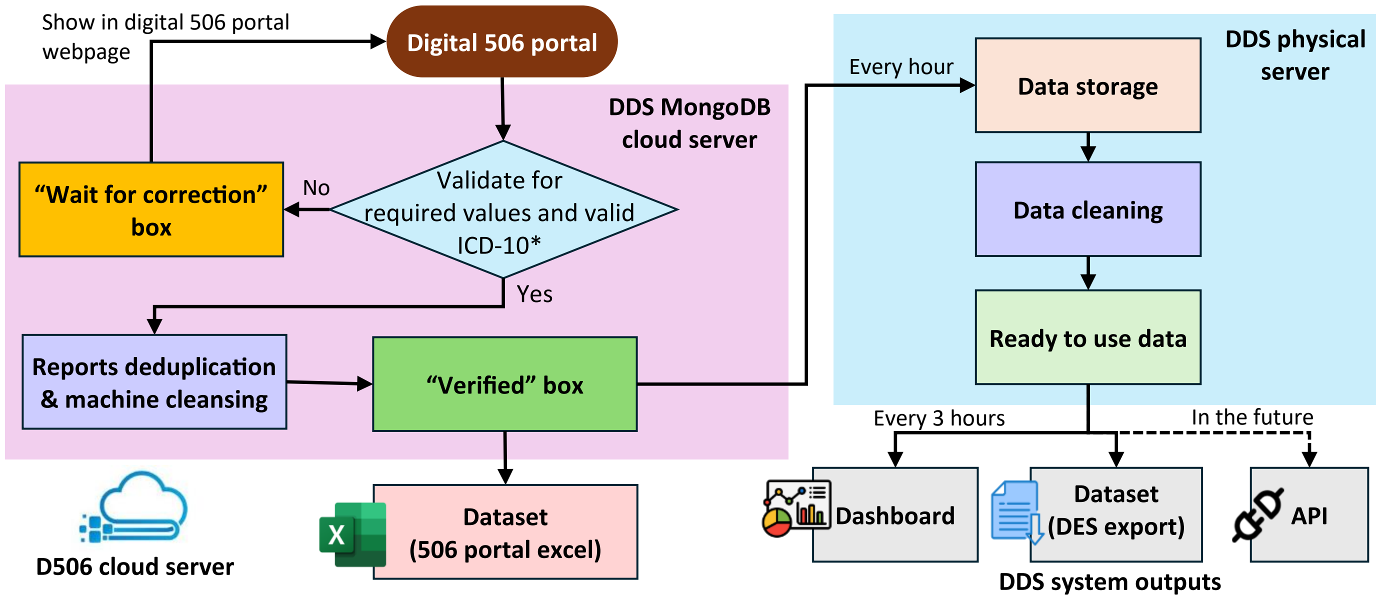


Figure 2. Data flow from Hospital X to the digital disease surveillance system database



**Even some reports met suspected influenza criteria (by symptoms) but had other ICD-10 diagnosis than J10–J11, they will be labeled as invalid ICD-10 and sent "Wait for correction" box. API: application programming interface. D506: digital 506. DDS: digital disease surveillance. DES: data encryption standard. ICD-10: International Classification of Diseases 10th revision.*

Figure 3. Data flow from digital disease surveillance to information users

Qualitative Assessment

Simplicity

The ICN found that the system was user-friendly, especially compared to previous standalone software, stating that "*At the first time I received the web portal link, I could use it instantly without any guidance*." The dashboard was easy to navigate and provided quick summaries. However, some limitations were identified, such as a limited number of data exports and no aggregated data compared to earlier R506 reports.

Flexibility

The DDS could be adapted to align with changing policies such as adding variables or diseases under surveillance, but it required technically skilled personnel, and modifications related to HIS needed approval from the private hospital committee.

Acceptability

Data from the DDS were used by private hospitals for decision-making, as mentioned by the hospital's vice director *"The timeliness and trustworthiness of situation reports help us in preparation of beds, medicine, staff and even the designing of vaccine packages"*. However, the ICN expressed: *"I tried using the API system, but the values are often incorrect. Thus, manual input to the online web portal is way faster."* This reaffirmed her concerns about its reliability leading her to prefer the previous R506 report form.

Stability

As the DDS is legally mandated under the Communicable Disease Act B.E. 2558, ongoing support from the public sector is ensured. System downtimes were minimal and usually planned. While data security and power backup were strong, a shortage of trained personnel and a lack of standard operating procedures were noted.

Automation

Despite the auto influenza case detection design by the DDS via the API, the ICN said that the data from this process is usually incomplete and inaccurate. Hence, the R506 form replaced this process to ensure the data quality.

Quantitative Assessment

Based on the DOE case definition, 142 HIS records were identified as influenza cases. The weighted sensitivity values (Table 1) for the DOE, physician diagnosis, and laboratory-based definitions were 9.3% (535/5,751 weighted records), 35.0% (622/1,776 weighted records) and 41.4% (723/1,746 weighted records) respectively. Analysis of 135 unreported DOE definition cases revealed reasons for underreporting, as 100 (74.1%) cases did not receive an influenza diagnosis. Among 35 influenza-diagnosed cases, 27 (77.1%) were outpatient cases or patients residing outside Nakhon Pathom, which led to exclusion for reporting (Figure 4). Among all reviewed records, 19 inpatients cases within the province were missing report due to operational factors: 16 (84%) were admitted outside working hours, 4 (21%) had negative RIDT but had clinical suspicion, and 2 (11%) were admitted during lunch hours.

Table 1. Positive predictive value and weighted sensitivity by case definition

Case definition	PPV (n=250)		Weighted sensitivity	
	n (%)	95% CI	n/total (%)	95% CI
Department of Epidemiology	205 (82.0)	76.7–86.6	535/5,751 (9.3)	8.6–10.1
Physician diagnosis	250 (100.0)	98.5–100.0	622/1,776 (35.0)	32.9–37.3
Laboratory-based	250 (100.0)	98.5–100.0	723/1,746 (41.4)	39.1–43.7

CI: confidence interval. PPV: positive predictive value.

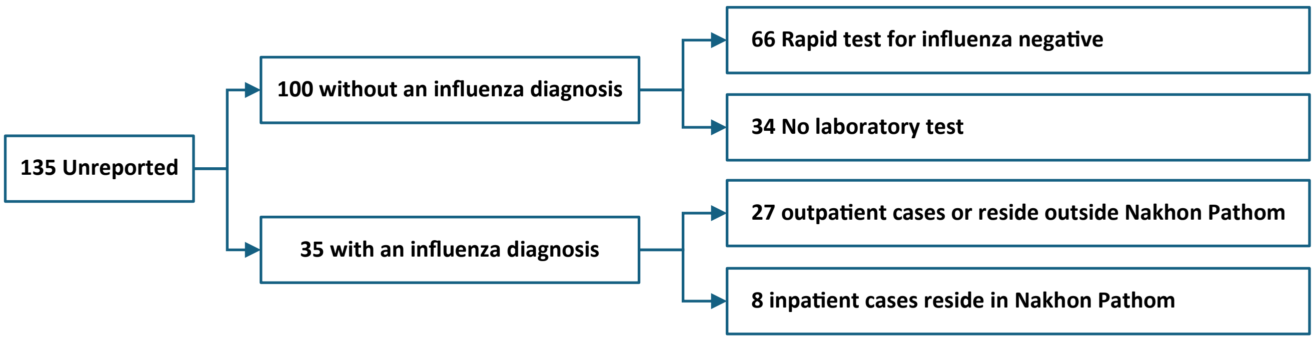


Figure 4. Components of 135 influenza cases based on Department of Epidemiology case definition that were unreported to the Digital Disease Surveillance system in 2024

The PPV (Table 1) of physician diagnosis and laboratory-based definition was 100% (250/250 records). However, the PPV of the DOE definition was slightly lower at 82.0% (205/250 records). Of the 45 reported cases that did not meet the DOE definition, 18 (40%) were for patients aged under 15 years old with no recorded cough, 14 (31%) were aged over 15 years old without cough, and 9 (20%) were aged under 15 years old despite having records on cough. Interviews with pediatricians suggested that children often presented with non-classic influenza symptoms such as fever with vomiting or rhinorrhea, and were not captured by the current DOE definition, which focused on fever and cough.

The completeness of reported influenza cases in the DDS was 100% (250/250) for age, gender, onset date, patient type (outpatient or inpatient) and current address (subdistrict) variables (Table 2).

The accuracy of variables showed more variability. Gender had the highest accuracy at 99.6% (249/250) followed by age and patient type at 98.4% (246/250). However, the accuracy was lower for current addresses at the subdistrict level and onset date (Table 2).

The median time from onset to visit was 1 day (IQR 1–2). The records that had diagnosis times on the same day as the patient visit were 94.8% (237/250). The median duration from diagnosis to report submission was 3 days (IQR 2–6), with 88.8% (222/250) of cases reported within 7 days.

Table 2. Completeness and accuracy of the Digital Disease Surveillance system reported-case in 2024 by variable

Variables	Completeness (n=250)		Accuracy (n=250)	
	n (%)	95% CI	n (%)	95% CI
Gender	250 (100.0)	98.5–100.0	249 (99.6)	97.8–100.0
Age	250 (100.0)	98.5–100.0	246 (98.4)	96.0–100.0
Patient type (OPD/IPD)	250 (100.0)	98.5–100.0	246 (98.4)	96.0–100.0
Address (subdistrict)	250 (100.0)	98.5–100.0	180 (72.0)	66.0–77.5
Onset date	250 (100.0)	98.5–100.0	157 (62.8)	56.5–68.8

OPD: outpatient department. IPD: inpatient department. CI: confidence interval.

For representativeness, the proportion of female cases in the DDS system closely aligned with the DOE, physician, and laboratory-based definitions. In contrast, DDS underrepresented elderly patients (≥60 years), who accounted for only 3% of DDS cases compared to 7% in the DOE definition. Patient type analysis showed a significant gap as DDS included only inpatient cases, whereas HIS indicated a large proportion of outpatient cases (Figure 5). As shown in Figure 6, monthly trends in DDS mirrored those in HIS, particularly during the seasonal peak periods (June to August).

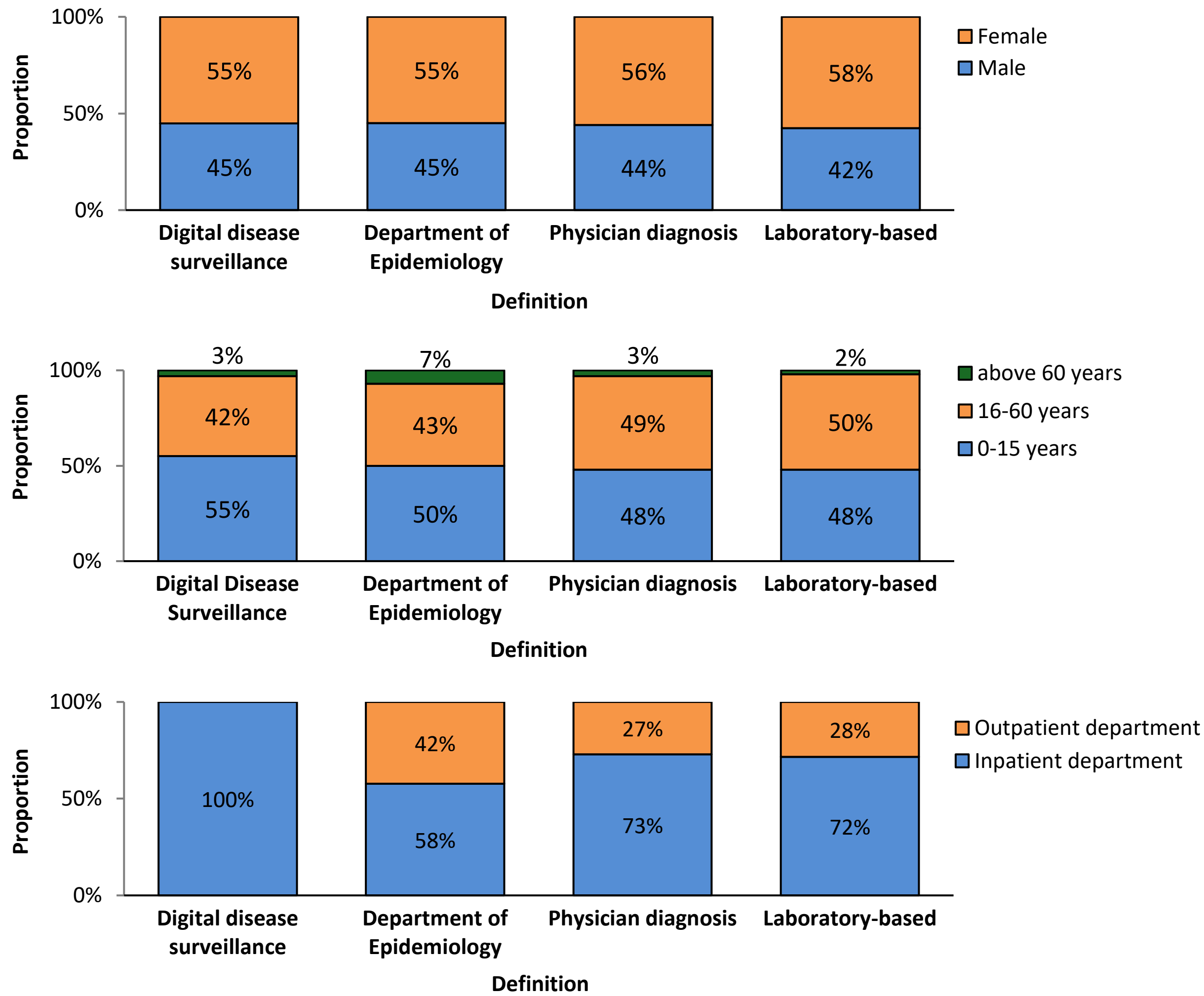


Figure 5. Representativeness of the DDS for gender, age group and patient type by case definition

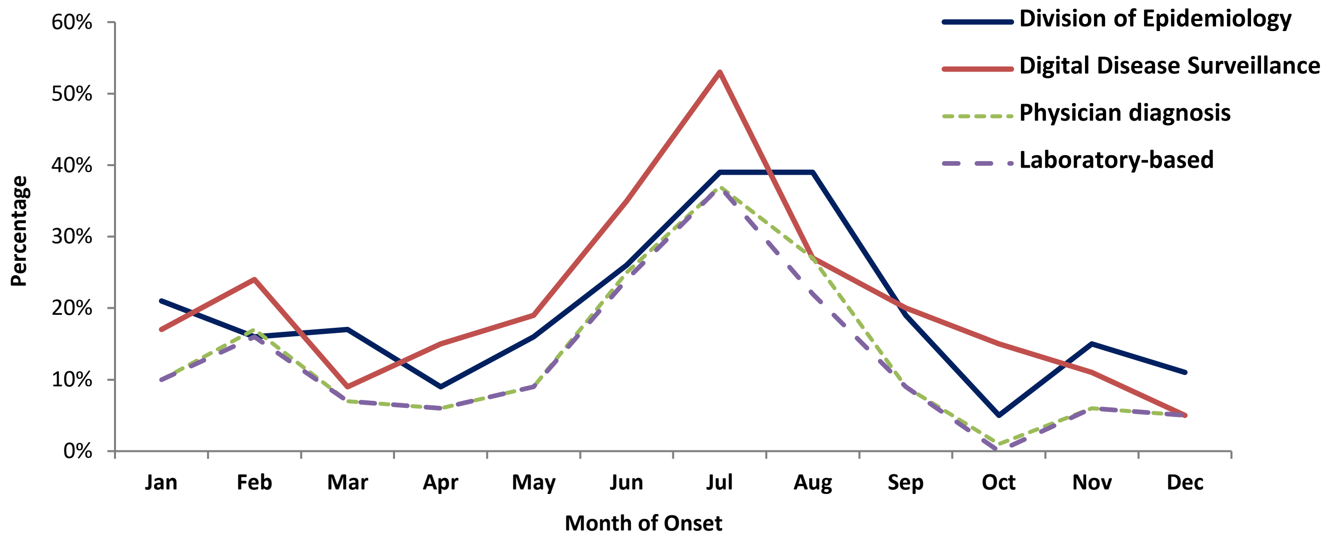


Figure 6. Representativeness of the DDS over month of onset by case definition

Discussion

The DDS system demonstrated significant strengths rooted in its simplicity, modern technology, and stability. It effectively fulfilled its primary objective of providing consistent influenza monitoring from local to national levels, and its applicability in private settings also aided resource management and vaccination campaign planning. This high level of utility and user acceptance was due to its minimal operational burden, facilitated by a technological infrastructure that included APIs, a web portal, and a real-time dashboard. Furthermore, its reliability and continuity were supported by national policies, legal mandates, and secure data management.

Despite its utility, the DDS system faced limitations, notably an unclear capacity for outbreak detection. While generally user-friendly, difficulties with data extraction hinder advanced epidemiological analysis. Furthermore, issues with incorrect data inputs via the API reduced user trust and overall system acceptance.

As shown in patient and data flow, there was no standard procedure for reporting that led to inconsistency across OPDs, the ER, and medicine and pediatric wards, resulting in only inpatient cases being reported to the DDS. These issues affected the accuracy and reliability of the data.

Currently, due to limitations of the API, all reports are manually entered, and this may cause delayed or missed reporting if the case numbers rise. Despite this, the system is deemed to be digitalized but it still necessitates manual operation. Improving the API could correctly automate data transfer, reduce staff workload, and improve the completeness, accuracy, and timeliness of influenza reporting.[9,10]

The sensitivity of the DDS at Hospital X was relatively low when assessed against the DOE definition, with a weighted sensitivity of 9.3%. This low value is likely due to the broad spectrum of clinical presentations that patients who meet the criteria may initially be diagnosed with other respiratory illnesses that mimic influenza such as the common cold, and acute bronchitis or even confirmed with other pathogens.[11] This issue has also been observed in previous evaluations of Thailand's R506 system, which reported sensitivities ranging from 5% to 25% due to similar diagnostic challenges.[12,13] Additional factors contributing to underreporting included the exclusion of outpatient cases and those residing outside Nakhon Pathom. This exclusion does not align with the Communicable Disease Act, which states the hospitals are responsible for reporting any cases of disease under surveillance who visit the hospital.[8] Furthermore, cases presenting outside of regular working hours were often missed either due to consultations with part-time clinicians or delays in influenza diagnosis until the following day after the visit. These findings highlight structural and operational gaps that reduce the reporting of influenza cases into the surveillance system.

The current system only captures about 9% of influenza cases at Hospital X. To improve surveillance accuracy in Thailand, integrating private hospitals into DDS and enhancing sensitivity and performance monitoring are vital.

The PPVs are higher than those from previous evaluations of the R506 system in Thailand, which reported values ranging from 12% to 30%.[12,13] The high value observed in this study may be attributed to validation steps taken before reporting, such as rechecking ICD-10 codes and incorporating RIDT before finalizing diagnoses. These pre-reporting steps help ensure that only clinically appropriate cases are submitted to the DDS system. However, the DOE definition itself may still require revision. For instance, it mandates the presence of a cough, which may not appear in pediatric patients despite other symptoms or positive laboratory results. A prior study revealed that 64% of patients with laboratory-confirmed influenza had fever and cough together.[14] This limitation highlights the need to adapt case definitions to be more inclusive of age-specific presentations, particularly among young children.

The results showed exceptional data quality, with 100% completeness across all key variables. Accuracy was also higher compared to prior evaluations.[11,12] This improvement may be attributed to the relatively smaller volume of cases, which allowed the ICN to review each case thoroughly. However, representativeness remains a challenge. The exclusion of OPD cases and those residing outside Nakhon Pathom from reporting resulted in discrepancies, highlighting the need for more inclusive reporting practices for a comprehensive surveillance picture.

Limitations

This study has three main limitations. First, misclassification bias may have occurred due to human error during medical record reviews. To address this, data extraction followed a standard operating procedure to improve consistency. Second, selection bias may exist, as laboratory-confirmed influenza cases that did not meet selected ICD-10 codes could have been excluded. However, this potential bias was minimized by using a comprehensive and inclusive list of ICD-10 codes to capture as many relevant cases as possible. Third, in the qualitative part, respondent bias may have occurred, as the local staff knew the evaluation was part of the function of the DOE and this might have caused them to express favorable answers.

Recommendations

Hospital X should report the patients from outside Nakhon Pathom and set clear procedures for reporting during weekends and after hours. In the long term, a fully automated API system with correct data extraction should be developed to reduce manual work. The Nakhon Pathom Provincial Public Health Office should provide regular training and communication with healthcare staff. The Division of Epidemiology should revise the influenza case definition to include laboratory-confirmed cases without strict symptom requirements, especially for children. The DDS dashboard and export features should also be improved for easier use.

Conclusion

The DDS-based influenza surveillance system offers clear strengths in simplicity, completeness, timeliness, and PPV, particularly when evaluated against physician diagnosis and laboratory-based definitions. However, sensitivity remains low under the current DOE definition, largely due to the exclusion of pediatric cases or cases with clinical presentations that did not match the DOE definition. The system also showed limited representativeness, especially for outpatients and non-local residents.

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Author Contributions

Thanaphon Yisankhun: Conceptualization, methodology, investigation, writing—original draft, writing—review & editing. **Watcharapol Rongdech:** Conceptualization, methodology, investigation, writing—original draft. **Kogkawee Raruenroeng:** Investigation. **Sethapong Lertsakulbunlue:** Investigation. **Wanchat Saowong:** Investigation. **Thanawadee Chantian:** Supervision, writing—original draft. **Nichakul Pisitpayat:** Supervision, writing—original draft. **Rapeepong Suphanchaimat:** Supervision, writing—original draft.

Ethical Approval

This study only involved interviews with participants who were anonymous, and therefore ethics approval was not required.

Informed Consent

Informed consent was obtained from all participants involved in the study.

Data Availability

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

Conflicts of Interest

The authors declare no conflict of interest.

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The authors did not receive funding.

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

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

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Investigation of an Influenza A(H3N2) Outbreak and Assessment of Vaccine Effectiveness at a Non-commissioned Officer Training Center, Saraburi Province, Thailand, 2025

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Abstract

On 13 Oct 2025, an influenza-like illness (ILI) outbreak was reported at a non-commissioned officer training center in Saraburi Province, Thailand. We investigated to verify the outbreak, describe epidemiological characteristics, identify risk factors and the causative agent, estimate vaccine effectiveness (VE), and implement control measures. We conducted a retrospective cohort study among 903 students and staff. A suspected case was defined by fever (body temperature ≥37.5 °C) or a history of fever, plus cough and at least one other related symptom (sore throat, rhinorrhea, myalgia, headache, fatigue, or dyspnea), with onset between 1–28 Oct 2025. Data were collected via an online questionnaire, and specimens were tested using real-time PCR. Poisson regression with robust error variance estimated adjusted risk ratios (ARR). Of 887 respondents (98.2%), 159 suspected cases (attack rate 17.9%) were identified. Influenza A(H3N2) was confirmed. The epidemic curve, peaking on 11 Oct 2025, was consistent with person-to-person transmission, and the basic reproduction number was estimated at 0.81–1.10. Significant risk factors included close contact with a patient (ARR 1.22; 95% confidence interval (CI) 1.06–1.42) and sharing personal items (ARR 1.20; 95% CI 1.06–1.36). Handwashing before meals was protective (ARR 0.80; 95% CI 0.72–0.89). The VE against clinical illness was 19.1% (95% CI -20.0%–43.9%). This outbreak was associated with personal hygiene-related risk factors. The VE was low and not statistically significant, which may be consistent with known vaccine limitations against A(H3N2) strains. The outbreak rapidly subsided following the implementation of public health control measures.

Keywords: influenza, vaccine effectiveness, non-commissioned officer training center

Introduction

Influenza is an acute infection caused by a segmented RNA virus.[1] Its genomic structure facilitates rapid antigenic drift and shift, necessitating continuous surveillance. The World Health Organization estimates 1 billion infections annually, resulting in 3–5 million severe cases and 290,000–650,000 deaths.[2,3]

Transmission occurs via respiratory droplets and aerosols, with an average incubation period of two days (range 1–4 days)[2,4,5] Viral shedding can begin one day before symptom onset and persist for 5–7 days. Clinical presentation involves abrupt fever and upper respiratory symptoms.[2,5] While mostly self-limiting, high-risk groups face severe, potentially fatal complications.[3]

Vaccine effectiveness (VE) varies seasonally based on the vaccine-virus antigenic match and host factors like age and immunocompetence. Systematic reviews estimate the pooled effectiveness of inactivated vaccines in healthy adults at approximately 59%.[6] Furthermore, VE may decline during the season (intra-season waning), particularly against A(H3N2) and B strains.[7]

In Thailand, influenza circulates year-round with a bimodal peak. Influenza activity in 2025 significantly exceeded the 5-year median; as of September, over 486,000 cases and 57 deaths were reported.[8] This surge elevates outbreak risks in congregate settings like training centers and military camps. Such environments facilitate rapid transmission due to high-density living, close-contact training, and stressors.[9,10]

In Thailand, the National Immunization Program provides free annual vaccinations to seven high-risk groups, such as pregnant women, young children, the elderly, and individuals with chronic diseases.[11] Organizations like the Royal Thai Army and Police also conduct campaigns to preserve workforce readiness. However, variable coverage and timing can leave some cohorts susceptible to infection during peak transmission periods.[12,13]

On 13 Oct 2025, a cluster of approximately 40 students with influenza-like illness (ILI) was reported at a non-commissioned officer (NCO) training center in Saraburi. Health authorities like Saraburi Hospital, Saraburi Provincial Health Office, the local Subdistrict Health Promoting Hospital, and the Office of Disease Prevention and Control Region 4 Saraburi, mobilized a joint Surveillance and Rapid Response Team (SRRT) to investigate the same day. The objectives were to verify the outbreak, describe epidemiological characteristics, identify risk factors and the causative agent, estimate vaccine effectiveness, and implement control measures.

Methods

Study Design, Setting, and Population

We conducted a retrospective cohort study, including both descriptive and analytical components, to describe epidemiological characteristics and identify risk factors at an NCO training center in Saraburi Province, Thailand. Located in the central region, Saraburi serves as a transportation gateway with high mobility. The study population comprised all students and staff, focusing on symptom onset between 1–28 Oct 2025.

Active Case Finding, Data Collection, and Case Definitions

We employed a two-phase data collection strategy using a self-administered online questionnaire (Google Forms).

Data included: (1) demographics (age, gender, dormitory and method of commute); (2) clinical history (symptoms, onset date, underlying conditions: chronic respiratory diseases, cardiovascular diseases, chronic kidney disease, neurovascular diseases, obesity, cancer, and diabetes); (3) exposure and risk behaviors (handwashing, masking, sharing personal items), sleep duration, and history of contact with sick individuals; and (4) vaccination and treatment (influenza vaccination history and oseltamivir usage).

Phase I; Initial mass screening (13–14 Oct 2025)

The SRRT conducted active case finding, requiring all students and staff to complete the questionnaire to establish baseline health and exposure history.

Phase II; Enhanced surveillance (13–28 Oct 2025)

Subsequently, we implemented enhanced surveillance with twice-daily (at 08:00 AM and 04:00 PM) screening for fever, respiratory symptoms, and oxygen saturation. Suspected cases completed the questionnaire. Active surveillance concluded on 28 Oct 2025 after exceeding the maximum incubation period with no new cases, though passive monitoring continued until the center's closure on 31 Oct 2025.

Data management

To address multiple submissions, we de-duplicated the dataset by retaining the most recent record per participant, ensuring the analysis captured the final disease status and symptom profile.

Case definitions

Cases were classified as follows: (1) suspected case—a student or staff member with a body temperature ≥37.5 °C or a history of fever, plus cough, and at least one of the following symptoms: myalgia, sore throat, rhinorrhea, headache, fatigue, or dyspnea, with onset between 1 Oct 2025 and 28 Oct 2025; (2) probable case—a suspected case that tested positive using an influenza rapid antigen test (RAT); (3) confirmed case—a suspected or probable case with laboratory confirmation of influenza virus infection by real-time polymerase chain reaction (RT-PCR) from a nasopharyngeal swab.

Laboratory Methods

Nasopharyngeal swabs were collected from suspected cases presenting to Saraburi Hospital with fever and cough. Specimens were screened by RAT; positive samples were sent to the Office of Disease Prevention and Control Region 4 Saraburi for RT-PCR subtype confirmation.

Data Analysis

Data were analyzed using R software, version 4.5.1 (R Core Team, Vienna, Austria).[14] We used *tidyverse* for manipulation and *gtsummary*/*flextable* for tables. Adjusted risk ratios (ARR) were calculated using multivariable Poisson regression with robust error variances (*sandwich* package). Statistical significance was defined as p-value <0.05.

Descriptive epidemiology

We analyzed data by person, place, and time using frequencies, percentages, and attack rates (AR). Person-level characteristics, risk behaviors, and symptoms were summarized. Time was visualized via an epidemic curve, and place by dormitory-stratified AR.

Analytical epidemiology

A retrospective cohort study was conducted to identify risk factors and estimate vaccine effectiveness.

- *Source population and sampling*

The source population comprised all students and staff residing at the center. Given the manageable population size, we employed a total enumeration (census) approach to invite all individuals, maximizing statistical power without sampling.

- *Variables*

Dependent variable: meeting the suspected case definition.

Independent variables included: (1) demographic characteristics and health (gender, age group, and presence of comorbidities); (2) method of commute to the center; (3) risk behaviors (handwashing, masking, sharing personal items, and sleep duration [5-point Likert scale]); (4) history of contact with sick individuals; (5) vaccination status.

- *Statistical analysis*

We calculated crude risk ratios (RR) with 95% confidence intervals (CIs) using Chi-square or Fisher's exact tests. Variables with p-value <0.1 were included in a multivariable Poisson regression model with robust error variances to estimate adjusted risk ratios (ARR). Vaccine effectiveness (VE) was calculated as VE=(1−RR) ×100 using crude RR, as vaccination status did not meet multivariable model inclusion criteria.

Estimation of Reproduction Number

To characterize transmissibility, we estimated: (1) Basic reproduction number (R_0) using the R_0 package via attack rate, exponential growth, and maximum likelihood methods for robustness; (2) Time-dependent effective reproduction number (R_t) to evaluate interventions, assuming a mean generation time of 3.2 days (SD 2.1).[15]

Environmental and Activity Assessment

In addition to the retrospective cohort study, we conducted an environmental walk-through of dormitories, the refectory, and training facilities to assess density, ventilation, and hygiene. Key staff were also interviewed regarding daily schedules and activities.

Results

Of 903 students and staff at the center, 887 (98.2%) participated. We identified 159 suspected cases (attack rate 17.9%). Most (96.9%) had mild-to-moderate symptoms and were managed on-site in isolation. Five (3.1%) severe cases (oxygen saturation <95%) were hospitalized. All responded well to treatment; no respiratory failure or deaths occurred.

Descriptive Epidemiology

All 159 cases were identified via active and enhanced surveillance. No cases were identified solely through passive reporting. All were male. The mean (standard deviation) age was 22.8 (2.96) years. The most affected age group was 21–25 years (52.8%). Regarding commuting methods, 80 (50.3%) traveled to the center either on foot, by bicycle, or in a private car, while 79 (49.7%) used public transportation. Four reported comorbidities (aggregated as binary due to low prevalence). Most (78.6%) had received the influenza vaccine after 1 Oct 2024. During their illness, 98 (61.6%) received oseltamivir treatment.

Common symptoms included rhinorrhea (87.4%), sore throat (86.8%), fatigue (65.4%), myalgia (60.4%), headache (55.4%), and dyspnea (28.9%).

Attack rates varied: Division 3 (21.8%), Division 2 (17.2%), and Division 1 (16.0%). Only one staff member was affected (Table 1).

The first case occurred on 1 Oct 2025; cases peaked on 11 Oct 2025, followed by a sharp decline from 13 Oct 2025 (Figure 1).

Table 1. Distribution of influenza cases and attack rates by population group, non-commissioned officer training center, Saraburi Province, Thailand, 1-28 Oct 2025

Population group	Total population	Number screened	Suspected cases	Probable cases	Confirmed cases	Total cases	Attack rate (%)
Division 1	290	287	46	0	0	46	16.03
Division 2	290	290	50	0	0	50	17.24
Division 3	290	284	59	0	3	62	21.83
Staff	33	26	1	0	0	1	3.85
Total	**903**	**887**	**156**	**0**	**3**	**159**	**17.93**

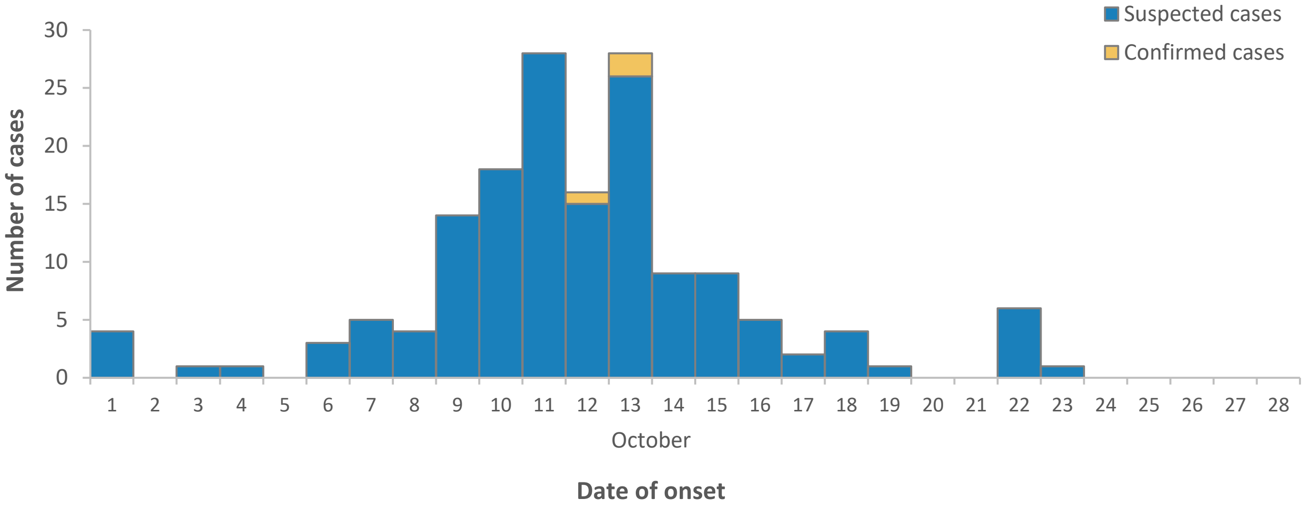

Figure 1. Epidemic curve of an influenza outbreak, non-commissioned officer training center, Saraburi Province, Thailand, 1–28 Oct 2025

Laboratory Findings

Of seven specimens collected, three were RAT-positive. Four underwent RT-PCR (including the three RAT-positives); three were confirmed as influenza A(H3N2) with cycle threshold values of 21.8–25.1. The single PCR-negative case had initiated oseltamivir prior to collection.

Analytical Epidemiology and Vaccine Effectiveness

Significant univariable factors included handwashing with soap and water before meals (*p*-value 0.012), close contact with patients (*p*-value <0.001), and sharing personal items (e.g., spoons, drinking glasses) (*p*-value <0.001) (Table 2).

Multivariable analysis identified three independent factors: handwashing with soap and water before meals (ARR 0.80, 95% CI 0.72–0.89, *p*-value <0.001), close contact with patients (ARR 1.22, 95% CI 1.06–1.42, *p*-value 0.011), and sharing personal items (ARR 1.20, 95% CI 1.06–1.36, *p*-value 0.008).

Vaccine effectiveness against suspected clinical illness was 19.1% (95% CI: –20.0% to 43.9%).

Reproduction Number

Estimated R_0 approximated 1.0 (attack rate 1.10, 95% CI 1.08–1.12; exponential growth 0.85, 95% CI 0.79–0.92; maximum likelihood 0.98, 95% CI 0.77–1.21). R_t peaked at 3.24 on 6 Oct 2025 (linked to a communal event) but dropped below 1.0 after 11 Oct 2025, coinciding with interventions and peak reporting (Figure 2).

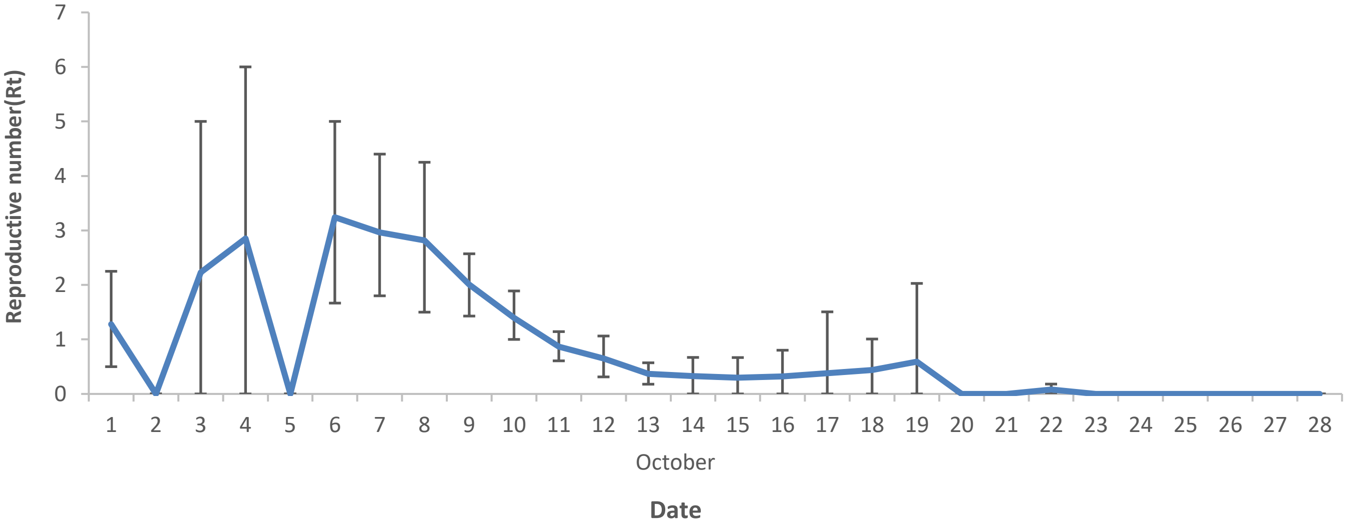

Figure 2. Time-dependent reproduction number (R_t) of the influenza outbreak, non-commissioned officer training center, Saraburi Province, Thailand, 1–28 Oct 2025

Table 2. Univariable and multivariable analysis of risk factors associated with influenza illness, non-commissioned officer training center, Saraburi Province, Thailand, 1-28 Oct 2025

Factor	Non-cases (%) (n=728)	Cases (%) (n=159)	Univariable analysis		Multivariable analysis	
			Relative risk (95% CI)	*P*-value	Adjusted RR (95% CI)	*P*-value
Gender						
Male	722 (81.95)	159 (18.05)	Ref	0.598	-	-
Female	6 (100.00)	0 (0.00)	Undefined			
Age group (years)						
0–15	0 (0.00)	0 (0.00)	Undefined	0.084*	0.90 (0.75–1.07)	0.312
16–20	176 (81.11)	41 (18.89)	Ref			
21–25	401 (82.68)	84 (17.32)	0.92 (0.64–1.34)			
26–30	121 (78.57)	33 (21.43)	1.13 (0.71–1.79)			
31–60	30 (96.77)	1 (3.23)	0.17 (0.01–0.78)			
≥60	0 (0.00)	0 (0.00)	Undefined			
Commute to center						
Walk/bicycle/private car	317 (79.85)	80 (20.15)	Ref	0.135	-	-
Public/shared transport	411 (83.88)	79 (16.12)	0.80 (0.59–1.09)			
At least 1 comorbidity						
Yes	8 (66.67)	4 (33.33)	Ref	0.244	-	-
No	720 (82.29)	155 (17.71)	0.53 (0.22–1.73)			
Influenza vaccination						
Unvaccinated	126 (78.75)	34 (21.25)	Ref	0.255	-	-
Vaccinated	602 (82.81)	125 (17.19)	0.81 (0.56–1.20)			
Handwashing before meals						
Never	42 (70.00)	18 (30.00)	Ref	0.012**	0.80 (0.72–0.89)	<0.001**
Rarely	82 (78.85)	22 (21.15)	0.71 (0.38–1.33)			
Sometimes	112 (76.19)	35 (23.81)	0.79 (0.46–1.43)			
Mostly	265 (84.39)	49 (15.61)	0.52 (0.31–0.92)			
Always	227 (86.64)	35 (13.36)	0.45 (0.26–0.80)			
Mask wearing						
Never	64 (80.00)	16 (20.00)	Ref	0.113	-	-
Rarely	107 (86.99)	16 (13.01)	0.65 (0.32–1.31)			
Sometimes	159 (80.71)	38 (19.29)	0.96 (0.55–1.78)			
Mostly	242 (84.91)	43 (15.09)	0.75 (0.43–1.35)			
Always	156 (77.23)	46 (22.77)	1.14 (0.66–2.07)			
Close contact with patient						
Never	113 (94.17)	7 (5.83)	Ref	<0.001**	1.22 (1.06–1.42)	0.011**
Rarely	112 (82.96)	23 (17.04)	2.92 (1.32–6.83)			
Sometimes	182 (85.45)	31 (14.55)	2.49 (1.17–6.17)			
Mostly	207 (80.54)	50 (19.46)	3.34 (1.62–8.07)			
Always	114 (70.37)	48 (29.63)	5.08 (2.46–12.3)			
Sharing personal items						
Never	254 (88.19)	34 (11.81)	Ref	<0.001**	1.20 (1.06–1.36)	0.008**
Rarely	93 (85.32)	16 (14.68)	1.24 (0.67–2.21)			
Sometimes	205 (83.00)	42 (17.00)	1.44 (0.92–2.28)			
Mostly	118 (76.13)	37 (23.87)	2.02 (1.27–3.23)			
Always	58 (65.91)	30 (34.09)	2.89 (1.76–4.72)			
Sleep 6-8 hours per day						
Never	9 (90.00)	1 (10.00)	Ref	0.519	-	-
Rarely	25 (80.65)	6 (19.35)	1.94 (0.33–36.6)			
Sometimes	71 (78.02)	20 (21.98)	2.20 (0.46–39.4)			
Mostly	213 (80.08)	53 (19.92)	1.99 (0.44–35.2)			
Always	410 (83.84)	79 (16.16)	1.62 (0.36–28.5)			

**p-value <0.1, **p-value <0.05. Multivariable results for ordinal variables (e.g., handwashing) are presented as a single adjusted risk ratio, representing the risk trend across categories, which were entered into the model as continuous ordinal variables. RR: relative risk. CI: confidence interval.*

Environmental and Activity Assessment

Environmental investigation revealed high transmission risks:

(1) Dormitories: trainees resided in long, two-story concrete buildings. Beds were arranged in two long rows. The spacing between adjacent beds was approximately 0.5 to 1.0 meters, indicating high physical proximity during sleep. Ventilation relied on large industrial fans, which, while reducing heat, likely facilitated the circulation of viral aerosols across the sleeping quarters.

(2) Refectory: the dining area had a seating capacity of 320, organized into tables of eight (four students facing four). This arrangement forced face-to-face interaction at close range (<1 meter) during meals. Furthermore, chairs were covered with fabric cloths (potential fomites), and food service staff were observed working without masks.

(3) Shared facilities: bathing facilities utilized a large communal water tub (dipping style), and water for handwashing sinks was available only during specific intervals, potentially hindering consistent hand hygiene.

(4) High-risk activities: the daily schedule (05:00 AM–09:00 PM) was strictly regimented. Key activities identified as high-risk included field training involving unmasked group exercises with loud vocalization. Two mass gathering events—the "welcome new students" (1 Oct 2025) and "senior-welcomes-junior" (6 Oct 2025)—coincided with the start of the outbreak.

Actions Taken

The SRRT implemented immediate enhanced surveillance with twice-daily screening by on-site nurses. Suspected cases were isolated. Clinical management followed a collaborative model: Saraburi Hospital physicians authorized oseltamivir, while center nurses managed daily care and monitoring.

Concurrently, the SRRT provided health education on symptoms and prevention via trainers and materials. Environmental measures included disinfecting high-touch surfaces.

Key non-pharmaceutical interventions (NPIs) included strict handwashing, mandatory masking for symptomatic cases (source control), and suspension of group activities. These measures continued until the center closed for term break on 31 Oct 2025.

Discussion

This investigation describes a rapid Influenza A(H3N2) outbreak in a high-density setting (attack rate 17.9%). This finding underscores the rapid transmission potential of influenza in such environments. This aligns with previous military and training centers studies (10–40%),[16] though lower than a 2017 military recruit unit in Chiang Mai report (40.8%).[17] While the AR in our study was lower, it confirms the profound vulnerability of this population. This vulnerability is likely driven by environmental and structural factors, such as high-density dormitories with closely arranged beds and a curriculum requiring continuous, close-contact group activities, which are highly conducive to the spread of respiratory droplets. The epidemic curve suggested propagated spread, with peaks coinciding with two major communal events that likely amplified transmission. Additionally, low cycle threshold values indicated high viral loads, further facilitating rapid spread.

Personal behaviors drove transmission. Close contact (ARR 1.22) and sharing items (ARR 1.20) were significant risks, inherently difficult to mitigate given structured training routines. Conversely, handwashing before meals was protective (ARR 0.80), aligning with evidence of 16–21% risk reduction.[18] Where physical distancing is operationally infeasible, reinforcing basic hygiene remains paramount.[19]

We observed a low, non-significant VE of 19.1% against clinical illness. This aligns with historical data showing reduced effectiveness for H3N2 (~33%), often attributed to rapid antigenic drift or egg-adaptive mutations during manufacturing. [20,21] Although the cohort received the 2025 Southern Hemisphere influenza vaccine approximately one month before the outbreak, we were unable to perform genetic sequencing or hemagglutination inhibition assays on the clinical specimens due to limited laboratory resources.[11] Therefore, while we strongly suspect antigenic drift or vaccine strain mismatch contributed to the low VE, this hypothesis remains presumptive and relies on the indirect evidence of the low clinical protection observed in this outbreak.

Despite the rapid spread of the outbreak, the R_0 ranged between 0.85 and 1.10. While R_0 is theoretically defined for a completely susceptible population, a large proportion of this cohort was vaccinated. Although vaccination coverage was high, the low VE implies that the vaccine conferred minimal protection. Consequently, the population remained functionally susceptible to this specific circulating A(H3N2) strain, validating the use of this estimate as an approximation of the virus's intrinsic transmission potential in this setting. This value is notably lower than the natural R_0 for seasonal influenza typically reported in congregate military settings, which often ranges from 2.68 to 4.84.[22] The suppression of the overall R_0 to near unity likely reflects the impact of early behavioral adaptations and the prompt initiation of control measures, which dampened the average transmission potential over the course of the outbreak. However, the true intensity of transmission is better illustrated by the time-dependent effective reproduction number, which peaked at 3.24 during the early phase. This early peak raises the critical question of whether the subsequent decline in cases resulted from the population reaching the herd immunity threshold. Based on the peak R_t of 3.24, the theoretical herd immunity threshold is approximately 69% (calculated as $1-1/R_t$). Yet, the observed AR was only 17.9%, significantly below this threshold. This discrepancy strongly suggests that the outbreak did not burn out naturally due to the depletion of susceptible hosts. Instead, the rapid reduction in R_t to below 1.0 was driven by the effective implementation of public health interventions—specifically patient isolation and strict hygiene enforcement—which truncated the transmission chain.

This investigation highlights the limitation of relying solely on mass vaccination in congregate settings. While essential, high coverage proved insufficient against H3N2, a subtype prone to antigenic drift and lower effectiveness.[20,22] Sole reliance creates a "single-point failure" risk, permitting rapid transmission when VE declines—a phenomenon common in military cohorts.[16,17] Consequently, we advocate for a resilient "vaccine-plus" strategy.[23] This multi-layered approach integrates vaccination with pre-emptive NPIs (e.g., hygiene enforcement, density reduction) to mitigate risk when vaccine protection is suboptimal.[19]

Limitations

This study has several limitations. First, self-reported data introduces potential recall bias. Second, using a broad clinical case definition rather than lab confirmation risks non-differential misclassification (potentially capturing other pathogens), which typically biases associations toward the null. Third, prioritizing symptomatic testing missed asymptomatic infections, likely underestimating transmission. Furthermore, unaccounted prior natural immunity in unvaccinated controls could further bias VE estimates toward the null. Finally, the study was underpowered to detect low VE. With a fixed cohort (n=887) and few unvaccinated controls (n=34), the sample size was insufficient to statistically confirm the observed protection (post-hoc requirement: n≈1,475).

Recommendations

We propose recommendations for military and residential training institutions globally:

(1) Institutionalize hygiene as a discipline: Hygiene protocols must be integrated into core disciplinary curricula rather than treated as optional advice. Mandatory handwashing before meals and strict prohibition of sharing personal items (e.g., utensils) should be enforced as standard operating procedures.

(2) Adopt a "vaccine-plus" strategy: Authorities should shift from sole reliance on vaccination to a multi-layered approach. Given suboptimal H3N2 protection, policies must mandate pre-emptive NPIs—such as density reduction and ventilation improvements—before intake, regardless of vaccination status.

(3) Enhance surveillance: Future investigations involving low VE despite high coverage should prioritize advanced molecular characterization (sequencing and culture). This is crucial for confirming antigenic mismatch and directly informing national vaccine strain selection.

Conclusion

We confirmed an influenza A(H3N2) outbreak at a Saraburi NCO training center (159 cases; AR 17.9%; peak 11 Oct 2025). Close contact and sharing items were risk factors; handwashing was protective. VE was 19.1%. Although R_0 was 0.85–1.10, R_t peaked at 3.24 before dropping below 1.0 following interventions. This demonstrates that rapid public health response effectively controls outbreaks in high-risk settings despite low vaccine effectiveness.

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Author Contributions

Panupong Tantirat: Conceptualization, data curation, formal analysis, investigation, methodology, software, supervision, validation, visualization, writing—original draft, writing—review & editing. **Sitthanon Jamhom:** Data curation, investigation, project administration, resources. **Jiraporn Kruksomrong:** Investigation, project administration, resources.

Ethical Approval

This investigation was initiated and conducted by Thai public health authorities (Saraburi Provincial Health Office and Saraburi Hospital) as an emergency public health response to an acute outbreak. The activity meets the criteria for "public health surveillance," which is broadly recognized and formally defined under international guidelines (such as the U.S. Common Rule 45 CFR 46.102(l)(2)) as distinct from “human subjects research”.

The primary objectives of this activity were disease control, prevention, and public health situational awareness, not the generation of generalizable scientific knowledge. Therefore, as this activity constituted routine public health practice and not research, it was determined to be exempt from formal review and approval by an Institutional Review Board. The investigation was nonetheless conducted in accordance with all relevant ethical principles, including the Declaration of Helsinki. All data were fully anonymized prior to analysis to ensure patient confidentiality.

Informed Consent

Informed consent was obtained from all participants involved in the study.

Data Availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Conflicts of Interest

The authors declare no conflict of interest.

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

During the preparation of this work, the author(s) used Gemini (Google) to translate the manuscript from Thai to English, search for relevant literature, enhance textual clarity, and refine the language for a formal academic tone. The content produced by this tool was reviewed and edited by the author(s), who accept full responsibility for the final text.

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A Food Poisoning Outbreak in a School from Progressive Contamination of Norovirus, Amnat Charoen Province, Thailand, February 2025

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Abstract

On 13 Feb 2025, students and staff at School A in Hua Taphan District, Amnat Charoen Province, Thailand, developed gastroenteritis symptoms. An investigation was conducted to confirm the diagnosis, describe outbreak characteristics, identify possible sources and risk factors, and provide recommendations. A suspected case was an individual present at the school between 11–24 Feb 2025 who experienced three or more loose or liquid stools within 24 hours or at least one episode of vomiting. Data was collected via questionnaires and hospital records. Rectal swabs and stool samples were tested, and the environment was assessed. A retrospective cohort study was conducted using multivariable Poisson regression with robust error variance to calculate adjusted relative risks (ARR). The attack rate was 30.2% (142/470). Common symptoms were nausea (85%), abdominal pain (79%), and vomiting (76%). The epidemic curve indicated a point-source exposure followed by secondary transmission. Norovirus was detected in 71.4% of clinical samples, including one asymptomatic food handler. The chicken rice meal served on 11 February, had the highest ARR of 4.37 (95% confidence interval (CI) 1.12–17.10). Students served later (grades 4–6) had a significantly higher risk compared to the early serving group (ARR 2.17, 95% CI 1.37–3.43), suggesting progressive contamination. The epidemiological and laboratory results suggested that the chicken rice meal, was likely contaminated by an infected asymptomatic food handler, which was the source of the norovirus outbreak. The study recommendations included improving food-handling practices, strengthening hand hygiene infrastructure, and ensuring regular maintenance of the water treatment system.

Keywords: norovirus, foodborne and waterborne outbreak, outbreak investigation

Introduction

Foodborne illnesses remain a major global public health concern, with the World Health Organization estimating 600 million cases and 420,000 deaths and the loss of 33 million disability-adjusted life years (DALYs).[1]

Norovirus is the leading cause of acute gastroenteritis worldwide. It is estimated to cause 685 million cases annually, including 200 million children under five. The virus is associated with approximately 200,000 deaths each year, particularly affecting young children, older adults, and individuals with compromised immunity. In addition to its health impact, norovirus imposes a substantial global economic burden, with annual costs estimated at 60 billion US dollars due to healthcare expenses and productivity losses.[2]

Thailand similarly faces a considerable burden; in 2024, the country reported 130,444 food poisoning cases, corresponding to an incidence of approximately 200 per 100,000 population.[3] Norovirus is a leading cause of acute gastroenteritis in Thailand, with schools frequently serving as outbreak sites. Most clusters occur during the cool season (September–February) when close contact and low temperatures enhance transmission. From 2017–2021, about three-quarters of reported outbreaks were linked to schools.[4,5] Outbreaks spread rapidly via person-to-person and foodborne routes, often affecting 10.0–30.0% of students, causing vomiting, diarrhea, and dehydration.[6] These events disrupt learning through absenteeism and temporary school closures, highlighting the need for strict hygiene, early case isolation, and environmental cleaning to limit spread.[7,8]

On 13 Feb 2025, the Department of Disease Control (DDC) was notified of a suspected foodborne illness outbreak at a school in Hua Taphan District, Amnat Charoen Province, Thailand, prompting the deployment of a Joint Investigation Team (JIT) comprising of DDC and local health staff. Conducted from 14–17 Feb 2025, the investigation aimed to confirm the diagnosis and outbreak, describe the epidemiological characteristics, identify potential sources and transmission risk factors, and recommend appropriate control measures.

Methods

Epidemiologic Study

A suspected case was defined as any student or school staff present at the school between 11–24 Feb 2025 who experienced three or more loose or liquid stools within 24 hours or at least one episode of vomiting. A confirmed case was defined as a suspected case with a laboratory-confirmed norovirus detected from a fresh stool or rectal swab sample, while an asymptomatic case referred to a person without gastrointestinal symptoms who tested positive for norovirus using the same diagnostic methods.

Active case finding was conducted through multiple approaches: students who visited the hospital were scheduled for follow-up interviews and questionnaires; room-by-room surveys were carried out by the JIT in every classroom; school staff received online health questionnaires; and for absent students, Google Form questionnaires were distributed via the class LINE group, a mobile messaging application widely used in Thailand, by homeroom teachers.

Data were collected using semi-structured questionnaires. For preschool students, questionnaires were completed by their parents, while older students completed them under the guidance of the JIT and teachers. Information collected included demographic characteristics, symptomatology, food items and consumption detail (including quantity, categorized into five levels: not eat, eat less than half, eat about half, eat more than half, and eat all) and source of drinking water.

A retrospective cohort study was conducted among all students and staff who were present at the school during lunch on 11 Feb 2025, for which data were collected using structured questionnaires to identify potential sources and risk factors associated with the outbreak. The estimated sample size required was 202 participants, based on exposure and attack rate assumptions from similar foodborne outbreaks reported in Thailand.[9,10] Descriptive analysis summarized demographic and clinical characteristics as proportions for categorical variables and medians with interquartile ranges for continuous variables. For the cohort study, risk ratios (RRs) with 95% confidence intervals (CIs) were calculated for each food item using a Poisson regression model with robust standard errors. This study used Poisson regression due to its ability to provide adjusted risk ratios, which is more understandable given that the disease was not rare among the affected population in this event.[11] Multivariable analysis was performed using the same model to calculate adjusted RRs, focusing on food items served during the most suspected meal and including variables with p-value <0.20 from the univariable analysis or those deemed epidemiologically relevant. Statistical significance was defined as p-value <0.05, and all analyses were conducted using R software (version 4.4.1) with the *tidyverse* package (version 1.3.1).[12]

Environmental Study

This study conducted environmental inspections of the school kitchen, food preparation areas, dishwashing stations and water supply system using the standard water and sanitation safety checklist from the Department of Health.[13] A walkthrough survey was carried out to observe hygiene practices, food storage conditions, and overall sanitation. Food handlers were interviewed to gather information regarding raw material sourcing, cooking procedures, and water collection and usage during meal preparation.

Environmental sampling included the collection of water samples from various risk points around the school. Coliform screening was conducted using two field test kits: the A.11 test for drinking water and the SI-2 test for food, utensils, and hand samples. These samples were tested for coliform bacteria using the SI-2 test kit, a peptone-lactose-bromocresol solution that detects lactose-fermenting bacteria through gas production and acidification. Residual chlorine levels in water samples were measured using the O-31 test, which contains an orthotolidine-arsenate solution that reacts with free residual chlorine. In addition, water and ice samples intended for drinking were collected for multiplex polymerase chain reaction (PCR) to detect key viral gastrointestinal pathogens, including norovirus, rotavirus, and adenovirus, while bacterial pathogens were assessed using bacterial culture.

Laboratory Study

For laboratory testing, stool and rectal swab specimens were collected approximately 10.0% from symptomatic cases who had not yet received antibiotics. Fresh stool samples were preferred because they provide higher pathogen detection sensitivity compared with rectal swabs, which were used only when stool could not be obtained.[14] All food handlers were also included in the laboratory investigation. All specimens were sent to the Bamrasnaradura Infectious Diseases Institute or the National Institute of Health for bacterial culture and PCR analysis to detect potential viral and bacterial gastrointestinal pathogens.

Results

Epidemiologic Study

A total of 470 individuals (430 students and 40 staff) were present at the school, which serves kindergarten level 2 through grade 6. The response rate to the questionnaire was 80.2% (377/470). Active case finding identified 142 cases. Of these, 139 were symptomatic students, one was a symptomatic staff member, and two were asymptomatic food handlers. Thirteen cases met the confirmed case definition, 127 were classified as suspected cases, and two were asymptomatic. Most cases managed their illness at home (68.0% did not seek medical care), while 29.2% visited the outpatient department and 2.8% required brief hospitalization.

The crude attack rate was 30.2% (142/470). Attack rates were lowest among preschoolers at 12.0–13.8%, increasing with age to 56.8% among grade 6 students, while only 2.5% of staff were affected. The median age was 9 years (interquartile range 7–11 years), and the male-to-female ratio (M:F) was 1.0:1.5. The most common symptoms were nausea (84.3%), abdominal pain (78.5%), and vomiting (76.0%), followed by fever (36.5%) and diarrhea (28.4%).

The first case developed symptoms at approximately 12:00 PM on 11 Feb 2025. The number of cases increased rapidly, peaking between 06:00 PM and 12:00 AM on 12 February, and declined sharply after 13 Feb 2025, consistent with the epidemiological pattern of a point common-source outbreak. In total, 47 cases (33.1%) developed symptoms 30–36 hours after the lunch meal on 11 February, aligning with the main surge in the epidemic curve (Figure 1).

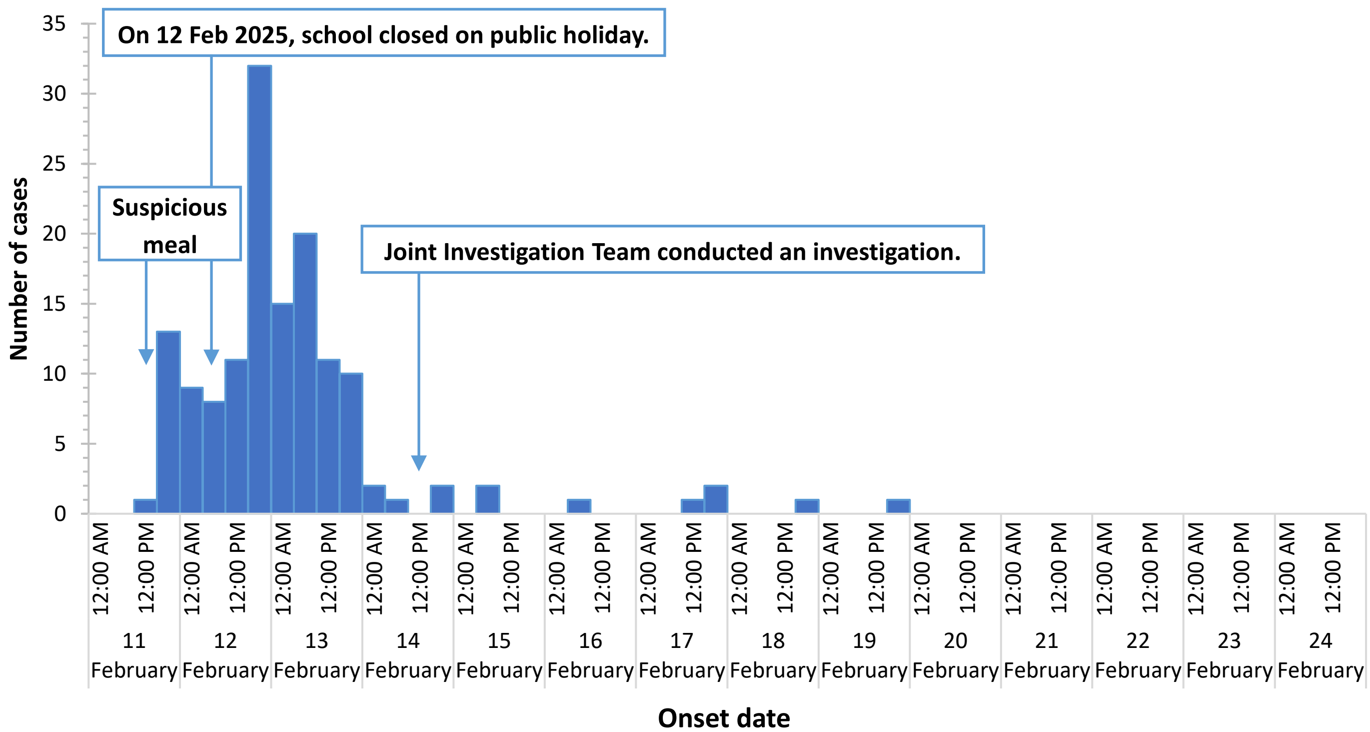

Figure 1. Number of food poisoning cases at a school in Hua Taphan District, Amnat Charoen Province, 11–24 Feb 2025, Classified by Date of Symptom Onset (n=142)

The highest attack rate was observed among those who consumed chicken rice (67.5%, 131/194). The school was closed on 12 Feb 2025, due to a public holiday, and no meals were served. The univariable analysis showed that the chicken rice meal had the strongest association with illness (crude RR 6.65, 95% CI 1.72–25.65). Meal-service timing also influenced risk: students in the intermediate serving group had twice the risk of illness (crude RR 2.00, 95% CI 1.25–3.19), and those in the late serving group had an even higher risk (crude RR 2.39, 95% CI 1.51–3.77) compared with the early serving group. In the multivariable model, the chicken rice meal remained independently associated with illness (adjusted RR 4.37, 95% CI 1.12–17.10), and elevated risks persisted for both the intermediate (adjusted RR 1.76, 95% CI 1.10–2.82) and late serving groups (adjusted RR 2.17, 95% CI 1.37–3.43) (Table 1).

Table 1. Crude and adjusted relative risks of food and water exposures associated with food poisoning at a school, Amnat Charoen Province, February 2025

Items	Exposed Attack rate (case/total)	Non-exposed Attack rate (case/total)	Crude RR (95% CI)	*P*-value	Adjusted RR (95% CI)	*P*-value
Chicken rice	67.5% (131/194)	6.5% (2/31)	6.65 (1.72–25.65)	<0.01*	4.37 (1.12–17.10)	0.03*
Steel dispenser water	44.8% (13/29)	63.6% (129/206)	0.80 (0.5–1.29)	0.36	0.80 (0.50–1.28)	0.35
Filtered water	63.7% (121/190)	46.7% (21/45)	1.22 (0.84–1.79)	0.30	1.17 (0.75–1.82)	0.50
Early serving group (Preschool 2–3)	25.8% (17/66)	81.0% (124/153)	Reference		Reference	
Intermediate serving group (Grade 1–3)	69.4% (59/85)	61.2% (82/134)	2.00 (1.25–3.19)	<0.01*	1.76 (1.10–2.82)	0.02*
Late serving group (Grade 4–6)	95.6% (65/68)	50.3% (76/151)	2.39 (1.51–3.77)	<0.01*	2.17 (1.37–3.43)	<0.01*

Adjusted for chicken rice, steel dispenser water, filtered water, and meal service timing. RR: risk ratio. CI: confidence interval.

Environmental Study

Groundwater served as the school's primary water source. Drinking water passed through a reverse osmosis system and an ultraviolet (UV) sterilizer, although the UV unit had been nonfunctional for two weeks and maintenance was suboptimal. Water used in the kitchen came from a separate line with ceramic filtration. Soap was not available at handwashing stations in the kitchen or nearby toilets. Students did not clean their food trays thoroughly after meals; visible food residues and moisture were often left on the trays. After use, trays were placed in a single stack while still wet, without adequate drying or sanitization, and were later reused for the next meal. There was no separation between cutting boards and knives used for raw meat and vegetables, presenting a risk for cross-contamination. The school had only two food handlers, each with over 20 years of experience, but neither had received formal food safety training (Figure 2).

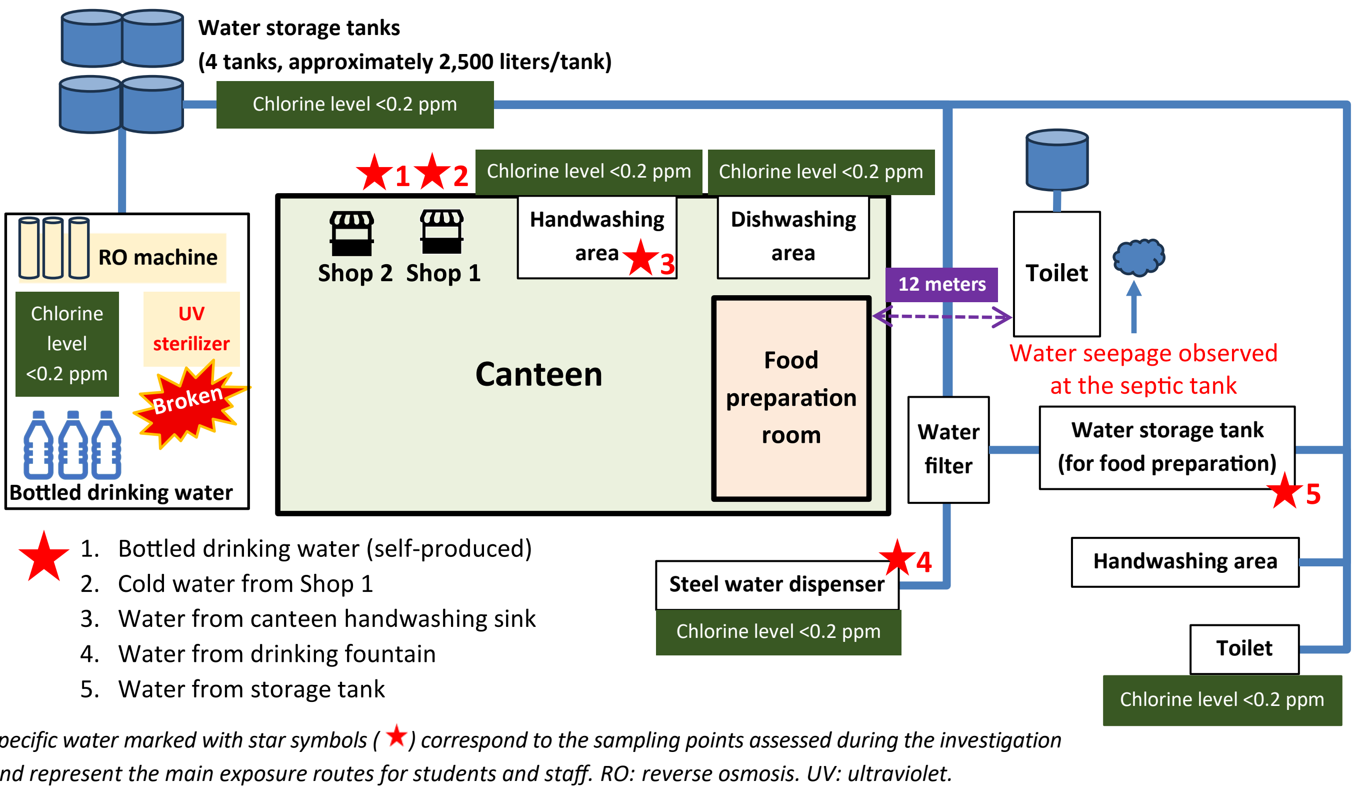

Figure 2. Layout of the canteen and water supply system at School A, Hua Taphan District, Amnat Charoen Province, Thailand

Raw chicken meat was pre-chopped at the supplier before delivery to the school. No cold storage was available at the school; therefore, ingredients were used on the same day of delivery, and cooking began immediately upon arrival in the morning.

On 11 February, the chicken rice lunch was prepared as follows. Food handler 1 rinsed raw chicken prior to cooking and later handled cooked chicken during portioning and serving. Food handler 2 prepared rice using grains stored in the kitchen. The rice was rinsed three times using water from the ceramic-filtered supply, then cooked in the chicken broth using a rice cooker. After cooking, the rice was left in the unplugged cooker for approximately one hour.

At 09:00 AM, final food assembly was performed. With gloves on, food handler 1 portioned the chicken onto individual trays, and food handler 2 scooped the rice. Teachers assisted with distribution. Preschoolers were served at approximately 10:30 AM, followed by grades 1–3 around 11:00 AM, and grades 4–6 around 11:30 AM.

Multiplex PCR detected no pathogens in water, ice, or kitchen tools such as knives, cutting boards, and trays. The drinking-water system showed no contamination by the A.11 test. Coliforms were detected in 70% (7/10) of surface and equipment samples, including food trays, spoons, plates, a water tap, one food handler's hand, and the handwashing sink in the girls' restroom. Several water sampling points around the school showed residual chlorine levels of <0.2 ppm, including outlets near Shop 1, Shop 2, the handwashing and dishwashing sinks, and the drinking water dispenser.

Laboratory Study

A total of 14 rectal swabs and stool samples were collected, including 12 from symptomatic cases and two from asymptomatic food handlers. Multiplex PCR detected at least one gastrointestinal pathogen in 92.9% of samples, and norovirus detected in 71.4% of the samples (Table 2). Food handler 1 tested positive for norovirus.

Table 2. Laboratory test results of rectal swab and stool samples from cases and food handlers, Hua Taphan District, Amnat Charoen Province, Thailand, February 2025

Pathogen	Cases (n=12) n (%)	Food handlers (n=2) n (%)	Total (n=14) n (%)
Any pathogen (PCR)	11 (91.7)	2 (100.0)	13 (92.9)
Norovirus	9 (75.0)	1 (50.0)	10 (71.4)
Astrovirus	3 (25.0)	-	3 (21.4)
P. shigelloides	2 (16.7)	1 (50.0)	3 (21.4)
Sapovirus	1 (8.3)	-	1 (7.1)
***Aeromonas* spp.**	1 (8.3)	-	1 (7.1)
EPEC	1 (8.3)	-	1 (7.1)
EAEC (culture)	1 (8.3)	1 (50.0)	2 (14.3)

PCR: polymerase chain reaction, EPEC: enteropathogenic Escherichia coli., EAEC: enteroaggregative Escherichia coli.

Action Taken

On 17 Feb 2025, after confirming norovirus in an asymptomatic food handler, the school was advised to immediately exclude the affected individual from food preparation. Hua Taphan Hospital provided risk communication and handwashing education to staff and students, while the investigation team reinforced essential hygiene practices and avoiding prolonged room-temperature holding of cooked food. The tray-drying method was improved by spreading trays under sunlight to reduce moisture. Chlorine was added to the school's water system to maintain residual chlorine levels at 0.5–1 ppm during the outbreak, with a plan to return to the routine maintenance level of 0.3–0.5 ppm once the situation was controlled.

Discussion

This study confirmed a norovirus outbreak among students and staff at the school, with epidemiologic and laboratory evidence indicating that the chicken rice served on 11 February, was the most likely vehicle, contaminated during preparation by an asymptomatic food handler infected with norovirus.

The identification of an infected, but asymptomatic handler was a critical finding. Norovirus is highly contagious, requiring a very low infectious dose (<100 viral particles) to cause illness.[15] Asymptomatic infection is common, with studies estimating that approximately 30% of norovirus infections present without symptoms.[16] Asymptomatic individuals can shed the virus in viral loads comparable to symptomatic cases and for up to 3–4 weeks.[17]

The observed timing of symptoms was consistent with the incubation period of norovirus, which ranges from 12 to 48 hours with a median of 33 hours.[18] A trailing distribution of cases from 14–18 February suggests subsequent secondary person-to-person transmission, a pattern commonly observed in school norovirus outbreaks given the virus's high transmissibility and environmental persistence.[19] The outbreak was characterized by upper gastrointestinal symptoms, particularly nausea and vomiting, a pattern typical of norovirus infection and distinct from the diarrhea-predominant presentation more commonly seen in bacterial foodborne illnesses.[20]

The chicken rice meal served on 11 February, was the most plausible primary source of infection, supported by a strong epidemiologic association and a clear biological link to food handler 1, who tested positive for norovirus. This handler performed several high-risk tasks, including rinsing raw chicken, handling cooked chicken, and serving cooked food items. Given this workflow, post-cooking contamination of the chicken rice was highly likely. A graded increase in risk was observed across the meal-service schedule, with students served later experiencing higher illness rates. Because norovirus does not multiply in food, this pattern is consistent with progressive contamination during the serving process, likely due to increasing viral transfer from food handler 1 as meal distribution progressed.[21]

Although norovirus was not detected in the water supply, extensive coliform contamination on 70% of sampled surfaces—including food trays, utensils, and the hands of a food handler—indicated substantial lapses in hygiene.[22] The school's water and sanitation systems were also compromised: the UV disinfection unit was non-functional, and residual chlorine levels were consistently below recommended standards.[23] In the absence of soap at handwashing stations, effective hand hygiene was not possible, increasing the likelihood that viral particles remained on the hands of an infected handler.[24] The practice of stacking trays while still wet further promoted cross-contamination, as moisture facilitates the persistence and transfer of enteric pathogens.[25] Collectively, these environmental deficiencies created conditions in which contamination introduced by a single infected food handler could spread widely, highlighting the need for reliable sanitation infrastructure alongside appropriate food-handler management.

Limitations

This investigation faced several limitations. Most cases were young children, which may have affected the accuracy of symptoms and food history reporting. To improve data quality, information was also obtained from parents and teachers. Recall bias was possible due to the retrospective nature of questionnaires, though data collection occurred promptly after the outbreak to minimize this issue. Detection of norovirus in a food handler occurred after illness onset, limiting confirmation of their role in transmission, but the epidemiological evidence and known potential for asymptomatic shedding support their involvement. Whole genome sequencing was not available to confirm genetic links between cases, although consistent clinical and laboratory findings suggest a common pathogen. Environmental samples were collected after cleaning, although before chlorination. Norovirus was not detected in water, or kitchen-surface samples, possibly because cleaning reduced its presence, although widespread coliform contamination still indicated poor environmental hygiene.

Recommendations

Teachers should reinforce proper student hygiene, particularly handwashing with soap, which was not available at the school's handwashing stations during the investigation. Kitchen practices should be improved by separating utensils for raw and cooked foods, ensuring trays are thoroughly washed and dried before reuse, and enforcing glove use when handling ready-to-eat items. Routine food-safety training and supervision should be coordinated by local health authorities in collaboration with the school administration, with the hospital providing technical support during outbreak response. The school should also repair and maintain its water treatment system, including restoring UV disinfection, performing regular reverse osmosis system maintenance, and maintaining residual chlorine at recommended levels.

Conclusion

A foodborne norovirus outbreak occurred at a school in Hua Taphan District, Amnat Charoen Province, Thailand, most likely caused by contaminated chicken rice, with subsequent secondary person-to-person transmission. Poor sanitation conditions may have further facilitated transmission. Recommendations focused on improving food-handling practices, strengthening hand hygiene infrastructure, and ensuring regular maintenance of the school's water treatment system to prevent future outbreaks.

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Author Contributions

Waritnun Anupat: Conceptualization, data curation, formal analysis, methodology, project administration, validation, visualization, writing—original draft, writing—review & editing. **Drunpob Srithammawong:** Conceptualization, data curation, validation. **Patchanee Plernprom:** Conceptualization, data curation, validation. **Pochana Choosang:** Conceptualization, data curation, validation. **Thanit Rattanathumsakul:** Methodology, supervision**. Chayanit Mahasing:** Methodology, resources, supervision, validation, writing—review & editing.

Ethical Approval

Since this study was a part of a routine public health outbreak investigation, 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 anupatwritnun@gmail.com).

Conflicts of Interest

The authors declare no conflicts of interest.

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A Design Thinking Approach to Developing an Innovative Board Game for Preventing Leptospirosis among Schoolchildren in Nan Province, Thailand

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Abstract

Leptospirosis is a major public health concern in Thailand. In 2024, Nan Province reported an increasing incidence of leptospirosis cases, with schoolchildren accounting for the majority, including one fatality. Entertainment-education is an effective public health communication strategy for school-aged populations, improving both understanding and engagement. This study applied a design-thinking approach to develop an innovative game-based intervention and assess its effectiveness in enhancing awareness, knowledge, and preventive practices related to leptospirosis among schoolchildren. The study employed a mixed-methods research and development design, conducted between January and September 2025. Qualitative methods were used to identify schoolchildren's needs and contexts, which informed the development of the Lepto Game, an interactive simulation board game. A quantitative one-group pre-post design was used to evaluate the intervention's effectiveness. Three main issues were identified: (1) limited communication between schoolchildren and healthcare providers about the disease and its symptoms, (2) low general awareness of leptospirosis, and (3) the need for more engaging and enjoyable health education tools. Among 132 schoolchildren who tested the intervention, satisfaction with learning was very high. In the quantitative study (n=124, 68.5% male, age 12–15 years), significant improvements were observed in mean scores for knowledge of exposure risks (0.395), symptoms (0.387), and self-care practices (0.556). Integrating design thinking with entertainment-education can create engaging interventions that effectively enhance awareness, knowledge, and preventive practices among schoolchildren.

Keywords: leptospirosis, innovative board game, design thinking, schoolchildren

Background

Leptospirosis is a significant public health concern in Thailand.[1–3] The disease is widespread in the northern and northeastern regions.[1] It is an acute zoonotic infection caused by *Leptospira* bacteria, for which rodents and domestic animals serve as common reservoirs. Transmission occurs primarily through direct or indirect contact with water, soil, or animal urine contaminated with the bacteria. In Thailand, leptospirosis is a recurring epidemic, with an annual incidence rate of approximately 4.25 cases per 100,000 population.[3] The rainy season increases rainfall and flooding, which heightens the risk of infection by creating conditions favorable for bacterial survival and transmission.[4,5] Living near rubber plantations and bathing in natural water sources have been identified as significant risk factors for severe leptospirosis in Thailand.[6] Additionally, evidence indicates that pathogenic serovars of *Leptospira* are circulating among livestock and domestic animals.[7]

In 2024, the incidence of leptospirosis in Thailand was 7.21 cases per 100,000 population. The death rate was 0.15 per 100,000 population, with a total of 94 deaths.[3] The northern and southern regions were the most affected, reporting the highest number of cases.[3] The age group over 60 years accounted for the highest number of cases. Inpatient department cases constituted 45.6% (2,135 cases) of the total reported cases (4,680).[3]

On 6 Aug 2024, Nan Provincial Health Office was notified of a severe leptospirosis case admitted to Nan Hospital. A 12-year-old girl developed high fever, headache, myalgia, and fatigue on 1 Aug 2024. She visited Mae Jarim Hospital (the district hospital) twice before being admitted and subsequently referred to Nan Hospital (the provincial hospital), where she died on 9 Aug 2024. According to Digital Disease Surveillance (DDS), Department of Disease Control data from 1 Jan to 30 Aug 2024, Mae Jarim District reported 28 leptospirosis cases, equivalent to an incidence rate of 174.9 cases per 100,000 population. The most affected age group was 10–14 years (n=11 cases), and schoolchildren predominated (n=18 cases). There was one death, resulting in a mortality rate of 6.3 deaths per 100,000 population, and the case fatality rate was 3.6%.

Gamification has emerged as a promising strategy in public health interventions across various domains, including health promotion, disease prevention, and disease management. Evidence suggests that a gamified approach can enhance participant engagement, acceptability, knowledge, and behavior change.[8,9] These interventions have demonstrated particular effectiveness among school-aged children due to their enjoyable and interactive nature.[10] Systematic reviews evaluating the use and effectiveness of board games in health education further highlight their potential to improve health knowledge and promote behavioral modification compared with traditional health education methods.[11,12] The design-thinking approach provides tools for understanding behavioral and experiential insights, integrating individual and community perspectives into public health programs, and generating creative and feasible solutions.[13]

The objectives of this study were to design an innovative game-based intervention and assess its effectiveness in enhancing awareness, knowledge, and preventive practices for leptospirosis among schoolchildren.

Methods

A mixed-methods study was conducted using a design-thinking approach to develop a public health intervention for school-aged children. The study comprised two components: (1) a qualitative study applying a design-thinking approach to explore insights, needs, perceptions, and contextual factors related to leptospirosis in order to design an innovative game-based prevention and control intervention, and (2) a quantitative study to assess the effectiveness of the developed intervention in improving awareness, knowledge, and preventive practices among schoolchildren.

Qualitative Study

The qualitative study applied the five steps of the design-thinking approach: empathize, define, ideate, prototype, and test. It was conducted between January and August 2025.

Empathize

Focus group discussion and in-depth interviews were conducted with key stakeholders, including nine schoolchildren aged 10–14 years, six parents, four teachers, and five healthcare providers in Nan Province, to explore their experiences, behaviors, and insights related to leptospirosis. A total of 24 participants were purposively selected as key informants. Four rounds of discussion were conducted, each lasting approximately three hours.

Define

Thematic analysis of interview data was used to identify core challenges, unmet needs, and contexts.

Ideate

Innovative ideas were brainstormed, and a storyboard for the prototype was developed.

Prototype

Initial prototypes were sketched and developed. These prototypes were then assessed and refined through iterative feedback from stakeholders.

Test

A focus group discussion and a survey were conducted with 132 schoolchildren from Mae Jarim School, aged 10–14 years, to evaluate the usability of the prototype and overall user experience.

Quantitative Study

Study design

A one-group pre-post quantitative design was used to evaluate changes in knowledge, attitudes, and practices (KAP) related to leptospirosis among schoolchildren following the implementation of the developed intervention. Participants completed a structured questionnaire assessing baseline scores prior to the intervention. After the intervention, the same questionnaire was administered again to measure changes in KAP.

Setting and sample size

The study was conducted from August to September 2025. A school in Mae Jarim District, Nan Province, was purposively selected due to its increased incidence and mortality from leptospirosis. The school is a public secondary school (grades 7–12) with 434 students. All schoolchildren aged 10–14 years in grades 7–9 were invited to participate. The sample size calculation applied the paired t-test (dependent samples) model by using the formula:

$$n = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 \times 2(1-\rho)}{d^2}$$

where d refers to the standardized mean difference between pre- and post-intervention scores, α denotes the probability of a type I error, ower $(1-\beta)$ represents the probability of detecting a true pre-post difference, and ρ represents the assumed proportion of participants with an acceptable level of knowledge about the disease; with d=0.26, α=0.05, power=0.80, and ρ=0.50.[14–17]

$$n = \frac{(1.96 + 0.84)^2 \times 2(1-0.5)}{0.26^2} \approx 116$$

The estimated sample size based on the above calculation was 116. The sample size was increased by eight participants due to the availability of additional schoolchildren, resulting in a final sample of 124 schoolchildren.

Data Collection

A self-administered questionnaire was developed based on a comprehensive review of current literature and existing validated instruments to assess knowledge, attitudes, and practices related to leptospirosis. The development process included item generation, content validation by three field epidemiologists and two zoonotic disease experts, and pre-testing with 10 participants to ensure clarity, relevance, and comprehensibility. The questionnaire consisted of 12 multiple-choice items: four on disease knowledge and risk behaviors, four on symptoms, and four on self-care practices. Each correct item was scored as one point, for a total possible score of 12.

Statistical Analysis

Descriptive statistics, including percentages, means, and standard deviations (SDs) were used to summarize the data. Paired t-tests were used to compare pre- and post-intervention mean scores for knowledge of leptospirosis, risk behaviors, exposures, symptoms, and self-care practices, with a statistical significance level of 0.05. Data analysis was conducted using Jamovi.[18]

Results

Qualitative Study

Empathize and define

Based on four focus group discussions involving 24 participants, three main issues were identified: (1) limited communication between schoolchildren and healthcare providers about the disease and its symptoms, (2) low general awareness of leptospirosis, and (3) the need for more engaging and enjoyable health education tools. Most schoolchildren reported delays in seeking medical care due to fear of visiting doctors or hospitals: *"I'm afraid to go to the hospital, and I only have my friend to take care of me"* (Student 3). Limited knowledge about leptospirosis and its symptoms further contributed to the delayed health-seeking behavior: *"I didn't know about leptospirosis until I heard the rumor that a student had died from it"* (Student 7). Additionally, some children who did not live with their parents had to care for themselves and relied on friends or teachers to accompany them to the hospital: *"If I have a mild sickness, I won't ask for help; only if it's severe I will ask my friend to help me"* (Student 4). Schoolchildren also expressed a desire for enjoyable and engaging team-based activities that they could participate in with their peers, such as playing games together. As some children noted, *"In my free time, I enjoy playing with my friends"* (Student 1,2,6,8,9).

Ideate

A brainstorming session was conducted to explore ideas for (1) developing engaging and enjoyable health education tools, (2) enhancing awareness of the disease, its symptoms, and self-assessment of symptom severity, and (3) improving communication of personal health conditions to healthcare professionals. An interactive board game on leptospirosis was identified as the final, refined concept. The game is designed for teams of two to five players and is based on a scenario in which participants travel with friends while managing their own risks of contracting *Leptospira*. Key risk scenarios include exposure to flooding, wading through water, walking through mud, and having open wounds. During gameplay, players experience simulated symptoms such as fever, myalgia, diarrhea, nausea, vomiting, conjunctivitis, jaundice, and subcostal pain following exposure to these risk situations and behaviors. The use of protective items such as boots, sneakers, bandages, and tepid sponges reduces or eliminates these symptoms, protecting against disease progression (Figure 1).

Prototype and test

Multiple prototypes of the Lepto Game were developed and tested among the developers, with iterative refinements leading to the final version. The final prototype was tested with 132 schoolchildren aged 10–14 years from Mae Jarim School. The mean satisfaction score reported by participants was 4.73 out of 5. Schoolchildren described the game as highly engaging and fun, with 71.2% expressing interest in replaying it. Additionally, 81.8% reported feeling more encouraged and confident about seeking medical care, and 85.6% noted improved understanding of leptospirosis. Participants expressed the greatest satisfaction with the game's enjoyable, exciting, and competitive elements.

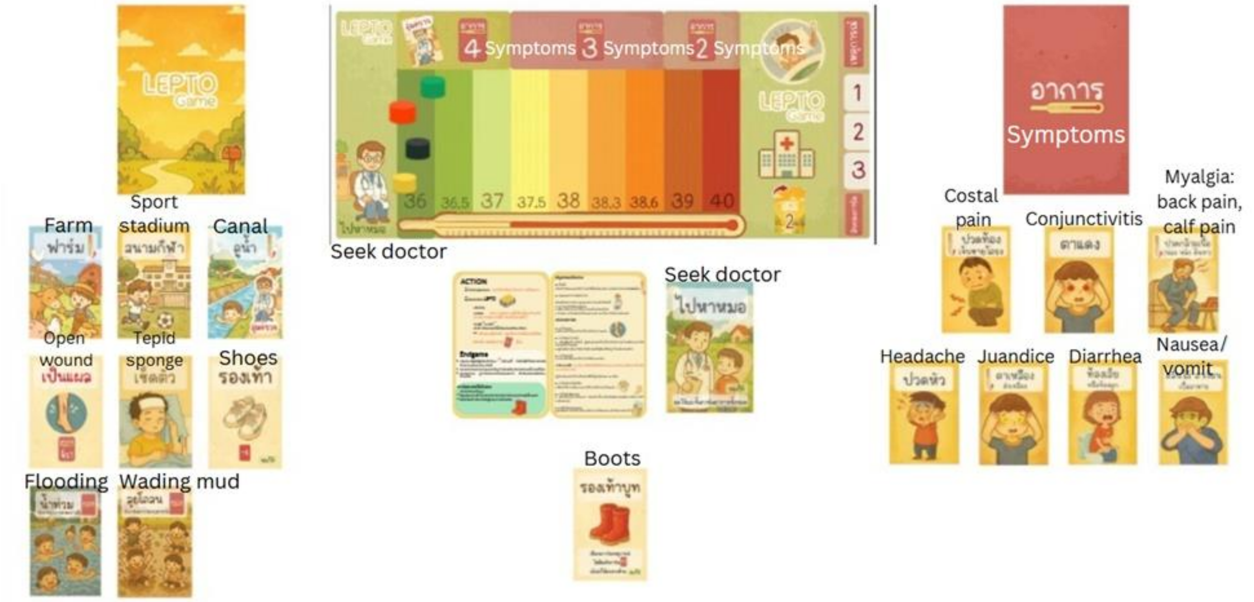

Figure 1. Final prototype of the Lepto Game, which includes a fever chart, visiting cards, risky event cards, risky behavior cards, protective wear cards, self-care card (yellow), and symptoms cards (red) with the rules and instructions in a box

Quantitative Study

A total of 124 schoolchildren from Mae Jarim school participated in the study. Most participants were male (68.5%) and aged 12–15 years, with a mean (SD) age of 13.60±0.94 years.

In the pre-test, the overall mean (SD) score for leptospirosis knowledge, symptoms, and self-care practice was 6.77±1.95 (out of 12). Among the knowledge domains, the highest mean score was observed for risk behavior related to exposure to water and mud with open wounds, whereas the lowest mean score was noted for knowledge of the pathognomonic manifestations, specifically calf pain.

In the post-test, the mean overall score increased to 8.10±1.85. The distribution of correct responses for disease knowledge, risk behaviors, exposures, symptoms, and self-care practices is presented in Table 1. The greatest improvement was observed in self-care practices, while the smallest improvement was seen in the knowledge of symptoms.

Table 1. Distribution of correct answers for disease knowledge, risk behaviors, exposures, symptoms, and self-care practices (n=124)

Variables	Pre-test n (%)	Post-test n (%)
Knowledge of exposure and mode of transmission		
• Leptospirosis is caused by exposure to contaminated water and soil through open wounds	82 (66.1)	112 (90.3)
• Most risky environment: damp, watery, and muddy areas	73 (58.9)	88 (71.0)
• Most risky behavior: exposure to water and mud with open wounds	108 (87.1)	115 (92.7)
• *Leptospira spp.* mostly found in flooding water	87 (70.2)	84 (67.7)
Knowledge of symptoms		
• Severe symptom of leptospirosis: costal pain	53 (42.7)	68 (54.8)
• Pathognomonic sign: calf pain	19 (15.3)	10 (8.1)
• Symptoms to seek medical care: fever and jaundice	62 (50.0)	84 (67.7)
• Information to inform doctors: body temperature and travel history	83 (66.9)	103 (83.1)
Self-care practices		
• Protection of leptospirosis: wearing closed-back, closed-toe shoes	61 (49.2)	84 (67.7)
• Proper home care: tepid sponge	44 (35.5)	75 (60.5)
• Avoid walking barefoot in mud	70 (56.5)	79 (63.7)
• Caution of contracting leptospirosis: seeking medical attention promptly for diagnosis and treatment	97 (78.2)	103 (83.1)

Paired t-test analysis indicated a significant increase in mean scores following the intervention. Specifically, scores for disease knowledge, risk behaviors, exposures, symptoms, and self-care practices all increased significantly after playing the Lepto Game (Table 2). The maximum total score was 12.

Table 2. Comparison of mean scores of disease knowledge, risk behaviors, exposures, symptoms, and self-care practices before and after the intervention (n=124)

Variables	Pre-test mean (SD)	Post-test mean (SD)	Mean difference	*P*-value*
Knowledge of exposure and mode of transmission				
• Leptospirosis is caused by exposure to contaminated water and soil through open wounds	0.66 (0.48)	0.90 (0.30)	0.242	<0.001
• Most risky environment: damp, watery, and muddy areas	0.59 (0.49)	0.71 (0.46)	0.121	0.007
• Most risky behavior: exposure to water and mud with open wounds	0.87 (0.34)	0.93 (0.26)	0.056	0.071
• *Leptospira spp.* mostly found in flooding water	0.70 (0.47)	0.68 (0.50)	-0.024	0.614
Knowledge of symptoms				
• Severe symptom of leptospirosis: costal pain	0.43 (0.50)	0.55 (0.50)	0.121	0.019
• Pathognomonic sign: calf pain	0.15 (0.36)	0.08 (0.27)	-0.073	0.049
• Symptoms to seek medical care: fever and jaundice	0.50 (0.50)	0.68 (0.47)	0.177	0.001
• Information to inform doctors: body temperature and travel history	0.67 (0.47)	0.83 (0.38)	0.161	<0.001
Self-care practices				
• Protection of leptospirosis: wearing closed-back, closed-toe shoes	0.49 (0.50)	0.68 (0.47)	0.185	<0.001
• Proper home care: tepid sponge	0.36 (0.48)	0.61 (0.49)	0.250	<0.001
• Avoid walking barefoot in mud	0.56 (0.50)	0.64 (0.48)	0.073	0.106
• Caution of contracting leptospirosis: seeking medical attention promptly for diagnosis and treatment	0.78 (0.42)	0.83 (0.38)	0.048	0.275

**p-values were calculated using a paired t-test. SD: standard deviation.*

Variables representing disease knowledge, risk behaviors, and exposures were also combined and analyzed by subgroup. The greatest change was observed in self-care practices, with mean scores increasing from 2.19 in the pretest to 2.75 in the post-test. Paired t-test analysis showed statistically significant increases across all grouped variables, including knowledge of exposure and mode of transmission, knowledge of symptoms, and self-care practices (Table 3).

Table 3. Grouped correct answer analysis of the disease knowledge, symptoms, and self-care practices

Variables	Pre-test mean (SD)	Post-test mean (SD)	Mean difference	*P*-value*
• Knowledge of exposure and mode of transmission	2.82 (0.98)	3.22 (0.85)	0.395	<0.001
• Knowledge of symptoms	1.75 (0.94)	2.14 (0.80)	0.387	<0.001
• Self-care practices	2.19 (0.99)	2.75 (1.03)	0.556	<0.001

**p-values were calculated using a paired t-test. SD: standard deviation.*

Discussion

The findings from this study emphasize the value of innovative approaches in health education. Insights derived from schoolchildren regarding their pains and unmet needs directly informed the development of the Lepto Game, an edutainment tool designed using design-thinking principles. This approach enabled the creation of an engaging, user-centered intervention tailored to schoolchildren's learning needs and satisfaction level. The Lepto Game effectively bridges gaps in knowledge, raises awareness, and promotes preventive practices related to leptospirosis, positively influencing children's health behaviors. Key success factors included the active involvement of end-users throughout the design process, which ensured relevance and engagement, and the incorporation of interactive, scenario-based learning that made abstract health concepts tangible and memorable. These factors contributed to high user satisfaction, improved knowledge retention, and greater motivation to adopt preventive behaviors. Evidence from meta-analyses further supports the effectiveness of entertainment-education in improving persuasive health outcomes.[20–22] Its age-appropriate and interactive design facilitates learning about leptospirosis risks, prevention, and health-seeking behaviors, while enhancing children's confidence in communicating health information.[23] Overall, applying design thinking in public health facilitates a deeper understanding of target populations, allowing interventions to be tailored to their real-world needs, preferences, and behaviors. In the context of health education, this approach provides a practical pathway for developing engaging, relevant, and impactful interventions that effectively promote health awareness, knowledge, and preventive practices.[24–26]

Low levels of awareness, knowledge, and preventive practices related to leptospirosis have been reported in many disease-endemic countries within Southeast Asia.[27–30] Public health interventions aimed at improving knowledge, attitudes, and practices should therefore be emphasized within health education programs.[13] Findings from this study demonstrated significant improvements in self-care practices, particularly in wearing proper footwear and using tepid sponging for fever management. These elements were key components of the Lepto Game. Significant improvements were also observed in children's understanding of risks associated with exposure to contaminated water and soil through open wounds, as these scenarios were actively experienced within the gameplay. Additionally, knowledge related to exposure to floodwater while walking barefoot outdoors did not show improvement, likely because this information was already familiar to participants prior to the intervention.[30,31]

The Lepto Game, as a novel health education tool, provides practical implications for school-based interventions by tailoring content to users' insights and needs, thereby reinforcing contextual knowledge. Meta-analyses have also indicated that the board games can effectively enhance knowledge, influence behavior and even impact biological outcomes.[32–34] However, careful attention to game design, player interaction, and implementation strategies is essential to maximize the effectiveness of entertainment-education approaches.[35] The Lepto Game also has the potential to be integrated into existing school systems cost-effectively, making it suitable for low-resource settings in leptospirosis-endemic countries.

Limitations

Interpretation of the mean difference for the variable of the pathognomonic signs of leptospirosis should be made with caution, as misemphasis in the symptom information presented on the Lepto Game symptoms card may have affected participants' responses. The use of tailored messages in board games may not fully address all knowledge gaps or accommodate the diverse experiences, cultural backgrounds, and learning styles of participants. Participants in the study were purposively selected by the school from the cluster where leptospirosis had occurred. As a result, the students who participated may have been more motivated, engaged, or interested in health education than the general student population. This selection process could have led to an overestimation of the intervention's effectiveness in terms of knowledge acquisition and retention. Additionally, the study employed a one-group pre-post design without a control group, which limits the ability to attribute observed improvement solely to the intervention. The study was conducted in a single school, which may limit the generalizability of the findings to other regions or populations with different sociodemographic characteristics. This study did not measure actual health outcomes or real-life preventive practices among schoolchildren, limiting the ability to assess the long-term behavioral impact of the intervention. Finally, the study did not compare the Lepto Game with conventional health education methods; therefore, future research should consider conducting a comparative study to evaluate the relative effectiveness of the intervention.

Recommendations

A design-thinking approach proves valuable for developing health education tools, as it helps address the specific needs of target users and maximizes their satisfaction. The Department of Disease Control (DDC), Ministry of Public Health, should apply design-thinking principles to empathize with and define the target population, enabling the development of tailored and impactful prevention and control interventions. The Lepto Game illustrates how a contextual, user-centered approach can enhance engagement, awareness, knowledge, and preventive practices among schoolchildren.

For a broader impact, the DDC could cooperate with the Office of the Basic Education Commission, Ministry of Education, to implement the Lepto Game in school classrooms, extracurricular activities, and community programs, with adaptations for diverse settings. Translating the game into English and other local languages could further expand its reach and effectiveness in leptospirosis-endemic countries. Future studies should evaluate the long-term impact of the Lepto Game on real-life health outcomes and preventive practices to confirm its effectiveness beyond the educational setting, and compare it with conventional health education methods to assess relative effectiveness.

Conclusion

This study suggests that integrating design thinking with entertainment-education can produce engaging, user-centered interventions that enhance awareness, target health knowledge, and promote preventive practices among schoolchildren to optimize learning outcomes. The Lepto Game demonstrates that tailored education tools to the needs and experiences of children can increase engagement and knowledge to adopt health behaviors. Incorporating interactive, scenario-based learning can effectively translate abstract health concepts into practical, actionable strategies leading to improved knowledge, attitudes, and preventive practices related to leptospirosis. To support broader implementation, adaptation of the Lepto Game should consider the socioeconomic context and characteristics of the target population.

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Author Contributions

Patcharin Tantiworrawit: Conceptualization, methodology, writing—original draft, writing—review & editing. **Panithee Thammawijaya:** Writing—review & editing.

Ethical Approval

This study did not require ethical approval, as it involved the development and evaluation of an educational tool without the collection of identifiable personal or sensitive health data. All participants were informed about the purpose of the study and provided voluntary consent to participate in the game and related assessments.

Informed Consent

Informed consent was obtained from all participants involved in the study.

Data Availability

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

Conflicts of Interest

The author declares that there are no conflicts of interest.

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

During the preparation of this work, the author used ChatGPT to correct grammatical errors and manage references. The content produced by this tool was reviewed and edited by the authors, who accept full responsibility for the final text.

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Uttar Tolarbagh Model—an Investigation of a COVID-19 Case Led to the First Localized Community Approach for Containment of COVID-19 in Dhaka City, Bangladesh, March–May 2020

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Abstract

On 23 Mar 2020, Uttar Tolarbagh, a two-square-kilometer walled-in area in Dhaka, was locked down to contain a COVID-19 outbreak. We evaluated whether localized restrictions on entry and exit points could prevent the spread of COVID-19. We traced contacts and conducted active surveillance from 20 Mar to 10 Apr 2020. Contacts were those within one meter of a confirmed COVID-19 case for ≥15 minutes between two days before and 14 days after the onset of symptoms. We collected swabs from all persons with respiratory symptoms. The positivity rate was calculated by dividing the number of positive samples by the total number of samples tested. The Uttar Tolarbagh House, Flat Owners' Association and the religious teacher of Masjidul Ahsan, the only mosque in Uttar Tolarbagh, discouraged local gatherings and ensured social distancing during mosque prayers. We identified 400 contacts; 156 were symptomatic and 16 tested positive, of whom eight were hospitalized and two died. SARS-CoV-2 PCR positivity rates among symptomatic contacts were 40% (2/5) before containment, 10% (15/152) during containment, and 0% (0/33) after containment. The last case's disease onset date was 5 April, and Uttar Tolarbagh remained COVID-19 free until 12 May 2020. Social distancing was observed by the field investigation team on the roads and within the mosque during the lockdown. Our findings suggest that the neighborhood lockdown, isolation of cases, quarantine and contact tracing, evacuation of COVID-19 patients, and community engagement helped to contain COVID-19 transmission in a densely populated area of Dhaka City.

Keywords: COVID-19, SARS-CoV-2, localized lockdown, contact tracing, outbreak

Introduction

At the beginning of the coronavirus disease 2019 (COVID-19) pandemic in Bangladesh, only travelers and their close relatives were infected.[1] The first reported cases were imported and sporadic; however, clusters were detected within two months. When clusters of cases were reported, the Institute of Epidemiology, Disease Control and Research (IEDCR), the government program responsible for investigating and controlling outbreaks, implemented non-pharmaceutical interventions to contain the disease and prevent further spread.[2] This policy was based on interventions implemented in China, Italy, and India. These countries used lockdowns, which were effective in reducing transmission.[3–5]

Through 12 May 2020, IEDCR investigated every reported COVID-19 case to describe the scope and magnitude of the pandemic and traced contacts to reduce transmission. On 20 March, a 73-year-old male with multiple comorbidities died from COVID-19. He was the second person in Bangladesh to die from the disease. He lived in Uttar Tolarbagh, which is close to the heart of Dhaka, the capital of Bangladesh. When IEDCR was notified, an investigation team was formed to identify other cases and contacts and to quarantine contacts. During the investigation, another 76-year-old male died in Uttar Tolarbagh on 22 Mar 2020. He was a contact of the first death case in Uttar Tolarbagh and tested positive for COVID-19. On 23 March, Uttar Tolarbagh was locked down by local officials in consultation with the IEDCR field investigation team in an attempt to contain the outbreak. The lockdown was lifted on 30 May 2020. This report describes the localized containment approaches and determines if these activities reduced or stopped transmission.

Methods

Study Design

We used a mixed-methods approach to evaluate five approaches to contain COVID-19 in a community.

Location and Timeframe

Uttar Tolarbagh is an urban community with an area of about two square kilometers and approximately 4,000 residents. A brick wall that is two meters high forms the border of Uttar Tolarbagh, and only one single-lane road passes through the community (Figure 1). Local officials started the containment on 23 March and ended it on 12 May 2020.

Study Population

A suspected case was defined as a resident of Uttar Tolarbagh who developed fever, cough, sore throat, or respiratory distress between 20 Mar and 30 May 2020. A probable case was defined as a suspected case who had contact with a confirmed case. A confirmed case was defined as any person who tested positive for reverse transcriptase-polymerase chain reaction (RT-PCR) (Da An Gene Co. Ltd, China) for COVID-19 and met the probable or suspected case definition. A contact was defined as any person who did not wear a mask and came within one meter of a confirmed case for ≥15 minutes between two days before and 14 days after onset of the case's symptoms. When someone thought that they might have COVID-19, local authorities instructed them to report this to the house committee for people living in apartment buildings or to the designated community leader for residents of other dwellings.

Data Collection

The field team investigated the outbreak and response from 20 Mar to 30 May 2020. Field team members interviewed suspected and probable cases in person using a semi-structured questionnaire that captured information regarding demographics, socioeconomic status, symptoms, signs, treatment, living situations due to the lockdown of Uttar Tolarbagh, and whether they were isolated. Samples were collected from symptomatic contacts and community members during interviews. Confirmed cases were interviewed by telephone.

We interviewed close relatives of cases that died to identify contacts. We interviewed confirmed cases who were alive and/or their close relatives to identify contacts. We also interviewed contacts to cross-check the contact event, as stated by the cases or their close relatives. All identified contacts of the confirmed cases were followed up daily for 14 days after their last exposure.

The field team conducted active surveillance for COVID-19 by visiting door to door within the community from 5 April to 11 April to screen people with symptoms to rule out suspected cases, which may have been missed by passive surveillance (the community hotline).

Approaches

Five containment approaches were implemented, guided by national recommendations for Nipah virus control and reports of containment strategies used in China.[6] These approaches were applied in a phased manner as the situation evolved.

Phase 1 (20 March): Initial localized containment

Local authorities initiated containment by locking down the building where the first confirmed case resided. Movement was restricted, and security personnel controlled entry through the main gate.

Phase 2 (20 March): Case finding through contact tracing and active surveillance

On the same day, authorities initiated systematic identification of suspected and probable cases through contact tracing, door-to-door active searches, and testing of symptomatic individuals.

Phase 3 (20 March): Isolation, quarantine, and referral of cases

Contacts of confirmed cases were instructed to quarantine at home. Confirmed cases were either isolated at home if symptoms were mild or referred to a dedicated COVID-19 hospital if they had severe illness or comorbidities.

Phase 4 (20 March): Establishment of event-based surveillance

A community hotline was established to identify additional suspected cases. Individuals reporting symptoms compatible with COVID-19 were assessed, and specimens were collected for confirmatory testing.

Phase 5 (23 March): Expansion of containment and restriction of gatherings

Following confirmation of the second case, containment was expanded to the entire Uttar Tolarbagh area. The main entrance gate was locked and the second gate was permanently closed; mass gatherings and meetings were prohibited, and movement within public and private spaces was restricted. Although no lockdown was imposed on the mosque—initially considered the suspected epicenter—authorities limited the number of people allowed to attend prayers to reduce crowding.

Qualitative Investigation

An anthropologist interviewed residents, regular mosque attendees, and local social groups in Uttar Tolarbagh in person and interviewed confirmed cases by telephone. The interviews were recorded and transcribed verbatim. Data were coded inductively by creating codes, which were organized into themes and subthemes.

Laboratory Investigation

Nasopharyngeal and oropharyngeal swabs were collected from Uttar Tolarbagh residents who developed fever, cough, sore throat, or respiratory distress from 20 Mar to 30 May 2020, and were tested within 24 hours by RT-PCR for severe acute respiratory syndrome coronavirus 2 at the IEDCR. Residents who tested positive were retested 14 days later to confirm they were no longer infectious.

Data Analysis

We conducted a descriptive analysis of demographic data and clinical information of COVID-19 cases and contact follow-up indicators. Positivity rates were calculated by dividing the number of positive samples by the total number of samples tested up to 12 May and expressed as a percentage. The numerator was the number of initial positive test results. Attack rates were calculated by dividing the number of positive samples by the total number of contacts identified through 12 May and expressed as a percentage. A spot map of buildings in which the confirmed COVID-19 cases lived in Uttar Tolarbagh was made using Google Maps.

Results

The index case was a 73-year-old male who lived in Uttar Tolarbagh and had no travel history outside the community for more than a month prior to the onset of symptoms. The second case was a 76-year-old male with no travel history outside Uttar Tolarbagh in the month prior to the onset of symptoms. Both cases were members of the mosque welfare committee and were known for consistently offering prayers in the front row of the mosque. An additional 15 confirmed cases were identified during the study period. All 17 confirmed cases lived in one of nine apartments in five buildings (Figure 1). Multiple cases were identified within several families. Among the confirmed cases, 17 (100%) had fever, 6 (35%) had cough, and 3 (18%) had difficulty breathing (Table 1).

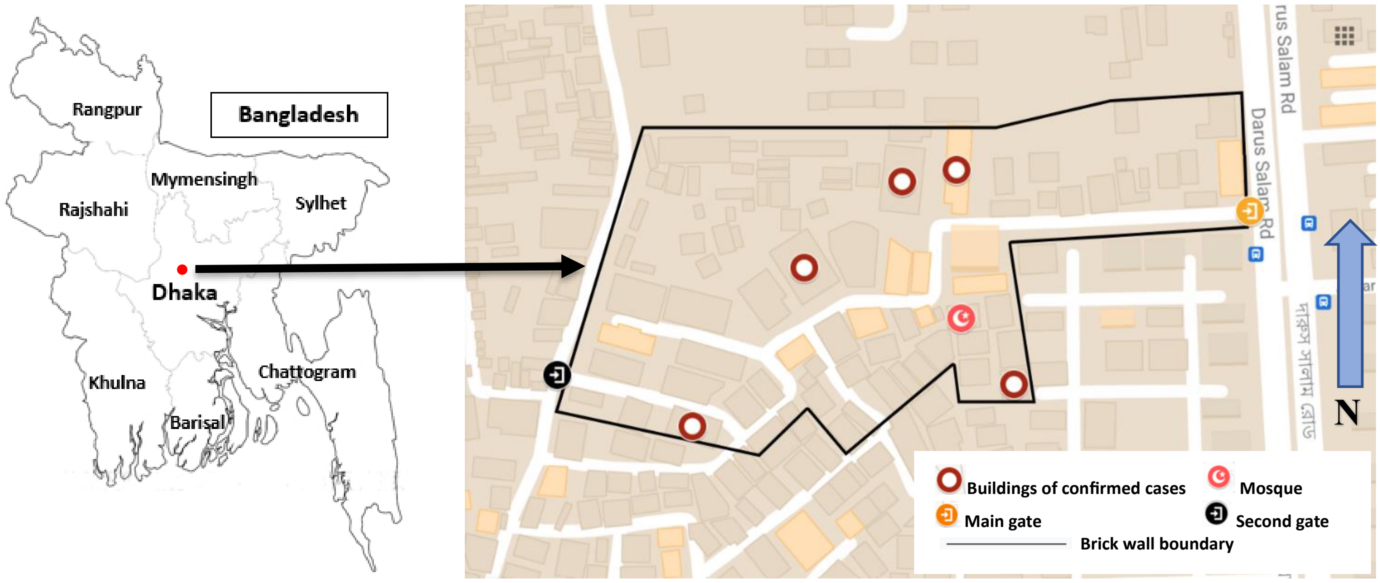

Figure 1. Map of Bangladesh (left) and Uttar Tolarbagh in Dhaka City (right), showing buildings with confirmed COVID-19 cases, 20 Mar–10 Apr 2020

Table 1. Clinical information of confirmed COVID-19 cases in Uttar Tolarbagh, Dhaka City, Bangladesh, 20 Mar–30 May 2020 (n=17)

Clinical information	n (%)
Signs and symptoms	
Fever	17 (100.0)
Cough	6 (35.3)
Difficulty breathing	3 (17.6)
Sore throat	2 (11.8)
Altered consciousness	2 (11.8)
Pneumonia	1 (5.9)
Myalgia	1 (5.9)
Comorbidities*	
Yes	6 (35.3)
No	11 (64.7)
Hospitalized	
Yes	8 (47.1)
No	9 (52.9)
Admitted to intensive care unit†	
Yes	1 (6)
No	7 (94)
Died	
Yes	2 (11.8)
No	15 (88.2)

**Comorbid conditions included diabetes mellitus, hypertension, cardiovascular disease, chronic kidney disease and chronic obstructive pulmonary disease. †Only hospitalized cases.*

Contact Tracing

Contact tracing began when the first COVID-19 case in Uttar Tolarbagh was diagnosed on 20 March and ended on 24 April as there were no confirmed cases after 5 April. We identified 400 contacts of confirmed cases, of whom 156 were tested, and 16 were positive. Three (5%) of the 120 contacts of the first confirmed case tested positive for COVID-19 (Figure 2 & 3).

Contact Findings

COVID-19 was detected in 15% (5/33) of regular mosque attendees, 5% (1/17) of the community contacts, and 9% (10/106) of household contacts (Table 2).

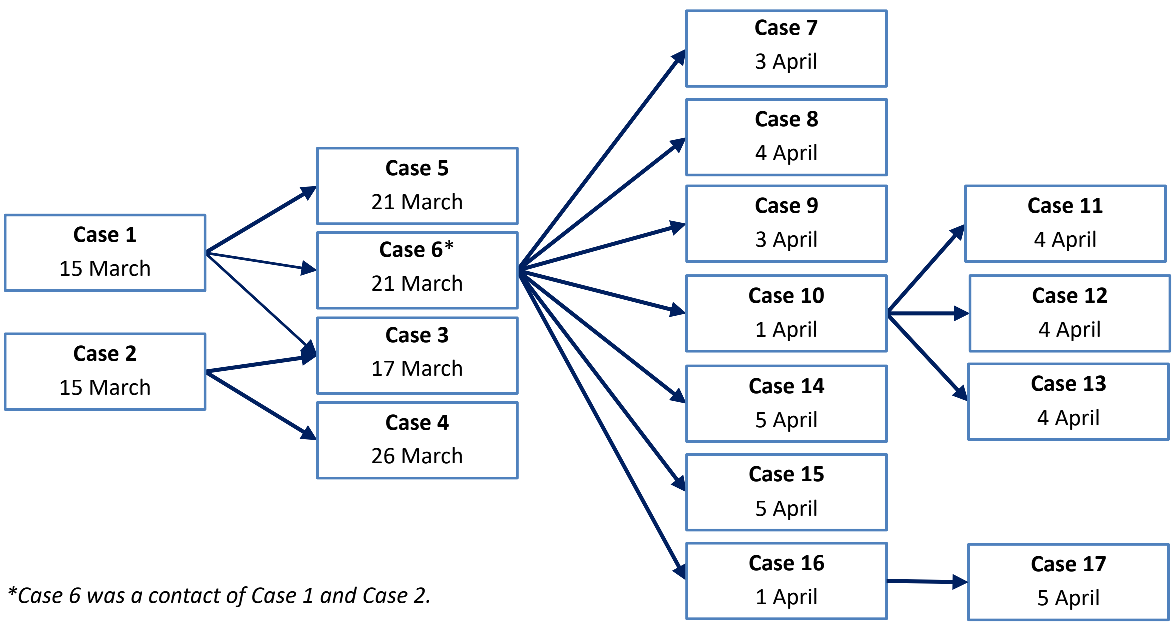

Figure 2. Diagram showing COVID-19 transmission from index case by date of symptoms onset in Uttar Tolarbagh, Dhaka City, Bangladesh, 20 Mar–30 May 2020

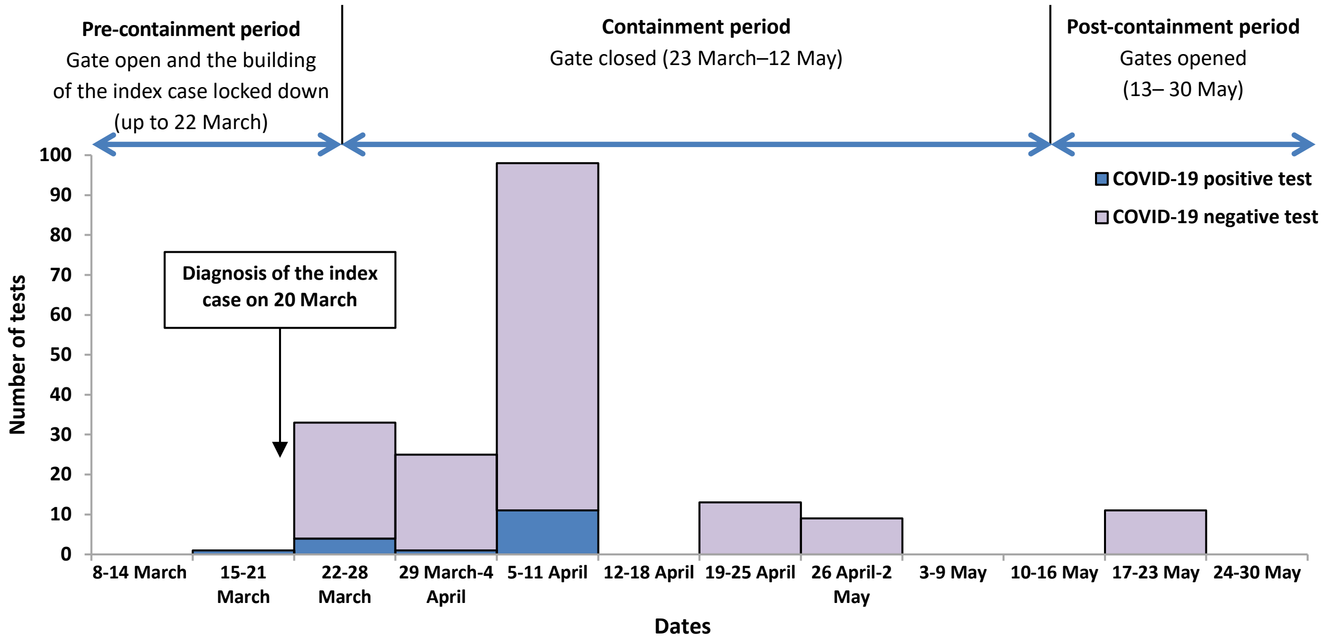

Figure 3. Epidemic curve of COVID-19 cases in Uttar Tolarbagh, Dhaka City, Bangladesh by day of their positive test result, 20 Mar–30 May 2020 (n=17)

Table 2. Positivity rate and attack rate among 156 symptomatic contacts of 17 confirmed COVID-19 cases in Uttar Tolarbagh, Dhaka City, Bangladesh, 20 Mar–12 May 2020

Characteristic	Total contacts	Number of persons tested	Positive by RT-PCR	Positivity rate (%)	Attack rate (%)
Gender					
Male	264	95	11	11	4
Female	136	61	5	8	3
Age group (years)					
11–20	45	13	2	15	4
21–30	62	24	2	8	3
31–40	143	41	5	12	3
41–50	82	47	2	4	2
51–60	56	19	3	16	5
61–70	9	9	1	11	11
71–80	3	3	1	33	33
Case source					
Contact tracing	302	58	5	8	2
Active case search	98	98	11	11	11
Location of contacts					
Community	72	17	1	5	1
Mosque	65	33	5	15	7
Household	263	106	10	9	3

Containment

The positivity rate among suspected cases was 40% (2/5) during the pre-containment period (15–22 March), and 10% (15/152) during the containment period (23 March–12 May). The 152 individuals represent symptomatic contacts identified and tested during containment. After containment (13–30 May), 33 symptomatic individuals from the community who reported through event-based surveillance were tested, and none were positive (0/33). During the study period, 190 symptomatic individuals from Uttar Tolarbagh were tested for COVID-19, of whom 17 tested positive, with an overall percent positivity of 9%. Positivity declined to 12% during 22–28 March and 4–11% through early April (Table 3).

The date of symptom onset of the last confirmed case was 5 April, and no confirmed COVID-19 cases were reported during containment up to 12 May.

Table 3. Percent positivity of symptomatic persons of Uttar Tolarbagh, Dhaka City, Bangladesh, 15 Mar–30 May 2020

Dates	COVID-19 test results			Percentage of positivity
	Total	Positive	Negative	
15 March–21 March	1	1	0	100*
22 March–28 March	33	4	29	12
29 March–4 April	25	1	24	4
5 April–11 April	98	11	87	11
19 April–25 April	13	0	13	0
26 April–2 May	9	0	9	0
17 May–23 May	11	0	11	0

**Index case*

Qualitative Findings

Since confirmed cases and many probable and suspected cases were identified within the same cluster, people residing in Uttar Tolarbagh perceived that they were stigmatized by others through phone calls or social media posts. We learned that some community members planned to leave the lockdown area of Uttar Tolarbagh at night once the identity of the deceased person and the confirmed case became known. Anxiety increased as the number of infected individuals and deaths in the community rose. Anxiety and fear were more common among those who attended routine prayers in the mosque, an event that occurred five times daily. After repeated awareness programs, people started maintaining personal protection measures as a part of infection control, reflecting a stage of personal commitment to mitigate the disease. Most people wore face masks when they went outside, and most were delighted about the lockdown, which they felt would keep them safe; however, a few people were annoyed by it.

Actions Taken

The Ministry of Health and Family Welfare of Bangladesh identified the approach in Uttar Tolarbagh as a model for other areas and later developed a localized containment approach of red, yellow, and green zones based on the rate of active cases in the community. Red, yellow, and green zones represented high risk (≥30 positive cases/100,000 population), moderate risk (4–29 positive cases/100,000 population), and low risk (≤3 positive cases/100,000 population), respectively. The National Islamic Foundation of Bangladesh declared and issued guidelines on behaving in religious ceremonies for Muslims during the COVID-19 pandemic. For example, they advised older persons and those with comorbidities to pray at home instead of coming to a mosque, emphasized strict personal and public hygiene, such as frequent handwashing, and the practice of social distancing to protect others.

Discussion

Contact tracing and active community engagement helped ensure early detection and isolation of cases and early treatment of patients, which likely limited the spread of COVID-19. In our study, all the new cases were among known contacts of confirmed COVID-19 cases. Other studies in China, Italy, and India have shown that contact tracing and containment within a specified area reduced transmission of COVID-19.[5,7,8]

The attendance of residents at religious gatherings in the mosque may have contributed to the spread of COVID-19 in Uttar Tolarbagh. The index case and the second case were both members of the mosque committee and prayed at the mosque; both developed symptoms on the same day. Case 6 was considered a superspreader because he infected seven contacts at the mosque and at home. Many factors can contribute to a super-spreading event, including immunosuppression, disease severity, viral load, large numbers of asymptomatic cases, and extensive social interactions.[9]

Household and family contacts are at higher risk than other close contacts due to prolonged and close exposure to infected individuals.[10,11] According to the characteristics of families in the study area, most of the members interacted in shared rooms, increasing the risk of disease transmission. Household contacts were the most affected group for COVID-19 infection in this study, suggesting the difficulty of home quarantine. Other studies in Thailand, India, and the United States have shown that household contacts have the highest risk of developing COVID-19.[5,12,13]

The reduction in the spread of COVID-19 was concurrent with the containment. The percentage of COVID-19 positive tests decreased after the third week, as community members began accepting the containment approach and maintained infection prevention and control measures. China, Italy, and India followed a containment strategy to eliminate the local transmission of COVID-19 outbreaks.[5,7,14] The containment strategy was highly successful in China, with very few new daily cases reported since March 2020. Italy's containment strategy helped manage the pandemic initially, but the strategy was implemented late, leading to a rapid increase in cases, indicating limited long-term effectiveness. For India, the containment strategy was less effective due to high population density, limited resources, and challenges in enforcing lockdown measures.[15]

For Bangladesh, a lower-middle-income country and one of the world's most densely populated, the implementation of containment measures faces challenges. Ambulance personnel frequently do not want to enter contained areas to evacuate severe COVID-19 cases or non-COVID-19 patients. Consequently, some patients were evacuated by personal means, some without proper protective measures, and getting an ambulance within a short notification time was often challenging. In Australia, the COVID-19 pandemic severely strained the Emergency Medical Services, leading to a marked deterioration in ambulance response times.[16] Beyond emergency transport, maintaining uninterrupted supplies of food, medicines, and household essentials during lockdowns was also difficult, particularly in densely populated urban neighborhoods and informal settlements. Overcrowding and multigenerational households further complicated adherence to quarantine and physical distancing guidelines. Religious practices posed additional challenges as mosques could not be fully closed due to their social and religious significance, and controlled and limited daily prayers continued, with small groups maintaining distancing and using personal protective equipment. Similar difficulties in enforcing and sustaining containment measures have been documented elsewhere.[5,7,14] Improvised and timely measures taken with proper coordination may help the country fight COVID-19. The government was not able to mitigate the situation alone; individual efforts from the citizens, direct involvement of the nation's public health experts, and international assistance were urgently needed.

Limitations

This study has several limitations. First, there were only 17 confirmed cases, likely too few from which to make definitive conclusions or recommendations. Second, different case detection methods were used during the study—namely, contact tracing and active surveillance—and so detection may have been low, and there may have been some bias from the differential case detection. Third, asymptomatic and minimally symptomatic COVID-19 cases are common, and many of these cases were not detected by either passive or active surveillance in this study. Fourth, no statistical measures were provided in this manuscript, so it is difficult to assess the importance of some of the findings. Fifth, the study lacked a comparison group, preventing any conclusions from being drawn about the effectiveness of the containment measures implemented.

Overall, the Uttar Tolarbagh model demonstrates that localized, community-based containment guided by national policies and adapted to local contexts may be a practical and effective approach for containing outbreaks of COVID-19 and possibly for other infectious diseases.

Recommendations

High-risk close contacts should be isolated or quarantined and monitored by local authorities. All stakeholders should assess the quantity and quality of these local quarantine places in the area for proper planning. Local authorities should strengthen the social distancing policy in public areas to prohibit religious or other gatherings.

To reduce COVID-19 transmission, we recommend that persons with COVID-19 isolate at home until they are no longer infectious and that exposed persons be quarantined to monitor for symptoms and avoid onward transmission. We recommend that a qualitative study be conducted to determine the acceptance of this approach.

Conclusion

This manuscript describes localized containment approaches and their effect on COVID-19 transmission. Community transmission of COVID-19 in Uttar Tolarbagh declined following implementation of containment measures, suggesting that a combination of lockdown, restricted mobility, mosque-based regulation, systematic contact tracing, quarantine and isolation, and community-driven event-based surveillance helped reduce transmission.

Our findings suggest that household and religious gatherings posed the greatest risk of spread, underscoring the need for strict adherence to social distancing in both domestic and religious settings. Community engagement was critical, though challenges of stigma, fear, and misinformation initially hindered cooperation. These appeared to be gradually mitigated through the visible implementation of public health measures.

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Author Contributions

Md. Faruk Ahmad: Conceptualization, methodology, investigation, project administration, data curation, formal analysis, visualization, writing—original draft, writing—review & editing. **Mallick Masum Billah:** Methodology, visualization, writing—review & editing. **Alden Keith Henderson:** Validation, visualization, writing—review & editing. **Mahbubur Rahman:** Methodology. **M Salim Uzzaman:** writing—review & editing. **ASM Alamgir**: Conceptualization. **Manjur Hossain Khan:** Validation. **Tahmina Shirin:** Resources. **Meerjady Sabrina Flora:** Conceptualization, funding acquisition, resources, supervision.

Ethical Approval

This response was exempt from Institutional Review Board review because it was a response to an acute public health event. Verbal informed consent was obtained before interviews or the collection of samples.

Informed Consent

Verbal informed consent was obtained before interviews or COVID-19 sample collection.

Data Availability

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

Conflicts of Interest

No conflicts of interest by all authors.

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Mass Psychogenic Illness in a School during a Human Papillomavirus Vaccination Campaign, Bangladesh, 2024

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Abstract

Mass psychogenic illness (MPI) poses a public health threat due to rapid spread, diagnostic difficulty, and potential to undermine public trust. Effective prevention and response require recognition of social and psychological risk factors with clear communication, education, and preparedness. On 30 Oct 2024, two students at a school in Gobindaganj, Bangladesh, developed symptoms such as shortness of breath, abdominal cramps, and body aches shortly after receiving the human papillomavirus (HPV) vaccine. Within hours, 17 more reported similar symptoms. This investigation describes the outbreak by person, place, and time, documents the response by health authorities and hospital staff, and outlines measures taken to maintain confidence in HPV vaccine safety. Health officials reviewed hospital records, interviewed students, teachers, vaccinators, and health officials, and evaluated vaccine storage and cold chain integrity. Among 80 vaccinated students, 19 developed symptoms, resulting in an attack rate of 24%. Five students were hospitalized, three had hypokalemia linked to hyperventilation. All fully recovered within 24 hours. No evidence was found of vaccine quality issues, cold chain failures, immunization errors, infectious causes, or environmental exposures. The symptom pattern, rapid spread, absence of an organic cause, and presence of psychological stressors led to classification of the event as MPI. Management focused on symptomatic care, reassurance about vaccine safety, and real-time public and media communication. Authorities also addressed vaccine misinformation through press briefings, community outreach, and engagement with religious leaders. This incident highlights the need to integrate MPI preparedness into immunization campaign planning to ensure rapid containment and sustained public trust.

Keywords: mass psychogenic illness, Bangladesh, vaccination, HPV, AEFI

Introduction

Mass psychogenic illness (MPI), also known as mass hysteria, mass sociogenic illness, or epidemic hysteria, is a phenomenon characterized by the rapid spread of symptoms within a socially connected group, in the absence of an identifiable physical or environmental cause.[1] As a primarily psychological and social phenomenon, MPI underscores the complex interplay between individual stress responses and group dynamics, often arising in high-stress or close-knit environments such as schools, workplaces, and religious or military settings.[2] MPI outbreaks are frequently associated with heightened anxiety about environmental, chemical, or infectious threats, reflecting evolving societal stressors and the influence of social networks.

MPI outbreaks predominantly affect socially cohesive groups, with women and younger individuals, particularly in school settings, more susceptible. Common triggers include psychological stress, fear, and rumor, which, when amplified by interpersonal and media communication, can result in the rapid propagation of symptoms such as shortness of breath, dizziness, fainting, nausea, and headaches. While the symptoms are transient and typically resolve with reassurance and environmental or psychological intervention, for public health authorities, the condition poses significant challenges, such as misdiagnosis, stigmatization, and unnecessary resource utilization.

MPI outbreaks are sporadic and typically short-lived, but their disruptive impact on communities and public health systems can be significant. Outbreaks have been documented globally across diverse cultural and socioeconomic contexts, with notable events such as a conversion disorder among students in New York, rashes at several schools in Sri Lanka, and neurological complaints at a girls' school in Australia.[3–5] Several unpublished outbreaks that occurred in Bangladesh during recent vaccine campaigns include schools in Borhanuddin (68 students), Kaliganj (40 students), Potuakhali (12 students), Lakshmipur (17 students), Rajshahi (7 students), Chittagong (21 students) and Rangpur (3 students).

An 18-day human papillomavirus (HPV) school vaccination campaign in seven divisions of Bangladesh was initiated on 24 Oct 2024 by the Ministry of Health and Family Welfare, Bangladesh, supported by United Nations Children's Fund (UNICEF), the Global Alliance for Vaccines and Immunization (GAVI), and the World Health Organization (WHO). On 30 Oct 2024, the local health authority of Gobindaganj was notified that students at a rural school experienced rapid onset of severe shortness of breath, abdominal cramps, and body aches after the HPV vaccination. This outbreak may be classified as an adverse event following immunization (AEFI) during a mass HPV vaccination campaign. We describe the outbreak in terms of person, place and time, document the role local health authorities and hospital staff played in managing the event, and outline steps taken to ensure the public maintains confidence in the safety of the HPV vaccine.

Methods

We conducted a descriptive study to identify epidemiological characteristics of the outbreak and actions taken by local health organizations. This consisted of interviewing vaccinated students, health staffs that treated them, their parents, and school and health officials who assisted with the response, and assessing the vaccine cold chain.

Since the Bangladesh Ministry of Health and Family Welfare does not have a definition for MPI, we used the expanded program on immunization (EPI), Bangladesh, definition as follows: (a) two or more people experiencing the same type of symptoms without an identifiable physical cause and little or no laboratory evidence of disease; (b) a rapid spread of illness symptoms occurring within a socially connected group; (c) event triggered by psychological stressors such as fear of illness, rumors, or perceived threats; and (d) symptoms typically resolving when the underlying psychological stress is addressed, or the group dynamics change.[6]

In Bangladesh, the WHO office uses the AEFI surveillance system definitions for all vaccines introduced by the government.[7] For this event to be classified as a reportable AEFI, at least one of the following conditions must be met: (a) vaccine product-related reaction; (b) vaccine quality defect-related reaction; (c) immunization error-related reaction; (d) immunization triggered stress response; or (e) coincidental event.

The Bangladesh EPI defines a non-serious adverse event as one in which individuals experience any of the following symptoms: fever, nausea, nodule at vaccination site, muscle pain, redness, swelling or joint pain on and around the site of injection, seizure with or without fever, headache, anaphylaxis, abscess, rash, cough, joint pain, unstoppable bleeding in the site of injection, unconsciousness, or fainting.[8] A serious adverse event is a death, deformity, an overnight hospital stay exceeding 24 hours, community concern, more than two people with the same symptoms, any congenital deformity, or other serious health-related event.

We defined a case as a student who had a serious adverse event within 24 hours after receiving the HPV vaccination at the school on 30 Oct 2024. Our analysis focused on students with a serious AEFI only.

To describe the actions taken during the event, the local health officials reviewed medical records of the students treated at the hospital, interviewed them and their guardians, and conducted laboratory investigations including complete blood count, serum electrolytes, serum creatinine, and electrocardiograph. Interviews and group sessions were conducted among the following groups:

Vaccinators: information obtained included the time that the students received the vaccine, the time they started vaccination, whether the cold chain was maintained, type and use of vaccine carrier, and disease history of the student.

Medical technologist: we asked about the maintenance of the cold chain, time of storage and state of the vaccine when stored, and the time and state of the vaccine before sending to vaccinators.

Teachers: we asked about the students' past medical illnesses and history of AEFI.

Treated students: we obtained medical history, whether breakfast was eaten in the morning, any similar history, and any other potential causal factors behind the illness.

Students not treated and guardians: we obtained history of illness of the students affected, and any other history related to this incident.

To describe the actions on maintaining vaccine confidence and safety, the authors examined the cold chain management at the district and sub-district level by interviewing the vaccinators and EPI medical technologist responsible for the storage of vaccines, the upper authority regarding vaccines responsible for cold chain management, and the WHO surveillance and immunization officer. We also checked freezer temperature logs, whether the ice pack used for the vaccines were frozen, the proper use of the freeze-free vaccine carrier used as recommended by WHO for this campaign, and the vaccine vial monitors and expiration dates.

To describe the actions taken to determine the role of hospital staff in managing the incident, we interviewed the vaccinators and EPI and hospital staff (doctors, nurses, consultants, and emergency attendants).

To describe actions taken to determine the role health authorities played in managing this event, we interviewed the vaccinators, EPI medical technologists, hospital authorities, and administrative authorities of the EPI program.

Verbal consent was obtained from the student's parents or guardians and assent from the students. The EPI programme officers also gave their verbal consent to conduct the investigation. To maintain confidentiality, personal identifiers were not collected, and interviews were conducted in private rooms.

Results

Describing the Event

On 30 Oct 2024, during the HPV vaccination campaign conducted by the Bangladesh EPI, the local health authority of Gobindaganj Sub-district of Bangladesh was notified that several girls from a rural school became ill just after receiving the HPV vaccine. The school contained 750 students, ranging from kindergarten to tenth grade, of which 120 (16%) were female. As this vaccination campaign was for 10–14-year-old girls only, the target population for HPV vaccination in this school was female students, of which there were 80 in this age bracket. The school assembly starts at 08:00 AM and usually ends at around 08:30 AM. Some students travel from afar and many arrive without having eaten breakfast. The school has no cafeteria and there are no shops selling food near the school.

Vaccinations began at 09:00 AM and within 10:00 AM total 80 female students were vaccinated in that school. One of the first girls to be vaccinated developed rapid onset severe shortness of breath, abdominal cramps, and body aches approximately one hour post-vaccination. Soon afterwards another girl developed the same symptoms. Since the vaccinators thought that these symptoms were due to the vaccine, they contacted a local pharmacist, who agreed that the symptoms were due to the vaccine. The vaccinators then contacted the AEFI focal person for this campaign in the subdistrict, who then advised the vaccinators to bring the students to the hospital.

After witnessing the first two students become symptomatic, 17 other students had a rapid onset of severe shortness of breath, abdominal cramps, and body aches after receiving the vaccine (Figure 1). The median age of the symptomatic students was 13 years (range 10–14 years). All were immediately transported to hospital. Five later reported that, on the previous day, they were afraid to be vaccinated, and did not have a good sleep that night. Eight girls reported that they often fell down at the assembly, even without vaccination or medicine, as they often skipped breakfast.

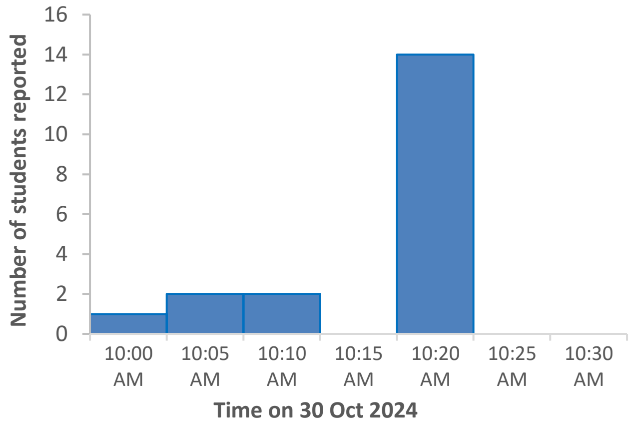

Figure 1. Symptom onset dates of a mass psychogenic illness among students in a village school, Gobindaganj, Bangladesh 2024

Upon arrival at the hospital, the students were treated symptomatically and given oxygen for hyperventilation and paracetamol for body aches (Table 1). Two agitated girls were given diazepam. Five girls had carpopedal spasms: three girls had hypokalemia, all had normal serum calcium levels and no changes in heart rate/rhythm on electrocardiogram. When many girls with similar symptoms were treated at the hospital, hysteria or mass psychogenic illness was suspected because similar events occurred in the country during the immunization campaign.

Table 1. Treatment provided to students at the hospital, Gobindaganj, Bangladesh, 2024

Treatment	Number of students	Percent
Low flow oxygen (0.5 L/min)	19	100
Paracetamol	9	47
Muscle relaxant	2	11
Antihistamine	11	58
Oral potassium	3	16

The most common symptoms were shortness of breath, headache, and body ache (Table 2). Thirteen students were treated and released within one hour of admission, one was hospitalized for one day, and five were hospitalized for three days. All students recovered without any complications. This outbreak was considered a serious AEFI because more than two people that were vaccinated were affected from the same locality at the same time, and more than two people were admitted to hospital for at least 24 hours. Infectious diseases, respiratory illness, foodborne or vector-borne illnesses, chemical exposures, neurological disorders, psychiatric conditions, and environmental toxins were systematically were ruled out through rigorous clinical evaluation, laboratory testing, and environmental assessments.

Table 2. Symptoms of students during a mass psychogenic illness event, Gobindaganj, Bangladesh, 2024

Symptom	Number of students	Percent
Shortness of breath	19	100
Headache	7	37
Body ache	3	16
Hand pain	2	11
Itchiness	1	5
Abdominal cramp	1	5

Attack Rate

Overall, 19 students (24%) reported adverse effects following HPV vaccination. The attack rate was relatively low for ages 10–12 years and increased from age 13 onward (Table 3). The number of ill students was highest in the 13-year-old age group (nine students), followed by the 14-year-old group (six students). Although the number of cases in the 15-year-old age group was low (two students), the attack rate was high (33%). The attack rate increased with grade and was highest in grade 9 (33%) (Table 4). Attack rates were lower in grade 5 (17%) and 8 (25%).

Table 3. Attack rates of a mass psychogenic illness among students by age, Gobindaganj, Bangladesh, 2024

Age (years)	Number of ill students	Number of students	Attack rate (%)
10	1	11	9
11	0	0	0
12	1	10	10
13	9	34	26
14	6	19	32
15	2	6	33
Total	**19**	**80**	**24**

Table 4. Attack rates of a mass psychogenic illness among students by school class, Gobindaganj, Bangladesh 2024

Grade	Number of ill students	Number of students	Attack rate (%)
5	2	12	17
6	6	27	22
7	6	25	24
8	1	4	25
9	4	12	33
Total	**19**	**80**	**24**

Vaccine Cold Chain Assessment

The HPV vaccine cold chain was assessed by the EPI medical technologist, the local authority responsible for cold chain management, and the WHO surveillance and immunization officer. They noted that the average temperature of the freezer containing the HPV vaccine was +4.5 °C (range: +3.0 to +5.5 °C) for the seven days before the incident date. Also, the ice packs used for the vaccines were not frozen properly due to a mechanical malfunction of the refrigerator that day; therefore, a freeze-free vaccine carrier was used during the campaign. However, monitored vaccine vials were in a usable state, intact, and the vaccine had not expired.

Local Health Authorities and Hospital Staff Managing the Event

Before this outbreak, local authorities prepared for an AEFI because of previous reports of MPIs occurring in HPV immunization campaigns in the country. The hospital prepared two rooms to receive students in case any developed an adverse event, and vaccinators were trained to recognize these adverse events and report them to the disease control medical officer. Staff also prepared emergency kits containing injectable adrenalin, paracetamol tablets, antihistamines, syringes, and cotton.

Local health authorities were surprised that 19 students developed adverse events. Local volunteers directed the teachers, parents, and press to a separate room from the students. A medical consultant who examined students at the hospital initially excluded an anaphylaxis reaction and suspected an acute exacerbation of a respiratory illness. While the first two students were examined and treated, more students who developed similar symptoms were being transported to the hospital. Because the symptoms were similar, physicians suspected a cluster of MPI and initiated steps to rule out other causes. The hospital authorities engaged one team of local volunteers to counsel the teachers and guardians that the adverse events were not due to the vaccine.

To identify additional cases, teachers contacted guardians to check for symptoms among students that were vaccinated and not hospitalized; however, no more students reported any symptoms.

Managing the Event

Dealing with reporters

Hospital staff and local authorities were confident that the adverse events experienced by the students were not due to the vaccine. They were confident because the HPV vaccine was piloted in 2016 in Gazipur and in 2023 in Dhaka Division where no serious AEFI was reported.

Ten to twenty reporters came to the hospital to cover this event. To answer their questions, the spokesperson for the hospital gave a press conference and stated that all students were examined, the symptoms were probably not due to the vaccine, and that other diagnoses were ruled out. The spokesman asked the reporters not to disturb the hospital staff as they needed to manage the patients smoothly. The next day, reporters were shown videos from the Directorate General of Health Services on the safety of HPV vaccination and were requested not to spread unfounded rumors to the public. The hospital physician provided updates of the hospitalized students to the reporters every 12 hours. The hospital authorities shared pictures on hospital web page and the public could see that the students were recovering, and that their illnesses were not serious.

Rumors

On social media, there were some posts claiming that vaccines were not allowed under Islamic law, made women infertile, and stopped girls from menstruating. The Directorate General of Health Services posted video messages on social media to address these rumors. The EPI office shared a video of girls who were vaccinated at Gazipur on 2016 and were later married. They shared the vaccine manufacturer documents that verified the endorsement of the vaccine by religious leaders. They also shared the video and comments of the Chairperson of the National AEFI committee and comments of several pediatricians and gynecologists. The Islamic Foundation engaged the national and local religious leaders to share this message to the public that the HPV vaccine was allowed under Islamic law and was safe.

Increasing public confidence in vaccination

During the press conference, reporters were informed that the cold chain for the HPV vaccines in Gobindaganj was maintained properly. Freeze-free vaccine carriers were used, and vaccines were checked for expiration dates and vaccine vial monitors were intact. Mass media was used to show the positive effects of HPV vaccination and videos of renown gynecological consultants were shared on social media.

Discussion

This mass psychogenic illness outbreak during a school-based vaccination campaign in Bangladesh illustrates a well-recognized pattern of psychosomatic events in group settings. In this event, students had an acute episode of dizziness, fainting, nausea, headaches, hyperventilation, and non-specific neurological symptoms, hallmarks of a previous MPI described in the literature.[2] Consistent with known MPI transmission patterns, symptoms appeared to spread through observation and suggestion rather than direct contact.[9] Environmental and psychological triggers, such as witnessing peers faint or hearing distressing rumors, likely played a role in symptom amplification.

As with any cluster of unexplained symptoms, a broad differential diagnosis was considered. Infectious diseases, respiratory illnesses, foodborne or vector-borne illnesses, chemical exposures, neurological disorders, psychiatric conditions, and environmental toxins were systematically ruled out through rigorous clinical evaluation, laboratory testing, and environmental assessments. This thorough process was crucial to avoid unnecessary interventions and to correctly identify the outbreak's psychogenic origin.

Adolescents, particularly females, are disproportionately affected by an MPI, especially in structured environments such as schools and workplaces.[1,10] Sociocultural influences, including greater tendencies toward somatization and different societal expectations regarding health reporting, may partly explain this gender disparity.[1] In this case, the combination of an organized school setting, strong peer networks, and anxiousness regarding introduction of a new vaccine, likely facilitated the propagation of symptoms. An additional factor was that several students had not eaten breakfast prior to receiving the vaccine in the morning. Weakness due to hunger or dehydration can predispose individuals to fainting or dizziness, contributing to the onset of symptoms and potentially intensifying the collective response. The range of temperatures that the vaccine was stored in the week before the cold chain inspection and on the second day of the event was +3.0 to +5.5°C and was within the recommended temperature range of +2.0 to +8.0°C. Consequently, the vaccine was stored at the recommended temperatures and was unlikely to be linked to the MPI. The attack rate was relatively low among students aged 10–12 years and increased from age 13 onward. Similarly, students in lower grades had relatively lower attack rates than students in higher grades. This suggests that older students may be at higher risk, possibly due to behavioral factors, environmental exposures, biological susceptibility, or onset of puberty.

The broader context in Bangladesh is also important. Previous MPI outbreaks associated with HPV vaccinations reveal the power of public perception and rumor in shaping responses to health interventions. Misinformation, often magnified by traditional and social media, can catalyze anxiety and symptom spread, complicating outbreak management.[11]

The response by local health authorities and healthcare providers was crucial in managing this outbreak. A rapid epidemiological investigation, the immediate ruling out of environmental and infectious hazards, and clear, transparent communication helped to prevent an escalation of the situation. Hospital teams played a vital role by triaging students, providing symptomatic treatment, and their reassurances minimized the reinforcement of symptoms and prevented unnecessary medical treatment. Such strategies are aligned with best practices for managing MPI outbreaks.[12] Importantly, when an MPI outbreak occurs during a vaccination campaign, it can seriously threaten public confidence in immunization efforts. Recognizing this risk, public health officials swiftly communicated findings to the community, engaged trusted healthcare workers to disseminate timely and accurate information, and emphasized the safety and importance of the HPV vaccine. Educational outreach and psychological support helped contain misinformation and regained public trust in vaccinations.

Although MPI outbreaks are often self-limited, they can produce significant public health and social consequences. Beyond the immediate health concerns, outbreaks can disrupt educational systems, strain healthcare resources, and cause vaccine hesitancy. Moreover, sensationalized media coverage can exacerbate the situation by perpetuating fear and misunderstanding.[1,13]

Epilogue

An MPI outbreak at a school in Boalkhali, Chattogram, on 29 Oct 2025, almost one year after the current outbreak, reaffirmed that swift medical evaluation on-site, psychological support, and transparent communication are crucial in limiting the spread of MPI outbreaks and maintaining public trust during an immunization campaign. That particular outbreak occurred during a countrywide typhoid vaccination campaign targeting 50 million children in Bangladesh. Twenty students developed pain, fainting, dizziness, and weakness shortly after vaccination. Drawing on lessons from the outbreak at the school in Gobindaganj Sub-district, the affected students were not transported to a hospital but moved to a separate room and treated on-site. A medical consultant and three physicians were sent to the school to evaluate, treat, and counsel the affected students. The students were monitored for three hours and released to their guardians when their symptoms subsided. To reassure others, local health officials visited the classrooms and explained that the symptoms were not caused by the vaccine. A total of 800 students received the typhoid conjugate vaccine that day, including 150 vaccinations administered after the MPI event.

Limitations

As this was a descriptive study, we were unable to identify risk or preventive factors or test hypotheses. Interviews were conducted only on ill students, with no comparison group. Therefore, an analytical study, such as case-control study, could not be conducted. Although we were confident of the sequence of events, their duration was subject to recall bias and therefore may be approximations.

Recommendations

Effective management requires rapid assessment, transparent communication, and reassurance to affected communities. Public health authorities must engage efficient and hardworking managers, trusted messengers, counter misinformation, and emphasize the safety and importance of vaccines during vaccination campaigns. Preventive strategies such as stress management, education, and media cooperation are essential to maintaining good vaccination coverage and public trust during and after MPI events. Epidemiologists should consider conducting analytical studies, such as case-control studies, to test hypotheses and identify risk factors.

Conclusion

Though medically benign, an MPI outbreak can cause significant disruptions such as school closures, absenteeism, stigma, and persistent anxiety in communities. When they occur during immunization campaigns, vaccine confidence may be undermined, contribute to misinformation, and lead to increased vaccine hesitancy. Public fear, especially if amplified by sensational media coverage, can reduce vaccination uptake and compromise public health goals. The coordinated, multidisciplinary response to the MPI outbreak during the vaccination campaign in Bangladesh highlights the necessity of early interventions, public reassurance, and open communication. Viewing an MPI outbreak as a legitimate public health phenomenon is crucial for ensuring community resilience and maintaining trust in vital public health interventions such as vaccination programs.

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Author Contributions

Jafrin Jahed Jiti: Investigation, methodology, writing—original draft. **Shahabuddin Manik:** Writing—review & editing. **Alden Henderson:** Supervision, writing—review & editing.

Ethical Approval

Ethical approval was exempt because this was a response to an acute health event.

Informed Consent

Verbal informed consent was obtained before interviews were conducted.

Data Availability

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

Conflicts of Interest

None.

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No AI was used to analyze the data or write the manuscript.

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The Grammar of Science: The Challenge of Competing Outcomes

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In many studies, multiple possible outcomes can occur. Sometimes, another event happens before the outcome of interest, potentially preventing it from occurring. This situation is known as a "competing risk." This paper discusses how to handle competing risks, which are common in epidemiological research, focusing on time-to-event analyses where individuals are followed from study entry until the event of interest, a competing event, or censoring.

Getting Started with Time-to-event Analysis

Time-to-event data describe how long it takes for a specific event to occur. Time-to-event analysis, or survival analysis, estimates the survival function, S(t)—the probability that an individual has not yet experienced the event at a given time. Depending on the study goal, analyses may compare survival between groups or assess how factors such as age, sex, socioeconomic status, or treatment affect the time to event.[1]

In time-to-event analysis, individuals are followed over time, and their hazard of experiencing the outcome, h(t), may change at each time point. The hazard represents the instantaneous risk of the event occurring at a specific time, given that the individual has not yet experienced it, reflecting how risk evolves over time rather than the total probability of the event. Those who experience the event are called "failures", while those who do not are considered "censored". Censoring occurs when an individual (1) does not experience the event by the study's end, (2) is lost to follow-up or withdraws, or (3) dies or experiences a different event during follow-up.[1] Because of censoring, survival analysis requires specialized methods beyond standard regression.

The Kaplan–Meier (KM) method estimates the proportion of individuals who remain event-free over time.[2,3] It assumes noninformative censoring, meaning that censored individuals would have had the same probability of experiencing the event as those who remained under observation. By including individuals with incomplete follow-up, KM provides a flexible and widely used tool for time-to-event analysis.[1]

Figure 1 illustrates 10 individuals followed over 14 months, showing who experienced the event of interest and who were censored. Those reaching the endpoint (death from the disease) are considered failures, whereas individuals who did not reach the endpoint were censored. Figure 2 presents the hazard function h(t) along with the KM curves for the survival function S(t) and the failure function F(t) (i.e., 1–S(t)) for the same dataset.

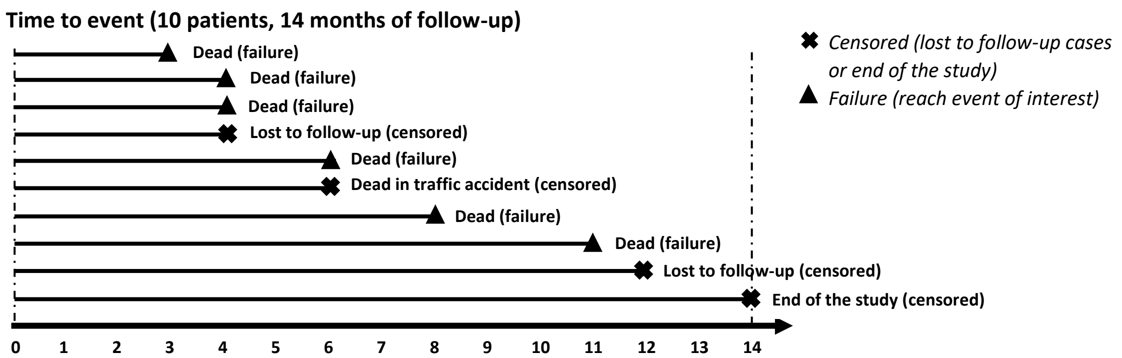
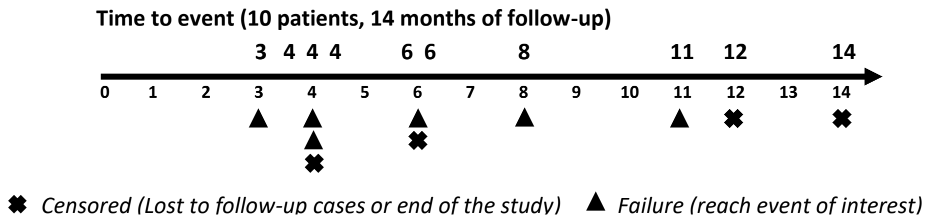


Figure 1. Event occurrence and censoring during 14-month follow-up



Time (month)	0	3	4	6	8	11	12	14
Event	0	1	2	1	1	1	0	0
Censored	0	0	1	1	0	0	1	0
Risk set	10	10	9	6	4	3	2	1
P(event)_h(t)	0/10	1/10	2/9	1/6	1/4	1/3	0/2	0/1
	0.00	0.10	0.22	0.17	0.25	0.33	0.00	0.00
P(no event)	1.00	0.90	0.78	0.83	0.75	0.67	1.00	1.00
P(survival)_S(t)	1	0.9 x 1	0.78 x 0.9	0.83 x 0.70	0.75 x 0.58	0.67 x 0.44	1 x 0.29	1 x 0.29
	1.00	0.90	0.70	0.58	0.44	0.29	0.29	0.29
P(failure)_F(t)	0.00	0.10	0.30	0.42	0.56	0.71	0.71	0.71

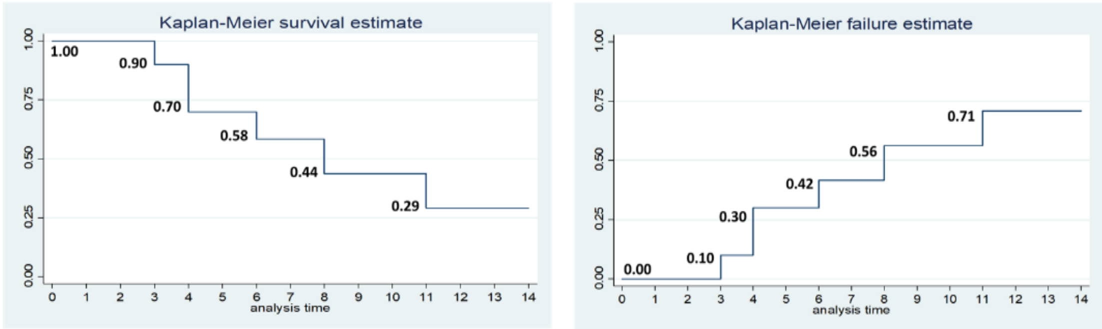


Figure 2. Estimated hazard, survival and failure over time

Competing Risks: Concept and Implications

In epidemiological studies, individuals may be at risk of multiple event types. In a standard time-to-event analysis, shown in Figure 3(a), the event of interest is disease-related death after treatment, with other events treated as censored. Another scenario, shown in Figure 3(b), involves cancer patients where events can occur as relapse or death, and relapse may later lead to death—an example of a multi-state event (not discussed in this paper).

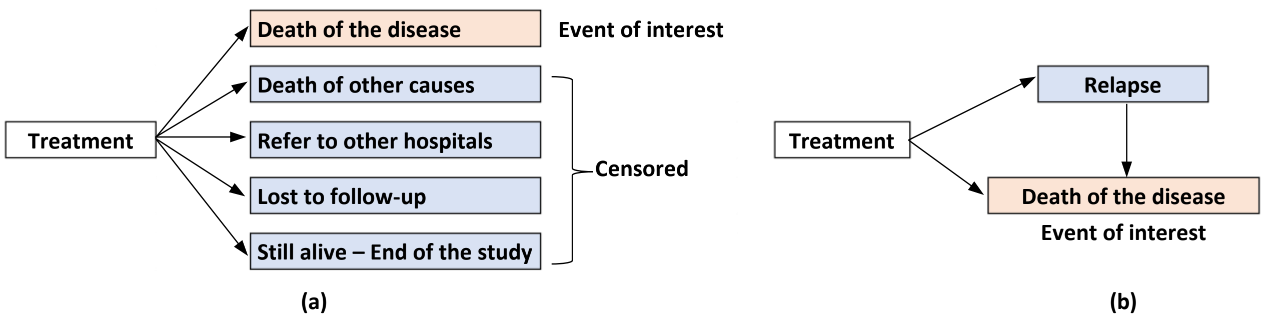


Figure 3. Event types: (a) disease-related death with censoring; (b) multi-state event

A competing risk situation arises when only one event can occur at a given time, thereby preventing other events—particularly the main event of interest—from occurring. In such cases, the probabilities of these events are interdependent.[4–6] For example, as shown in Figure 4, when analyzing time to death among patients with chronic kidney disease (CKD), other important events may act as competing risks or censored observations. Similarly, in cancer research, outcomes such as local recurrence and metastasis can serve as competing risks.

Researchers need to decide which events count as competing risks and which should be treated as censored. Noninformative censoring means that the reason someone leaves the study has nothing to do with their chance of experiencing the event of interest. Informative censoring happens when people leave the study for reasons related to their event risk—for example, if sicker patients are more likely to drop out. In such situations, informative censoring can be viewed as a competing risk because it affects the chance of observing the main event and may bias the results if not handled correctly.[3]

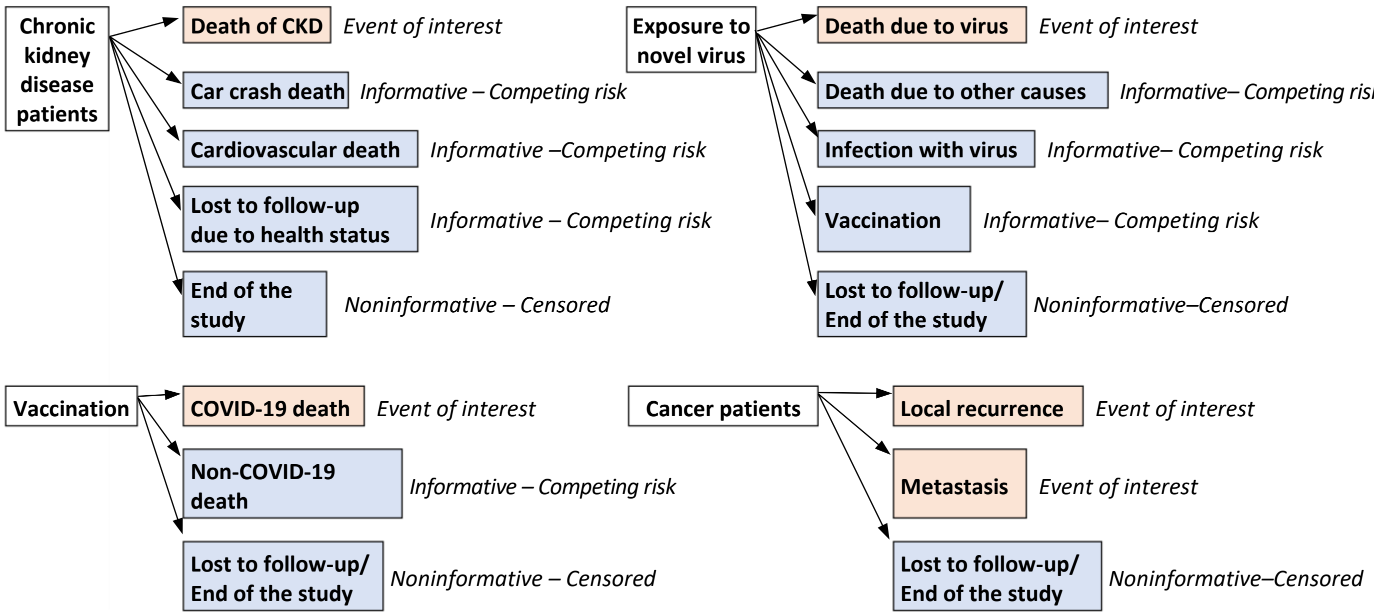


Figure 4. Examples of different competing risks events

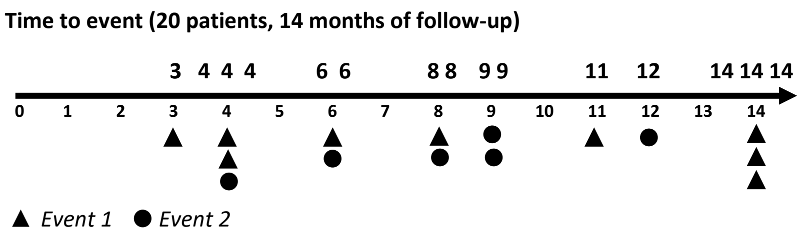
Ignoring other possible events can give misleading results.[7,8] When there is a competing risk situation, the KM method will treat competing events as censored, assuming that competing events are independent—like standard censoring—which is often unrealistic.[1,4]

Competing Risks: Analysis & Models

Competing risk regression is usually based on two types of hazard: the cause-specific hazard (CSH) and the subdistribution hazard (SDH). In the presence of competing risks, CSH and SDH produce different hazard functions for the same event. While both account for competing risks, they use different risk sets, which leads to different interpretations of covariate effects.[9]

Cause-specific Hazard

The cause-specific hazard (CSH) measures the risk of a specific event occurring at a particular time, considering only individuals who have not yet experienced any event.[6,9] The group of individuals who are still at risk at a given time is called the risk set. Once someone experiences a competing event, they are removed from the risk set and no longer contribute to the calculation of the hazard for future times. Figure 5 illustrates a scenario in which 20 patients are followed over time, and each can experience Event 1, Event 2, or no event (censored). From Months 0 to 3, all 20 are in the risk set. At month 3, one person experiences Event 1 and none experiences Event 2, giving a CSH of 1/20=0.05 for Event 1 and 0/20=0.00 for Event 2. At month 4, 19 people remain in the risk set because one individual has already had Event 1. That month, two people experience Event 1 and one experiences Event 2, resulting in a CSH of 2/19≈0.11 for Event 1 and 1/19≈0.05 for Event 2. This process continues over time, showing the instantaneous risk of each event among those still in the risk set.

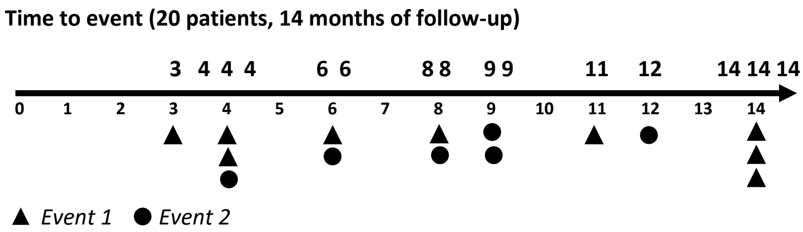


Time (month)	0	3	4	6	8	9	11	12	14
Event 1	0	1	2	1	1	0	1	0	3
Event 2	0	0	1	1	1	2	0	1	0
Risk set	20	20	19	16	14	12	10	9	8
Specific h(t) – Event 1	0/20	1/20	2/19	1/16	1/14	0/12	1/10	0/9	3/8
	0.00	0.05	0.11	0.06	0.07	0.00	0.10	0.00	0.38
Specific h(t) – Event 2	0/20	0/20	1/19	1/16	1/14	2/12	0/10	1/9	0/8
	0.00	0.00	0.05	0.06	0.07	0.17	0.00	0.11	0.00

Figure 5. Cause-specific hazard (CSH) schematic

Subdistribution Hazard

The subdistribution hazard (SDH) is a method used to estimate the probability of different events when competing risks are present. Unlike the CSH model, which removes individuals from the risk set once they experience a competing event, the SDH keeps these individuals in the risk set along with those who are still event-free. This approach allows direct estimation of the cumulative incidence of each event while still using a Cox regression framework.[6,10] The SDH function shows the risk of a specific event at a given time, including both people who haven't had any events yet and those who have experienced competing events.[9] As shown in Figure 6, suppose 20 patients being followed over time, where they can experience Event 1, Event 2, or be censored. From months 0 to 3, all 20 are in the risk set. At month 3, one person experiences Event 1 and none experiences Event 2, so the SDH=1/20=0.05 for Event 1 and 0/20=0.00 for Event 2. At month 4, the risk set for Event 1 is now 19 (one person already had Event 1), while the risk set for Event 2 remains 20, since no one has had Event 2. That month, two people have Event 1 and one has Event 2, giving SDH=2/19≈0.11 for Event 1 and 1/20=0.05 for Event 2. This continues over time, showing how the SDH accounts for competing events while estimating the probability of each specific event.



Time (month)	0	3	4	6	8	9	11	12	14
Event 1	0	1	2	1	1	0	1	0	3
Risk set – Event 1	20	20	19	17	16	15	15	14	14
SubD_h(t) – Event 1	0/20	1/20	2/19	1/17	1/16	0/15	1/15	0/14	3/14
	0.00	0.05	0.11	0.06	0.06	0.00	0.07	0.00	0.21
Event 2	0	0	1	1	1	2	0	1	0
Risk set – Event 2	20	20	20	19	18	17	15	15	14
SubD_h(t) – Event 2	0/20	0/20	1/20	1/19	1/18	2/17	0/15	1/15	0/14
	0.00	0.00	0.05	0.05	0.06	0.12	0.00	0.07	0.00

Figure 6. Subdistribution hazard (SDH) schematic

Cumulative Incidence Function

The Cumulative incidence function (CIF) is used instead of standard methods like KM, which can overestimate the risk when competing events are present.[11] The CIF shows the probability that a specific event occurs by a certain time while taking competing events into account.[6,12,13] When there is only one type of event, the CIF is the same as 1–KM. With multiple competing events, the CIF is calculated from cause-specific hazards but does not assume that the events are independent, providing a more accurate estimate of event probabilities.[6,14]

The CSH and cause-specific cumulative incidence function (csCIF) measure the event rate among those still at risk, but they assume that different events do not influence each other, which may not always hold true.[6] In contrast, the SDH and subdistribution cumulative incidence function (sdCIF) account for competing events by keeping individuals who have already experienced competing events in the risk set, along with those who are still event-free.[6] This approach allows direct calculation of the cumulative probability of each event over time. The SDH can also show how covariates affect this probability through the subdistribution hazard ratio (SHR). Models such as the Fine and Gray SDH model are especially useful for predicting an individual's absolute risk of an event while accounting for competing risks.[10,13]

Interpretation and Application of Competing Risks Models

The CIF is calculated by integrating the hazard over time, weighted by overall survival. The hazard ratio (HR) represents the relative change in the instantaneous risk among individuals who are still event-free. As an example adapted from a COVID-19 vaccination study, suppose 10,000 people are followed for one year.[15] Vaccination status is the exposure, COVID-19 death is the event of interest, non-COVID-19 death is treated as a competing event, and those who survive the year are censored. Using a CSH model (Cox), the hazard ratio is HRvax=0.40 (95% CI 0.32–0.51), meaning vaccinated individuals have a 60% lower instantaneous risk of COVID-19 death among those still alive and event-free. Using a SDH model

(Fine & Gray), the subdistribution hazard ratio is SHRvax=0.65 (95% CI 0.54–0.78), reflecting a 35% lower cumulative incidence of COVID-19 death over 1 year, accounting for competing deaths. At 12 months, the CIF shows 0.8% for vaccinated and 2.0% for unvaccinated individuals, thus a risk difference between the two groups is 1.2 percentage points.

The choice of hazard function in competing risks analysis depends on the research question. As noted in the literature, the CSH is most useful for etiologic research, which seeks to understand what causes an event and how risk factors directly affect it.[3,6,11,15,16] In contrast, the SDH is better suited for prognostic research, which focuses on predicting the overall chance of an event over time while accounting for competing events. SDH models also estimate the cumulative incidence, making them more useful for real-world risk prediction.

Returning to the COVID-19 vaccination study example, the CSH model shows how vaccination affects the immediate risk of COVID-19 death among people who are still alive and have not experienced any event, reflecting the biological effect of the vaccine. The SDH model, on the other hand, takes competing events—such as death from other causes—into account and shows how vaccination affects the overall cumulative risk of COVID-19 death, which is more useful for predicting outcomes in the population. We can say that SDH model estimates effects in relation to the cumulative incidence, making their results closely tied to—and therefore strongly influenced by—the frequency of competing events in the population. In contrast, the CSH model evaluates effects independently of how often competing events occur, underscoring the greater robustness and stability of CSH estimates when competing-risk incidence varies.[6,13]

When reporting CSH and SDH models, always include the CIF to visualize event probabilities over time. Clearly indicate whether hazard ratios come from a CSH or SDH model, because their values and interpretations differ. Remember, SDH reflects cumulative incidence in the presence of competing events and does not measure the exact causal effect of a covariate.

Guidelines for Researchers

Competing risk models are most useful when follow-up is long enough to observe a sufficient number of events. Because there is no simple test for informative censoring, it is important to ensure that individuals with and without events were handled consistently. These models are typically considered when competing events are fairly common—affecting ≥10% of the population or occurring as often as the primary event.[1]

Competing risks analysis considers multiple types of events, giving more accurate predictions for individual outcomes. However, it can be biased if exposures or conditions change over time. In such cases, multistate models are preferable, as they track individuals through multiple states—such as treatment, relapse, and death—capturing complex transitions over time.[16]

When you have multiple outcomes, don't settle for just one—pick the method that tells the whole story.

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