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Surveillance Report

Letter to the Editor

To contact us:

Western Pacific Surveillance and Response
World Health Organization
Office for the Western Pacific Region
United Nations Avenue
1000 Manila, Philippines
wpsar@who.int
https://ojs.wpro.who.int/

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The first outbreak of herpes gladiatorum in Thailand: an investigation of boxing gyms in Phuket, May–August 2022

Suppasit Srisaeng,[a] Kusuma Swangpun,[b] Arriya Panchaiyaphum,[b] Pilailuk Akkapaiboon Okada,[c] Warodom Sornsurin,[a] Panuwat Naraart[d] and Thanawadee Chantian[a]

Correspondence to Suppasit Srisaeng (email: mumiman@gmail.com)

Objective: The objectives of this study were to describe the characteristics of Thailand's first reported outbreak of herpes gladiatorum in Thai-boxing gyms and to provide recommendations for reducing the risk of transmission.

Methods: Hospital reports of atypical rashes appearing among Thai-boxing trainees triggered investigations at three gyms in Phuket during May–August 2022. Semistructured questionnaires were used to collect data from gym owners, trainers and trainees. Skin and blood specimens were collected for reverse transcription–polymerase chain reaction testing for herpes simplex virus type 1 (HSV-1), antibodies to HSV-1 and other pathogens; genomic sequencing was performed on culturable samples. The environmental investigation included walk-through surveys, a review of each gym's web site, and testing of surfaces and water specimens.

Results: Nine cases of herpes gladiatorum were confirmed and one was suspected, all in non-Thai trainees. Attack rates in Gyms I, II and III were 21.4%, 11.5% and 2.6%, respectively. Risk behaviours included sparring with partners who had a rash, sharing equipment and neglecting to shower before training. HSV-1 was detected on gym equipment and surfaces, and cultures from skin lesions and blood samples revealed a genomic linkage between two cases in Gym II, identified as belonging to the East Asian Clade II strain. Disinfection of equipment reduced exposure to HSV-1.

Discussion: The first outbreak of herpes gladiatorum in Thailand was confirmed in 2022. Genomic sequencing suggested local transmission within Thailand, with the virus introduced independently into each gym. Skin-to-skin contact was likely the main mode of transmission; environmental findings indicated a lower risk of transmission via gym surfaces. Recommendations to prevent future outbreaks include stricter regulations for pre-fight screening and improved gym cleaning and hygiene among trainers and trainees.

Herpes gladiatorum (HG), a skin infection caused by herpes simplex virus type 1 (HSV-1), is prevalent in athletes who participate in high-contact sports such as wrestling and boxing.[1] The virus spreads through direct contact with lesions or mucosal secretions, and is most contagious when sores are present.[2] However, asymptomatic shedding, which occurs in 4–25% of cases, also facilitates transmission.[3]

Early, or prodromal, symptoms of HG include malaise, anorexia and fever; painful skin vesicles develop within 4–11 days following exposure,[4] typically on the forearm, face and neck, and most frequently on the right side of the body. HG is commonly misdiagnosed as bacterial folliculitis.[4,5] Around half of cases experience recurrent infections, which are usually milder.[6] Although severe complications are rare, ocular infection with HSV is a common cause of blindness in United States of America, and untreated herpes encephalitis has a 70% fatality rate.[4]

HSV-1 infection is relatively common. Data from 2012 suggest that two thirds (67%) of the global population younger than 50 years (3.7 billion persons) are infected with HSV-1; in South-East Asia, the proportion is 59%, or 432 million persons.[7] A 2019 systematic review

[a] Field Epidemiology Training Program, Division of Epidemiology, Department of Disease Control, Ministry of Public Health, Nonthaburi, Thailand.
[b] Phuket Provincial Public Health Office, Ministry of Public Health, Nonthaburi, Thailand.
[c] National Institute of Health of Thailand, Nonthaburi, Thailand.
[d] Office of Disease Prevention and Control Region 11, Department of Disease Control, Ministry of Public Health, Nonthaburi, Thailand.
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concluded that 73% of adults in Asia have antibodies to HSV-1.[8]

Prior to 2022, there were no recorded outbreaks of HG in Thailand. However, the emergence of mpox in May 2022 raised surveillance awareness of rash-causing diseases. The Bamrasnaradura Infectious Diseases Institute (BIDI) notified the Division of Epidemiology at the Department of Disease Control, Ministry of Public Health, and several hospitals in Phuket notified the Provincial Public Health Office, about clusters of atypical rashes occurring in patients linked to three Thai-boxing gyms, triggering a joint investigation team to assess these gyms (Gyms I, II and III). This team, which comprised representatives from the Provincial Public Health Office, the Office of Disease Prevention and Control Region 11, and the Division of Epidemiology at the Department of Disease Control, conducted its investigations during May to August 2022. On-site investigations were conducted within 2 days of notification of the most recent case in each gym.

The aims of this study were twofold: (i) to describe the characteristics of Thailand's first confirmed outbreak of this disease and (ii) to make recommendations to prevent and control outbreaks.

METHODS

Study population

On-site investigations were initiated on 26 May at Gym I, 27 June at Gym II and 12 August at Gym III. A second investigation was conducted at Gym II on 7 July to allow for more detailed interviews and specimen collection. Across the three gyms, 114 of 257 individuals were interviewed and examined for the presence of a rash, including gym owners, trainers, trainees and other staff. The following case definitions were employed.

- **Suspected case:** A person who trained or worked in any of the three gyms between May and August 2022 and developed a rash (i.e. macules, papules, vesicles, pustules or crusts), with or without fever, sore throat, headache, myalgia or lymphadenopathy.
- **Confirmed case:** A suspected case with a positive result from a reverse transcription–polymerase chain reaction (RT–PCR) test for HSV-1.
- **Risk contact:** A person who had direct skin-to-skin contact with a suspected or confirmed case during training or sparring sessions, or had used shared equipment, such as target pads, gloves or punching bags.

Data collection

Convenience sampling was used to interview the individuals present at each gym and examine them for rashes during the on-site investigation. Individuals not present on investigation days were interviewed by telephone. Individuals reporting rash symptoms over the telephone were further assessed at the gym, their accommodation or a hospital. Ten suspected cases were identified through this process and were interviewed in detail using a semistructured questionnaire. Ten Thai trainers from Gym II were also interviewed in detail. The questionnaire covered demographic information (e.g. sex, age, nationality), medical history (e.g. date of symptom onset, underlying conditions, prior herpes infections, symptoms, treatment), exposure history (e.g. sparring with symptomatic partners) and hygiene behaviours (e.g. equipment sharing, showering before training). The owners of Gyms I and III did not consent to interviews.

Laboratory testing

Specimens from throat swabs, lesion fluid, lesion scrapes, lesion swabs and/or blood were collected and tested at the National Institute of Health of Thailand using RT–PCR for mpox, HSV-1, HSV-2, varicella–zoster virus and *Treponema pallidum*. RT–PCR results with a cycle threshold (Ct) value of ≥40 cycles were classified as "not detected." Higher Ct values typically indicated viral loads below the detection limit. Blood samples were additionally tested for HSV-1 antibodies. Genomic sequencing was performed on six culturable HSV-1 specimens from four cases. Viral genomic sequences were quality-trimmed and assembled into consensus sequences, then aligned against the HSV-1 reference genome (National Center for Biotechnology Information reference sequence for HSV-1 strain 17: NC_001806.2).[9,10] A phylogenetic tree was constructed using W-IQ-TREE version 1.6.11 with maximum likelihood analysis.[11] Geographical data for each isolate were overlaid onto the tree.

Environmental study

Walk-through surveys were conducted in all three gyms to gather information relating to the facilities, sanitation measures, cleaning protocols, the use of personal protective equipment and training practices. The gyms' web sites were reviewed to gather information about staff, facilities and training programmes. From Gym II, surface swabs and water samples from the pool, toilets and water supply were collected and sent to the National Institute of Health of Thailand for RT–PCR for HSV-1. Free chlorine levels in water samples were tested on-site.

RESULTS

Descriptive study

Setting and context

Including owners, trainers, and adult and teenage trainees (i.e. younger than 18 years), 47 individuals had links to Gym I, 66 to Gym II and 144 to Gym III. Gyms II and III were large and offering training in mixed martial arts (MMA) as well as Thai boxing. The duration of training programmes ranged from 1 to 2 weeks for amateurs to 2 to 3 months for professional fighters. Training sessions were held twice daily, Monday to Saturday (7:00–10:00 and 16:00–18:00). Sessions typically began with a 30-minute run of 3–5 km, 10 minutes of skipping rope, and 30 minutes of stretching and shadowboxing. Morning sessions included an hour of clinching and sparring in 4–5 rounds of 3 minutes each, with 2-minute rest periods and 4–12 partner rotations, ending with 15 minutes of stretching. Evening sessions focused on bag and pad work (i.e. striking punching bags and targets held by a trainer). Saturday sessions featured Thai-boxing pre-fight ritual dancing and full-body training techniques involving frequent upper-body contact. Thai-boxing techniques and clinches are shown in **Supplementary Fig. 1**.

Case characteristics

Of the 114 individuals interviewed or examined for rash, 10 had rash symptoms consistent with HG and were classified as suspected cases; nine were tested by RT–PCR to confirm their diagnoses (**Table 1**). One suspected case (a Russian female) was not tested because she left Gym I after the owner prevented her from training. The 10 cases were all non-Thai nationals (seven from Europe, one from New Zealand, one from Russian Federation and one from the United States). The median age was 27 years (interquartile range [IQR]: 21–29 years) (data not shown). All nine confirmed cases were male; one had a history of asthma and another had a prior herpes infection (**Table 1**). The predominant symptom of confirmed cases was a vesicular rash, occurring mainly on the right forearm (7/9 cases, 78%), the right side of the face (5/9, 56%) and the left forearm (4/9, 44%) (**Fig. 1**; **Supplementary Fig. 2**). Additionally, three cases (3/9, 33%) had fever and two (2/9, 22%) had enlarged lymph nodes (data not shown).

Case timeline and distribution

Onset in the first case was 15 May, and the outbreak peaked on 21 May in Gym I, with three cases. Thereafter, Gym II reported sporadic cases and Gym III had one case (**Fig. 2**). A timeline of contacts between confirmed cases and sparring partners at Gyms I and II is shown in **Fig. 3**. It was not possible to construct a meaningful timeline for Gym III, as we were unable to trace many of the 12 known sparring partners of the one suspected case.

Mr A commenced training at Gym I on 6 May and developed facial vesicular rashes by 15 May, marking his exposure period. He continued training with close-contact sparring until 21 May, after which he sought medical treatment. Mr B interacted with Mr A on 16 May. By 19 May, he exhibited a vesicular rash that spread to his neck and caused painful and swollen lymph nodes, leading him to cease training and rest at a hotel on 21–22 May. Financial pressures compelled him to participate in a professional fight on 23 May, at which time he had an open wound on his forehead. Mr C sparred with Mr B on 19 May, and Mr D sparred with Mr A, who had a rash, on 18 May. Mr E sparred with Ms F on 13–21 May; Ms F (the unconfirmed case) also had a rash during this period of time, but Mr E was unaware of her rash because she always wore long-sleeved clothing. Mr C, Mr D and Mr E are brothers, and they all developed rashes that were initially misdiagnosed as bacterial skin infections by a clinic or pharmacy. As their symptoms worsened, they flew to Bangkok for treatment at a private hospital, which subsequently notified BIDI of a suspected mpox cluster. Other trainees noticed large groups of vesicles on Ms F's body during May, and despite being advised to rest on 24 May, she resisted and departed the gym (**Fig. 3a**).

Table 1. **Characteristics of herpes gladiatorum cases (*N* = 10) and their risk contacts (*N* = 92) at three Thai-boxing gyms, Phuket, Thailand, May–August 2022**

Characteristic	Gym			Total
	I	II	III	
Cases				
Confirmed	5	3	1	9
Suspected	1	0	0	1
Sex (male/female)	5/1	3/0	1/0	9/1
Ethnicity (White/Asian)	6/0	2/1	1/0	9/1
Country of nationality	Ireland 4 Portugal 1 Russian Federation 1	England 2 New Zealand 1	USA 1	10
Previous HSV infection	0	1	0	1
Underlying disease	No	No	1 (asthma)	1
No. interviewed or examined for rashes/total no.				
Owner/manager	1/1	1/1	2/2	
Non-Thai trainee	18/24	12/20	21/30	
Non-Thai MMA trainee	0/0	0/21	0/50	
Thai trainee	3/6	0/0	0/0	
Thai trainer	6/6	10/10	10/21	
Non-Thai trainer	0/0	3/3	7/7	
Thai teenage trainee	1/10	1/5	0/0	
Worker	0/0	6/6	12/34	
No. interviewed or examined/total no. in gym	29/47	33/66	52/144	114/257
No. of risk contacts/total no. interviewed or examined[a]	28/29	26/33	38/52	92/114
Attack rate[b]				
Overall	21.4% (6/28)	11.5% (3/26)	2.6% (1/38)	10.9% (10/92)
Non-Thai trainees	33.3% (6/18)	25.0% (3/12)	4.8% (1/21)	19.6% (10/51)

HSV: herpes simplex virus; MMA: mixed martial arts.

[a] A risk contact was a person who either had skin-to-skin contact with a suspected or confirmed case, specifically during training or sparring sessions (direct contact), or had used equipment that had been used by a suspected or confirmed case (indirect contact), such as target pads, gloves or punching bags.

[b] The attack rate was calculated as the number of cases divided by the total number of risk contacts.

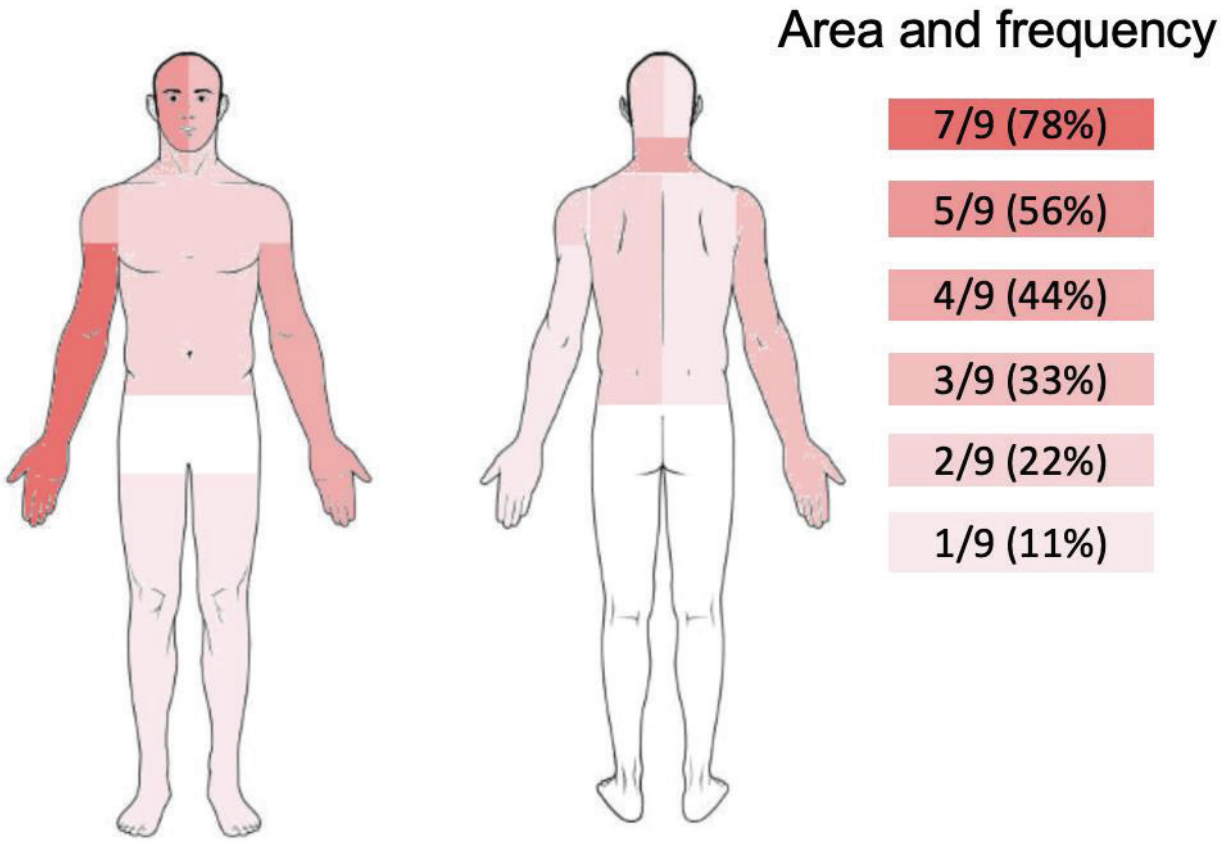
Three of the nine confirmed cases trained at Gym II, where 33 potential risk contacts were identified. Mr G began training on 21 June and developed groups of vesicles on 23 June. Despite the rash, he sparred with Mr I on 24 June. Mr I developed a rash on 6 July, and the next day he participated in a professional fight for financial reasons. Mr H developed vesicles on 28 June and sparred with Mr I; both were trained by the same Thai trainer (**Fig. 3b**).

Gym III's single confirmed case (Mr J) began training on 27 June and sparred with a rash-affected partner. His symptoms emerged on 5 August. He then obtained medication from a nearby pharmacy, but it was ineffective. He was hospitalized 2 days later.

At Gym I, six confirmed and suspected cases and 28 risk contacts were interviewed or assessed for rash, yielding an overall attack rate of 21.4% (6/28), rising to 33.3% (6/18) among non-Thai trainees (**Table 1**). The overall attack rates in Gyms II and III were lower, at 11.5% (3/26) and 2.6% (1/38), respectively, but again the rates were elevated among non-Thai trainees, at 25.0% (3/12) and 4.8% (1/21), respectively.

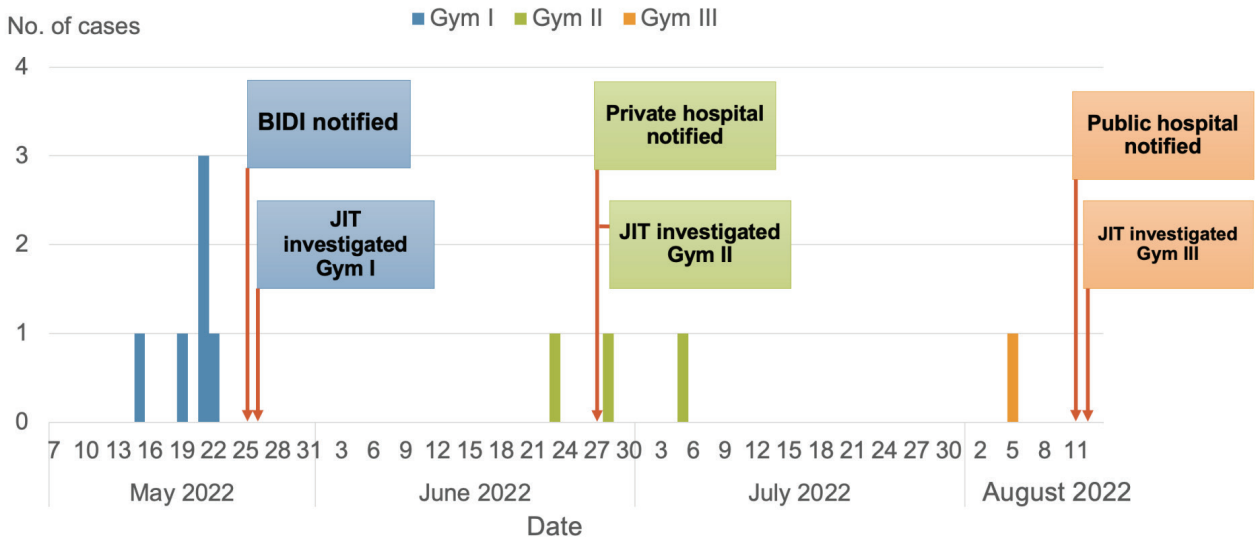
Seven confirmed cases and one trainer were known to have sparred with rash-affected individuals. All trainers and one case shared boxing gloves, and

Fig. 1. **Location of rash among nine confirmed cases of herpes gladiatorum, Phuket, Thailand, May–August 2022**[a]



[a] Colours represent the occurrence of rashes, ranging from the most frequent location (dark red) to the least frequent (pale pink) or to places where rashes were not seen (white).

Fig. 2. **Date of onset of symptoms of herpes gladiatorum at three Thai-boxing gyms, Phuket, May–August 2022 (*N* = 10)**



BIDI: Bamrasnaradura Infectious Diseases Institute; JIT: Joint Investigation Team.

Fig. 3. **Timeline of cases of herpes gladiatorum in (a) Gym I and (b) Gym II, Phuket, Thailand, May–August 2022**

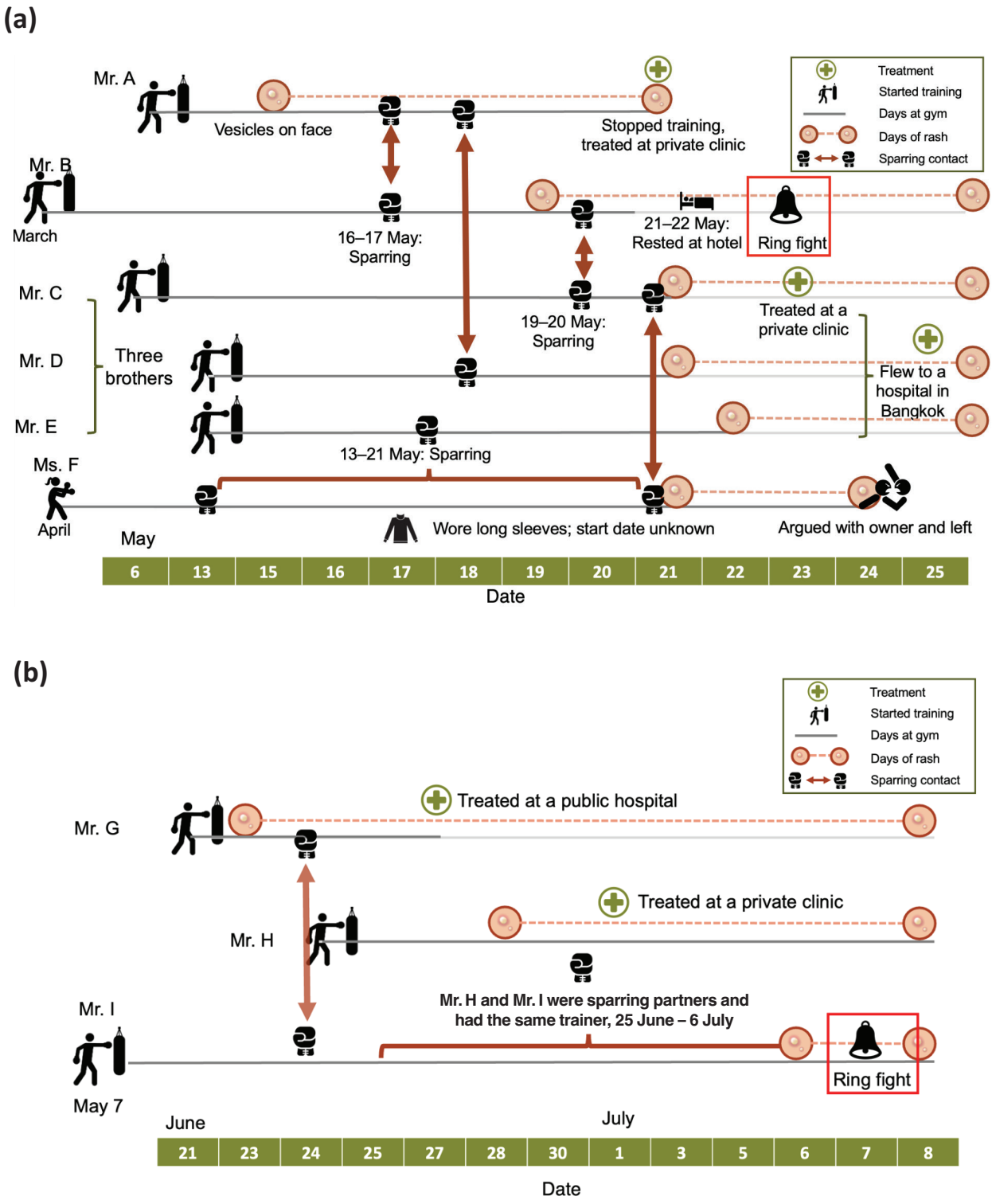


Table 2. **Results of laboratory testing of human specimens and environmental samples collected during an investigation of an outbreak of herpes gladiatorum, Phuket, Thailand, May–August 2022**

Type of specimen	Result[a]					
	HSV-1	HSV-2	HSV IgG or IgM antibody	Monkeypox virus	Varicella–zoster virus	*Treponema pallidum*
Human[b]						
Throat swab	5/5	0/2	–	0/9	0/2	–
Lesion fluid	6/6	0/3	–	0/9	0/3	–
Lesion scrape	7/7	0/5	–	0/8	0/4	0/1
Lesion ulcer	3/3	0/3	–	–	0/3	–
Blood	2/3	0/2	0/3	0/6	0/2	–
Environmental surfaces[c]						
MMA floor mat	0/1	–	–	–	–	–
Fitness floor and equipment	0/1	–	–	–	–	–
Target pad	1/1	–	–	–	–	–
Boxing ring rope and corner	1/1	–	–	–	–	–
Boxing ring floor	1/1	–	–	–	–	–
Uncleaned sand-bag	1/1	–	–	–	–	–
Cleaned sandbag	0/1	–	–	–	–	–
Boxing gloves	0/1	–	–	–	–	–
Water	0/3	–	–	–	–	–

HSV: herpes simplex virus; IgG: immunoglobulin G; IgM: immunoglobulin M; MMA: mixed martial arts.

[a] Results are the number of positive specimens/total number collected. Dashes indicate not applicable or not tested.

[b] Specimens were collected from the nine confirmed cases.

[c] Environmental samples were collected only from Gym II.

everyone used a shared sandbag. Four cases rarely showered before training, one often did and four always did, while among the trainers, one often showered before training and eight always did (data not shown).

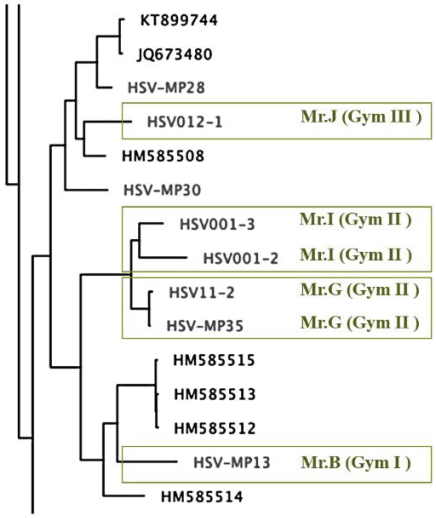
Environmental study

Gym I comprised a large, roofed and open-sided space (40 × 70 m) with two boxing rings and a smaller enclosed room (10 × 20 m). Sanitation was a concern, with subpar toilet facilities and inconsistent cleaning practices. Boxing gloves, pads and other shared equipment, such as sandbags, leg guards and headgear, were often left uncleaned overnight. Some trainers and trainees resided at an adjacent three-storey apartment complex where the water system was unreliable; this meant that they frequently used the gym's bathroom facilities.

Gym II was larger, offering a Thai-boxing gym, an MMA gym and a fitness centre, as well as accommodation for trainers and guests. The Thai-boxing gym measured 20 × 25 m, and had two boxing rings and 30 sandbags, and equipment was stored on shelves. The gym area was disinfected twice daily. Accommodation for trainers consisted of eight rooms, each with a bathroom, but cleaning practices varied widely among occupants. The on-site hotel, which also had eight rooms, was cleaned daily.

Gym III, covering 120 × 50 m, was the largest training facility, providing 12 boxing rings, around 50 sandbags, a full-size MMA cage, an indoor weight room, a yoga studio, training areas for MMA and Brazilian jiu-jitsu, and a fitness area. The facility was well maintained, with 34 workers responsible for daily cleaning. However, the insides of gloves and target pads were not cleaned,

Fig. 4. **Phylogenetic tree of confirmed cases of herpes gladiatorum in Phuket, Thailand, May–August 2022[a]**



Trainee	Gym	Type	Clade	Sequence length[b]
Mr B	I	Lesion swab	II	149 838
Mr G	II	Lesion scrape	II	128 857
Mr G	II	Lesion fluid	II	151 190
Mr I	II	Lesion fluid	II	139 765
Mr I	II	Lesion fluid	II	146 854
Mr J	III	Lesion swab	II	151 669

[a] The tree was constructed based on the analysis of six specimens from four confirmed cases among trainees.
[b] HSV-1 has a genome size of approximately 152 000 base pairs.

despite daily use. The on-site hotel, with 10 rooms, was also cleaned daily by the staff.

Laboratory tests

Specimens were collected from a total of nine suspected cases at all three gyms, while environmental surface samples were obtained only from Gym II. Among the nine confirmed cases, seven were confirmed by positive lesion scrape and three by positive swabs from lesion ulcers. The median Ct value of HSV-1 ranged from 18.7 (IQR: 16.3–26.3) in lesion scrapes to 25.3 (IQR: 24.9–26.9) in throat swabs (data not shown). All samples tested positive for HSV-1; the other pathogens were not detected: HSV-2, mpox virus, varicella–zoster virus and *T. pallidum* (**Table 2**). HSV-1 was found in environmental samples from target pads; a boxing ring floor, and ropes and corners; and an uncleaned sandbag (Ct: 34–36); none were culturable. Water samples from the gym and pool bathrooms showed chlorine levels of 0.25 mg/L; pool water samples contained 2.5 mg chlorine/L.

A phylogenetic tree was constructed using data from six specimens obtained from four confirmed cases (**Fig. 4**). All specimens belonged to Clade II, which is the East Asian strain.[10] The specimens from Mr G and Mr I, who both trained at Gym II, were found to be in the same phylogenetic node.

DISCUSSION

We identified nine confirmed and one suspected case of HSV-1 infection in three Thai-boxing gyms in Phuket. The first confirmed case trained at Gym I but had no known prior contact with persons exhibiting rash symptoms before the onset of his own. Identifying the source of his infection is likely to be challenging, as HSV-1 infection can result in people becoming lifelong, asymptomatic carriers.[7] Seven of the nine cases had a history of training in sparring and clinching with partners who had a rash, implying transmission through skin contact and an epidemiological link.

The attack rate among non-Thai trainees ranged from 4.8% to 33.3%. In contrast, none of the Thai trainers or trainees were found to have HSV infections. Differences in hygiene habits may have contributed to this discrepancy. While four of the nine non-Thai trainees reported infrequently showering before training, nine out of 10 Thai trainers regularly showered before training. Chlorine levels in the bathrooms met national health standards. Furthermore, four of the nine non-Thai trainees continued to train despite exhibiting symptoms, a behaviour that could facilitate the further spread of infection. However, the lack of data about the showering habits of Thai trainees, along with incomplete information about sparring partners, limited our capacity to fully

assess the role of behavioural factors as contributors to higher attack rates in non-Thai trainees.

The distribution of skin rashes and training practices appear to be correlated. The most common areas of the body with a rash were those that made contact during clinching training practices, when trainees use their hands and arms to grasp the back of their opponent's neck (**Supplementary Fig. 1** and **2**). Most rashes were distributed on the right side of the body. This pattern aligns with the fact that most trainees are right-oriented. A similar observation was made in a report of an HG outbreak among wrestlers in the United States.[1]

Two cases with infection confirmed later participated in professional fights while displaying rash symptoms. One of these fighters, who had multiple rashes, had refrained from training in the gym for 2 days before the fight. However, he chose to participate in a fight due to financial constraints. That trainees took part in fights despite having rashes is concerning for two reasons. First, it indicates a lack of enforcement of current Boxing Committee regulations governing pre-fight physical examinations[12] and, second, it underscores the economic pressures that can lead fighters to overlook their health.

All three non-Thai trainees whose blood was tested for HSV-1 antibodies were found to have undetectable antibody levels. This finding is consistent with evidence that suggests the prevalence of HSV-1 antibodies is decreasing in high-income countries.[13,14] In contrast, the Thai trainees generally had lower socioeconomic status, a demographic that has been associated with higher levels of HSV-1 antibodies and a higher degree of immunity to the virus.[15] While not definitive, it does seem that differences in socioeconomic status at both the country and individual levels may form part of the explanation for the higher attack rates observed in non-Thai trainees.

Genomic sequencing revealed the presence of the East Asian strain (Clade II), which is the predominant strain within Asia.[10] This distribution suggests that the confirmed cases might have contracted the infection in Thailand. Notably, specimens from two trainees from Gym II shared the same phylogenetic node. Since these individuals had engaged in close-contact sparring, epidemiological and genomic evidence suggests a direct link between the two cases. However, cases from the three gyms were grouped on distinct branches of the phylogenetic tree; this means that, although all cases are Clade II, there is no compelling evidence to suggest a direct transmission link between the gyms. It is plausible that the virus was introduced to each independently.

In Gym II, HSV-1 was found on a target pad, a boxing ring rope and an uncleaned sandbag. Despite these items being frequently used by trainers and trainees, especially the universally shared target pad, no rashes were reported among the Thai trainers. The high Ct values and non-culturability of the surface specimens suggested the presence of inactive viral remnants, indicating a lower risk of transmission via these surfaces. Sampling the sandbag before and after cleaning with disinfectant revealed an absence of HSV-1 after cleaning, suggesting that the disinfection practices effectively reduced the risk of transmission from this surface. The specimens from the fitness and MMA sections of the gym were all negative for HSV-1, and these areas were not frequently used by the confirmed cases.

Public health actions and recommendations

All confirmed cases were seen by doctors at primary care facilities and advised to rest at their accommodation until their rash resolved. Gym owners and trainers were provided with health education and instructions about how to check their skin for signs of infection. The water system at the apartment adjacent to Gym I was repaired.

Subsequent to the investigation, the joint investigation team issued guidelines that covered infection control measures, including routine disinfection, personal hygiene and screening for skin lesions before competition. Educational materials about atypical rash diseases were distributed to all Thai-boxing gyms and stadiums in Phuket. In addition, a surveillance system was established to monitor atypical rash diseases in Phuket. Other follow-up actions have included recommending that regulators introduce stricter requirements for pre-fight physical examinations, as well as rules that bar trainees with active infections from participating in training and fights. The joint investigation team also provided recommendations to gym owners, trainers and trainees regarding the need to maintain high standards of hygiene in gyms, including ensuring that boxers shower before training sessions

and avoiding sharing equipment, such as boxing gloves and protective gear. Regular cleaning and disinfection of common training areas – such as boxing rings, equipment and mats – were recommended to minimize the risk of surface transmission. Advice was offered to gym owners, staff and trainees to raise awareness about HG and the risk of skin-to-skin infections.

Limitations

The main limitation of this study is that cases of HG were likely missed, resulting in attack rates that are probably underestimates. Investigations were conducted between 4 and 11 days after onset of the first symptoms, possibly due to an initial misdiagnosis of HG as a bacterial skin infection and consequent delayed notifications. In addition, the relatively short duration of training courses (typically 1–2 weeks) and high turnover rates of trainees limited our ability to trace all potential risk contacts. The owners of Gyms I and III did not permit the team to interview the staff or collect samples from facility surfaces, which limited the investigation.

Conclusions

Outbreaks of HG were confirmed in three Phuket Thai-boxing gyms. Non-Thai trainees, all of whom came from high-income countries, had the highest attack rates, possibly because of differences in hygiene practices or lower levels of immunity, or both. Genomic analyses suggested local transmission within Thailand, likely through skin-to-skin contact. This study underscores the need for stricter gym hygiene practices, including regular showering before training and not sharing equipment, as well as stricter regulations for pre-fight screening to reduce the risk of transmission of skin infections.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

This research adhered to the ethical guidelines of the Ministry of Public Health of Thailand. Informed consent was obtained from all participants, and their privacy was rigorously protected throughout the study.

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Genomic sequencing identifies tuberculosis cluster in inner-city Sydney boarding house, Australia, 2022

Eunice Stiboy,[a,b] Standish Rigava,[c] Anthea Katelaris,[a] Vicky Sheppeard,[a,d] Anna Glynn-Robinson,[b] Yasmeen Al-Hindawi,[c] Hazel Goldberg,[e,f] Kerrie Shaw,[g] Vitali Sintchenko,[h,i] Elena Martinez,[h] Taryn Crighton,[h] Ellen Donnan[i] and Anthony Byrne[c,k]

Correspondence to Anthea Katelaris (email: anthea.katelaris@health.nsw.gov.au)

Objective: In 2022, the New South Wales TB Program was notified of genomically clustered *Mycobacterium tuberculosis* isolates from two smear-positive tuberculosis (TB) patients diagnosed 3 months apart. Secondary investigations found they resided in the same Sydney boarding house. The objective of this study was to investigate this cluster and conduct active case finding among contacts.

Methods: We conducted a site visit to understand transmission risk, reviewed patient histories, performed a risk assessment and conducted on-site TB contact screening, including interferon-gamma release assay testing. Long-term residents were also screened via chest X-ray. Past residents were referred to local TB services.

Results: Four residents with TB disease were identified, three of whom were genomically linked to the cluster. The exposure period in the boarding house was determined to be from January 2021 to September 2022. All residents and staff were considered contacts requiring screening. Of the 91 contacts identified, 37 (41%) completed screening, including 20 (22%) who attended the on-site clinic. Among those screened, one resident with TB disease (patient 4) and three residents and one staff member with TB infection were identified.

Discussion: This cluster highlights the role of genomic sequencing in detecting TB transmission. The first three patients were infectious for prolonged periods before diagnosis, likely facilitating transmission in communal areas. In multidwelling buildings with TB exposures, contact screening of all residents may be required when prolonged exposures are found. Strategies to increase screening completion should be further explored.

Australia has one of the world's lowest incidence rates of tuberculosis (TB) and has maintained this status through excellent TB control over the last three decades, despite its proximity to countries with some of the highest incidences in the world.[1] In 2018, Australia reported 1438 TB notifications, representing a rate of 5.8 per 100 000 people, with 89% of people with TB disease (active TB) reported in people who were born overseas.[1] In the 4 years from 2015 to 2018, the most frequently reported countries of birth for people with TB disease diagnosed in Australia were China, India, Nepal, the Philippines and Viet Nam.[1]

In 2022, the rate of TB in New South Wales (NSW) was 6.5 per 100 000 people, with these notifications comprising 41% of the total notifications in Australia.[2] The majority (n = 481, 91%) of the 528 notified people with TB disease were reported as having been born overseas, with the most frequently reported countries of birth being India and Nepal.[2] Notification rates by country of birth

[a] South Eastern Sydney Public Health Unit, New South Wales Health, Sydney, New South Wales, Australia.
[b] National Centre for Epidemiology and Population Health, Australian National University, Canberra, Australian Capital Territory, Australia.
[c] St Vincent's Health Network Sydney, Sydney, New South Wales, Australia.
[d] School of Public Health, University of Sydney, Sydney, New South Wales, Australia.
[e] Consultant in Respiratory and Tuberculosis Medicine, Prince of Wales Hospital, Sydney, New South Wales, Australia.
[f] Sydney Eye Hospital and Royal Prince Alfred Hospital, Sydney, New South Wales, Australia.
[g] South Eastern Sydney Local Health District, New South Wales Health, Sydney, New South Wales, Australia.
[h] New South Wales Mycobacterium Reference Laboratory, Institute of Clinical Pathology and Medical Research, New South Wales Health Pathology, Westmead, New South Wales, Australia.
[i] Sydney Infectious Diseases Institute and School of Medical Sciences, The University of Sydney, Sydney, New South Wales, Australia.
[i] New South Wales Tuberculosis Program, Communicable Diseases Branch, Health Protection New South Wales, Sydney, New South Wales, Australia.
[k] University of New South Wales, Sydney, New South Wales, Australia.
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ranged from 104.7 per 100 000 people for those born in Nepal to 0.9 per 100 000 for those born in Australia.[2]

During 2016, NSW Health introduced routine whole genome sequencing (WGS) for all *Mycobacterium tuberculosis* isolates, which has allowed for the surveillance of circulating strains, detection of genotypic drug susceptibility, differentiation of TB endogenous relapse from exogenous reinfection, inference of transmission pathways and cluster detection to guide public health responses, as well as detection of laboratory cross-contamination.[3,4] Routine WGS has the potential to allow for better targeting of contact tracing interventions and prevention strategies.[4]

With Australia being a country of low incidence for TB, transmission among the general population is expected to be uncommon, with most incident TB generated by reactivation of TB infection (latent TB infection) acquired overseas.[5,6] Local transmission is occasionally recognized among households, but less commonly in health-care facilities or congregate settings such as prisons or facilities for people experiencing homelessness.[6] This can result in delayed identification of transmission, which may have a significant epidemiological and public health impact.[5] A comprehensive understanding of local epidemiology and transmission is crucial in low-incidence countries, as detailed by the World Health Organization's *Framework towards TB elimination in low-incidence countries*.[6] The Framework outlines the requirement for tailored approaches to contain local outbreaks, with rigorous contact investigations and outbreak management being essential elements for control of TB in low-incidence settings.[6]

We report a cluster of TB cases in a boarding house in inner-city Sydney, NSW, which was detected via routine WGS.

METHODS

In November 2022, the South Eastern Sydney Local Health District's Public Health Unit (PHU) and the chest clinic at St Vincent's Hospital (SVH) were notified by the NSW Health TB Program of genomically clustered *M. tuberculosis* isolates from two TB patients with a single nucleotide polymorphism (SNP) difference on routine WGS. At the time of diagnosis of these patients (3 months apart), it was apparent that they shared the same residential address, a boarding house in inner-city Sydney, but were not known to one another or identified during individual patient follow-up when prompted about boarding house exposures.

Epidemiological investigation

Epidemiological investigation was undertaken by the SVH chest clinic in accordance with the NSW TB control and contact management guidelines.[7,8] Each patient was interviewed at the time of diagnosis, and a risk assessment and follow-up of disclosed contacts were undertaken. Following WGS results, the boarding house was contacted and a list of residents who stayed in the boarding house during the exposure period was obtained. An inspection of the boarding house was undertaken to assess transmission risk. The boarding house manager was interviewed to determine the movements of staff and residents within the building.

Boarding house screening

During the preliminary investigation, one of the patients reported that a relative who had previously lived with them in the boarding house had been diagnosed with pulmonary TB after leaving Australia. Investigations into this patient found their symptom onset was approximately April–May 2021, so the potential risk period was updated to begin in January 2021 (to include a margin of uncertainty).

We conducted a risk assessment to determine the screening strategy. We established that all boarding house residents, staff and visitors (who resided there for ≥7 days) warranted contact tracing and screening for TB infection for the period from January 2021 to September 2022 (when the second patient was admitted to hospital).

Laboratory methods

WGS was performed on all culture-positive isolates by the Mycobacterium Reference Laboratory NSW. Briefly, DNA was extracted from pure cultures by an in-house method, and a library constructed using Nextera XT (Illumina, San Diego, CA, United States of America). Sequencing was performed using NextSeq 500 (Illumina) with a 150-bp paired-end protocol using NextSeq 500/550 v2 kits. Analysis was performed as described by Lam et al., after samples passed quality control and were mapped

Table 1. **Summary of TB screening results for all residents and staff (N = 94) of a boarding house, Sydney, NSW, Australia, 2022**

	Current residents	Past residents	Staff	Total	%
TB disease	3	1	0	**4**	**4**
Positive IGRA	3	0	1	**4**	**4**
Negative screening	17	14	1	**32**	**34**
Not screened – unable to contact	0	22	0	**22**	**23**
Not screened – contacted but declined screening	7	1	3	**11**	**12**
Not screened – contacted but did not attend or lost to follow-up	5	16	0	**21**	**22**
Total	**35**	**54**	**5**	**94**	**100**

IGRA: interferon gamma release assay; NSW: New South Wales; TB: tuberculosis.

against the reference genome of *M. tuberculosis* H37RV.[3] Clustering was defined as isolates having ≤12 SNPs.

Contact tracing methods

Identified contacts were screened for TB infection via a single interferon-gamma release assay (IGRA), as it was more than 8 weeks since last exposure to an infectious patient. Residents identified as long-term (defined as living in the boarding house for >2 years) were considered higher risk and offered a chest X-ray (CXR) in addition to IGRA testing.[9,10]

Residents and staff of the boarding house were offered screening at a one-off clinic held at the boarding house. History of TB symptoms, previous TB exposures, TB vaccination, and demographic details, including country of birth and duration of residence or work at the boarding house, were collected. Blood for IGRA testing was collected on-site, and long-term residents were given a referral for a CXR that could be conducted nearby. Current residents and staff who did not attend the on-site clinic were referred to the local chest clinic.

Past residents and staff were contacted by phone and notified of the potential TB risk. After their TB risk history was obtained, they were referred to their nearest chest clinic for screening and follow-up. They were also sent written information on exposure. The NSW TB Program provided support by facilitating the use of a call centre initially set up for COVID-19 contact tracing. Attempts to contact past residents were made in two rounds of calls on different dates, with up to three calls per round. Contact attempts were made via e-mail, if available. Contacts in other health districts in NSW were referred to their local chest clinic, and those living in other states or territories were notified to their jurisdictional TB programme for follow-up.

RESULTS

Including the three people with TB disease identified at the start of the investigations, we identified 94 people living or working in the boarding house during the period of interest from January 2021 to September 2022. No visitors were identified during the exposure period. During the contact investigations, a fourth resident with TB disease (patient 4) was diagnosed during a routine medical exam for an unrelated health condition, bringing the total number of TB patients in the building to four (4%) of 94 people. A summary of the cohort can be found in **Table 1**.

TB disease patients

We identified four people with fully susceptible TB disease in this cluster. Their demographic and clinical characteristics are summarized in **Table 2**.

Patient 1, a female in her 20s, presented to the hospital emergency department in July 2022, with a 4-month history of weakness, weight loss, fever, chills and non-productive cough. Sputum testing was both culture- and smear-positive for TB. She reported that increasing breathlessness and cough meant she had spent considerable time using the shared stairwell to reach her room. While she did report TB exposure during childhood, we considered this diagnosis to be

Table 2. **Summary of patients with TB disease and contacts with positive IGRA who were identified during contact screening of residents of a boarding house, Sydney, NSW, Australia, 2022**

Patients with TB disease				
	Patient 1	**Patient 2**	**Patient 3**	**Patient 4**
Sex	Female	Female	Male	Male
Onset	April 2022	August 2022	~May 2021	Asymptomatic
Symptoms	Cough, 10 weeks Fever Night sweats Weight loss	Cough, unknown duration Iron deficiency Weight loss Nausea, vomiting	Undefined respiratory symptoms	Asymptomatic
Laboratory and imaging results	Sputum microscopy (3+) and culture-positive for AFB Cavities on CXR	Sputum microscopy (2+) and culture-positive for AFB Cavities on CXR	Reported to have cavities on imaging	Bronchoscopy microscopy, PCR and culture positive for AFB Subtle changes on routine CT scan
Diagnosis	July 2022	October 2022	~August 2021 (overseas)	December 2022
Risk factors	Childhood exposure to TB	Diabetes	Childhood exposure to TB	COPD Previous unrelated TB exposure, 2019[a]
Country of birth	Low-incidence country	Low-incidence country	Low-incidence country	Australia
Screened contacts with positive IGRA				
	Contact 1	**Contact 2**	**Contact 3**	**Contact 4**
Sex	Male	Male	Female	Male
Arrival in boarding house	April 2016	March 2014	March 2017	Staff, lives off-site
Symptoms	Asymptomatic	Asymptomatic	Asymptomatic	Asymptomatic
Laboratory results	IGRA-positive CXR-negative	IGRA-positive CXR-negative	IGRA-positive CXR-negative	IGRA-positive CXR-negative
Diagnosis	December 2022	December 2022	December 2022	December 2022
Previous risk factors	N/A	N/A	N/A	Born and lived in high-incidence country
Country of birth	Australia	Australia	Australia	High-incidence country

AFB: acid-fast bacilli; COPD: chronic obstructive pulmonary disorder; CT: computer tomography; CXR: chest X-ray; IGRA: interferon gamma release assay; NSW: New South Wales; N/A: not applicable; PCR: polymerase chain reaction; TB: tuberculosis.

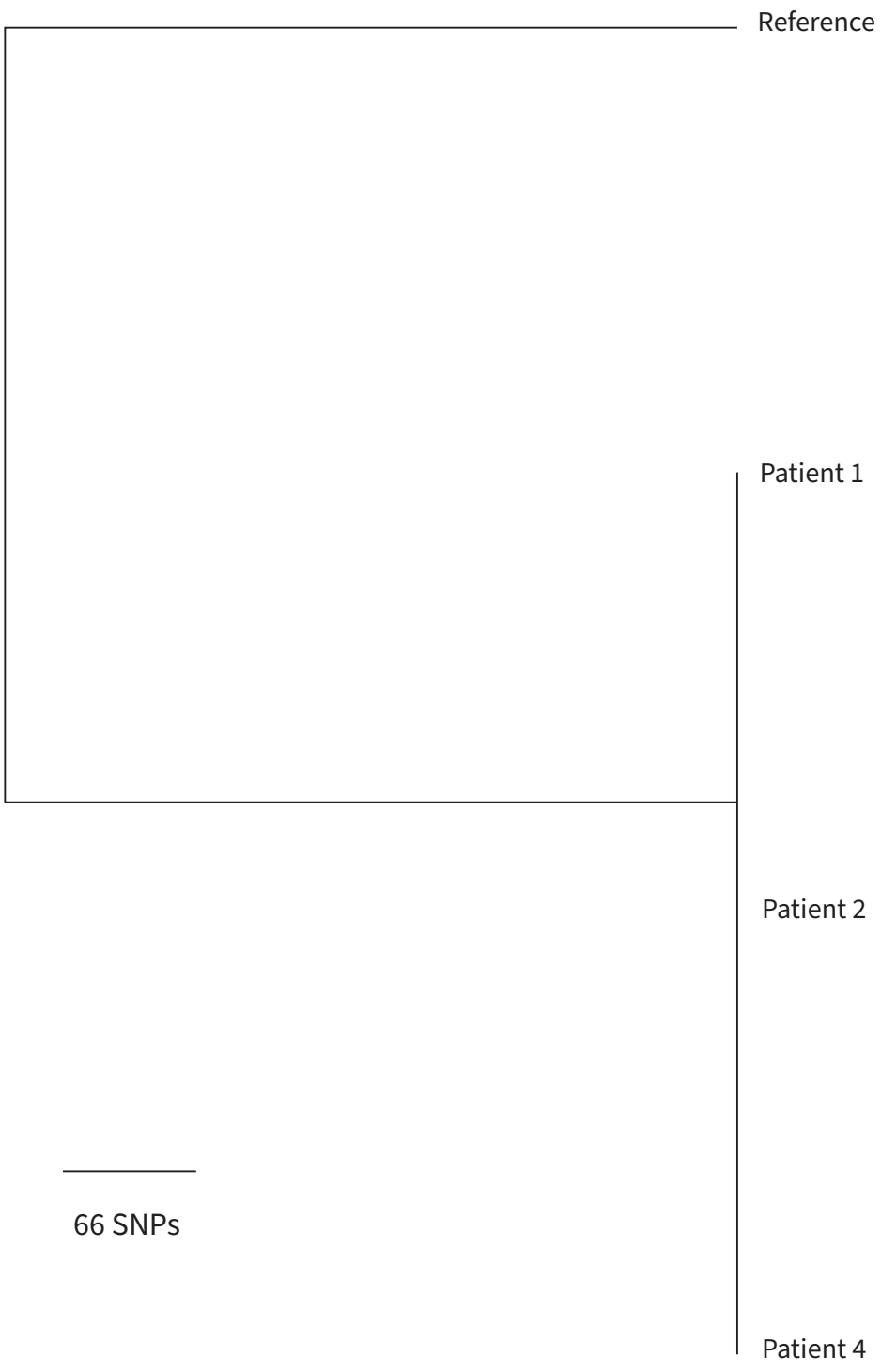
[a] TB infection treated.

from a more recent exposure to her relative, patient 3 (below). During her initial interview, she confirmed her residential address to be the boarding house, but no high-risk contacts were identified (as defined in the NSW TB contact investigation guidelines).[8] As she reported no contact with other residents apart from her relative (patient 3) and did not spend time in the communal areas with other residents, no additional screening was undertaken at the facility.

Patient 2, a female in her 50s, was admitted to hospital in September 2022 with abdominal pain, a 6-week history of weight loss, nausea and vomiting, iron deficiency and a cough of unknown duration. Sputum testing was both culture- and smear-positive for TB. The SVH chest clinic noted the same residential address as patient 1 on diagnosis, but no high-risk contacts were identified or additional screening undertaken at the boarding house at the time of diagnosis, as patient 2 also reported no contact with other residents. Neither patient 1 nor 2 identified one another when initial contact tracing was undertaken.

In the weeks following the diagnosis of patient 2, *M. tuberculosis* isolates from patients 1 and 2 were found to be very closely related. WGS results indicated a single SNP difference between *M. tuberculosis* isolates from patients 1, 2 and 4. An isolate from patient 3 was not

Fig. 1. **Maximum likelihood phylogenetic tree of *M. tuberculosis* genomes sequenced from three patients in a TB cluster in a boarding house, Sydney, NSW, Australia, 2022**



NSW: New South Wales; SNP: single nucleotide polymorphism; TB: tuberculosis.

All isolates belong to the European American lineage. The reference isolate used in mapping is *M. tuberculosis* H37Rv (GenBank Accession number NC. 00962).

available for genomic sequencing. A phylogenetic tree summarizing the genomic sequencing is shown in **Fig. 1**.

The genomic sequencing results of isolates from patients 1 and 2 triggered the cluster investigation. Both patients were re-interviewed, and patient 1 reported that her relative, patient 3, who had previously lived in the boarding house, had returned to their home country 11 months earlier in August 2021, where he was diagnosed with TB disease.

Patient 3, a male in his 20s, was diagnosed with TB outside of Australia. Patient 1 reported that the onset of her relative's cough was approximately April or May 2021 and that a CXR in their home country showed cavities. Patient 3 lived in the boarding house from January 2020 to August 2021. We consider patient 3 the likely source case in this cluster.

Patient 4 was a male in his 70s and was identified as a resident contact in the building. When routine imaging for chronic obstructive pulmonary disorder (COPD) in November 2022 showed subtle changes, he underwent further investigation. TB sputum smear and culture were negative; however, bronchoscopy specimens from December 2022 were positive for acid-fast bacilli on microscopy and culture. WGS showed his *M. tuberculosis* isolate was genomically linked to isolates from patients 1 and 2.

Contact tracing and screening for TB infection

There were 91 residents and staff during the exposure period who required contact screening: 53 (58%) were past residents; 33 (36%) were current residents; and five (5%) were staff. There were 23 (25%) long-term residents in the cohort; duration of stay in the boarding house was unavailable for six (7%) contacts. Of the 91 residents and staff identified, 69 (76%) were contacted on-site, or by phone or e-mail. Twenty-two (24%) were uncontactable.

Of the 69 residents and staff contacted, screening was not completed for 32 (46%) contacts: 21 (30%) were lost to follow-up, including two (10%) considered high-risk; and 11 (16%) declined to be screened, including six (55%) considered high-risk. Of the 37 (54%) contacts who completed screening, 20 (54%) attended the on-site clinic, 13 (35%) attended an NSW Health chest clinic and four (11%) were referred interstate. One (3%) screened contact was diagnosed with TB disease (patient 4). Four (11%) contacts returned a positive IGRA and 32 (87%) returned a negative IGRA. Of the 32 that returned a negative IGRA, two (6%) were symptomatic with a normal CXR and two (6%) were asymptomatic with an abnormal CXR. These four contacts were placed on CXR surveillance. A summary of the contact follow-up is shown in **Fig. 2.**

The four IGRA-positive residents and staff are described in **Table 2**. Three were current long-term residents at the boarding house and were born in Australia with no known prior TB exposure or screening history. They were all asymptomatic and had normal CXRs. One reported going into the room of patient 1 on several occasions while she was unwell. The other two residents had no known direct exposure to any of the patients. The fourth IGRA-positive contact was a staff member who was born in a high-TB burden country, was asymptomatic and had a normal CXR. A timeline of the patients with TB disease and TB infection is summarized in **Fig. 3**.

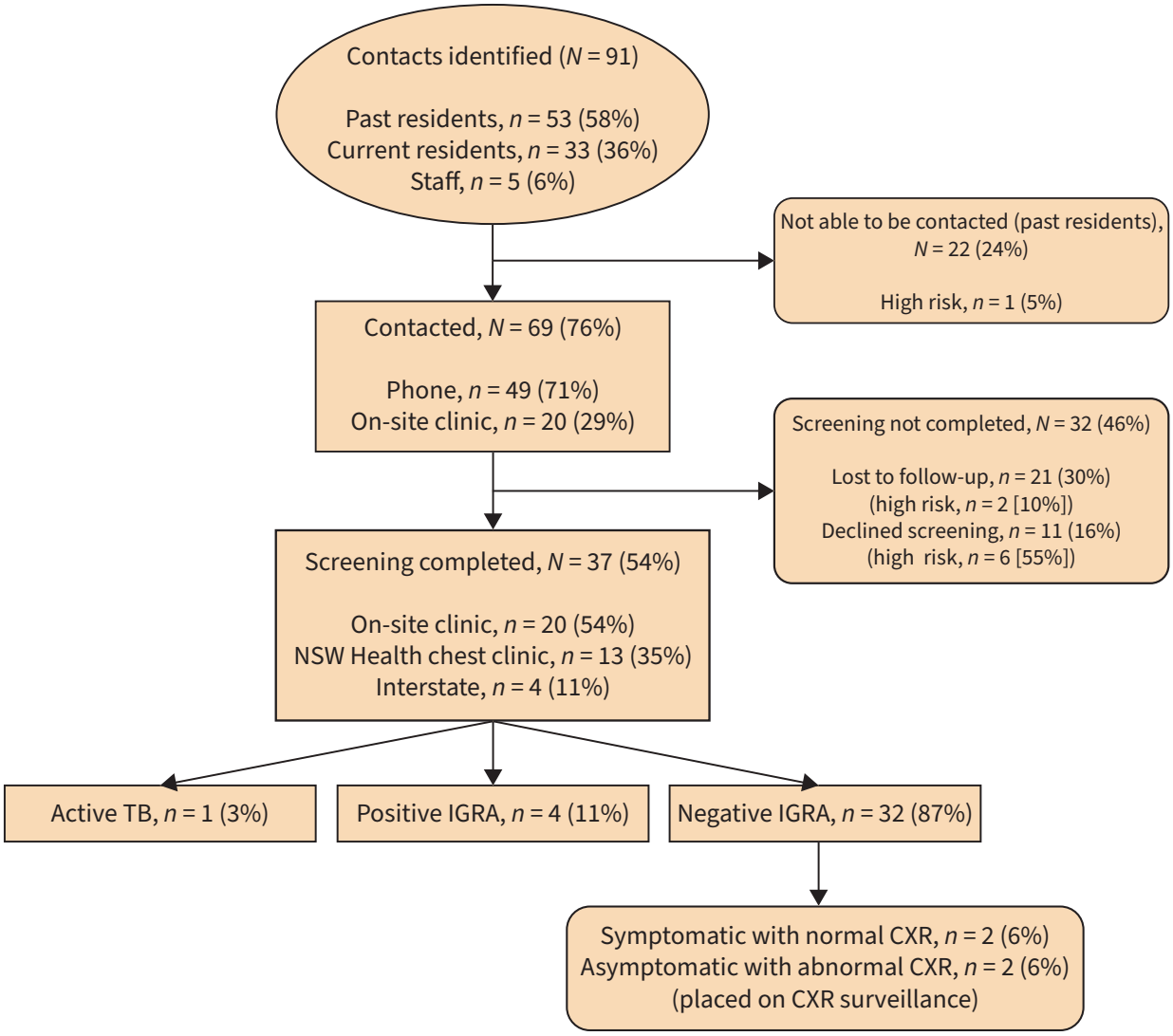
Environmental investigation results

The environmental investigation revealed that the boarding house provided both short- and long-term accommodation options and consisted of five floors including a communal rooftop. The staircase was narrow and had a landing halfway between each floor. Each floor consisted of individual studio apartments (some with private bathrooms), with shared bathrooms and toilets on each floor. The corridors were narrow and poorly ventilated. A communal laundry used by all residents was located on the rooftop. A floorplan was created based on the site visit. A review of the room history revealed that each patient with TB disease had, at some point, while infectious, resided on the same floor as a resident found to have TB infection. Patients 1 and 3 changed apartments multiple times, resulting in movement between floors.

DISCUSSION

We present a cluster of four patients with TB disease and four contacts with TB infection residing within the same boarding house in inner-city Sydney. Patients 1, 2 and 3 were symptomatic for long periods before diagnosis, facilitating transmission, most likely in the communal

Fig. 2. **Flow chart of follow-up for the 91 contacts identified during investigation of a TB cluster in a boarding house, Sydney, NSW, Australia, 2022**



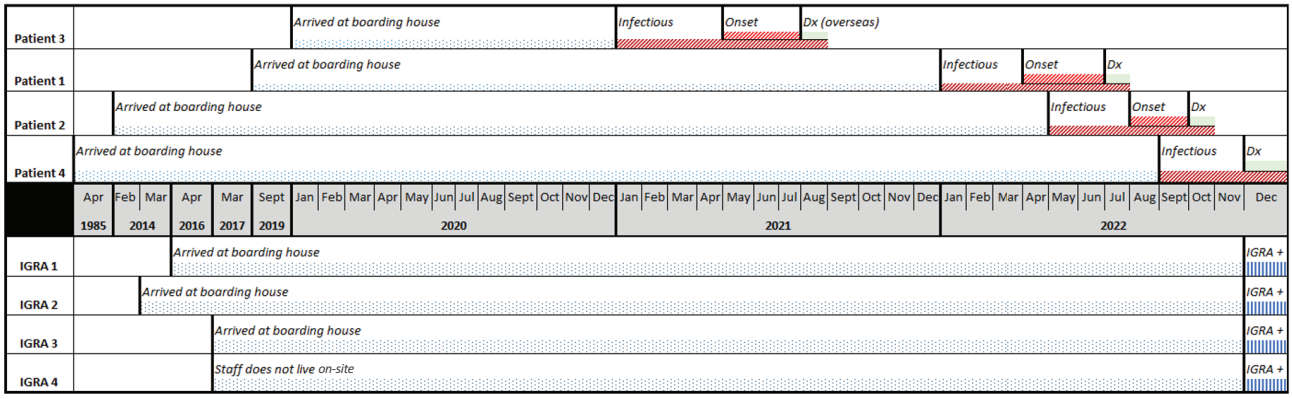
CXR: chest X-ray; IGRA: interferon gamma release assay; NSW: New South Wales; TB: tuberculosis.

areas. The identification of this cluster has highlighted the importance and value of routine genomic sequencing of TB isolates in confirming a TB cluster in a low-incidence setting such as Australia. We have also demonstrated the value of broad contact screening when transmission has occurred in a residential building.

A major strength in the identification of this cluster was the routine application of genomic sequencing, which was able to detect genomic relatedness between patient isolates. This facilitated a prompt and targeted public health investigation and follow-up. Strong collaboration between the local chest clinic, the PHU, the NSW TB Program and pathology service, and the early formation of an outbreak management team were crucial in coordinating the cluster investigation.

The local chest clinic that conducted the patient interviews had established a working relationship with the manager at the boarding house who assisted in facilitating the distribution of risk communications to current residents and establishing the on-site clinic within a week of the investigation commencing. This ensured residents at the boarding house were provided with convenient options for screening, thus enabling our ability to promptly conduct contact follow-up and screening.

Fig. 3. **Timeline of patients with TB disease and TB infection in a boarding house, Sydney, NSW, Australia, 2022**



Dx: diagnosis; IGRA: interferon gamma release assay; NSW: New South Wales; TB: tuberculosis.

While there were many strengths in this investigation, there were also limitations. Despite intensive contact investigation efforts, we were unable to get in touch with a large proportion of the contacts identified and suspect that this may have been due to many of the former temporary residents having returned overseas. Also, we contacted a considerable number of contacts and informed them of their exposure, but they did not complete screening. This means some patients with TB infection and TB disease associated with this cluster may have been missed. Reasons why contacts did not complete screening, and whether this stemmed from health system or patient factors, remain unknown. Further work is required to understand why people do not complete TB screening if we are to increase screening completion rates and maintain a low incidence of TB in Australia. TB testing and treatment are free in public clinics in NSW, irrespective of eligibility for government-funded health care. However, we learned that a few contacts who had attempted screening were deterred from completion when they were referred to private pathology services and asked to pay a fee. In addition, some temporary residents may have been concerned that TB testing would impact immigration visas.[11,12]

Some patients were potentially exposed to several infectious patients, but we were unable to elicit the exact transmission pathways from either WGS (due to the limited SNP differences) or the patient epidemiology. One of the key questions left unanswered from this cluster was the possibility of more than one chain of transmission among the known patients. Understanding how TB was transmitted between the residents would have assisted in providing a more precise risk stratification of people in the facility. Another limitation is that we did not know whether the people with positive IGRA tests were linked to this exposure. Also, three of the four people with positive IGRA tests who had no known history of prior TB exposure cannot be ruled out, as none had received prior screening for TB infection. The fourth patient with TB infection was born in a high-burden country for TB, and we were unable to ascertain if their TB infection was a result of exposure from the boarding house or from their country of birth.

Despite the limitations of our investigation, the value of routine genomic sequencing of *M. tuberculosis* isolates for public health investigations is beneficial and is considered the gold standard for the assessment of transmission and strain relatedness.[13] The identification of closely related strains allows for detection of clusters that may indicate recent transmission and require more intensive public health investigation and follow-up.[13] The usefulness of routine WGS was demonstrated in this investigation, as clustering was only identified after genomic sequencing results were notified, which then expanded our contact and active case finding investigation. As NSW Health Pathology performs sequencing of all TB cultures, there is a possibility of detecting future cases related to this cluster, as all new sequences are compared to historical isolates. Although we were unable to determine the exact transmission pathways of this cluster, when more genomic diversity is present, genomic sequencing has the potential to suggest the direction of transmission.[4] Despite our investigation displaying the utility of routine genomic sequencing for TB programme development and control, results should be interpreted along with epidemiological or clinical information.[4,14]

Outbreaks of TB pose a significant risk to communities and, if left without intervention, they add to the incidence of TB disease and prevalence of TB infection, threatening the maintenance of low TB incidence and increasing the risk of local transmission.[15] Therefore, contact investigation and robust outbreak management are essential elements for TB control in low-incidence settings.[16] When local transmission is suspected, or an outbreak identified, a coordinated and prompt response based on a multidisciplinary approach is required.[17] A risk assessment to prioritize contact follow-up based on the infectiousness of the index patient and intensity of exposure should be considered. TB case investigation forms could be modified to include a question on type of dwelling, thus highlighting higher-risk settings at an early stage of contact identification.[18] This approach to the risk assessment and epidemiological investigation could help optimize resources, which are often stretched in TB programmes.[15]

Conclusion

This cluster has demonstrated the value of routine genomic sequencing to identify clustering and local transmission of TB, leading to targeted public health investigation. We have shown the importance of robust outbreak investigation using a multidisciplinary team, with broad screening and multiple follow-up strategies in this boarding house environment, where residents did not necessarily know each other. Despite intensive contact tracing efforts, we could not complete screening for a substantial proportion of contacts, suggesting that methods to improve TB contact screening completeness should be explored. If countries with low TB incidence are to progress to elimination, investment in routine genomic sequencing and robust public health investigation should be commonplace in TB management guidelines and policies.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

This public health investigation was conducted under the New South Wales Public Health Act 2010 as part of routine public health follow-up; hence, no ethics committee approval was required.

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Noncommunicable disease communication campaigns in the Pacific Region: strengths, challenges and lessons learned from an online survey and poster analysis

Ferdinand Strobel[a] and Solène Bertrand Protat[a]

Correspondence to Ferdinand Strobel (email: strobelf@protonmail.com)

Objective: Noncommunicable diseases impose a significant and growing burden in Pacific island countries and territories, prompting health authorities to implement media-driven communication campaigns as part of their broader strategies to address these diseases and promote health. This analysis was undertaken to assess the strengths and limitations of these campaigns and identify areas for improvement.

Methods: A semi-structured online survey, conducted between August and October 2023, and a visual content analysis were used to examine noncommunicable disease-related communication in Pacific island countries and territories. Distributed through the Pacific Community's Public Health Division focal-point network, the survey was designed to gather qualitative insights on campaign development, evaluation, audience targeting, challenges and success factors. Public health posters from the Pacific Community's archives were analysed using a semiological approach to categorize their enunciative functions.

Results: Thirty-four survey responses from 12 Pacific island countries and territories were received. Tobacco was the top campaign issue, followed by nutrition, physical activity and cancer awareness; social media was the primary communication channel. Most respondents (80%) rated their campaigns as only moderately successful. Actions needed to enhance the impact of communications included better planning, more preliminary research, sustainable funding, skilled staff and greater cross-sector collaboration. Most noncommunicable disease-related posters (70%) served a representational function by portraying reality as designed by public health authorities. While most posters incorporated local cultural elements and vernacular languages, they were predominantly authoritative (46%) or neutral (44%) in tone. Furthermore, 73% were not tailored to specific target groups.

Discussion: Enhancing communication requires greater resourcing, transdisciplinary approaches and stronger audience engagement. More research-informed strategies that integrate behavioural science could improve interventions that promote healthier choices. Achieving this necessitates closer collaboration across disciplines, and stronger partnerships and engagement with communities.

Noncommunicable diseases (NCDs) such as cardiovascular diseases, cancers, diabetes and chronic respiratory diseases are the leading cause of premature death in Pacific island countries and territories (PICTs).[1] More than 80% of adults are overweight or obese, 33% have elevated blood pressure and 40% exhibit high cholesterol.[2] Diabetes prevalence is among the highest globally, with rates exceeding 20% in several nations.[3] The burden of NCDs on families, health-care systems and national economies is such that PICT leaders have described the situation as a "human, social and economic crisis" and a threat to sustainable human development.[4]

PICTs are responding by improving health-care service delivery for screening, management and care.[5] Many are also adopting population-level policy measures recommended by the World Health Organization (WHO) to regulate tobacco and alcohol, and to promote access to nutritious foods and physical activity.[6] However, many health systems remain overwhelmed and under-resourced, and regulatory measures around tobacco control, alcohol

[a] Public Health Division, The Pacific Community, Nouméa, New Caledonia.
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and food are often inconsistently implemented and poorly enforced.[7]

As part of their response to the public health threat posed by NCDs, many PICTs have employed communication campaigns to promote healthier lifestyles. Communication can shape public understanding of NCD risk factors and influence health behaviours. However, to be effective, communication must be culturally sensitive, linguistically appropriate and grounded in local context. The use of multiplatform approaches (for example, mass media, social media, posters, interpersonal communication) can increase message reach and reinforce impact. Evidence suggests that well-designed communication can help shift social norms and influence policy changes towards healthier lifestyles.[8,9]

Several PICTs have implemented media-driven communication initiatives as part of their NCD prevention strategies. Distinct from direct, interpersonal or individual forms of communication, media-driven initiatives are influenced and facilitated by various forms of public media including television, radio, newspaper, and the public display of banners and posters. However, thus far, the evaluation of the effectiveness of NCD-related communication in PICTs has been limited.

The aim of this study, which has been ongoing since 2017, was to inform a Pacific Community (SPC) capacity-building project on NCD prevention communication. Its objectives were to generate insights from practitioners' lived experiences of NCD prevention and to produce actionable recommendations to enhance the design and implementation of future communication efforts. We conducted an online survey as the primary method of data collection and complemented it with a poster analysis as an additional source of evidence.

METHODS

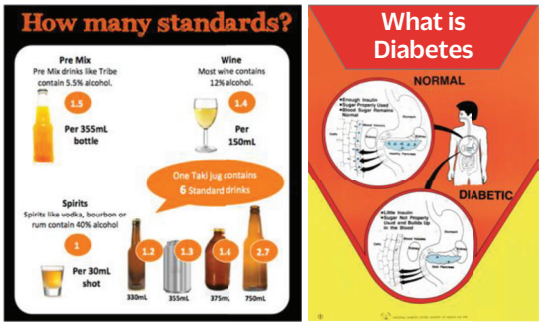
We conducted a semi-structured questionnaire-based online survey using Google Forms, which was distributed to all 22 PICTs through SPC's Public Health Division (PHD) NCD focal-point network. The NCD focal points are officials of health ministries (or departments) who are mandated to liaise with the PHD on all matters related to NCDs. These individuals were contacted by e-mail and asked to pass on the survey link to relevant personnel within their ministries or affiliated entities (for example, health promotion units) that are directly responsible for or involved in NCD prevention communication and health promotion. Participation was voluntary and anonymous; only the identity of participating country or territory was recorded. The independent principal researcher (FS) was the only person who had sight of respondents' e-mail addresses, ensuring that all information was kept confidential.

The questionnaire was specifically created for this study, as there was no existing standardized relevant questionnaire that suited this research. Moreover, since this research was primarily intended to inform a SPC capacity-building project, the design of the questionnaire was guided by the needs of the project rather than the need to ensure comparability with other studies. Our questionnaire design approach was theoretically grounded in the Socio-ecological Model,[10] which enabled us to explore not only message design, but also institutional constraints, community dynamics and broader system-level communication challenges.

The questionnaire comprised 13 questions – eight open-ended and five closed – and aimed to gather qualitative data on campaign development, evaluation, themes, audience targeting, perceptions of success, success factors and challenges (questionnaire available upon request). Respondents were first asked if they were directly involved in a communication campaign on NCDs. They were also invited to provide recommendations for improving NCD-related communication campaigns based on their direct experience. Prior to dissemination, the questionnaire was reviewed by SPC's bilingual public health experts for quality assurance and translation accuracy (French and English versions).

Data analysis identified thematic areas that aligned with the questionnaire. These comprised three broad themes: campaign execution (success and challenge factors); the relevance of messaging for the target audience (specificity, messaging/content adequacy, relevance of channels, cohesiveness and consistency); and engagement for impact (public engagement, accessibility, follow-up services outcome and impact observed). The qualitative data from the questionnaires were manually reviewed and the responses were categorized by theme. Data were entered into Microsoft Excel for descriptive analysis.

Fig. 1. **Examples of posters by enunciative functions**[a]

Representational function: "Represents reality"	Constructive function: "Constructs reality"
Referential posters (examples from Fiji)  – Provides facts – Explanations – Non-abstract, descriptive discourse – Realistic illustration and text – No adjectives, no slogans	**Mythical posters (examples from French Polynesia)**  – Health = happiness = success (or unhealthy = danger) – Slogan – Analogies – Idea of prevention invested with meaning – Exploits major cultural references – Personalized, affirmative exchange
Substantial posters (examples from Fiji and Wallis)  – Aesthetic emotion – Exploits aesthetic values – Reality revealed abruptly – Close-up to highlight the issue (or product) – Construction figures illustrating casue and effect	**Oblique posters (examples from Wallis and Tonga)**  – Produces the meaning to be constructed – Uses the medium (the form that helps produce meaning) – Appeals to the reader's competence – Uses metaphors/imagination Note: in this example the poster "substitues" a well-known alcohol advertisement image, an example of counter-marketing.

[a] Classification method.[11]

Source: Pacific Community archives.

In addition, we analysed undated public health posters that addressed NCDs. They were sourced from SPC's PHD archives and analysed using a matrix to identify source, theme, text presence, figures, language, visual style, cultural references, tone, target and motivator. Posters were categorized by their enunciative functions using Lebel's method for analysing public health images,[11] distinguishing between "representational" and "constructive" functions. Representational function includes referential and substantial compositions, while constructive function includes mythical and oblique compositions. Examples of each type of poster are shown in **Fig. 1**.

RESULTS

Online survey

A total of 34 responses were received from 12 of the 22 PICTs. Of the 34 respondents, 29 (85%) were at that time directly involved in NCD prevention communication campaigns (100% in the Pacific island countries [PICs] and 75% in the territories). Respondents represented New Caledonia (n = 11), French Polynesia (n = 8), and Cook Islands, Fiji, the Republic of the Marshall Islands, the Federated States of Micronesia, Nauru, the Commonwealth of the Northern Mariana Islands,

Palau, Papua New Guinea, Samoa, the Solomon Islands, Tokelau, Tonga, Tuvalu, Vanuatu, and Wallis and Futuna (n = 15, one from each). The over-representation of the territories in the responses is attributed to larger resources, including staff dedicated to NCD communication in the French territories compared with PICs. Tobacco control was the top campaign issue, followed by nutrition and physical activity. Cancer awareness, especially breast cancer through campaigns like Pink October, was also prominent. Diabetes was frequently addressed due to its high prevalence. A campaign on youth screen addiction highlighted digital health issues. Integrated campaigns targeting multiple risk factors were common.

The most used channels were websites/social media, press and radio/television (each employed by over 80% of survey respondents). Around half reported employing posters, community discussions and health-worker interventions. Least used were champions (by 38%), artistic productions and preaching in a religious setting (by less than 30%). Social and mass media were preferred for effective dissemination, but community discussions, one-to-one engagement, school programmes, champions, storytelling, arts, roadshows and workplace initiatives, although less used, were also considered important channels. The value of employing multiple channels was acknowledged.

Overall, 62% of respondents stated that messages were designed for audiences in local languages, and over half reported engaging communication professionals. Preliminary research and message testing were less common (35–38%), and evaluation and follow-up even more so (18–21%). Borrowing standard messages from other countries was a more frequent practice in PICs (64%) than in the territories (20%). Among PIC respondents, only 28% stated that campaigns included preliminary studies, compared with 45% from the territories. The use of communication professionals was also a less common practice in PICs than in the territories (29% vs 70%), a further indication of greater resource availability in the territories. Cultural aspects and beliefs were crucial but often underconsidered. The need to address information access inequalities was identified as a major challenge.

Although performance evaluation is not often current practice, most respondents (82%) agreed that using Knowledge, Attitude, Practice and Behaviour surveys to evaluate campaigns would be beneficial. Two thirds (68%) agreed that specific evaluation methods should be integrated, while 50% supported using general NCD surveys like WHO STEPwise. Other methods, such as monitoring the uptake of NCD prevention services (for example, screening, risk assessment, dietary advice or ending tobacco use) were mentioned by 15% of respondents.

Most respondents rated their campaigns as moderately successful (**Fig. 2**). Responses to open-ended questions providing qualitative information on respondents' perception of success factors and challenges are summarized in **Table 1**, grouped by theme (execution, relevance and engagement). Respondents highlighted that campaign execution success was enhanced by access to adequate funding, trained staff, effective planning, use of evidence-based messaging, consistent strategies (for example, annual campaigns), robust evaluation tools (for example, pre-post measures, behavioural outcomes) and policy support (for example, tobacco taxes). Challenges included limited funding and resources, staffing shortages, geographical barriers, inconsistent leadership and low-quality campaign evaluations. Respondents stressed the importance of approaching NCD communication collaboratively by involving multiple sectors, engaging more with civil society and local/traditional structures, and adopting a consistent approach. Respondents mentioned the need to invest more resources in planning and evaluation, including implementing a testing phase, to understand more precisely what makes the message "work" and "focusing more on how to do this". In relation to planning, respondents also spoke of the need to be "ready for a high level of public response and ensuring that the infrastructure can handle this, especially support or screening services".

Messaging relevance was considered most successful when tailored, relatable and actionable messages were targeted at clearly defined audiences, delivered through multiple channels and repeated consistently. Current challenges arose from inadequate audience research, low community involvement and reliance on non-local materials that lacked cultural relevance.

Respondents agreed that audience engagement is key for impact but said that it was not practiced enough. They stressed the importance of managing public perceptions of health issues, particularly when

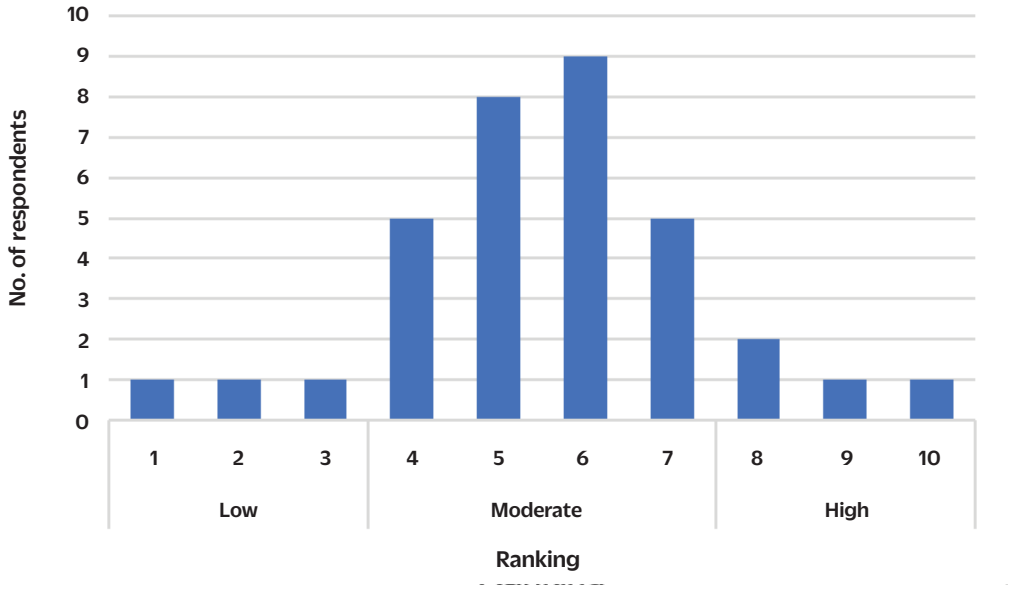
Table 1. **Success and challenge factors of campaigns identified by survey respondents (*N* = 34), August–October 2023**

Dimension	Success factors: When or why campaigns were more successful	Challenges: When or why campaigns were less successful
Campaign execution	**Resourcing** – Adequate funding and resources – Membership of companies/partners include financial participation – Staffing is adequate – Technical and media resource availability (e.g. websites, tools) **Planning** – Well-planned – Staff trained, including communication professionals – Evidence-based messages used – Pre- and post-evaluation surveys undertaken – Strategy consistent (e.g. same date every year) **Accompanying policy measures (campaign reinforces them, informs about them)** – Enforcement activity on legal acts (e.g. tobacco control) – Specific support to policy change, such as raised taxation on tobacco or new regulations (e.g. no smoking in public areas) **Evaluation tools/metrics** – Engagement tallying is automated on social media – Media coverage is monitored – Actions taken within the population are monitored when tools in place	**Funding and capacity** – Funding is rarely adequate in all aspects of campaign design and implementation – Suboptimal technical capacities (research, graphic design, social marketing) **Technological and operational issues** – Inadequate infrastructure, poor communication networks – Outreach made difficult by geography (outer islands) – Staffing (not enough, not qualified enough) – Planning and managing resource and time-intensive campaign elements is a challenge – Absence of well-thought-through overall communication strategy for NCDs **Leadership and political buy-in** – Suboptimal support from leaders and lawmakers – Engagement with leaders and lawmakers difficult when they change constantly **Evaluation** – Not systematic, embedded and specific – Difficult to measure and attribute success in complex system
Relevance of messaging for target audience	**Target specificity** – Target group defined and understood – Messaging adapted to knowledge level of audience – Country-specific and evidence-based information is used in a way the target audiences can relate to **Messaging** – Strong, evidence-based information (explanations, advice, risk informed) – Empowering and positive messages (positive depiction, relatability and inclusiveness of content) – Practical, actionable and non-judgemental – Shock visuals, suggestive images in some cases when most relevant **Message dissemination/retention** – Multimedia dissemination and use of networks (actual and digital) – Communication accompanied by goodies, gifts and games – Marketing element (through partnerships with companies or social marketing) **Cohesiveness and consistency** – Across campaigns and channels – Extensive multichannel distribution – Consistent and persistent campaigning (length/repetition of exposure)	**Ensuring content/context adequacy** – Most difficult in the absence of strong research element on market audience – Community members insufficiently involved in key stages of campaign – Difficulties in ensuring campaign messages are contextually appropriate (due to lack of engagement, research, etc.) – Materials “borrowed” rather than created locally

Dimension	Success factors: When or why campaigns were more successful	Challenges: When or why campaigns were less successful
Engagement for impact	**Community/public engagement** – Multistakeholder engagement (partnerships and collaborations between sectors) – Stakeholder motivation – Issue/s perceived as collective challenges – Consistency of approach and messages across sectors – Involvement of target audience/s in content development (to ensure content is relatable) **Accessibility and follow-up services available** – Availability of supportive services (e.g. quitline for smokers, adequate foods for diabetics, expert advice online or though app services) – Offers of practical resources for self-monitoring (BMI measurement, step counter, apps on mobile phones) **Positive outcome and impact** – Tangible outcomes observed (e.g. weight loss, decrease in smoking rates) – Changes in businesses (healthier options on offer, changes in marketing practices) – Awareness increases among specific groups (youth, parents) – Behaviour changes observed through research (knowledge, attitudes, practices and behaviour studies)	**Unaddressed issues of public perception and awareness that are beyond the realm of the public health sector** – Difficulties engaging specific demographic groups (e.g. "youth, who might ignore messages") – Campaign often too general as a result – Population perceptions of health issues or NCD risk (e.g. "not seeing obesity as an illness", "imported foods more attractive", physical activity "inappropriate for elders or mothers/married women", competing with appealing and well-funded advertising for unhealthy foods, tobacco and alcohol)

BMI: body mass index; NCD: noncommunicable disease.

Fig. 2. **Distribution of survey respondents' success ranking of NCD communication campaigns (*N* = 34), August–October 2023**



NCD: noncommunicable disease.

sources of information abound and when interpretation can differ between communicators and audiences. They recommended collaborating with multiple stakeholders, forming cross-sector partnerships, involving target audiences in message design, and providing accessible follow-up services. They highlighted the catalytic role played by laws and policies (when enforced) to facilitate behaviour change.

Common barriers included tackling what were referred to as "public misconceptions" around health (for example, "obesity not necessarily perceived as an issue"), difficulty engaging specific audiences, such as youth and generic campaigns that overlook community needs, the inability of the public to initiate and sustain behaviours due to their living or social environments (for example, "high cost and seasonality of healthy food options"), and competition from well-funded unhealthy product advertising within the same realm of communication. Respondents recommended collaborating with "well-known individuals in communities" and "leveraging social networks" to overcome such barriers, as well as using more innovative and "daring" approaches to "keep people motivated", including one-to-one and group interactions, both in person and through technology and incentives. Continuous support was considered critical to ensuring long-term engagement and helping individuals "stick to behaviours". Respondents also stressed the need for sustained action within communities, citing the integration of routine health activities into workplaces as a case in point.

Poster analysis

We analysed 284 public health posters addressing a broad range of health issues including reproductive health, hygiene, parasitic infections, and both communicable diseases and NCDs. NCD-related themes accounted for 54% of all posters. Among the NCD-related posters, themes most depicted were diet and nutrition (63%), tobacco (10%) and diabetes (8%).

Most posters featured cultural references specific to the Pacific or individual PICTs, incorporating local characters, traditional patterns and typical landscapes. Approximately one third used vernacular languages, and another third used English. Bilingual and trilingual posters were less common, but the latter were more common than the former due to contributions from Vanuatu and Wallis and Futuna.

Posters primarily adopted authoritative injunctions (46%) or neutral tones (44%), with fewer using enthusiastic, humorous or dramatic tones. Most posters did not include explicit motivators, but when motivators were present, positive motivators were most prevalent: "happiness" was the most common (22–23%), followed by "fear" (11%). The majority of NCD posters were not targeted at specific subpopulations (73%). Specific age groups were targeted in 14% of posters, genders in 10% and ethnic groups in 8%.

The majority of NCD posters (70%) served the representational function, portraying reality as designed by public health authorities (**Fig. 3**). Slightly more than half of the representational NCD posters were referential (providing factual content), and just under half were substantial (using aesthetics to evoke emotions). Most of the remaining posters (29%) were constructive, but within this subset, most were "mythical" posters relying on cultural references to associate health with positive values (**Fig. 1**). NCD posters predominantly used artistic drawings (50–56%) and photographs (27–37%). The choice of style often reflected the intended function, with artistic drawings used for constructive posters and photographs for representational ones.

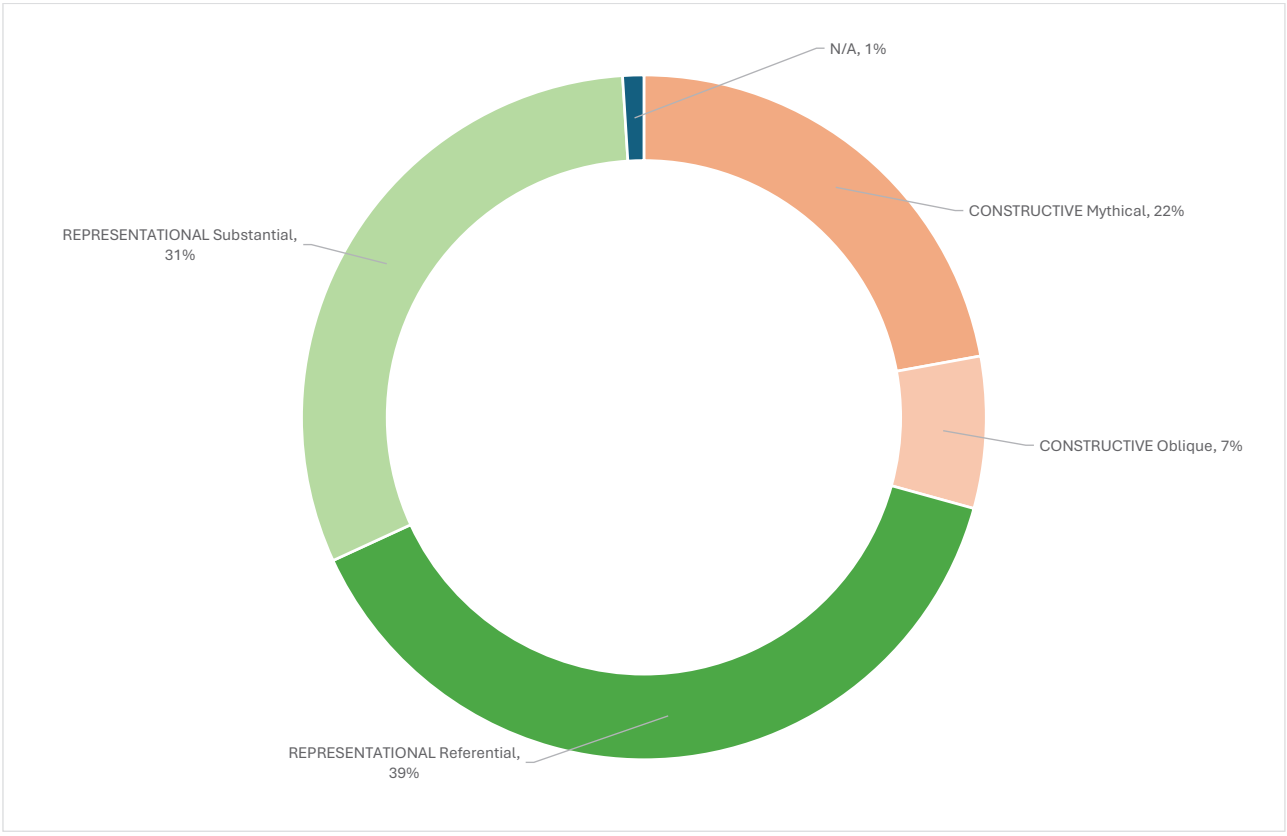
DISCUSSION

Communication campaigns are widely used to raise awareness of preventable diseases and promote healthier behaviours. However, their impact – as most of the respondents in this study acknowledged – is often mixed, in part due to underlying social and structural conditions that shape health-related behaviours, but are less amenable to change.[12]

A central challenge is that messaging alone rarely achieves behaviour change.[13] While cognitive or attitudinal shifts may occur, their translation into lasting behaviours is difficult, especially for NCD risk factors because recommended behaviours often conflict with ingrained, highly socialized habits and require immediate costs without immediate rewards.[14] Nevertheless, there have been some successes in the region. Studies have shown that campaigns can influence social norms when they are rigorously planned and use graphic, emotionally resonant messages and multiple platforms.[15] Anti-smoking campaigns exemplify this. Emotive and evidence-based messaging sustained over time, coupled with legislation and regulation enforcement, can cut across demographics and be effective. As a result, tobacco use has been steadily declining across the region.[16]

Our survey responses reflected a strong belief in the importance of context and the need for messaging to be accompanied by broader measures, such as healthier

Fig. 3. **Distribution of posters[a] by function (*N* = 153)**



N/A: not applicable.

[a] Noncommunicable disease posters only.

food access, fiscal incentives, and infrastructure and regulatory measures. Several respondents mentioned the crucial roles played by workplaces, communities, laws and policies (particularly in the case of tobacco) in sustaining change. While support for a settings approach that addresses "people and places"[13] is strong among PICTs,[17] implementation of supportive measures and policies is often limited in practice[7] and hindered by technical and political barriers.[12,18,19] This perspective was echoed by our respondents who listed suboptimal support from leaders and legislators as a key barrier to successful communication campaigns, along with poor planning, ill-defined communication strategies, limited resources and weak interdisciplinary collaboration.

Consistent with reports in the literature, our respondents noted that few communication campaigns are adequately informed by preliminary research, leading to critical social, cultural, economic and political dynamics being largely ignored. As a result, campaigns tended to overemphasize personal responsibility while neglecting systemic factors.[19–21] Moreover, as several respondents noted, communication campaigns for NCD prevention can easily be overshadowed by the commercial marketing of unhealthy products, which often leverage these social and cultural dynamics more effectively.[11]

Other shortcomings in NCD prevention communication highlighted by our respondents included insufficient cultural competency and insufficient local adaptation. They mentioned, for example, that local concepts of health and traditional medicine are generally not considered and that messages are often "imported from developed countries". Studies have shown that most tailored interventions in the Pacific lacked cultural competency and sustainability.[22] This is exemplified by the case of obesity which, as indicated by respondents, is considered a sign of high social status and thus desirable in many Pacific island societies. Anthropologists have pointed out that obesity in the region has also arisen from complex societal interdependencies that are not addressed let alone understood by standardized media

campaigns.[23,24] In contrast, there is ample evidence that culturally adapted approaches rooted in local traditions and values are more effective and can improve clinical outcomes.[22,25,26] It has also been suggested that Pacific communities' interconnectedness, which in some ways contributes to NCD risk, could also be harnessed to do the opposite, that is, promote healthy behaviours.[20,24]

Perhaps not surprisingly, and as noted by our respondents, digital media are increasingly the favoured communication channels due to their low cost, wide reach and interactivity. The evidence relating to social media's effectiveness is mixed. Some studies showed minimal impact,[27] while others found that in a hyperconnected world, peer influence and community reinforcement can facilitate positive change.[21,28] However, respondents warned of growing inequalities in information access and the new challenges posed by social media health communication, concerns also expressed in the literature. The 2019 measles crisis in Samoa[29] and the COVID-19 pandemic are just two examples of how misinformation and "deliberate obfuscation" can influence opinion and policy-making in public health.[30]

Several respondents highlighted the importance of community engagement as a driver of successful communication. Numerous Pacific scholars have advocated for evidence-based, community-driven efforts to enhance cultural specificity of health promotion messaging and ensure local ownership.[20,26,31] Yet in practice, and as noted by our survey respondents, community involvement in framing messages is often limited due to resource constraints. Respondents also linked poor community engagement to insufficient contextualization of messaging. Health promotion scholars agree[32] and some sociologists argue that NCD prevention messaging has tended to over-rely on individual responsibility, holding individuals "morally accountable" for disease prevention and public health. This has obscured the structural determinants of disease and thus discounted the need for more fundamental change.[18] This past focus on the individual was also evident from the poster analysis.

Theory-driven approaches to intervention design are emerging as a potentially effective way of overcoming recognized health communication challenges. The COM-B model and Behaviour Change Wheel, developed by behavioural epidemiologists and psychologists, offer practical tools to identify behavioural drivers and link them to effective interventions and supporting policies. Such tools have demonstrated potential to improve the design, implementation and consistency of behaviour change strategies across public health domains.[33] Evidence in support of social marketing and "engaging communication" as alternatives to traditional persuasive strategies is also growing.[34–37] Social marketing employs segmentation, competition analysis, positive messaging and audience involvement. Successful interventions like TRUTH and VERB use counter-marketing to challenge harmful products,[38] and adaptations for Pacific islander communities in New Zealand have shown positive outcomes among youth.[39] While a systematic review[40] concluded that even partial use of social marketing elements can yield more positive results than conventional campaigns, social marketing is no panacea. Its full potential remains unrealized in the Pacific, where the complete social marketing mix – product, price, place, promotion – is rarely applied in the public health field.[15]

We acknowledge several limitations in our study. The online survey was conducted using a relatively small number of public health practitioners, which may have affected the generalizability of our findings. The use of a non-standardized questionnaire limited comparability with other studies. The reliance on self-reported data represents another potential source of bias, including the possibility of socially desirable responses. Similarly, the degree of subjectivity in our analysis of public health posters, which was based on semiotic interpretation, did not include data on audience reception. This limited our ability to assess how messages were perceived by target populations. Moreover, while posters are a widely used, longstanding and common communication tool across the region, they represent only one medium among a broader array of strategies. Despite these limitations, we believe our findings remain relevant and meaningful within the scope of our study and may be considered by health authorities in the region seeking to strengthen their NCD prevention communication endeavours.

Conclusion

NCD communication campaigns in the Pacific have heightened awareness and broadened public dialogues about health. However, they appear to have often fallen short in prompting sustained behavioural change. Our study suggests that to enhance their impact, campaigns

must evolve beyond top-down, information-driven tactics and be integrated into broader policy measures and structural reforms. Our findings are consistent with both the current literature and the paradigm that effective communication for NCD prevention should be part of a more systemic approach that addresses living conditions, market trends, cultural nuances and community dynamics, while leveraging interconnectedness and new technologies.

Future efforts should aim to transform the interplay between individuals, their environment and the commercial influences that impact NCD risk vulnerability. The focus should be on four priorities throughout the communication cycle, from design to evaluation: formative research; the systematic evaluation of current health communication practice; cultural tailoring; and community engagement.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

The authors affirm that this research adheres to the highest ethical standards for scientific research and publication. All procedures performed in the study comply with relevant ethical guidelines and institutional policies of SPC.

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Hepatitis B prevalence, knowledge and attitudes among health-care workers and antenatal mothers attending a tertiary hospital in South Tarawa, Kiribati: insights from a 2022 cross-sectional study

Thomas Russell,[a] Vikash Sharma[b] and Alice Lee[c]

Correspondence to Thomas Russell (email: kirirussell@gmail.com)

Objective: Hepatitis B virus infection is hyperendemic in Kiribati (~15% prevalence rate), with vaccination and antiviral treatment being the mainstays of control. Prevalence, knowledge and attitudes among health-care workers and antenatal mothers are poorly understood.

Methods: A cross-sectional, descriptive study was conducted among health-care workers and antenatal mothers at Tungaru Central Hospital on South Tarawa, Kiribati in 2022. The study included hepatitis B virus serology and a bilingual questionnaire.

Results: Fifty-one health-care workers and 49 women receiving antenatal care participated in the study. Most health-care workers (98.0%) had heard of the hepatitis B virus and most (54.9%) exhibited a moderate level of knowledge. Less than half (46.9%) of the antenatal mothers had heard of the hepatitis B virus and most (63.3%) had a low level of knowledge. Most health-care workers (60.8%) and half of antenatal mothers (49.0%) had satisfactory attitudes towards screening, care-seeking and vaccination, and 93.9% approved of adult catch-up vaccination. Hepatitis B virus prevalence was 23.0% (15.7% of health-care workers, 30.6% of antenatal mothers).

Discussion: Extensive educational campaigns for antenatal mothers are needed to enhance awareness of the infection, while training for health-care workers on transmission, prevention and treatment is critical for informing and galvanizing action on hepatitis B virus.

Hepatitis B virus (HBV) was declared a global public health threat in 2016 by the World Health Organization (WHO).[1,2] Global elimination goals have been set with targets to be achieved by 2030.[1] HBV is an enveloped virus that primarily infects the liver and can cause both acute and chronic infection.[3,4] Its transmission is via blood and body fluids, with mother-to-child transmission (MTCT) during delivery being the most common route in developing countries.[4] Other transmission routes are sexual encounters with an infected partner, needle-stick injuries and unsafe infection control practices.[4] WHO estimates that, in 2022, approximately 304 million people lived with chronic HBV infection, with 1.2 million new infections annually and over 1 million deaths attributable to cirrhosis and hepatocellular carcinoma.[4] Treatment is highly effective, with long-term therapy required in the majority of cases.[5] Functional cure is seen in some patients, in which cessation of antiviral treatment is possible.[5] Hence, preventive strategies remain central in achieving elimination with universal provision of timely infant HBV birth-dose vaccination, preferably within 24 hours of birth, followed by three subsequent doses at least 4 weeks apart.[4]

[a] Department of Internal Medicine, Tungaru Central Hospital, Ministry of Health and Medical Services, Tarawa, Kiribati.
[b] School of Medical Sciences, College of Medicine, Nursing and Health Sciences, Fiji National University, Suva, Fiji.
[c] Department of Gastroenterology and Liver Services, Concord Repatriation General Hospital, University of Sydney, Sydney, New South Wales, Australia.
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The WHO Western Pacific Region is home to a quarter of the world's population and bears the highest burden of HBV globally, with a prevalence rate of 7%.[2,6] Pacific island countries and territories (PICTs) have disproportionately higher prevalence rates compared to the more developed counterparts within the Region.[7–10] The majority of deaths in the Region caused by viral hepatitis are attributed to HBV, including deaths from acute hepatitis (72%), liver cancer (53%) and liver cirrhosis (30%), according to 2019 WHO data.[7] Although inroads have been made in addressing the burden of disease among PICTs with several inaugural treatment programmes having been established, access to treatment remains challenging.[6,11,12] There are limited studies published on HBV in PICTs.

The Republic of Kiribati is a large ocean state PICT comprised of 33 coral atolls scattered over an expanse of 3.5 million square kilometres in the Pacific Ocean, making it one of the most remote locations in the world – both internationally and domestically.[13,14] The country has a population of over 135 000 and provides free health care.[15] Its vulnerability to the effects of climate change is well documented, and it is one of three PICTs designated as a least developed country by the United Nations.[16,17] Hyperendemic in Kiribati, HBV has a pooled prevalence rate of 15%,[10,18] doubling regional averages, and compounded by high rates of hepatitis D virus (HDV) coinfection (~41%).[10] A hepatitis B treatment programme in the country has existed since 2018, which supports screening efforts and antiviral treatment using contextualized WHO guidelines that include antenatal mothers (ANMs), and prioritizes health-care worker (HCW) screening, vaccination and access to antiviral therapy, as appropriate.[11]

The Western Pacific Region and its Member States, which includes Kiribati, have followed the WHO Expanded Programme on Immunization (EPI) with the gradual and decisive introduction of vaccination against vaccine-preventable diseases (VPDs) to PICTs, as outlined in the *Regional strategic framework for vaccine-preventable diseases and immunization in the Western Pacific 2021–2030*.[19] Universal vaccination of newborns was introduced in 1989 to Kiribati; however, supplies were often insufficient or inconsistently available.[20] By 1995, a project managed by the United Nations International Children's Fund (UNICEF) and supported by WHO helped to establish a reliable supply chain and technical support for 10 PICTs.[18] To date, the immunization schedule specifies vaccinations at birth and at 6, 10 and 14 weeks of age. The hepatitis B vaccine administered at birth is a monovalent vaccine, while a pentavalent (DTP-Hib-HepB) vaccine is used for the subsequent three doses.[21,22]

The ANMs and HCWs form an important population cohort pivotal to addressing ongoing transmission of HBV. Transmission of HBV at birth via MTCT is the most common route, with preventive measures in place to mitigate its impact, while the nature of a HCW's occupation exposes them to increased risks of contracting as well as transmitting the virus. Existing national guidelines and policies reflect the importance of HBV screening among ANMs and HCWs.[23,24] The latest local data on HBV prevalence of 9% is from a WHO 2002 serosurvey of ANMs that was part of a sexual transmission infection study.[25] To date, there are no official data on the prevalence of HBV among HCWs in Kiribati. Prevention of HBV remains the mainstay of control efforts, and the knowledge and attitudes of HCWs and ANMs are key. Given the lack of existing data on this topic, the objectives of this study were to assess the prevalence, knowledge and attitudes towards HBV among HCWs working on the capital island of South Tarawa and ANMs attending an antenatal clinic at the tertiary-care national referral hospital, Tungaru Central Hospital (TCH).

METHODS

Study design, setting and sample

A cross-sectional study was conducted over a 3-month period from 1 September to 30 November 2022. The study site was TCH located in Nawerewere village on South Tarawa island. A convenience sampling method was employed to recruit as many participants as possible.

Study participants

Participants invited to take part in the study were HCWs aged ≥18 years employed by the Ministry of Health and Medical Services (MHMS) working on South Tarawa and ANMs aged ≥18 years attending the antenatal clinic at TCH. All participants were required to provide written informed consent before their inclusion in the study.

This was facilitated with the provision of a bilingual Participation Information Form, as well as a Withdrawal Form to emphasize the enrolled person's voluntary participation and withdrawal at any point.

HBV serology testing

The purpose of the study was explained to consenting participants. Approximately 2 mL of serum were drawn from the antecubital fossa of each participant and placed in a red cap (dry) tube by laboratory staff at TCH national laboratory. Samples were then tested for the presence of hepatitis B surface antigen (HBsAg) using the pre-qualified Determine™ HBsAg2 immunochromatographic point-of-care (POC) test strips – sensitivity 100%,[26] specificity 99.6–100%[26,27] – according to the manufacturer's instructions. Due to the limited number of POC test strips available during the study period, testing was limited to participants who either had never been tested for HBsAg or whose previous HBsAg test was older than 6 months. Documented HBsAg results that were within 6 months old and confirmed on either their antenatal folders, patient folders or TCH's laboratory register were considered valid. Both cohorts were tested using the Determine™ HBsAg2 POC test strips.

Study survey

Consenting respondents completed a structured survey adapted from Abeje and Azage (2015)[28] in the presence of a researcher who could answer any clarifying questions, either face-to-face or via teleconference. The survey collected data on basic sociodemographic characteristics, as well as knowledge of and attitudes towards HBV and vaccination. The survey, structured in English, was translated into Gilbertese, and was reviewed via discipline specialists to ensure relevance, readability, clarity and comprehensiveness of the knowledge and attitude items. It was subsequently piloted by 10 HCWs and 10 ANMs to assess clarity and usability and consequently modified and finalized.

Scoring knowledge and attitude

The survey contained categorical self-assessment questions (3 levels: yes, no, not sure/I don't know). The "not sure/I don't know" response was used to minimize the guessing effect and was scored as incorrect. Questions covered demographic characteristics, knowledge of HBV status, risks of exposure to HBV, knowledge of HBV infection, knowledge of HBV prevention and control measures, and knowledge of HBV vaccination. There were 14 knowledge-based questions and six attitude-based questions. The total knowledge (range 0–14) and attitude (range 0–6) scores for each respondent were calculated, with 1 point given for a correct response and none for an incorrect one. Data were collected via a hybrid model – either remotely via teleconference calls or in-person at the hepatitis or antenatal clinic at TCH. The mean total knowledge and attitude scores were determined to assess the level of knowledge and attitude based on Bloom's cutoff categories,[29,30] which are divided into three levels based on percentage scores: high-level (80–100%), moderate-level (60–79%) and low-level (<60%). Assessment of attitude was also scored accordingly and categorized as either satisfactory (80–100%), neutral (60–79%) or unsatisfactory (<60%).[29,30]

Data management and analysis

Raw data were deidentified and entered into Microsoft Excel for cleaning and coding, with regular backup files saved and stored in Microsoft's OneDrive file hosting service, which is a personalized, password-protected, secure data storage account accessible only to the primary investigator. Incomplete or missing data were omitted from the final analysis. Descriptive analyses were undertaken, with the mean and standard deviation used to summarize continuous variables, and categorical variables were summarized using frequencies and proportions.

RESULTS

Sociodemographic characteristics of participants

The sociodemographic characteristics of participants are displayed in **Table 1**. A total of 103 individuals consented to participate in the study (51 HCWs, 52 ANMs), with three excluded due to incomplete data entry (1) and being underage (2). The final number for analysis was 100 (51 HCWs, 49 ANMs). Among HCWs, a plurality were in the 18–29-year age category (47.1%), and most were married (54.9%) and had achieved tertiary education (90.2%). Among ANMs, most were

Table 1. **Demographic characteristics and HBV seroprevalence of surveyed health-care workers and antenatal mothers, South Tawara, Kiribati, 2022**

Characteristic	Health-care workers (*N* = 51)		Antenatal mothers (*N* = 49)	
	n	%	*n*	%
Sex				
Female	32	62.7	49	100
Male	19	37.3	–	–
Age group (years)				
18–29	24	47.1	28	57.1
30–39	21	41.2	19	38.8
40–49	4	7.8	2	4.1
≥50	2	3.9	–	–
Partnership status				
Married	28	54.9	33	67.3
De facto	8	15.7	14	28.6
Single	12	23.5	1	2
Divorced	2	3.9	1	2
Widowed	1	2.0	–	–
Education achieved				
Primary	–	–	1	2.0
Secondary	4	7.8	37	75.5
Tertiary	46	90.2	9	18.4
Vocational	1	2.0	2	4.1
Employment				
Unemployed	–	–	28	57.2
Nurse	26	51.0	1	2.0
Medical officer (doctor)	15	29.4	–	–
Laboratory technician	8	15.7	–	–
Health officer	2	3.9	–	–
Physiotherapist	–	–	1	2.0
Government employee	–	–	5	10.2
Self-employed	–	–	2	4.1
Other[a]	–	–	12	24.5
HBV seroprevalence				
HBsAg-positive	8	15.7	15	30.6
HBsAg-negative	43	84.3	34	69.4

HBsAg: hepatitis B surface antigen; HBV: hepatitis B virus.

[a] Employed by nongovernmental entities, private companies or faith-based organizations.

from the same age category as HCWs (57.1%), married (67.3%), unemployed (57.2%) and educated to the secondary level (75.5%).

Prevalence of HBV among participants

The prevalence of HBsAg positivity among all participants was 23.0% (23/100). The HBsAg seropositivity rate was 15.7% (8/51) among HCWs. All positive cases were new cases not previously identified. The HBsAg seropositivity rate among ANMs was 30.6% (15/49). Among seropositive ANMs, 13.3% (2/15) were new cases not previously identified. **Table 1** shows the HBsAg prevalence for each cohort.

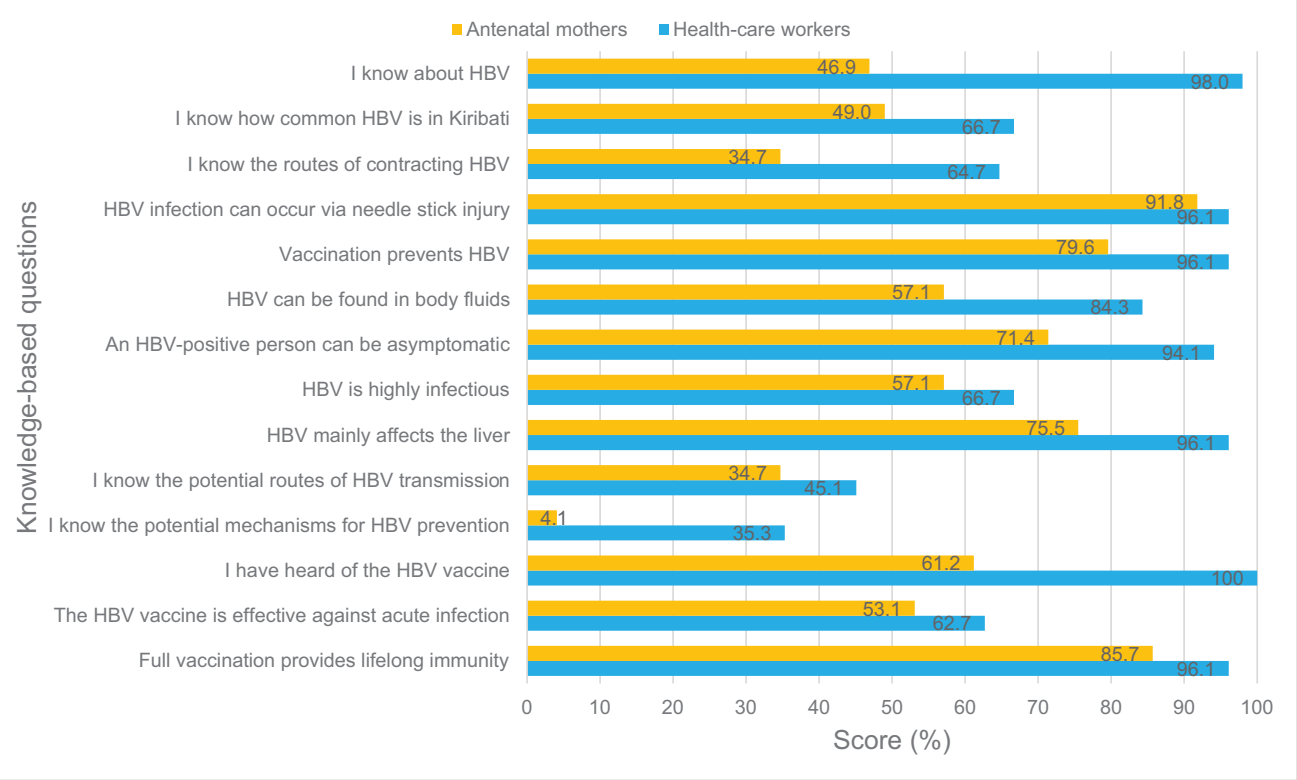
Assessment of HBV knowledge among participants

A total of 14 questions were used to assess participants' knowledge of HBV infection, transmission, prevention and vaccination (**Fig. 1**). Assessment of each cohort's knowledge is presented separately below.

HBV knowledge among health-care workers

The mean knowledge score for HCWs was 11.0 ± 1.6 out of 14 (78.6%), with 37.3% displaying high-level knowledge and 54.9% showing moderate-level knowledge (**Table 2**). The majority of HCWs (98.0%) had heard about

Fig. 1. **Knowledge-based scores about HBV among health-care workers (*N* = 51) and antenatal mothers (*N* = 49), South Tawara, Kiribati, 2022**



HBV: hepatitis B virus.

Table 2. **HBV knowledge and attitude scores of surveyed health-care workers and antenatal mothers, South Tawara, Kiribati, 2022**

Variable	Category (%)	Score	Health-care workers (*N* = 51)			Antenatal mothers (*N* = 49)		
			n	%	Mean ± SD	*n*	%	Mean ± SD
Knowledge	High (80–100)	12–14	19	37.3	11.0 ± 1.6	1	2.0	7.9 ± 1.8
	Moderate (60–79)	9–11	28	54.9		17	34.7	
	Low (<60)	<9	4	7.8		31	63.3	
Attitude	Satisfactory (80–100)	5–6	31	60.8	4.7 ± 0.8	24	49.0	4.0 ± 0.8
	Neutral (60–79)	4	17	33.3		18	36.7	
	Unsatisfactory (<60)	<4	3	5.9		7	14.3	

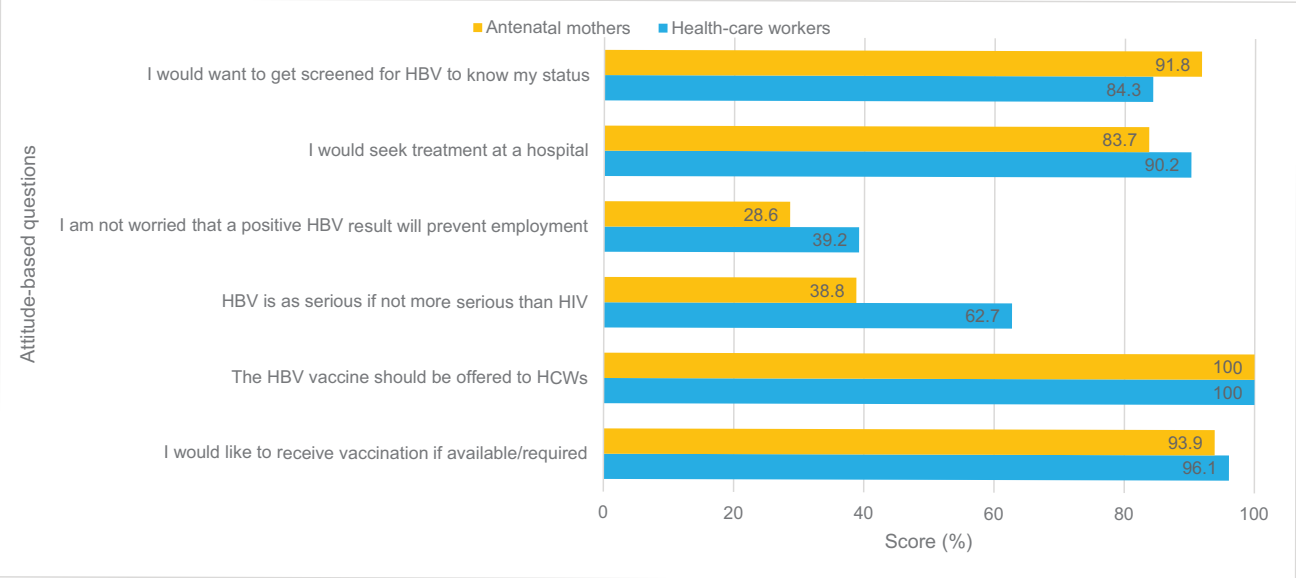
HBV: hepatitis B virus; SD: standard deviation.

HBV. HCWs exhibited moderate-level knowledge of HBV prevalence in Kiribati (66.7%), infectivity of HBV (66.7%) and effectiveness of vaccination for acute infection (62.7%). HCWs had low-level knowledge when asked to correctly identify potential routes of transmission (45.1%) and mechanisms to prevent HBV (35.3%) (**Fig. 1**).

HBV knowledge among antenatal mothers

The mean knowledge score for ANMs was 7.9 ± 1.8 out of 14 (56.4%), with most ANMs (63.3%) showing low-level knowledge (**Table 2**). Less than half of ANMs (46.9%) knew about HBV. ANMs exhibited moderate-level

Fig. 2. **Attitude-based scores about HBV among health-care workers (*N* = 51) and antenatal mothers (*N* = 49), South Tawara, Kiribati, 2022**



HBV: hepatitis B virus; HCW: health-care worker; HIV: human immunodeficiency virus.

knowledge about HBV vaccination (61.2%), infectivity of HBV (57.1%) and that HBV mainly affects the liver (75.5%). ANMs had low-level knowledge concerning routes of HBV transmission (34.7%) and mechanisms to prevent HBV (4.1%) (**Fig. 1**).

Assessment of attitudes of participants towards HBV

A total of six questions were posed to assess the participants' attitudes towards HBV screening, health-seeking behaviour, severity of condition relative to human immunodeficiency virus (HIV) and vaccination (**Fig. 2**). Assessment of each cohort's attitude is presented separately below.

Attitudes of health-care workers towards HBV

The mean attitude score for HCWs was 4.7 ± 0.8 out of 6 (78.3%), with the majority (60.8%) expressing satisfactory attitudes towards HBV (**Table 2**). They had satisfactory attitudes regarding HBV screening (84.3%), health-seeking behaviour (90.2%) and vaccination (96.1%) but neutral attitudes when viewing HBV as a serious condition relative to HIV (62.7%) (**Fig. 2**).

Attitudes of antenatal mothers towards HBV

The mean attitude score for ANMs was 4.0 ± 0.8 out of 6 (66.7%), with almost half of ANMs (49.0%) exhibiting satisfactory attitudes towards HBV (**Table 2**). They had satisfactory attitudes towards HBV screening (91.8%), health-seeking behaviour (83.7%) and vaccination (93.9%), but unsatisfactory attitudes when viewing HBV as a serious condition relative to HIV (38.8%) (**Fig. 2**).

DISCUSSION

The objective of this study was to assess the prevalence of HBV, as well as knowledge and attitudes towards HBV among HCWs and ANMs in a resource-limited country where HBV is hyperendemic. A high prevalence of HBV was found in both cohorts. Additionally, an underwhelming level of knowledge of HBV among HCWs and ANMs was observed, while both cohorts had satisfactory attitudes towards HBV.

The prevalence of HBsAg seropositivity was high in this study. The prevalence rate among HCWs is analogous to national rates. Among ANMs, the prevalence rate is much higher and is likely influenced by the participation of known HBsAg-positive ANMs already attending the hepatitis clinic. The small sample size may have been biased, as HBsAg-positive ANMs on South Tarawa are referred to the hospital's antenatal clinic for care. To the best of our knowledge, our study is the first to assess knowledge of and attitudes towards HBV in a PICT and the first to provide the prevalence rate of HBV among HCWs. This prevalence rate was still higher when

compared to other countries' reported seroprevalence rates such as Cameroon (11%),[3] Ghana (12%),[31] Sudan (12%),[32] Ethiopia (14%),[33] the Solomon Islands (14%)[34] and Viet Nam (15–20%).[35] The study in Cameroon carried out HBsAg testing by using the Monalisa HBsAg ULTRA ELISA kit,[3] whereas the others did not specify and reported on existing national rates. Kiribati's sustained high prevalence rates call for the MHMS to strengthen prevention of MTCT (PMTCT) strategies by ensuring HBV testing is accessible at primary health-care levels and that standardized pathways to link cases to care are followed.

Most of the HCWs exhibited a moderate level of knowledge, comparable to other studies assessing HCWs' knowledge of HBV. In Cameroon, Akazong et al.[3] reported that 85% of HCWs had heard of HBV and 68% were assessed to have adequate knowledge on the route of transmission. In Ghana, Botchway et al.[31] found that 61% of HCWs had adequate knowledge of HBV vaccination, while in Afghanistan, Roien et al.[36] found that the overall knowledge score among HCWs was 87%, although insights into possible reasons for this were not highlighted. Lower scores were described by Hang Pham et al.,[35] who noted a median knowledge score of 60% among HCWs in Viet Nam. Our research on the HCW population did not calculate a sample size, as this was the first study of its kind in the setting and such an estimate proved difficult. However, compared to the samples in the Cameroon and Ghana studies, the level of knowledge displayed was lower than expected. Despite HCWs having heard of HBV and acknowledging how common it is in the country, they exhibited limited additional knowledge. This reflects the need for ongoing awareness, investment and evaluation of HCW training on HBV. It is likely that the lack of focused health awareness and educational activities designed for HCWs contributes to this subpar level of knowledge and should be addressed.

The majority of ANMs showed a low level of knowledge, which has also been described in similar studies with larger sample sizes than ours. In Ghana, a study by Dun-Dery et al.[37] assessing expectant mothers' knowledge about HBV MTCT stated that the general knowledge score was 46% and identified that young age (<35 years), marital status, educational level, employment status and multigravidity were strong predictors of knowledge among the 450 ANMs surveyed. In Saudia Arabia, Al-Essa et al.[38] recruited 422 ANMs via a systematic sampling method and reported that only 47% of participants recognized blood as a transmission route when assessing pregnant women's perceptions and attitudes towards HBV. Furthermore, two separate studies in Ethiopia, with significantly larger sample sizes determined by fixed calculations, reported that 90%[33] and 73%[39] of ANMs had poor knowledge of HBV. Given the impact of hepatitis B in Kiribati as one of the country's most major health-care burdens, the low level of knowledge in our study was unexpected. It likely reflects the gap in awareness – among the general population as well as in hepatitis and antenatal clinics. There has also been inertia due to a lack of access to therapy until recently, with a subdued sense of urgency towards the seriousness of HBV infection. ANMs are a critical target population of PMTCT strategies. Limited knowledge will likely pose barriers towards antiviral treatment of pregnant mothers, leading to lower rates of acceptance and the risk of further transmission.

The majority of HCWs in this study exhibited satisfactory attitudes towards testing, care-seeking and vaccination – the latter being important given the availability of a HCW catch-up vaccination programme. A study conducted in Sudan[32] found that most participants (86%) had a favourable attitude towards HBV prevention measures. In the Cameroon study, only 44% of HCWs had a positive attitude towards HBV, possibly attributable to an inadequate level of knowledge on the route of transmission among the study population.[3] As the treatment programme rolls out in Kiribati, this study will help identify areas that require ongoing attention. HCWs must be supported with ongoing training, ensuring that it is undertaken in a format that is locally appropriate given the various backgrounds and training histories of the health-care workforce. Decentralized care is core to the hepatitis care effort; success is dependent on a trained health force. A multifaceted training programme including face-to-face, remote online, case-based and didactic talks is being rolled out. Ongoing capacity-building is needed, with close monitoring to increase impact.

Most of the ANMs in our study had satisfactory attitudes. This finding is comparable to the study by Gebrecherkos et al.[39] in Ethiopia, in which 86% of ANMs had never been screened for HBV, but 53% of respondents would seek further investigation and treatment if they were diagnosed with HBV – a positive attitude. Another study in Ethiopia by Dagnew et al.[33] found that 60% of ANMs were willing to be screened for HBV and that

their favourable attitudes towards HBV were significantly associated with good monthly income, living in urban areas, achieving good education, being primigravid and having a history of HBV vaccination. In Kiribati, routine antenatal screening for HBsAg is only available for ANMs registered at health facilities on South Tarawa. There is limited access to HBsAg testing elsewhere, and MHMS should urgently address this service gap. Bearing in mind our study findings, perhaps satisfactory attitudes towards HBV screening and prevention reflect a strong inclination among ANMs to support mechanisms that are offered as beneficial and protective for their unborn child. Another reason is that it may reflect general societal acceptance of HBV and rational health recommendations that are meant to preserve life. Further research in this domain will be needed to evaluate these insights.

There were several limitations to this study. First, it covered a cross-section of HCW and ANM participants from an urban setting, where health-care services and information are relatively more accessible than in rural settings, and the results cannot be generalized. Second, the use of a convenience sampling method enabled known HBV patients to participate in the study, which influenced the overall HBsAg prevalence rate of the study. Third, the limited number of HBsAg tests during the study limited the sample size, making the reported seroprevalence rate less predictive of the entire population.

Conclusion

This study reaffirms the previously reported high rates of HBV among ANMs (31%) and provides insights into the possible high rates among HCWs (16%). The demonstrated moderate level of knowledge among HCWs and the low level of knowledge among ANMs illustrate the need for enhanced training, awareness and education on HBV for both cohorts. It is recommended that the national hepatitis programme, supported by the MHMS, conducts training workshops addressing HBV surveillance and management for all HCWs involved in antenatal services on South Tarawa. Training needs to highlight PMTCT, which will upskill HCWs and enhance the necessary theoretical knowledge to allow them to confidently impart knowledge to ANMs. Crucial to this, HBsAg POC testing capacity must be available at all health facilities in the country and be enabled by: trained and motivated staff; the establishment of reliable distribution systems; and the use of secure data recording and reporting systems. Finally, the catch-up HBV vaccination afforded to HCWs should also be provided to all eligible women of child-bearing age, prior to pregnancy. Central to these activities would be sufficient funding for a sustainable programme which, for a resource-constrained setting such as Kiribati, would mean not only the engagement of willing development partners but also strong political will and commitment to the necessary budgetary allocation.

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Conflicts of interest

TR received support from SPC for travel and supplies to conduct data collection. The other authors have no conflicts of interest to declare.

Ethics statement

Approval was obtained from the Kiribati Ministry of Health and Medical Services and from the Fiji National University's College Human Health Research Ethics Committee (CHHREC ID 176.19). Consenting participants were offered pre-test counselling on the risk of venipuncture and implications of a positive test. Post-test counselling and linkage to care were provided for all participants with a positive HBsAg test. Study materials (survey printing, stationery) was funded by SPC.

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Investigation of a measles outbreak in Brondong subdistrict, Lamongan district, Indonesia, 2023

Konstantinus Ua,[a] Lucia Yovita Hendrati,[b] Kornelius Langga Son,[c] Siti Shofiya Novita Sari,[b] Erni Astutik[b] and Sigunawan[d]

Correspondence to Konstantinus Ua (email: uakonstantinus@gmail.com)

Objective: Lamongan District Health Office received a report of a suspected measles outbreak from a community health centre and two hospitals in Brondong subdistrict, Lamongan district, Indonesia. An outbreak investigation team was deployed to verify the diagnosis and to determine the magnitude of the outbreak.

Methods: This retrospective, 1:1 matched case-control study involved 51 suspected or laboratory-confirmed measles cases and 51 controls selected from household contacts and/or playmates within the same village who did not have measles. Data on case characteristics, clinical symptoms, vaccination status, as well as contact and travel histories were collected via interview. Blood specimens were collected from 25 of the children for laboratory confirmation. Univariate and multivariable logistic regression analyses were conducted to investigate risk factors for measles infection.

Results: Nineteen of the 51 measles cases (37.3%) were laboratory-confirmed. All 51 cases exhibited fever and rash (100%) and ranged in age from 11 months to 12 years; 29 (56.9%) were female, and 32 (62.7%) were hospitalized. Over half of the cases occurred in Sedayulawas village (31/51, 60.8%), showing a propagated epidemic pattern. The index case was a 2-year-old girl. Transmission predominantly occurred within the same village through household or playmate contacts. Immunization status and contact history were significantly associated with measles infection.

Discussion: The measles outbreak was attributed to a decline in immunization coverage, particularly for the second dose of the measles-rubella vaccine. This decrease was driven by multiple factors, including the impact of the COVID-19 pandemic, misconceptions related to religious beliefs, and the long interval between the first and second vaccine doses, which contributed to the patients who were lost to follow-up. Collectively, these factors increased the vulnerability of children to measles infection.

Measles is a highly contagious disease, spread by contact with infected nasal or throat fluids (via coughing or sneezing) or by inhaling air exhaled by a person with measles. The virus remains active and contagious in the air or on infected surfaces for up to 2 hours.[1] Measles infection can lead to severe illness, complications and even death.[1] Children aged <5 years face heightened risks of severe complications, with 1–3 out of every 1000 infected children succumbing to respiratory and neurological issues.[2]

Despite the commitment of the Government of Indonesia to eliminate measles and rubella by 2023, cases of measles have increased in recent years. In 2022, a total of 55 measles outbreaks were reported in 12 of the country's 38 provinces and, during the first quarter of 2023, outbreaks were reported in 18 provinces. Indonesia's elimination strategy has focused on achieving uniform 95% measles and rubella vaccine (MR) coverage through immunization campaigns and programme integration.[3] However, according to United Nations Children's Fund (UNICEF) and World Health Organization (WHO) estimations, the persistently low MR immunization coverages of below 95% over the past 3 years (2020–2022), which was further exacerbated by the COVID-19 pandemic, left approximately 0.8 million

[a] Indonesia Field Epidemiology Training Program, Universitas Airlangga, Surabaya, Indonesia.
[b] Epidemiology Division, Department of Epidemiology, Biostatistics, Population and Health Promotion, Faculty of Public Health, Universitas Airlangga, Surabaya, Indonesia.
[c] Indonesia Epidemiological Association, Jakarta, Indonesia.
[d] Lamongan District Health Office, East Java Province, Indonesia.
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and 0.6 million children undervaccinated for MR1 and MR2, respectively,[4,5] thereby jeopardizing the 2023 elimination goal.

Between 1 January and 3 April 2023 alone, a total of 2161 measles cases (848 laboratory-confirmed and 1313 clinically suspected) were reported across Indonesia. One of the affected provinces was East Java, which includes Lamongan district.[6] By the end of 2023, Lamongan district had recorded a total of 253 suspected and confirmed cases across its 18 subdistricts, a significant increase over the 22 recorded cases in 2022.[7]

In early July 2023, Lamongan's district health office (DHO) was notified of six children diagnosed with clinical measles, with symptoms of fever, rash, cough and conjunctivitis, who were treated at either a community health centre or one of two hospitals.[8] This report describes the results of a subsequent comprehensive epidemiological investigation of the measles outbreak in the two affected villages, Brondong and Sedayulawas, in Brondong subdistrict, Lamongan, East Java.

METHODS

Study design and population

A 1:1 matched case-control study design was used as the basis of the investigation. Suspected and confirmed measles cases were identified from Lamongan DHO reports for June and July 2023. Case definitions were based on WHO definitions of suspected and confirmed measles cases:[9]

1. Suspected case: fever and generalized maculopapular (non-vesicular) rash with at least one of the following: cough, coryza or conjunctivitis, in any child aged 0–12 years presenting or residing in Brondong and Sedayulawas villages between June and July 2023.

2. Confirmed case: any suspected case with measles IgM antibodies between June and July 2023.

Matched controls were recruited from the pool of children (aged 0–12 years) who had none of the above-mentioned symptoms and resided in the same household as the cases or were playmates (that is, had contact with a case during June–July 2023).

Data collection

Face-to-face interviews with parents, using a standard questionnaire developed by the Ministry of Health, were conducted to collect data on participants' characteristics, including age, sex, symptoms, rash onset, home address, health-care facilities visited, immunization history, contact history with measles cases within 2 weeks, measles history and travel history. Secondary data sources were also used, including surveillance data, medical records, laboratory results from specimen testing, population and coverage data on MR immunization; these data were obtained from community health centres, local hospitals, the referral laboratory and the Lamongan DHO.

Data analysis

Descriptive analysis was used to describe the characteristics of the study cohort. Univariate analysis using the χ^2 test was performed to calculate crude odds ratios (cORs), 95% confidence intervals (CIs) and *P* values for the association between potential risk factors and measles infection. Risk factor variables that were significant at the level of $P < 0.25$ in univariate analysis were selected for inclusion in a multivariable logistic regression analysis. For adjusted odds ratios (aORs), two-sided *P* values of <0.05 were considered to indicate significance, and 95% CIs were calculated. Variables included in the multivariable analysis were sex, age group, immunization status, contact history and travel history.

All statistical analyses were performed using STATA version 16.

RESULTS

Descriptive epidemiology

A total of 51 measles cases were identified during the study period. Of the 25 serum samples collected, 19 were positive for measles IgM. The age of cases ranged from 11 months to 12 years (median 5 years). The age group with the highest age-specific attack rate was children aged 5–9 years (24, 47.1%), followed by those aged <5 years (21, 41.2%). Females accounted for 29 cases (56.9%). Thirty-two cases (62.7%) were hospitalized, while the remaining 19 cases (37.3%) sought outpatient

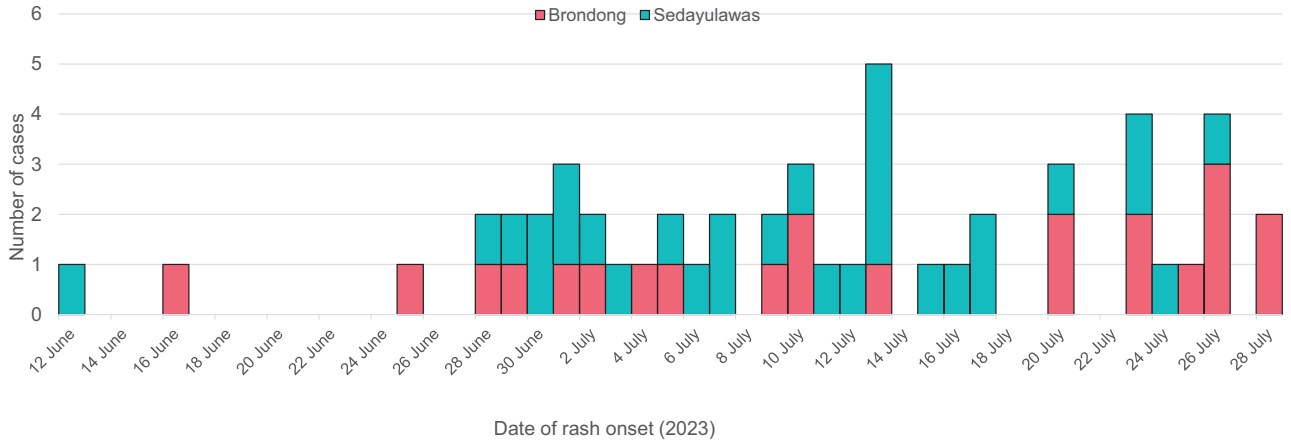
Table 1. **Characteristics of measles cases and controls, Brondong and Sedayulawas villages, Lamongan district, East Java, Indonesia, 2023 (*N* = 102)**

Characteristic	Cases (*n* = 51)		Controls (*n* = 51)	
	n	%	*n*	%
Sex				
Male	22	43.1	29	56.9
Female	29	56.9	22	43.1
Age group, years				
0–4	21	41.2	10	19.6
5–9	24	47.1	30	58.8
10–14	6	11.8	11	21.6
Symptoms				
Fever	51	100.0	NA	NA
Rash	51	100.0	NA	NA
Cough	49	96.1	NA	NA
Cold	9	17.6	NA	NA
Red eyes	23	45.1	NA	NA
Diarrhoea	4	7.8	NA	NA
Other	5	9.8	NA	NA
Place of residence				
Sedayulawas village	31	60.8	34	66.7
Brondong village	20	39.2	17	33.3
Case type				
Suspected	26	51.0	NA	NA
Laboratory confirmation (+)	19	37.3	NA	NA
Laboratory test (-)	6	11.8	NA	NA
Place of care				
Hospital	32	62.7	NA	NA
Health centre	19	37.3	NA	NA
MR immunization status				
Received one or two doses	3	5.9	11	21.6
Not immunized	48	94.1	40	78.4
Contact history				
Yes	35	68.6	22	43.1
No	16	31.4	29	56.9
Travel history				
Yes	33	64.7	21	41.2
No	18	35.3	30	58.8

MR: measles-rubella vaccine; NA: not applicable.

treatment at a health centre. In addition to fever and rash, most cases had cough (96.1%) and nearly half had conjunctivitis (45.1%). Over half of cases were from Sedayulawas village (31, 60.8%). Only three of the 51 cases (5.9%) had received at least one dose of measles vaccine. In terms of contact history, 35 cases (68.6%) had contact history with measles cases within 2 weeks of rash onset, while 18 cases (35.3%) had no record

Fig. 1. **Epidemic curve of a measles outbreak in Brondong and Sedayulawas villages, Lamongan district, East Java, Indonesia, 2023 (*N* = 51)**



Source: Lamongan District Health Office.

of travelling to areas with measles outbreak status (**Table 1**).

The earliest date of rash onset among the 51 measles cases was 12 June 2023. Cases steadily increased from 1 July onwards, peaked around 13 July, and ended on 28 July (**Fig. 1**). The index case was a 2-year-old girl from Sedayulawas village.

Measles risk factors

Multivariable analysis indicated that only immunization status and contact history were significantly associated ($P < 0.05$) with measles infection. Not being immunized increased the odds of measles more than 4-fold (aOR: 4.7, 95% CI: 1.1–20.6) relative to being immunized. Contact with a measles case in the preceding 2 weeks increased the odds of measles by a factor of 3.6 (aOR: 3.6, 95% CI: 1.4–8.9) relative to no contact (**Table 2**).

Vaccination coverage

In Lamongan district, average coverage of MR1 (at 9 months) declined from 95.1% in 2019 to 86.2% during the COVID-19 pandemic, while coverage of MR2 (at 18 months) fell from a pre-pandemic level of 73.1% to 65.4%.[8] Brondong village experienced a similar drop in MR1 coverage, by 12.2% from 100.7% in 2020 to 88.5% in 2022. However, relative to the district average, MR2 coverage rates were much lower, only reaching 8.7%, 6.4% and 10.1% in 2020, 2021 and 2022, respectively. The situation was similar in Sedayulawas village, where MR1 coverage decreased by 8.8% from 101.1% to 92.3% over the same 3-year period, with coverage below 95% in both 2021 and 2022. MR2 coverage also remained low, at less than 10% between 2020 and 2022 (8.2%, 6.1% and 6.3%, respectively).[7]

DISCUSSION

Despite Indonesia's efforts to eliminate measles by 2023, new cases continue to emerge in various regions, including Lamongan district. Outbreaks have occurred in Brondong and Sedayulawas villages, where there is a high proportion of unvaccinated children. Vaccination coverage data for the district as a whole and for the affected villages show marked declines in MR vaccine coverage from pre-pandemic levels, especially for MR2. Studies conducted in other countries have shown that low MR vaccine coverage and weak immunization delivery systems can lead to the buildup of groups of children susceptible to measles, increasing the risk of outbreaks.[10–12]

This study showed a strong association between vaccination history and measles infection and underscores the importance of maintaining MR immunization coverage levels above 95%, particularly among children aged <5 years who are most vulnerable to the effects of measles. This effort is essential in establishing herd immunity and preventing measles outbreaks.[11,12]

Table 2. **Logistic regression analysis of factors associated with measles outbreak, Brondong, Lamongan, East Java, Indonesia, 2023**

Risk factor	Measles status		Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)
	Cases	Controls		
Sex				
Male	22	29	Ref	Ref
Female	29	22	1.7 (0.7–4.1)	1.9 (0.8–4.7)
Age group, years				
0–4	21	10	3.85 (0.1–39.6)	2.3 (0.5–8.8)
5–9	24	30	0.9 (0.1–14.5)	1.0 (0.3–3.5)
10–14	6	11	Ref	Ref
Immunization status				
Received one or two doses	3	11	Ref	Ref
Not immunized	48	40	4.4 (1.1–25.8)	**4.7 (1.1–20.6)**
Contact history				
No	16	29	Ref	Ref
Yes	35	22	2.9 (1.2–7.0)	**3.6 (1.4–8.9)**
Travel history				
No	18	30	Ref	Ref
Yes	33	21	2.6 (1.1–6.3)	2.3 (0.9–5.5)

Bold values are statistically significant ($P < 0.05$).

This study also showed an association between contact history and measles infection, which is consistent with that of other studies, including one conducted in Ethiopia.[13] In contrast, we found no association between travel history and measles infection. This suggests that transmission occurred predominantly within the Brondong subdistrict, presumably via household contacts, with few imported cases. A previous outbreak investigation conducted in two villages in Jiken subdistrict, Blora Regency, reached a similar conclusion.[14]

The recent COVID-19 pandemic has undoubtedly contributed to the recent decline in MR vaccination coverage and increase in measles cases in many parts of Indonesia. However, there are also likely other underlying factors that have contributed to low MR vaccine coverage, especially of MR2, that are more unique to Indonesia. These include parents or caregivers refusing to vaccinate their children due to religious beliefs (concerns that vaccines are not halal or are haram) and parental concerns about the incidence of adverse events following immunization. The high drop-out rate between the first and second dose is particularly concerning. Anecdotal evidence suggests that this may be due in part to a belief that one dose is sufficient, and the second dose is not necessary. Another reason might be recent changes to the MR2 immunization schedule. The latter has been cited as a factor in an Ethiopian study where changes to the measles vaccine schedule, which were more inconvenient for caregivers, were ranked alongside displacement as one of the most frequently cited reasons for not bringing children to clinics for their second measles vaccination (24.1%).[15] This was closely followed by misunderstandings about immunization. This study also reported very high drop-out rates among Muslim study participants (77.1%).

Our study had several limitations. Controls were limited to household contacts and playmates within the same villages. In addition, some cases may have been missed due to time constraints and limited opportunities for specimen collection. The immunization status of respondents was based on verbal reports. Most participants did not have vaccination cards or proof of vaccination, so recall bias was unavoidable. Despite these limitations, this outbreak investigation confirmed the

pattern of measles infection in young children (0–9 years) and the clustering of measles cases in the same village.

Based on this investigation, it is recommended that outbreak response immunization be conducted to prevent measles transmission in the affected areas. In addition, MR1 and MR2 immunization coverage should be increased in those areas and districts where coverage is currently below the national target (<95%). In addition, a strategy is needed to reduce MR2 dropout by conducting home visits and improving the provision of MR vaccines through better coordination between health services and the community. At the national level, cross-sectoral coordination should be improved to increase and maintain vaccination coverage across Indonesia. In addition, health promotion should be conducted to increase public understanding and awareness of measles immunization, and the early detection and monitoring of suspected measles cases should be conducted through active and passive surveillance.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

This outbreak investigation in Brondong subdistrict was conducted as part of an urgent public health response under the authority of the DHO and in line with national outbreak response regulations. As the activity was a non-research public health activity carried out during an emergency, formal ethical clearance was not sought. All procedures adhered to standard outbreak investigation protocols, and only data essential for case verification and public health action were collected. Verbal consent was obtained from parents or guardians prior to interviews, while all clinical assessments (including specimen collection and testing) were conducted by authorized health facilities and laboratories under the supervision of the DHO. For this report, only secondary data from laboratory results were used, and no personal information or identifiers were included in either the analysis or this publication. Throughout the investigation, the team upheld the ethical principles of confidentiality, beneficence and respect for individuals, while prioritizing rapid control of the outbreak to protect affected communities.

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Investigation of an outbreak of typhoid fever in a rural district of East Malaysia, 2019

Jun Fai Yap,[a,b] Ester Barnad[b] and Muhammad Jikal[b]

Correspondence to Muhammad Jikal (email: drmj@moh.gov.my)

Objective: Following the notification of two cases of typhoid fever to the Kudat District Health Office in February 2019, an investigation was conducted in a rural district in Sabah, East Malaysia, to determine the extent, characteristics and source of the outbreak.

Methods: This epidemiological study used both active and passive case detection. Environmental samples were taken from water sources, food-handling areas and waste sites, and were analysed for the presence of *Salmonella enterica* serotype Typhi as part of the standard protocol during an announced typhoid fever outbreak. Clinical specimens underwent culture and sensitivity testing, with samples that were positive for *S.* Typhi analysed using pulsed-field gel electrophoresis to determine clonal relationships.

Results: A total of 35 cases of typhoid fever were identified during 3 months. Twenty-eight cases (80.0%) occurred among Sabah's indigenous ethnic groups, and 12 of these (34.3%) occurred in people aged 7–17 years. The index case, along with six other cases, had a history of consuming smashed fried chicken from a local restaurant. Analysis revealed three clonal clusters of *S.* Typhi isolates, with a dominant pattern found in 18 cases, which included the index case and a food handler from the implicated restaurant. Two paediatric patients experienced a relapse after initial treatment with intravenous antibiotics.

Discussion: The source of the outbreak was most likely the infected restaurant worker who prepared chicken without wearing gloves; transmission most likely occurred through contaminated food or surfaces. Immediate steps to control the outbreak included chlorinating water wells, disinfecting waste disposal areas and promptly vaccinating all food handlers, including those working in street food settings. Recommendations for preventing future outbreaks include strengthening surveillance systems for acute gastroenteritis, conducting education campaigns to promote safe food-handling practices and implementing measures to improve vaccination coverage against typhoid fever among food handlers.

Typhoid fever is a bacterial infection primarily caused by *Salmonella enterica* serotype Typhi (*S.* Typhi). The incubation period is 1–2 weeks on average, following which gastrointestinal symptoms may develop, comprising abdominal distension, diffuse abdominal pain, and constipation and/or diarrhoea. Other systemic symptoms include prolonged fever, general malaise, skin rash (i.e. rose spots), myalgia and headache.[1] If left untreated, severe organ-specific complications may ensue, including delirium, stupor, myocarditis, intestinal haemorrhage, bowel perforation or overwhelming sepsis leading to death.[2]

A proportion of typhoid fever survivors become asymptomatic, chronic carriers of *S.* Typhi. The presence of asymptomatic carriers presents challenges for controlling this disease. Carriers can shed the bacteria in their stool for many years, often harbouring the *S.* Typhi bacterium on cholesterol gallstones in their gallbladder, where they form biofilms.[3] Bacteria excreted by carriers can exhibit multiple genetic variations, which further complicates source-tracing and the control of outbreaks.[4]

Humans are the sole reservoir of *S.* Typhi, and transmission occurs primarily through contaminated food or water. Although antimicrobial treatments have significantly reduced the incidence of typhoid fever in high-income countries, it remains endemic in lower-income countries, including in Fiji, Malaysia and the Philippines in the World Health Organization's Western Pacific Region.[5–7] In these countries, ongoing challenges with sanitation, health-care access and public health infrastructure contribute to the endemicity of this communicable disease.

[a] Institute for Public Health, National Institutes of Health, Ministry of Health, Selangor, Malaysia.
[b] Sabah State Health Department, Ministry of Health, Kota Kinabalu, Sabah, Malaysia.
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In Malaysia, typhoid fever is a notifiable disease under the Prevention and Control of Infectious Diseases Act 1988 and must be reported to the nearest district health office within 7 days of a diagnosis. The annual incidence typically lies in the range of 10.2–17.9 cases per 100 000 population;[8] however, higher rates have consistently been recorded in East Malaysia, particularly in Sabah, a state located on the island of Borneo, where the disease remains endemic. Although in Malaysia typhoid fever is predominantly a rural disease associated with reduced access to clean water and sanitation, outbreaks have occurred in rapidly urbanizing areas, where cases have been linked to street food vendors and restaurants with poor hygiene.[8]

On 17 February 2019, the Kudat District Health Office, in a largely rural district of Sabah state, received notification of a laboratory-confirmed case of typhoid fever. When a food handler also tested positive for *S.* Typhi at the district hospital on 21 February 2019, the national criteria for declaring an outbreak were met. This led to the declaration of the first outbreak of typhoid fever in Kudat on 22 February 2019.

The aim of this report was to describe the outbreak investigation, the sociodemographic characteristics of the cases and the control measures that were implemented once the source of the outbreak had been identified. Based on these findings, the report also recommends actions to mitigate future outbreaks.

METHODS

Study design

This is a descriptive epidemiological study of individuals with confirmed *S.* Typhi infections.

Epidemiological investigation

A case was defined as any individual presenting with fever or constitutional symptoms in the Kudat district of Sabah state between 20 January and 27 May 2019 (when the outbreak was declared over) and whose clinical specimen tested positive for *S.* Typhi. A carrier was defined as an asymptomatic contact whose clinical specimen tested positive for the bacterium.[9]

Both active and passive case-finding strategies were employed. Active case detection involved interviewing all identified cases and their close contacts using a standardized form for food- and waterborne diseases. Close contacts, regardless of whether they were symptomatic, provided samples for stool culture and testing for *S.* Typhi. Passive case detection was conducted by alerting health facilities in the district to report any suspected cases of typhoid fever. Furthermore, all health clinics and nearby hospitals were issued directives to collect stool samples from all cases of acute gastroenteritis presenting with fever. These cases were notified to the Kudat District Health Office and referred for early disease control measures. Patients experiencing severe diarrhoea were also referred for treatment and hospital admission.

Questionnaires were used to collect data about the date of symptom onset, sociodemographic characteristics (e.g. sex, age, ethnicity, occupation, citizenship) and potential sources of exposure. Cases were also asked about their food consumption during the 2 weeks before symptom onset, particularly whether they ate at restaurants.

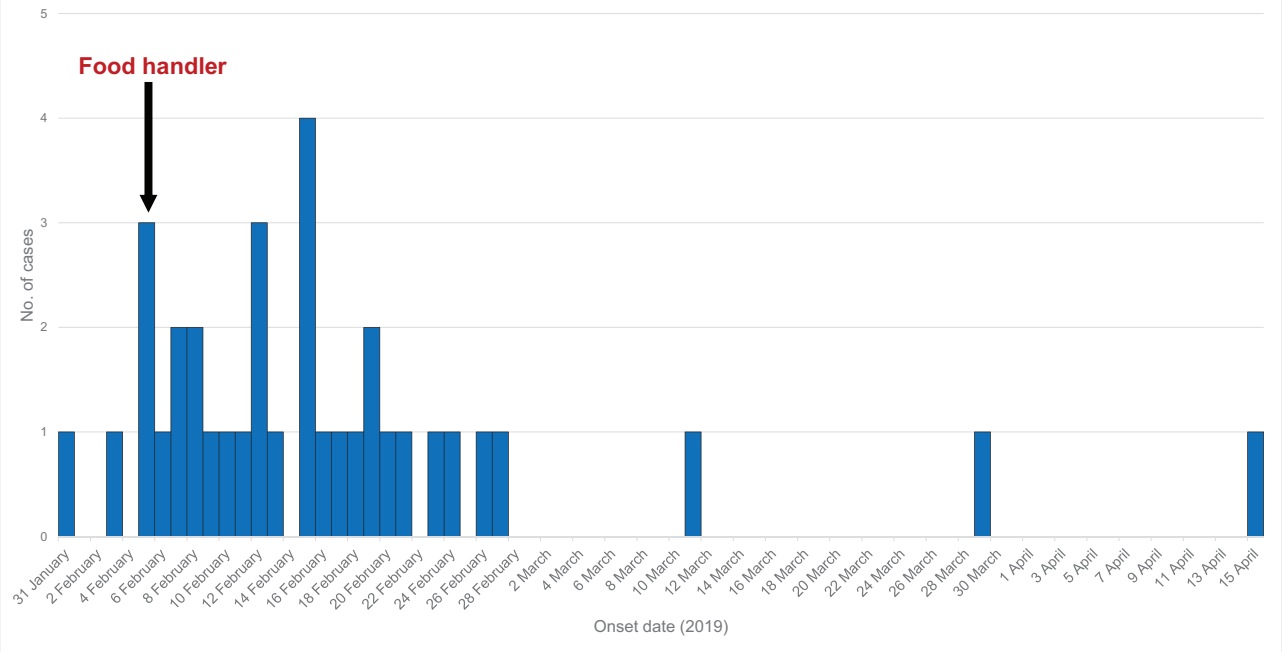
Environmental investigation

Combined inspections, comprising licensing visits (to verify restaurant licence status, as irregular renewals may compromise cleanliness standards), environmental sampling and food standards assessments, were carried out in various locations within the district. Water and food samples were collected from water sources, food-handling areas of restaurants and waste disposal sites and tested for the presence of *S.* Typhi at the Public Health Laboratory in the Kota Kinabalu district of Sabah state. All restaurants with an identified epidemiological link to the confirmed cases were included in the environmental investigation. This targeted approach ensured comprehensive assessment of all potential sources of foodborne infection and helped to trace possible routes of transmission within the affected areas.

Laboratory investigation

Culture and sensitivity tests for *S. enterica* Typhi and other *Salmonella* species were conducted on clinical specimens (i.e. blood or stool samples) from suspected cases and close contacts of confirmed cases identified through active case detection, as well as from symptomatic individuals presenting at health facilities. Isolation of *S.* Typhi from a clinical sample was considered a positive

Fig. 1. **Epidemic curve of an outbreak of typhoid fever, Kudat district, Sabah, East Malaysia, February–April 2019 (*N* = 35)**



laboratory result. Positive samples were then subjected to pulsed-field gel electrophoresis (PFGE) to identify clonal relationships between the isolates.

RESULTS

A total of 35 cases of typhoid were notified in Kudat district. Symptom onset of the index case was on 31 January 2019; the last date of symptom onset was 15 April 2019 (**Fig. 1**). The index case was a 3-year-old boy who was seen at Kudat Hospital on 13 February 2019 with fever, diarrhoea, abdominal pain, vomiting and loss of appetite. A blood culture sample subsequently tested positive for *S.* Typhi, and the result was reported to the Kudat District Health Office on 17 February 2019.

During the course of the 3-month outbreak, a total of 67 cases of acute gastroenteritis were reported to the Kudat District Health Office, including the index case. Clinical samples were obtained from all 67 cases, of which 35 (52.2%) were confirmed as positive for *S.* Typhi. All cases but one (97.1%) were Malaysian citizens, and 28 (80.0%) were of Sabah native ethnicity (**Table 1**). Around half of the confirmed cases were male (18, 51.4%). Children aged 0–17 years accounted for a large proportion of the cases (17, 48.6%). All 35 cases presented with fever and were hospitalized, but none died. Other common symptoms included diarrhoea (17, 48.6%), abdominal pain (16, 45.7%), dizziness (15, 42.9%) and malaise (15, 42.9%).

All 35 cases were identified through passive case detection. Cases were found in 20 villages in this rural district. Notably, the index case and six other cases had a history of consuming smashed fried chicken (or *ayam penyet*) at a local restaurant, where a food handler worked who tested positive on 21 February 2019, suggesting a common source of enteric infection.

A total of 202 environmental swab samples and 98 food samples were collected, mainly from restaurants, but all were negative for the bacterium. One food sample, identified as mud clams (or *lokan*), tested positive for *S.* Oslo. Of the 113 water samples tested, none were positive for *S.* Typhi. However, environmental inspections revealed poor sanitation practices and inadequate handwashing facilities in restaurants, including the one where the food handler who tested positive for *S.* Typhi worked.

Altogether, three (0.5%) of the 584 stool samples collected from close contacts of the 35 confirmed cases

Table 1. **Characteristics of 35 laboratory-confirmed cases of *Salmonella enterica* serotype Typhi infection, Kudat district, Sabah, East Malaysia, February–April 2019**

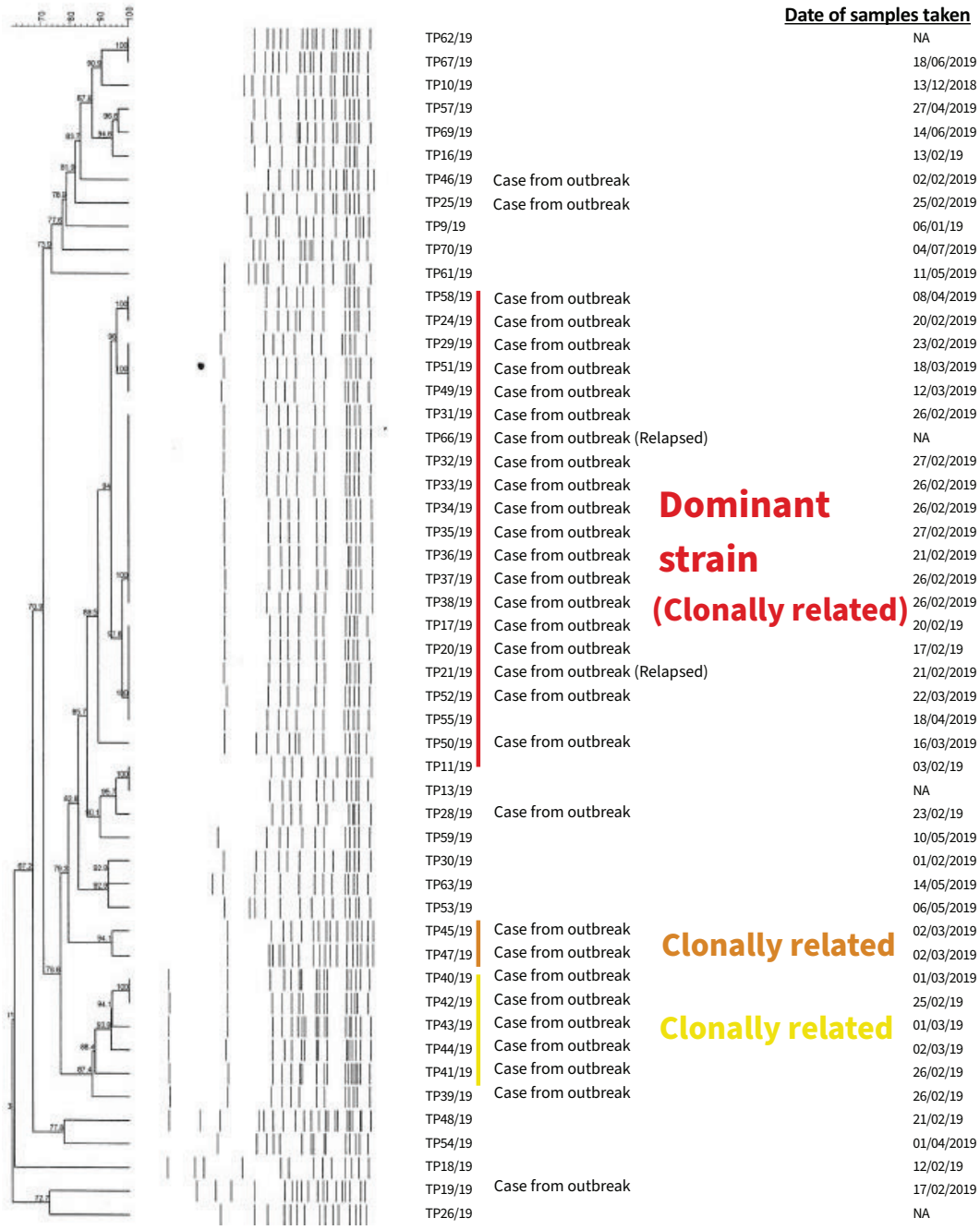
Characteristic (no. of respondents)	No.	%
Sex (*n* = 35)		
Male	18	51.4
Female	17	48.6
Age group (years) (*n* = 35)		
0–6	5	14.3
7–12	5	14.3
13–17	7	20.0
18–55	16	45.7
>55	2	5.7
Ethnicity (*n* = 35)		
Sabah native	28	80.0
Chinese	3	8.6
Iban	2	5.7
Malay	1	2.9
Jawa Banjar	1	2.9
Occupation (*n* = 30)		
Student	13	43.3
Employed	14	46.7
Unemployed	3	10.0
Citizenship (*n* = 35)		
Malaysian	34	97.1
Non-Malaysian	1	2.9
Symptoms (*n* = 35)		
Fever		
Yes	35	100.0
No	0	0
Diarrhoea		
Yes	17	48.6
No	18	51.4
Abdominal pain		
Yes	16	45.7
No	19	54.3
Dizziness		
Yes	15	42.9
No	20	57.1
Malaise		
Yes	15	42.9
No	20	57.1
Loss of appetite		
Yes	14	40.0
No	21	60.0
Nausea or vomiting		
Yes	13	37.1
No	22	62.9
Headache		
Yes	11	31.4
No	24	68.6

were positive for *S.* Typhi (data not shown). Eleven (1.9%) samples were positive for other *Salmonella* serotypes, including *S.* Weltevreden (*n* = 8), *S.* Lexington (*n* = 2) and *S.* Ohio (*n* = 1) (data not shown). Despite being asymptomatic, the three contacts who tested positive for *S.* Typhi were treated with a full course of intravenous antibiotics in hospital.

The PFGE dendrogram was based on 31 samples from 30 cases; it identified three clonal clusters of *S.* Typhi isolates, with a dominant pattern found in 19 samples (**Fig. 2**). Notably, the PFGE analysis showed that the food handler and 17 other cases, including the index case and one relapsed case, shared the same dominant clonal pattern, confirming community-wide transmission. The other two clonal patterns were observed in two and five cases. The presence of three distinct PFGE patterns suggests that the outbreak may have resulted either from multiple sources or from the introduction of three different strains at different times. However, the predominance of a single PFGE pattern indicates a primary source of infection, likely contributing to the sustained transmission within the community, and it strengthens the hypothesis implicating the restaurant where the food handler worked as a likely source of the outbreak.

Having pinpointed restaurants as potential sources of typhoid fever, control measures were promptly implemented in all affected localities. These included chlorinating domestic water wells, disinfecting public toilets and sanitizing waste disposal areas. These measures were supported by health education campaigns that highlighted the importance of safe food-handling practices, directed at both restaurant workers and the general public. Steps were also taken to strengthen surveillance for and reporting of cases of acute gastroenteritis in local health facilities to improve early detection of suspected cases of typhoid fever.

Fig. 2. **Dendrogram of pulsed-field gel electrophoresis results for *Salmonella enterica* serotype Typhi, representing 31 samples from 30 cases, Kudat district, Sabah, East Malaysia, 2019**



NA: not available.

Post-investigation follow-up actions included implementing regular inspections of food establishments to ensure compliance with advice regarding sanitation and hygiene practices. A formal re-evaluation of the food establishments, conducted by public health officers, revealed improvements in cleanliness. Typhoid vaccinations were strictly mandated for all food handlers, including street food vendors. Education programmes continued, focusing on raising community awareness about typhoid fever and emphasizing the importance of consuming safe food and water. After approximately 3 months, on 27 May 2019, the typhoid outbreak was officially declared over.

Two paediatric patients relapsed after their initial antibiotic treatment and hospital discharge. The first

relapsed case was the index case, who was initially treated with intravenous ampicillin (25 mg/kg four times per day for at least 1 week), but was readmitted within 3 months with abdominal pain; a repeat blood culture confirmed *S.* Typhi infection, and he was treated with intravenous ceftriaxone (100 mg/kg twice per day for 2 weeks). The second relapsed case was a 13-year-old boy originally treated with intravenous ceftriaxone (2 g/day for 2 weeks). He too was readmitted within 3 months with fever, diarrhoea and abdominal pain. The presence of *S.* Typhi was confirmed via repeat blood culture, and he was treated with intravenous meropenem (1 g three times per day for 1 week) before being discharged for a second time. Unfortunately, due to limited resources, blood samples were not analysed further to compare the first and second infections.

DISCUSSION

Our investigation suggested a common-source outbreak, most likely epidemiologically linked to an infected food handler working at a restaurant where the index case and a further six cases reported consuming smashed fried chicken. However, the sources of the additional 27 cases remain unclear. The food handler performed kitchen tasks, such as preparing and cutting chicken, but did not wear gloves while performing these tasks. This raises the possibility that the transmission of *S.* Typhi bacteria could have occurred through direct contact with contaminated food items or surfaces. The lack of proper handwashing facilities in the restaurant may have facilitated the spread of the pathogen.

This study observed a high prevalence of cases in school-aged children, a trend that aligns with findings from other countries.[10] A high prevalence of typhoid fever in children has been attributed to the fact that good hygiene habits, such as handwashing, are often less well developed in children. In this setting, malnutrition, which weakens the immune system and is common among children aged 5–12 years in Sabah, was likely an additional contributory factor.[11]

Practising good personal hygiene and regular handwashing and maintaining proper sanitation reduces the transmission of *S.* Typhi among vulnerable populations. Other important control measures include ensuring strict adherence to contact protocols in clinical settings; such precautions should remain in place throughout a patient's hospitalization, until three consecutive stool cultures, taken 48 hours after completing antibiotic therapy, are confirmed as negative.[9]

Vaccination against typhoid, which can prevent at least 50% of cases of typhoid fever during the first 2 years after vaccination, also has a role to play,[12] and in Malaysia it is mandatory for all food handlers. Regulations for food handlers also stipulate that they should have booster doses every 3 years, as immunity is not lifelong. However, the lack of surveillance data and lack of enforcement of vaccination record-keeping means that it is difficult to assess compliance with regulations, but it is likely that coverage of typhoid vaccine is suboptimal among food handlers in restaurant settings. Moreover, vaccination is not 100% effective and ideally should be complemented by other nonpharmacological measures to prevent transmission.[13]

The relapses in two paediatric patients after their initial antibiotic treatment could have been due to either re-exposure to contaminated sources after their discharge from hospital or an inadequate immune response. Additionally, if the patients had developed a chronic carrier state, that may have allowed bacteria to persist and cause a recurring infection. Determining the precise cause of these relapses would require further genotypic investigation.

Since the outbreak, laboratory capacity has been enhanced to support more detailed molecular epidemiology studies, including introducing whole genome sequencing, which will facilitate better understanding of the genetic diversity of *S.* Typhi in Sabah in the future.

That cases relapsed, despite adherence to clinical protocols during initial admission, including the requirement for three negative stool samples before discharge, raises concerns about the possibility of multidrug-resistant *Salmonella*. The bacterium is considered multidrug-resistant if it is resistant to at least three broad-spectrum antibiotics used empirically for treatment, such as ampicillin, chloramphenicol and co-trimoxazole.[14] Extensively drug-resistant *Salmonella*, however, has evolved to additionally resist fluoroquinolones or even third-generation cephalosporins. This growing antibiotic resistance highlights a critical challenge in treating typhoid fever. Malaysia has yet to report any instances of extremely drug-resistant *Salmonella*;[15] nonetheless,

there is the potential for additional undetected cases or importations of resistant bacteria.

The outbreak investigation faced several limitations, including the inability to conduct whole genome sequencing to compare the Sabah *S.* Typhi isolates with those from other areas, particularly neighbouring countries, such as Indonesia and the Philippines. Additionally, due to resource constraints, not all samples were subjected to PFGE. This constraint, in particular, limited understanding of the outbreak's molecular epidemiology and the ability to verify the source of the outbreak. Underreporting of cases through passive surveillance and potential recall bias during active case detection also posed significant limitations. In addition, the use of a standardized questionnaire prevented the collection of data about other risk factors, such as handwashing habits and food preparation practices. These limitations, combined with other logistical constraints, such as challenges in identifying an appropriate control group, precluded the use of a more robust approach to establish causality.

Conclusions

This outbreak investigation identified 35 laboratory-confirmed cases of typhoid fever, a high proportion of which occurred in children. All cases presented with fever and required hospitalization, but there were no fatalities. Results from the PFGE analyses linked the outbreak to a food handler at a local restaurant, indicating common-source transmission. The swift implementation of control measures effectively curtailed further spread. Nevertheless, it is crucial to ensure ongoing vigilance and to enhance existing public health infrastructure. This outbreak highlights the urgent need for vaccination against typhoid among food handlers.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

This study was approved by the Ministry of Health Malaysia.

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School outbreak of coxsackievirus A16 in Antipolo City, Philippines, October 2022

Daniel SP Garcia III,[a] Alireza S Faiyaz MF,[b] Nino D Rebato,[c] Mariz Zheila Blanco-Payuyo,[d] John Bobbie Roca[d] and Concepcion G Lat[e]

Correspondence to Daniel SP Garcia III (email: danielgarciathe3rd2019@gmail.com)

Objective: An investigation team was deployed to determine the cause of an outbreak of a cluster of cases of fever and rash in a public elementary school in Antipolo City, Philippines, after the Public Health Unit was notified on 24 October 2022. The team also aimed to identify the source of the outbreak and to guide prevention measures.

Methods: Active case-finding for hand, foot and mouth disease was conducted at the school. A suspected case was defined as any learner who developed acute febrile illness with a papulovesicular rash on the palms and soles of the feet during 16–30 October 2022. Interviews with key informants were conducted and included school staff and parents. Oropharyngeal swabs were collected for polymerase chain reaction (PCR) testing.

Results: Nineteen suspected cases of hand, foot and mouth disease were detected, predominantly in grade 1 learners (16, 84%). Most cases (14, 74%) were 6 years old, and just over half were male (11, 58%). The first case occurred in a 6-year-old in grade 1 who attended class with a papulovesicular rash. Twelve learners (63%) from the same section developed symptoms, two of whom were seatmates of the first case. Two out of the 10 swabs collected were tested by PCR, both of which were positive for coxsackievirus A16.

Discussion: The causative agent of this outbreak was identified as coxsackievirus A16. Disease transmission occurred through close contact with the index case and possibly through shared classroom objects. Follow-up actions included dissemination of a memorandum about preventing the disease to all public elementary and secondary schools that emphasized symptom screening (i.e. for fever and rash), self-isolation at the onset of symptoms, regular disinfection of classroom surfaces and regular handwashing, especially before and after eating.

Hand, foot and mouth disease (HFMD) is an acute, infectious disease that mostly affects children worldwide. Caused by coxsackievirus A16 (CV-A16) and other enteroviruses, HFMD spreads quickly, causing outbreaks that can lead to closures of nurseries, day cares and schools.[1] Symptoms include low-grade fever, mouth sores and rashes, which are commonly found on the hands and feet. This disease is highly contagious, and cases can remain infectious for weeks after symptoms have resolved.[2] Asymptomatic individuals can also transmit the virus.[1]

In south-eastern Asia, where the disease is endemic, outbreaks are commonly caused by CV-A16. Case numbers tend to surge during the middle of the year, especially when the humidity is high.[3] In the Philippines, HFMD is an immediately notifiable disease and must be reported promptly to public health authorities. In 2022, the Philippines Department of Health reported a total of 3365 cases of HFMD distributed across the country.[4]

On 24 October 2022, the Public Health Unit of Antipolo City was notified of a cluster of cases of fever and rash in a public elementary school. The following day, a team of field epidemiologists was deployed to investigate the health event to determine the cause of the cluster and the likely transmission route. A secondary objective was to provide recommendations for controlling the outbreak and for preventing future outbreaks.

[a] Field Epidemiology Training Program, Intermediate Course, City Epidemiology, Health Statistics, Disaster and Response Unit, Antipolo City Health Office, Rizal, Philippines.
[b] City Epidemiology, Health Statistics, Disaster and Response Unit, Antipolo City Health Office, Rizal, Philippines.
[c] Municipal Human Resources Management, Government of San Jose de Buan, Samar, Philippines.
[d] Regional Epidemiology Surveillance Unit, Center for Health and Development Region 4A, Department of Health, Manila, Philippines.
[e] Antipolo City Health Office, Rizal, Philippines.
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METHODS

Study setting

Antipolo City is located in Rizal province, Philippines, and has a population of 887 399.[5] A total of 10 200 learners attended the elementary school involved in the outbreak. The school has adopted a double-shift schedule for classes (i.e. children attend either in the mornings or afternoons) and accommodates around 5000 learners per shift, with an average class size of 50.[6] At the time of the outbreak, there were 1591 learners in grade 1 distributed between 18 classrooms. Each classroom had two sections, and pupils spent most of their time in the same classroom and section.

Study design and case definitions

On 25 October 2022, members of the outbreak investigation team visited the school and conducted active case-finding activities. A suspected case was defined as any learner who developed or had developed acute febrile illness with a papulovesicular rash on the palms and soles of the feet during the period 16–30 October 2022. A confirmed case was a suspected case with positive laboratory results for human enteroviruses that cause HFMD.[7] An epidemiologically linked case was a suspected case whose illness was not laboratory-confirmed, but whose symptoms were temporally and geographically related to a laboratory-confirmed case or who was in a chain of transmission with another epidemiologically linked case.

Data collection and analysis

Parents and guardians of suspected cases provided consent before being interviewed using a structured questionnaire to collect demographic data and information about clinical symptoms and exposure history. The school nurse and class adviser were also interviewed to gather information about learners' seating arrangements, school sanitation and hygiene protocols, and children's behaviour during their time at school. The head of the City Epidemiology, Health Statistics, Disaster and Response Unit (CESDRU) of the Antipolo City Health Office was interviewed to determine whether other cases of HFMD had occurred in the city. The medical records of the cases who consulted the village health centre in the school's catchment area during 16–30 October 2022 were reviewed. School clinic records were also reviewed. The investigation team assessed learners' proximity to and use of points of entry and exit. Sanitary facilities were also inspected. Data were managed using Microsoft 365 Excel 2021.

For a descriptive analysis, frequencies and percentages were used to express the demographic characteristics of HFMD cases, and their grade, classroom section, date of onset, signs and symptoms, and history of travel. An epidemic curve, based on the date of symptom onset, was generated to illustrate the epidemiological connections between cases. A spot map, based on information about learners' movements, was created to understand transmission patterns and factors that may have contributed to the spread of disease.

Laboratory investigations

Oropharyngeal swabs were collected from suspected cases and preserved using BioSci Universal Transport Medium (Shenzen Dakewe Bio-engineering Co., Shenzen, China) prior to testing at the National Reference Laboratory. The specimens were tested for enteroviruses and coxsackievirus using semi-nested polymerase chain reaction (PCR), with a detection target of the 5′ untranslated region.

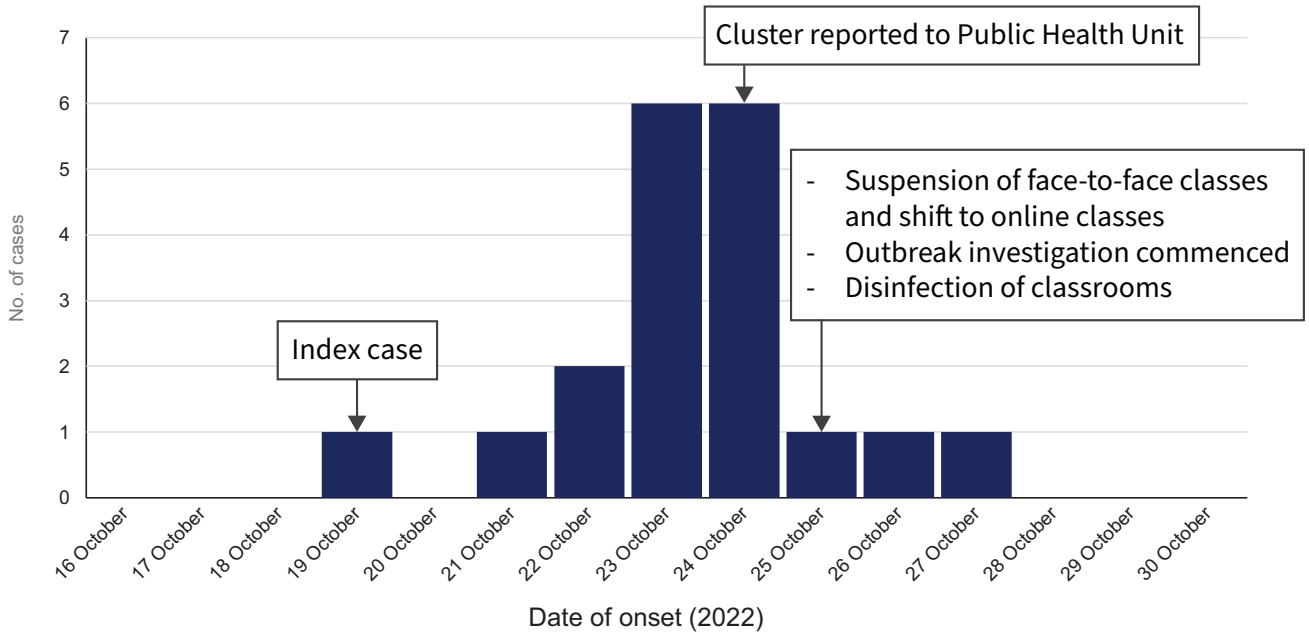
RESULTS

Descriptive analysis

A total of 19 suspected cases of HFMD were identified. The earliest date of symptom onset was 19 October and the latest was 27 October; the peak occurred on 23–24 October (**Fig. 1**). Case numbers decreased after 25 October, when face-to-face classes were suspended and teaching shifted to online and modular learning. All cases presented with fever and papulovesicular rash on the palms and soles of the feet.

The index case was a 6-year-old female first grader in section A who attended school in the mornings and whose symptoms were first noticed on 19 October 2022. She had attended mass at a nearby church 3 days before symptom onset. No other travel history was noted, and there were no other cases of HFMD at her home or in her community. Twelve of the suspected cases were from

Fig. 1. **Epidemiological curve of cases of hand, foot and mouth disease at a public elementary school, by date of onset, Antipolo City, Rizal province, Philippines, 16–30 October 2022 (*N* = 19)**



the same school section as the index case, and two of them had sat next to the index case. Two first graders from section B's afternoon shift who had used the same armchair as the index case also subsequently developed symptoms (**Fig. 2**).

Grade 1 learners (i.e. those aged 5 to 6 years) accounted for the greatest proportion of cases (16, 84%). Just over half were male (11, 58%), and the majority were aged 6 years (14, 74%) (**Table 1**). In addition to fever and papulovesicular rash, the majority experienced asthenia, or general weakness (16, 84%), and around half (10, 53%) had mouth sores. A smaller number had headaches or abdominal pain (8 each, 42%), and 4 (21%) experienced other signs and symptoms, including loss of appetite, nausea or vomiting (**Table 1**). Grade 1 section A had the highest attack rate (13/44, 30%), followed by grade 1 section B (2/46, 4%) (**Table 1**). A review of school records revealed no reports of HFMD during the past 5 years.

Key informant interviews

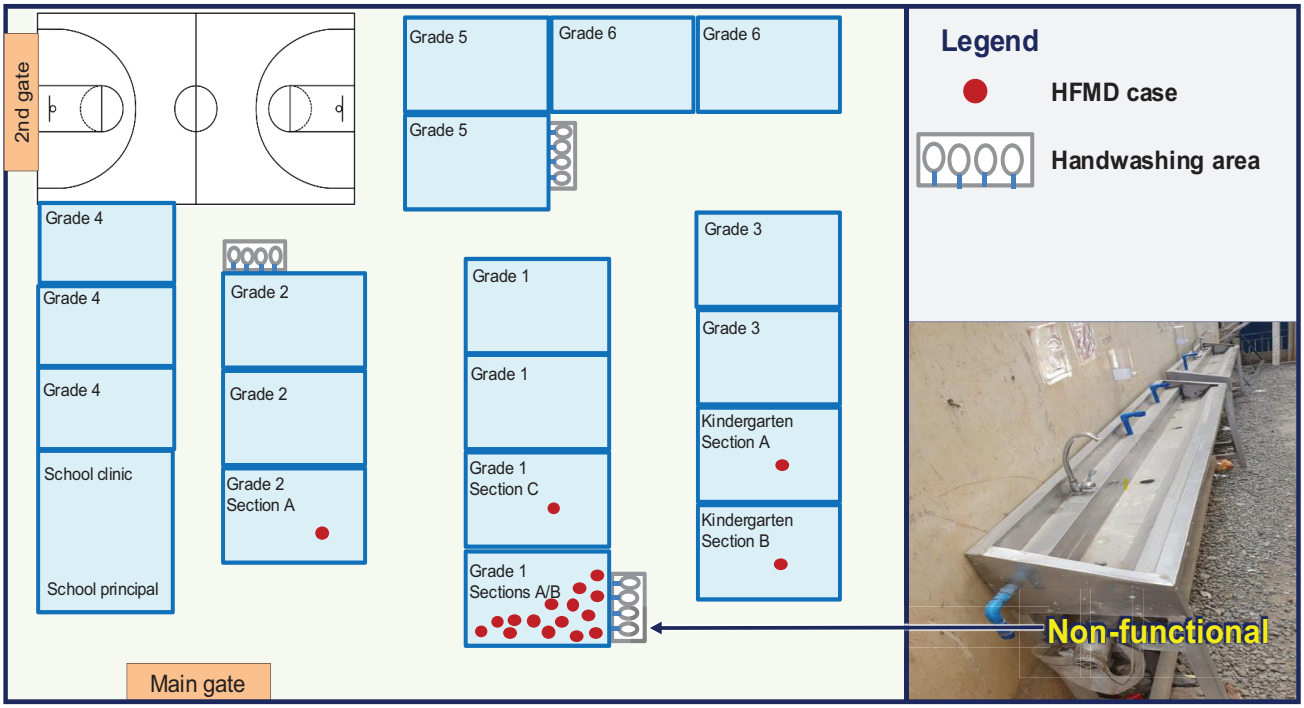
The mother of the index case was unaware of the signs and symptoms of HFMD and let her child attend school thinking it was an ordinary rash. According to the class adviser and the school nurse, all learners had their temperature checked as they entered the classroom (before classes started at 06:00). However, children were not routinely screened for other symptoms. According to CESDRU, no outbreaks of HFMD had been previously identified or detected in the city.

Environmental inspection and laboratory testing

Environmental inspection revealed inadequate handwashing areas, with leaks rendering some facilities nonfunctional. The assigned handwashing area for grade 1 section A was not functional due to a leaking pipe (**Fig. 2**). Learners were observed failing to wash their hands regularly. Few learners used alcohol-based sanitizer inside the classroom for hand hygiene before and after eating. During break time, learners were seen pushing and hugging one another, and running inside and outside the classrooms. Most of the learners engaging in these behaviours were males.

A total of 10 specimens were collected and two were tested by PCR. Both of these samples, which were from seatmates of the index case, were positive for CV-A16. The remaining eight samples were not tested, and these cases were classified as epidemiologically linked.

Fig. 2. **Spot map of cases of hand, foot and mouth disease in a public elementary school, Antipolo City, Rizal province, Philippines, 16–30 October 2022 (N = 19)[a]**



HFMD: hand, foot and mouth disease.

[a] School buildings are 3 to 4 storeys. Only the ground floor classrooms are shown.

DISCUSSION

Our investigation confirmed that the cluster of cases of fever and rash in a public elementary school in Antipolo City, Rizal province, Philippines, were HFMD caused by CV-A16. The outbreak was traced to a learner in grade 1, and disease transmission occurred through close contact with the index case and possibly through shared classroom objects. A review of records and interviews with CESDRU staff suggested that this event constituted the city's first report of HFMD in a public school setting.

Our investigation indicated that insufficient hand hygiene practices and a lack of symptom screening allowed the virus to spread unchecked within the school. Because learners were not regularly screened for rash at the school gate and when they entered their classrooms, the index case was able to attend classes while she had a papulovesicular rash but was afebrile. According to an HFMD rapid evidence review, people with the disease are most contagious during the first week of infection.[8]

All cases had mild and self-limiting symptoms, consistent with coxsackievirus infections. Studies conducted in China, southern Viet Nam and Pangasinan province in the Philippines have previously also identified CV-A16 as the cause of HFMD outbreaks in which the majority of affected individuals had only mild symptoms.[9–11] In contrast, more severe presentations of HFMD are more commonly linked to infection with other enteroviruses.

The index case was from grade 1 section A, which had the highest attack rate. Our spot map analysis revealed that the two cases who tested positive for CV-A16 were seatmates of the index case. Moreover, the two cases from the school's afternoon shift used the same chair as earlier-onset cases from the morning shift. Collectively, these patterns suggest transmission via an inanimate object. Previous studies, including one in a childcare centre in China and another in a kindergarten in Hong Kong Special Administrative Region (China), have established that HFMD can be transmitted through contact with contaminated objects.[12,13] Coxsackieviruses can remain viable and infective on hard, nonporous surfaces, including chairs and tables, for up to 2 weeks.[14] Inadequate disinfection of surfaces that are frequently touched, poor handwashing practices, and the close-

Table 1. **Characteristics of cases of hand, foot and mouth disease at a public elementary school, Antipolo City, Rizal province, Philippines, 16–30 October 2022**

Characteristic	No. (%) of cases (N = 19)	No. (%) of males (n = 11)	No. (%) of females (n = 8)
Age (years)			
5	2 (11)	2 (18)	0 (0)
6	14 (74)	7 (64)	7 (88)
7	2 (11)	1 (9)	1 (13)
8	1 (5)	1 (9)	0 (0)
Signs and symptoms[a]			
Fever	19 (100)	11 (100)	8 (100)
Papulovesicular rash	19 (100)	11 (100)	8 (100)
Asthenia (general weakness)	16 (84)	11 (100)	5 (63)
Mouth sores	10 (53)	8 (73)	2 (25)
Headache	8 (42)	6 (55)	2 (25)
Abdominal pain	8 (42)	5 (45)	3 (38)
Other[b]	4 (21)	2 (18)	2 (25)
Grade and section (no. of learners)[c]			
Kindergarten			
Section A (n = 34)	1 (3)	1 (3)	0 (0)
Section B (n = 31)	1 (3)	1 (3)	0 (0)
Grade 1			
Section A (n = 44)	13 (30)	7 (16)	6 (14)
Section B (n = 46)	2 (4)	1 (2)	1 (2)
Section C (n = 48)	1 (2)	0 (0)	1 (2)
Grade 2			
Section A (n = 45)	1 (2)	1 (2)	0 (0)

[a] Interviewees could provide multiple responses.

[b] This category includes loss of appetite, nausea and vomiting.

[c] These values are the attack rate, calculated as a percentage (the number of cases/the total number of learners).

contact nature of children's behaviours likely played roles in the transmission of HFMD in this setting. The unknown source of exposure for the index case implies asymptomatic transmission, aligning with findings from a study in China in which HFMD was spread by individuals without symptoms.[15]

This study had several limitations. Being descriptive, it does not test a hypothesis or identify risk factors. Another limitation is the low testing rate; only two out of 10 specimens were tested due to resource constraints. Nevertheless, the two positive results coupled with the consistent clinical presentation and strong epidemiological linkage among cases were considered sufficient evidence to identify the responsible pathogen as CV-A16.

Actions taken to control the spread of the outbreak in the school – a shift to online and modular learning in the affected classes, prompt screening for symptoms, isolation at the onset of symptoms, disinfection of surfaces and ensuring frequent handwashing – proved effective, and no new cases were reported in the school after 27 October. However, 1 month later, a cluster of new cases occurred at another elementary school in the same province.

In the wake of this investigation, the team made a series of recommendations – aimed at both schools and local authorities – for improving control of and preventing

HFMD. For schools, the recommendations included screening learners for symptoms (i.e. fever and rash) when they enter their classroom, disinfecting frequently touched surfaces and objects, and implementing strict rules about handwashing. The team also recommended that the local government of Antipolo City promote health education, strengthen community detection of HFMD and advocate for self-isolation at symptom onset.

In further follow-up action, a public health report was submitted by CESDRU to the Department of Education in Antipolo City. This led to the creation and dissemination of a departmental memorandum to reinforce awareness and prevention of HFMD and the provision of functional handwashing facilities in all public elementary and secondary schools. The memorandum also directed the Department of Education to facilitate a symposium about preventing HFMD for parents at all schools. In a more recent initiative, started in 2024, the Public Health Unit and school authorities are working jointly to establish a digitized symptom-based disease surveillance system in schools.

In conclusion, our investigation and subsequent actions underscore the importance of rapid containment, health education and sustained public health collaboration to effectively respond to HFMD outbreaks in school settings. Ensuring coordinated efforts between schools and local health authorities is crucial to maintaining proactive and prevention-oriented school and health systems.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

Ethics approval was not required as the investigation was conducted as part of routine public health response activities under the authority of Republic Act No. 11332.

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The potential impact of COVID-19 on tuberculosis trends in Japan

Lisa Kawatsu[a] and Kazuhiro Uchimura[b]

Correspondence to Lisa Kawatsu (email: kawatsul@med.nagoya-cu.ac.jp)

The COVID-19 pandemic impacted tuberculosis epidemiology worldwide, and Japan was no exception. This report analysed Japan's national tuberculosis surveillance data to explore the potential impact of COVID-19 on tuberculosis, by age group and place of birth, and to explore possible reasons behind the impact, if any. Overall since 2019, the observed number of notified cases was significantly lower than the number of expected cases. However, closer examination revealed that among Japan-born patients, this was true only for those aged 35–54 years and ≥65 years, while among those aged 25–34 years, the observed number of notified cases significantly exceeded the expected cases. Among foreign-born patients, the observed number of notified cases was significantly lower than that of expected cases for those aged 0–24 years and ≥65 years. Examination of changes in the modes of detection during the pre- and post-COVID-19 periods revealed that the impact of COVID-19 affected screening opportunities for tuberculosis among various populations differently, which in turn may partially explain the discrepancies between the observed and expected cases among those in different age groups and with different places of birth. A detailed study may be helpful in further understanding the interaction between the impact of COVID-19 on tuberculosis in the short and long-term.

The COVID-19 pandemic has undoubtedly impacted global efforts to control tuberculosis (TB). The World Health Organization has estimated that worldwide in 2020 compared with 2019 there was an 18% reduction in TB case detection, a 15% reduction in the number of people treated for drug-resistant TB, and a 21% decrease in the number of people receiving preventive therapy for latent TB infection.[1,2] For the first time in more than a decade, TB mortality has increased as well.[2] Additionally, it has been shown that the pattern of disruption has varied across regions and countries, probably due to differences in how the COVID-19 pandemic affected TB epidemiology and TB-related health services in local settings.[3,4]

In Japan, the TB notification rate had gradually been declining, with the annual rate of decline ranging between 4% and 5% since the 1980s; the rate reached 8.2 cases/100 000 population in 2022, with 10 235 newly notified cases.[5] Its epidemiology in Japan is unique in that approximately 70% of patients are aged ≥65 years, with the greatest number of cases occurring among those aged 85–89 years, followed by those aged 80–84 years. The proportion of foreign-born persons with notified TB is increasing yet still small, accounting for 11.9% of total cases in 2022.[5]

COVID-19 was first reported in Japan in January 2020. By the end of April 2023, when the Government of Japan officially downgraded COVID-19 from a class 2 to a class 5 infectious disease (i.e. no longer requiring mandatory notification), a cumulative total of approximately 30 million cases and 70 000 deaths had been recorded.[6] Although the age structure among people notified with COVID-19 changed over time – with a greater number of cases being younger people during the latter part of the epidemic – COVID-19 has consistently taken its toll on the elderly: throughout 2021–2023, approximately 85% or more of COVID-19 mortality was reported among those aged ≥70 years.[7] We thus hypothesized that COVID-19 had affected TB epidemiology unevenly. This report aimed to conduct a detailed examination of the potential impact of the incidence of COVID-19 on the reported incidence of TB, with cases aggregated by age group and place of birth (i.e. Japan-born or foreign-born), and to explore the possible reasons for any impact.

[a] Graduate School of Nursing, International Health Nursing, Nagoya City University, Aichi, Japan.
[b] Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association, Tokyo, Japan.
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JAPAN'S TB SURVEILLANCE SYSTEM

Japan introduced its first nationwide computerized TB surveillance system – the Japan TB Surveillance System (JTBS) – in 1987. TB is a notifiable disease, and public health centres are responsible for collecting data about notified patients and entering them into the system. The data are summarized monthly and annually, and selected aggregated data are available online (https://jata-ekigaku.jp/english) and as annual reports. Mechanisms to ensure data quality include the system's automatic verification programme, as well as regular training attended by staff from public health centres.[8] However, as with any national surveillance system, it is not designed to collect data for research purposes. Thus, some of the information is self-reported, such as country of birth, history of homelessness, HIV status and whether the person has diabetes mellitus, and the JTBS is not linked with any other clinical or health database.

METHODS

Using data from the JTBS, we analysed monthly trends in TB case notification in Japan between 1 January 2017 and 31 December 2022. We explored the potential impact of the COVID-19 pandemic on TB notifications by developing a model to predict the number of expected notifications from January 2020 to December 2022 based on monthly data about reported cases occurring from January 2017 to December 2019. We conducted an augmented Dickey–Fuller test to confirm the stationarity of the time series data, then selected the optimal model from among the autoregressive integral moving average (known as ARIMA), Holt–Winters method, and time series regression models, with the mean absolute percentage error (or MAPE) serving as the evaluation index. Post-prediction analysis involved the evaluation of residuals. Quantile–quantile plots, normality tests, correlation analyses and tests of means between predicted and measured values were conducted to validate the assumptions and performance of the prediction model. We generated predictive models for each age group (0–24, 25–34, 35–44, 45–54, 55–64 and ≥65 years) and place of birth (Japan-born, foreign-born and total).

Furthermore, in an attempt to explain the possible reasons behind any changes in the observed and expected trends, we examined the modes of detection for the notified cases. The modes of detection are mandatory data fields and are entered as one of 14 categories, the details of which can be found elsewhere.[9] These 14 categories were regrouped into the following, for the purposes of this study: "routine health check" (i.e. a chest X-ray conducted as part of a general health check during entry to university or as part of an annual health check at a workplace or certain social welfare institutions, which are mandatory under the law), "contact investigation" (i.e. for family and casual contacts of active TB cases), "screening at clinical settings with TB symptoms" (i.e. a chest X-ray conducted at a hospital for outpatients presenting with TB symptoms), "screening at clinical settings for other diseases/symptoms" (i.e. a chest X-ray conducted at a hospital for out- and inpatients presenting with other symptoms or seeking care for other disease), and "others and unknown". The proportions of modes of detection by age group and place of birth for those patients newly notified in 2019 were described, and the percentage change in the number of cases detected in 2019 and 2020 was calculated for mode of detection, age group and place of birth.

All analyses were conducted using R statistical software (version 4.3.2, http://cran.r-project.org; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Between 2019 and 2020, the notification rate fell from 11.5 to 10.1 cases/100 000 population. The annual rate of decline since 2019 far exceeded that of prior decades, at 10.6%. The number of notified cases also fell, from 14 460 in 2019 to 12 739 in 2020 (**Table 1**). The numbers similarly fell for both Japan-born and foreign-born patients (**Tables 2** and **3**).

Figures 1–3 show the observed and expected numbers of cases by month, from 2017 to 2022, by age group and place of birth. Overall, the observed number of notified cases was significantly lower than the expected number of cases (**Fig. 1**). However, a closer examination revealed that among Japan-born patients, this was true only for those aged 35–54 years and ≥65 years, while among those aged 25–34 years, the observed number of notified cases significantly exceeded that of the expected cases (**Fig. 2**). Among foreign-born patients, the observed number of notified cases was significantly lower than that of expected cases for those aged 0–24 years and ≥65 years (**Fig. 3**).

Table 1. **Total no. of newly notified cases of tuberculosis, by age group and year, Japan[a]**

Age group (years)	Year					
	2017	2018	2019	2020	2021	2022
0–24	816	863	798	632	574	474
25–34	1127	1079	915	882	798	685
35–44	1007	858	837	655	556	479
45–54	1246	1158	1093	876	813	666
55–64	1397	1235	1115	971	846	742
≥65	11 196	10 397	9702	8723	7932	7189
Total	16 789	15 590	14 460	12 739	11 519	10 235

[a] The total includes Japan-born and foreign-born patients as well as those for whom their country of birth is unknown; the last group is not summarized in the tables because of their small numbers.

Table 2. **No. of newly notified cases of tuberculosis who were born in Japan, by age group and year, Japan**

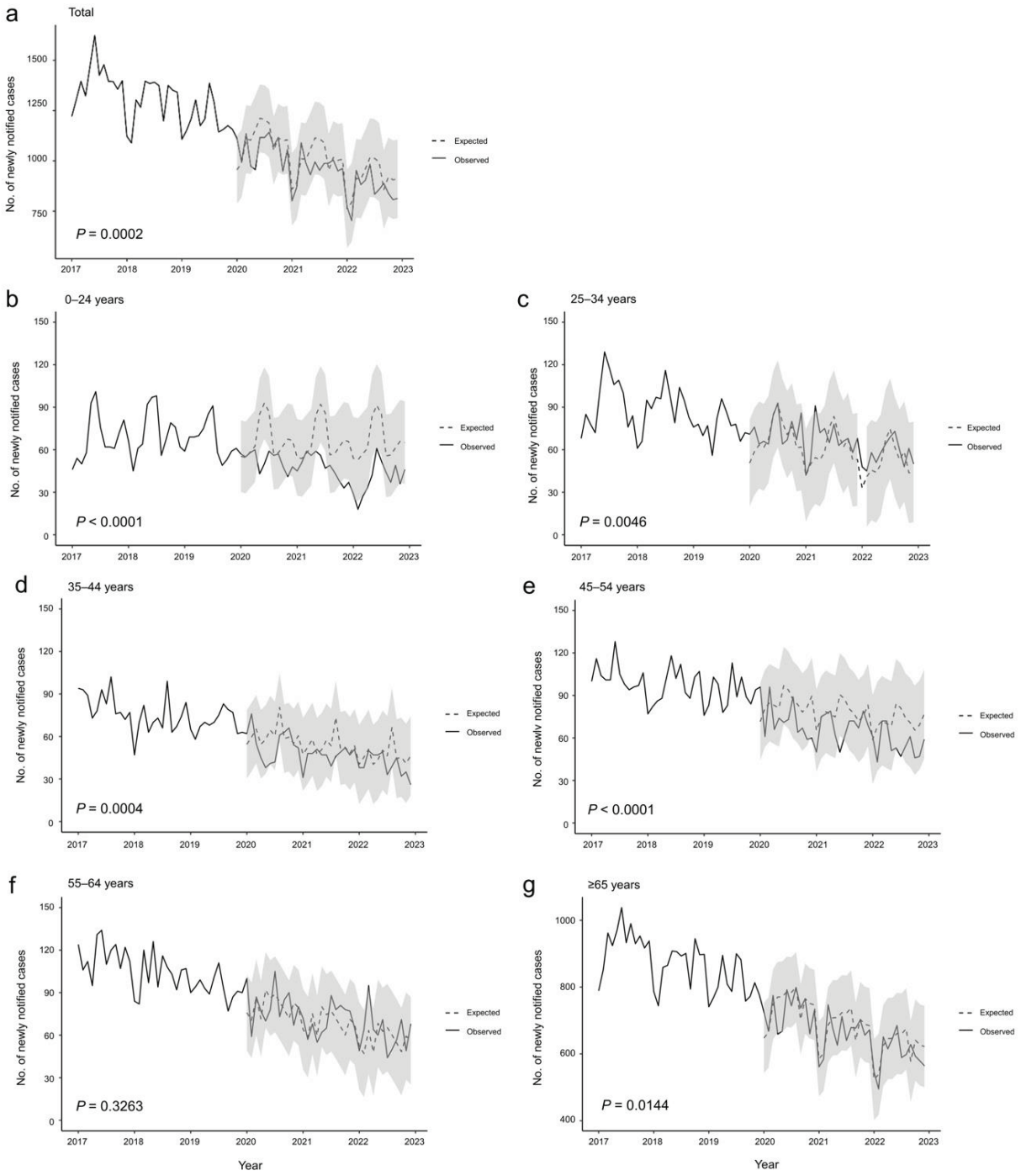
Age group (years)	Year					
	2017	2018	2019	2020	2021	2022
0–24	289	274	228	189	193	117
25–34	531	446	360	331	258	202
35–44	747	637	642	435	376	291
45–54	1083	1001	954	752	664	545
55–64	1274	1148	1038	899	760	664
≥65	10 609	10 064	9345	8474	7558	6854
Total	14 533	13 570	12 567	11 080	9809	8673

Table 3. **No. of newly notified cases of tuberculosis who were foreign-born, by age group and year, Japan**

Age group (years)	Year					
	2017	2018	2019	2020	2021	2022
0–24	514	583	564	437	374	352
25–34	565	625	549	546	526	469
35–44	219	200	186	214	167	171
45–54	114	139	117	110	127	100
55–64	65	56	52	54	54	60
≥65	53	64	73	50	65	62
Total	1530	1667	1541	1411	1313	1214

For both Japan- and foreign-born patients, the main mode of detection was "screening at clinical settings with TB symptoms", followed by "routine health check" for younger age groups, and for older age groups by "screening at clinical settings for other diseases/symptoms" (**Figs. 4a**, **5a**). Among Japan-born patients, the number of cases detected via "screening at clinical settings with TB symptoms" declined for all age groups, but to varying degrees, with those aged 35–44 years having the largest decline (reduction of 22.9%), followed by those aged 45–54 years (reduction of 19.4%). Furthermore, while approximately 30% of those aged 0–44 years were detected via a "routine health-check", the number of cases detected via this mode declined significantly for those aged 0–24 and 35–44 years (respective reductions of 46.4% and 47.8%). Conversely, those aged 25–34 years saw only a modest reduction of 9.2%. Furthermore, the number

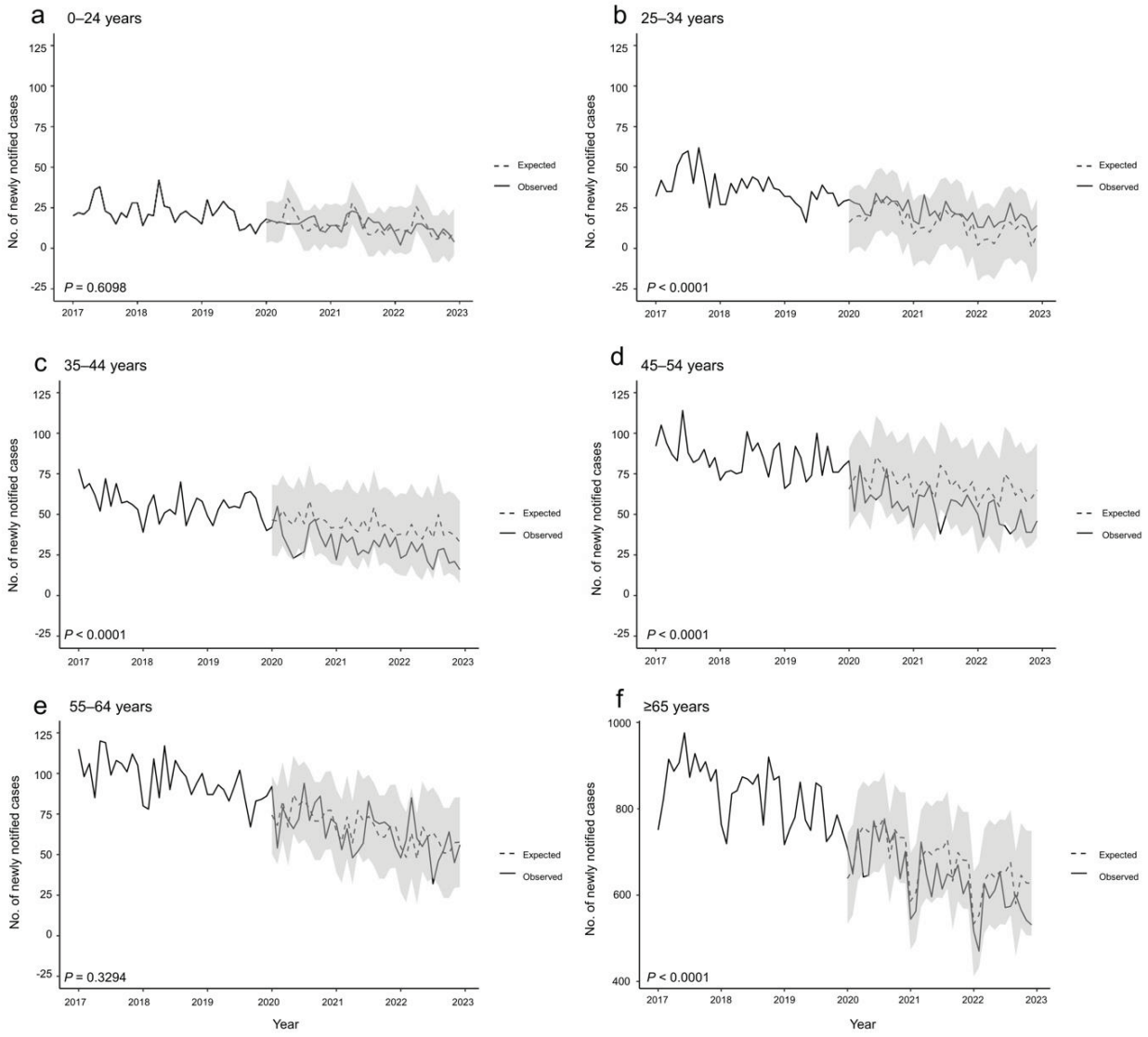
Fig. 1. **Observed and expected number of monthly notifications of active cases of tuberculosis in Japan, by age group, all patients, 2017–2022**



of cases detected via "screening at clinical settings for other diseases/symptoms" increased for those aged 0–44 years, most notably among those aged 25–34 years (increase of 46.7%).

In contrast, among foreign-born patients, the number of cases detected via "screening at clinical settings with TB symptoms" increased for those aged 25–34 and 35–44 years (respective increases of 26.3% and 19.7%), as did

Fig. 2. **Observed and expected number of monthly notifications of active cases of tuberculosis, Japan-born patients, by age group, 2017–2022**

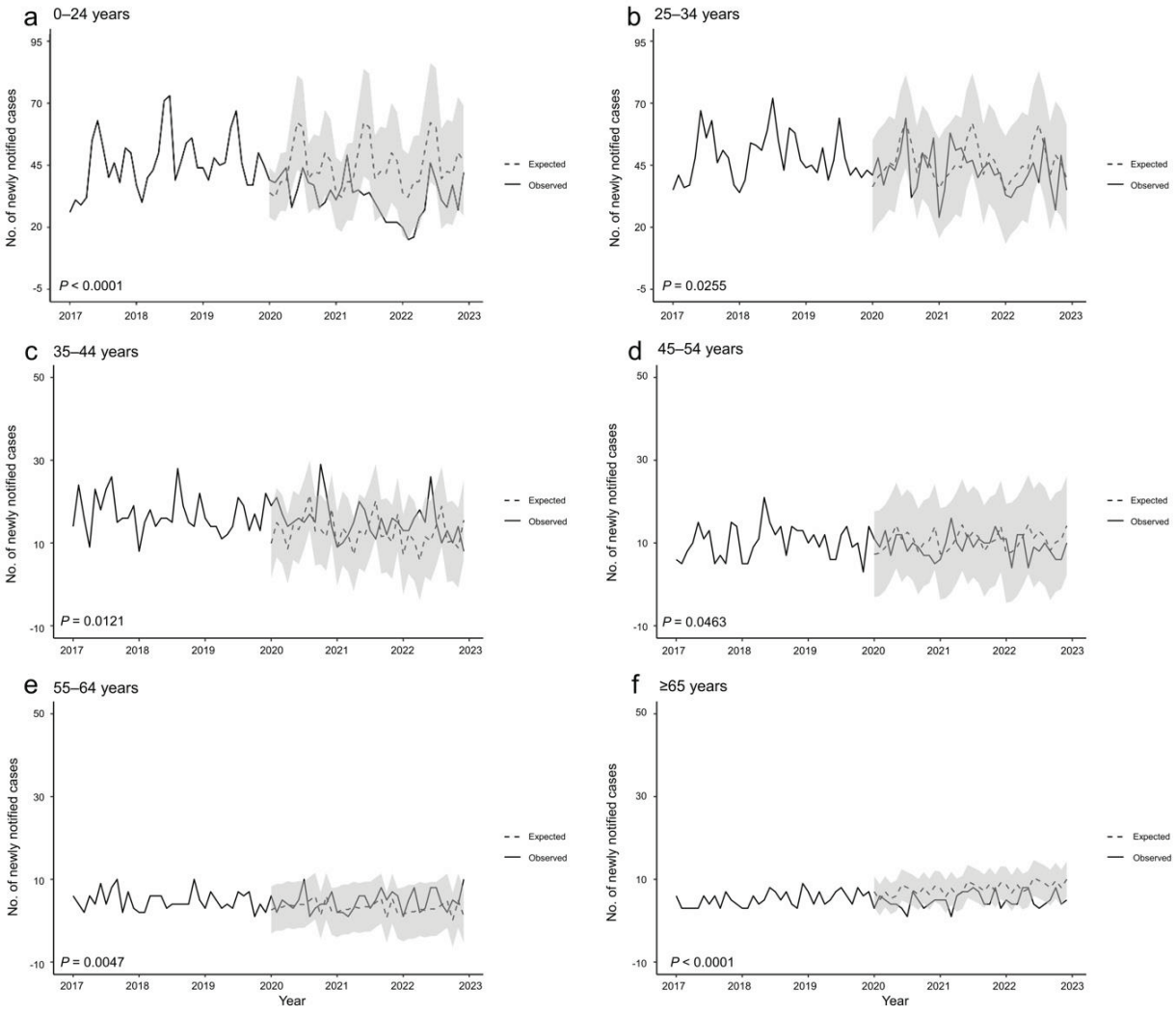


the numbers detected via "screening at clinical settings for other diseases/symptoms" for those aged 35–44 years (increase of 122.2%). The number of cases detected via a "routine health check" declined for all age groups.

DISCUSSION

Both the number of notified TB cases and notification rates declined dramatically between 2019 and 2020, and they continued to do so until the end of 2022. Considering that TB notification did not undergo any systemic changes – that is, there were no changes in the definition of a notifiable case or in contact investigation procedures[10] – it is likely that the declines were not system-based. Overall, the observed number of notified cases was below what was expected based on past trends, a phenomenon similarly observed in several other regions and countries.[11–13] However, there was considerable variation in the relationship between the trends in notified and expected cases by age group and place of birth. Indeed, previous studies have identified a bidirectional impact of the COVID-19 pandemic on TB epidemiology.[3,4,14] Thus, for example, a decrease in community and nosocomial contacts due to lockdown and increased mask-wearing

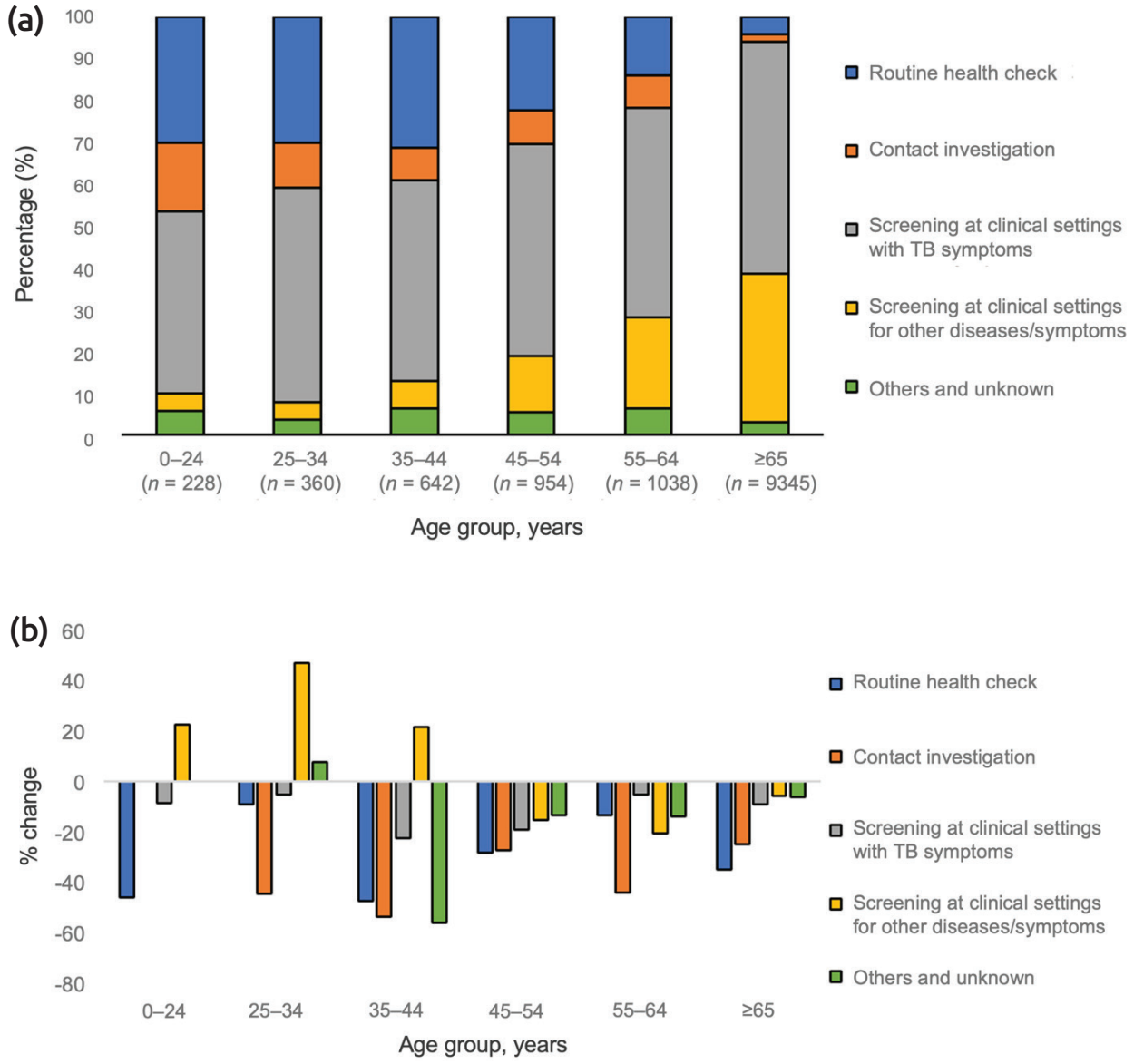
Fig. 3. **Observed and expected number of monthly notifications of active cases of tuberculosis, foreign-born patients, by age group, 2017–2022**



may have directly reduced opportunities for acquiring TB infection, and a decrease in access to TB testing and treatment enrolment due to lockdowns, disruptions in TB services and economic hardship may have reduced TB notifications.[14] Alternatively, an increase in household contact, and delays in testing and treatment may have increased the risk of TB infection.[14] It has also been suggested that the COVID-19 pandemic may have aggravated poverty and food insecurity,[15] which in turn may have increased TB disease burden. Decreases in vaccination against TB with Bacille Calmette–Guérin[16] and coverage of preventive therapy have also been reported from the Republic of Korea,[17] again likely having negative impacts on TB epidemiology.

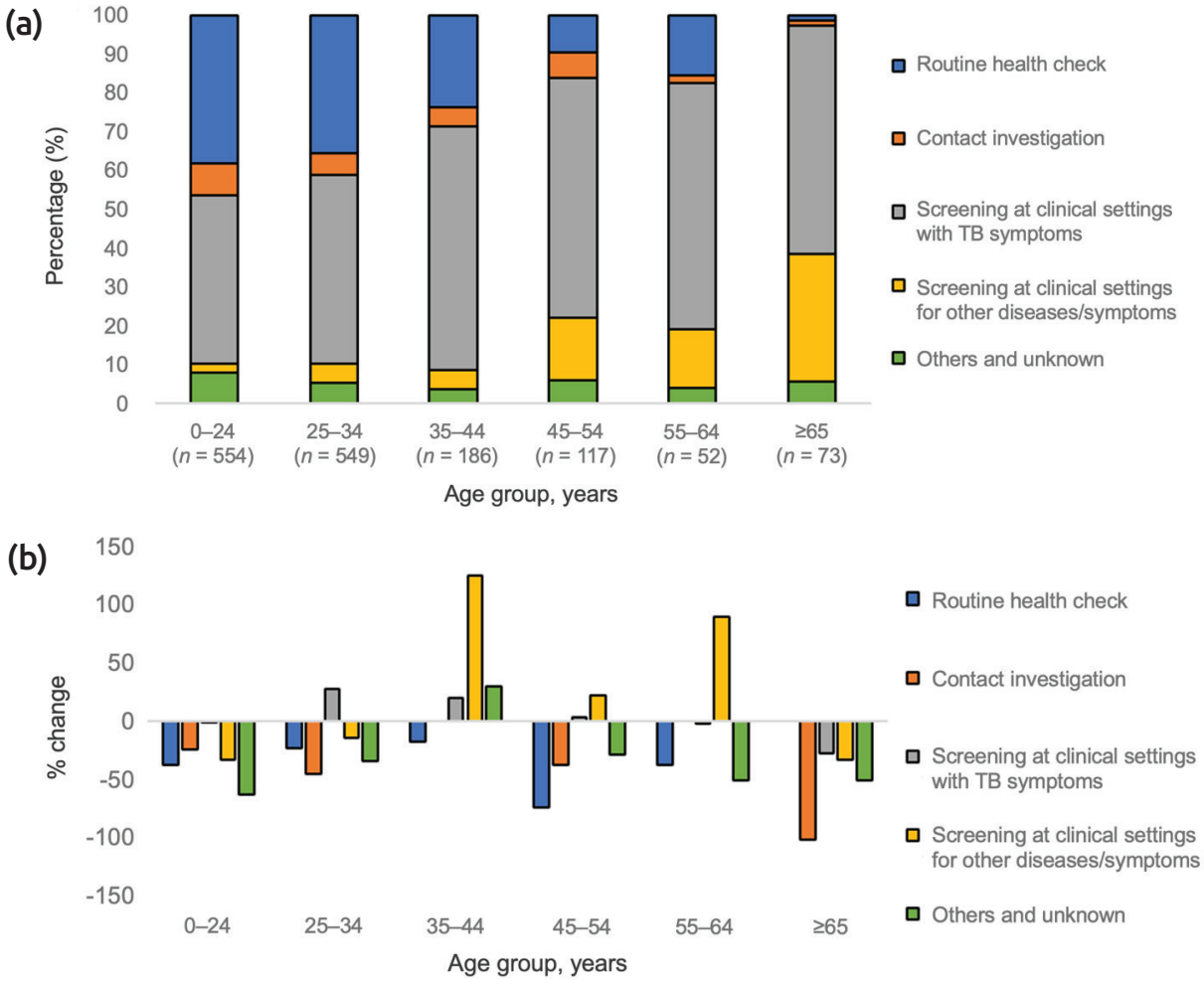
In Japan, among Japan-born patients, the observed number of notified cases was below what was expected for those aged 35–54 years and those aged ≥65 years. This may partially be due to underdetection of TB, especially among elderly people with COVID-19. One study has shown a decline in the number of acid-fast bacteria cultures being submitted to a commercial laboratory.[18] However, that study lacked age-specific data, and a detailed study of TB mortality is warranted to further investigate this possibility. Another possible reason for the lower number of notified cases is the decreased opportunities for routine TB screening, as well as suppression of health-care-seeking behaviour and health-care utilization in general. In Japan, annual

Fig. 4. **Percentage and change in the numbers of newly notified cases of active tuberculosis (TB), by age group and mode of detection, Japan-born patients (a) Active cases of TB newly notified in 2019, by age group and mode of detection (*N* = 12 567); (b) Percentage change in the numbers of newly notified active cases, by age group and mode of detection, 2019–2020**



health check-ups for employees, including chest X-rays, are legally required for most workplaces. For those aged ≥65 years, as well as for unemployed and self-employed persons, health check-ups are available and organized by local health authorities.[19] However, especially during the early phases of the COVID-19 pandemic, employees were strongly encouraged (but not mandated) to work remotely, thus limiting opportunities for workplace-required health check-ups.[20] Furthermore, restrictions on social movement and fear of acquiring COVID-19 from health-care workers, often based on stigma,[21] further discouraged people in Japan from accessing health-care facilities. As a result, take-up rates of health check-ups dropped across the country, by as much as approximately 40%, according to one study.[22] These observations are also reflected in the decrease in the number of cases

Fig. 5. **Percentage and change in the numbers of newly notified cases of active tuberculosis (TB), by age group and mode of detection, foreign-born patients (a) Active cases of TB newly notified in 2019, by age group and mode of detection (*N* = 1541); (b) Percentage change in the numbers of newly notified active cases, by age group and mode of detection, 2019–2020**



detected via the routes of "routine health check" and "screening at clinical settings with TB symptoms".

It is also worth noting that, unlike other age groups, those aged 25–34 years experienced the minimum reduction in the number of cases detected via "screening at clinical settings with TB symptoms" and the "routine health check" routes, which comprised approximately 70% of modes of detection. The reasons for this are unclear; however, this might explain why the actual number of cases did not decrease as expected. Furthermore, the number of cases detected via "screening at clinical settings for other diseases/symptoms" increased considerably for this age group. This could indicate that TB was detected unexpectedly, as young people who otherwise would not have visited a hospital regularly sought medical care because they became more health-conscious during the COVID-19 pandemic. Indeed, several small-scale studies of students and workers have indicated that people have become more conscious of their diet, exercise and sleep practices.[23,24] Many people also visited clinics for screening, either simply to reassure themselves before travelling or to receive discounts under the "Go to Travel" campaign, a government-led campaign that provided

discounts for travel and leisure activities within Japan in return for people being vaccinated against or tested for COVID-19.[25] Another possible explanation is coinfection with TB and COVID-19. Several studies have shown that COVID-19 severity may be worsened by TB.[26,27] Thus, young people with underlying TB may have had severe COVID-19, encouraging them to seek medical care, during which they were concurrently diagnosed with TB.

The impact the COVID-19 pandemic had on foreign-born cases with TB aged 0–24 years was probably more straightforward. The majority of foreign-born TB patients in Japan are students and workers, including technical trainees from high-burden countries.[5] Compared with older age groups, these foreign-born TB patients tend to be diagnosed relatively soon after their arrival in Japan – that is, within 1 to 2 years.[5] Hence, border closure measures, which Japan first implemented in April 2020 (and that lasted until restrictions were fully lifted in April 2023, with the number of foreign visitors plummeting by 99.2% at the peak),[28,29] directly reduced the number of TB notifications from incoming foreign-born persons. However, it is likely that TB among older working-age groups developed several years after migrating to Japan, either as reactivation of a previous infection acquired before arriving in Japan or as an infection newly acquired after migrating to Japan, and thus these groups were less affected by border measures related to the pandemic. This may also partially be reflected in the increase in the number of cases detected via "screening at clinical settings with TB symptoms" and also via "screening at clinical settings for other diseases/symptoms" for those aged 35–44 years. As for those aged ≥65 years, due to the small number of cases, it was difficult to ascertain any meaningful changes in the mode of detection between 2019 and 2020.

Our analysis is not without limitations. First, since the JTBS is not designed to collect data for research purposes, some of its data rely on self-reporting and may not be accurate. Second, the JTBS and surveillance data for COVID-19 are not linked; hence, our results are prone to the limitations of an ecological study.

Conclusion

TB epidemiology in Japan was impacted, both positively and negatively, by the COVID-19 pandemic. Overall, TB notifications fell below what was expected; however, both the direction and the degree of impact differed by age group and place of birth. How the pandemic impacted TB notifications might be explained by complicated interactions between both individual and societal factors. A detailed study, possibly a qualitative study, may be helpful in further understanding the interaction between the COVID-19 pandemic and TB in the short and long-term.

Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

Since the study utilized only anonymous data, it was not deemed necessary to undergo ethical review by the Institutional Review Board of Nagoya City University.

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Antimicrobial resistance in bloodstream isolates of *Escherichia coli* and *Staphylococcus aureus* from a provincial hospital, Cambodia, 2020–2022

Sivhour Chiek,[a] Vichet Orn,[a] Rina Dork,[a] Sreypeou Hem,[a] Sophanna Phai,[a] Phally Kheng,[a] Bunranai Thoeun,[a] Seila Kak,[a] Sidonn Krang,[b] Sovann Ly,[b] Sopheap Oeng[c] and Paul Turner[d,e]

Correspondence to Paul Turner (email: pault@tropmedres.ac)

Antimicrobial resistance (AMR) is a global concern. However, in Cambodia, as in other countries in the World Health Organization's Western Pacific Region, the magnitude of the problem is largely unknown. Thus, this study aimed to determine the prevalence of AMR in common pathogens, namely *Escherichia coli* and *Staphylococcus aureus,* isolated from blood cultures at one provincial hospital, a national sentinel site for AMR surveillance, during a 3-year period. Sample processing and analysis were conducted at the hospital's on-site microbiology laboratory. Blood cultures were processed manually, and conventional methods were used for bacterial identification. Antibiotic susceptibility testing (AST) was performed by disk diffusion and Etest minimum inhibitory concentration measurement, in accordance with current Clinical and Laboratory Standards Institute guidelines. Blood culture data from 1 January 2020 to 31 December 2022 were extracted from the hospital's microbiology database and, for the AST analysis, deduplicated to include results only for the first isolate per patient per year. Of 6102 blood cultures collected, 529 (9%) were positive. The most common blood culture pathogens found were *E. coli* (150, 28% of positive isolates) and *S. aureus* (65, 12% of positive isolates). For *E. coli*, resistance to ceftriaxone was detected in 110/148 (74%) isolates and resistance to imipenem in 3/147 (2%). For *S. aureus*, 18/56 (32%) isolates were methicillin-resistant, but vancomycin resistance was not detected. These rates of resistance to first-line treatments are of concern and have the potential to negatively impact patient outcomes.

Antimicrobial resistance (AMR) has emerged as a significant global public health threat, with nearly 5 million deaths linked to resistant bacteria in 2019.[1] Bacterial AMR also leads to treatment difficulties and longer hospital stays, resulting in increased health-care costs.[2]

It is essential to understand the true scale of AMR to inform risk management and identify opportunities for timely mitigation. The World Health Organization (WHO) established the Global Antimicrobial Resistance and Use Surveillance System (GLASS) in 2015 to enable countries to collect and share microbiological and antimicrobial use data.[3] This surveillance system targets six bacterial species commonly isolated from clinical samples globally, including *Escherichia coli* and *Staphylococcus aureus*, both dominant causes of bloodstream infections.

By the end of 2022, 92 countries had contributed AMR data to GLASS, including 10 from WHO's Western Pacific Region. Despite the growth of the GLASS database, large gaps remain in the global AMR dataset.[1] Although Cambodia has been reporting some data to GLASS since 2018, according to a review published in 2019, the scale of the AMR problem in Cambodia remains largely unknown.[4] This study aimed to provide contemporary data about AMR in Cambodia by determining its prevalence in *E. coli* and *S. aureus* isolated

[a] Battambang Provincial Referral Hospital, Battambang, Cambodia.
[b] Communicable Disease Control Department, Ministry of Health, Phnom Penh, Cambodia.
[c] Management4health and Integrated Quality Laboratory Services, Phnom Penh, Cambodia.
[d] Cambodia–Oxford Medical Research Unit, Angkor Hospital for Children, Siem Reap, Cambodia.
[e] Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom of Great Britain and Northern Ireland.
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from blood cultures submitted between 2020 and 2022 to Battambang Provincial Referral Hospital (BPRH), one of several sentinel sites belonging to Cambodia's national AMR surveillance system.

METHODS

Study site

BPRH, located in the north-west of the country, is a complete level-3 health-care facility, with a catchment area of around 1 million people. The hospital has 390 beds and departments for adult medicine, surgery, paediatrics, intensive care and obstetrics. The on-site microbiology laboratory processes around 3600 clinical samples per year from hospitalized patients and those attending surrounding health-care facilities. The laboratory participates in the national external quality assurance programme.

Blood culture practices and processing

National standard operating procedures for AMR surveillance recommend blood culture for hospitalized patients with fever and a suspected bacterial infection. At BPRH, blood cultures are processed manually. For adults, 10 mL of blood are collected for culture from two different sites and inoculated into a pair of 100-mL aerobic culture bottles (containing brain–heart infusion broth + 0.025% sodium polyanethol sulfonate). For children, 1–5 mL of blood are inoculated into a single 50-mL aerobic bottle. The blood culture bottles are then incubated in a static incubator at 35 °C (± 2 °C) for up to 7 days. All bottles are checked daily for signs of growth, including for turbidity, gas bubbles and haemolysis. If growth is detected, the bottle is Gram stained and subcultured onto a range of media. Additionally, blind subculture to chocolate agar and Gram stain are performed after 1 day of incubation for all bottles. Bacterial identification is done using conventional methods: catalase and coagulase for *S. aureus*; and oxidase, indole, and a panel of five biochemical tests for *E. coli* and other Gram-negative bacteria.

Antimicrobial susceptibility tests (ASTs) are done by disk diffusion and measurement of Etest minimum inhibitory concentration, following Clinical and Laboratory Standards Institute guidelines and standards (M02 and M100).[5,6] Specific species or groups of species were tested against standard panels of antimicrobial agents. Susceptibility to cefoxitin was tested as a surrogate agent for oxacillin and methicillin to report *S. aureus* resistance results for cloxacillin and cefazolin. Vancomycin was tested against *S. aureus* isolates only when cefoxitin resistance was detected.

Data analysis

Microbiology data were extracted from the national laboratory information system into a Microsoft Excel spreadsheet. Data were deduplicated to include only those results obtained from the first isolate per patient per year for each species (*E. coli* and *S. aureus*). Data summaries and graphs were generated using R, version 4.3.0 (R Core Team, Vienna, Austria), with the AMR, Harrell Miscellaneous (known as Hmisc) and tidyverse packages.[7] The χ^2 test was used to explore trends in resistance to key GLASS surveillance antimicrobials (i.e. ceftriaxone for *E. coli* and methicillin for *S. aureus*).

RESULTS

Hospital and laboratory summary

Between 1 January 2020 and 31 December 2022, 52 326 patients were admitted to BPRH: 17 947 in 2020, 16 312 in 2021 and 18 067 in 2022. During this period, 6102 blood cultures were processed by the microbiology laboratory: 5107 (84%) from hospitalized patients and 995 (16%) from patients attending external health-care facilities.

Blood culture data

Growth was detected in 826/6102 (14%) blood cultures. Of these, 297 were contaminated by skin flora (growth of coagulase-negative staphylococci, *Micrococcus* spp., *Corynebacterium* spp. or *Bacillus* spp.), leaving a total of 529 true positives. *E. coli* and *S. aureus* were the most common pathogens isolated from blood cultures, detected in 150 (28%) and 65 (12%) of positive cultures, respectively (**Table 1**).

Table 1. **The 10 most common pathogens isolated from blood cultures analysed at a sentinel surveillance site for antimicrobial resistance, Cambodia, 2020–2022 (*N* = 529)**

Species or species group	No. of isolates	% of true positive isolates
Escherichia coli	150	28.4
Staphylococcus aureus	65	12.3
Burkholderia pseudomallei	61	11.5
Klebsiella pneumoniae	47	8.9
Non-fermenting Gram-negative rods[a]	40	7.6
Acinetobacter spp.	24	4.5
Other Enterobacterales[b]	16	3.0
α-haemolytic (viridans) streptococci	12	2.3
Pseudomonas aeruginosa	12	2.3
Aeromonas spp.	9	1.7
Enterococcus spp.	9	1.7

[a] This group refers to oxidase-positive non-lactose-fermenting Gram-negative bacilli not speciated by available tests.
[b] This group refers to oxidase-negative Gram-negative bacilli not speciated by available tests (i.e. excluding *E. coli* and *K. pneumoniae*).

Antimicrobial susceptibility data

Escherichia coli

After deduplication, there were 148 *E. coli* blood culture isolates with AST data (**Fig. 1**). Resistance to the following was common: ampicillin (143/148, 97%; 95% confidence interval [CI]: 92–99%), ceftriaxone (110/148, 74%; 95% CI: 67–81%), co-trimoxazole (97/119, 82%; 95% CI: 73–88%) and ciprofloxacin (110/147, 75%; 95% CI: 67–82%). Resistance to the following was rare: amikacin (2/148, 1%; 95% CI: 0–5%), imipenem (3/147, 2%; 95% CI: 0–6%) and meropenem (2/148, 1%; 95% CI: 0–5%). AST results stratified by patient's age (<18 years, ≥18 years) are summarized in **Table 2**. There was no trend in resistance to ceftriaxone over time (73% [30/41] in 2020, 77% [49/64] in 2021, and 72% [31/43] in 2022; χ^2 for trend $P = 0.90$) (data not shown).

Staphylococcus aureus

After deduplication, there were 56 *S. aureus* blood culture isolates with AST data (**Fig. 2**). Resistance to methicillin was detected in around one third of isolates (18/56, 32%; 95% CI: 20–46%), but there was no evidence of resistance to vancomycin in the subset of isolates tested (0/25, 0%; 95% CI: 0–14%). AST results stratified by patient's age are summarized in **Table 3**. There was no trend in methicillin resistance over time (44% [7/16] in 2020, 17% [3/18] in 2021, and 36% [8/22] in 2022; χ^2 for trend $P = 0.75$) (data not shown).

DISCUSSION

Analysis of blood culture data from BPRH for 2020–2022 revealed that the most frequently isolated pathogens associated with bloodstream infections were *E. coli* and *S. aureus*; resistance to key first-line antibiotics was common in both species. More specifically, our study found that 74% of *E. coli* isolates were resistant to ceftriaxone and that 32% of *S. aureus* isolates were resistant to methicillin, proportions that are considerably higher than the 48% and 22%, respectively, reported by a nongovernmental hospital-based study conducted in Phnom Penh in 2007–2010.[8] However, resistance rates were similar to those reported to GLASS in 2022, when data were pooled from Cambodia's eight sentinel surveillance sites (including this hospital). According to the pooled data, 74% (95% CI: 69–79%) of *E. coli* isolates were resistant to third-generation cephalosporins and 68% (95% CI: 62–100%) of *S. aureus* isolates were methicillin-resistant.

The AMR rates at BPRH for 2020–2022 were higher than those reported to GLASS by adjacent countries. For 2022, Thailand reported rates of 34% (95% CI: 31–36%) for resistance to third-generation cephalosporins in *E. coli* and 8% (95% CI: 6–9%) for methicillin resistance in *S. aureus*, with the Lao People's Democratic Republic

Table 2. **Antimicrobial resistance in *Escherichia coli* blood isolates, stratified by patient's age group, Cambodia, 2020–2022**

Antimicrobial class	Antibiotic	Adult[a]				Paediatric[a]			
		Total	Susceptible	Intermediate	Resistant	Total	Susceptible	Intermediate	Resistant
Amphenicols	Chloramphenicol	143	125 (87.4)	4 (2.8)	14 (9.8)	5	5 (100.0)	0 (0)	0 (0)
Folate antagonists	Co-trimoxazole	114	16 (14.0)	4 (3.5)	94 (82.5)	5	2 (40.0)	0 (0)	3 (60.0)
Fluoroquinolones	Ciprofloxacin	142	20 (14.1)	14 (9.9)	108 (76.1)	5	2 (40.0)	1 (20.0)	2 (40.0)
Aminoglycosides	Amikacin	143	137 (95.8)	4 (2.8)	2 (1.4)	5	5 (100.0)	0 (0)	0 (0)
	Gentamicin	143	74 (51.7)	1 (0.7)	68 (47.6)	5	2 (40.0)	0 (0)	3 (60.0)
Carbapenems	Imipenem	142	137 (96.5)	2 (1.4)	3 (2.1)	5	5 (100.0)	0 (0)	0 (0)
	Meropenem	143	139 (97.2)	2 (1.4)	2 (1.4)	5	5 (100.0)	0 (0)	0 (0)
Third-generation cephalosporins	Ceftazidime	142	55 (38.7)	27 (19.0)	60 (42.3)	5	5 (100.0)	0 (0)	0 (0)
	Ceftriaxone	143	35 (24.5)	0 (0)	108 (75.5)	5	3 (60.0)	0 (0)	2 (40.0)
Penicillins	Amoxicillin + clavulanic acid	141	69 (48.9)	15 (10.6)	57 (40.4)	5	4 (80.0)	1 (20.0)	0 (0)
	Ampicillin	143	4 (2.8)	0 (0)	139 (97.2)	5	1 (20.0)	0 (0)	4 (80.0)

[a] Values are n(%). Adults are those aged ≥18 years. Paediatric cases are those aged <18 years.

reporting rates of 53% (95% CI: 46–59%) and 56% (95% CI: 39–72%), respectively. Unfortunately, Viet Nam did not submit AMR data for 2022 to GLASS.[9]

With the current data, it is difficult to make meaningful comparisons of AMR rates between countries in the Region. Inherent biases in surveillance data, which can arise from differences in patient populations and selective utilization of clinical diagnostic microbiology,[10] are likely to generate either under or overestimates of the true burden of AMR prevalence. In many locations, including Cambodia, AMR surveillance is in the early stages of implementation, and prevalence estimates are prone to these types of biases. Nevertheless, several factors may be more specific to Cambodia and may have a bearing on its rates of AMR. For example, in many parts of the country, it is common for patients to seek treatment from private health-care providers or use antibiotic self-treatment before being admitted to a government hospital. This practice may contribute to the selection of AMR in bacteria and thus overestimate the true prevalence of AMR in blood cultures, by inhibiting the growth of susceptible organisms.[11] Such practices may also be indicative of the wider issue of the inappropriate and excessive use of antibiotics. Om et al., for example, found that the drivers of AMR in Cambodia encompass the improper use of antibiotics in humans,[12] marked by excessive reliance on broad-spectrum antibiotics such as ceftriaxone.[13]

There are several limitations to this current study. First, the data cover only a 3-year period and involve a relatively small number of isolates, limiting their representativeness. In addition, the dataset is a blend of community-acquired and hospital-acquired infections. Furthermore, the absence of clinical data and the lack of comprehensive information regarding the patient population present challenges in determining the impact of AMR.

However, the study also has several strengths. The blood culture positivity rate was 9%, suggesting that clinician uptake of diagnostic microbiology services was reasonable, and this reflects a positive attitude towards identifying bacterial infections in patients presenting to BPRH. However, confirming adequate coverage would require an audit of the clinical records of patients with relevant clinical syndromes to determine blood culture collection metrics. Other strengths

Fig. 1. **Antimicrobial resistance in *Escherichia coli* blood isolates, Battambang, Cambodia, 2020–2022**

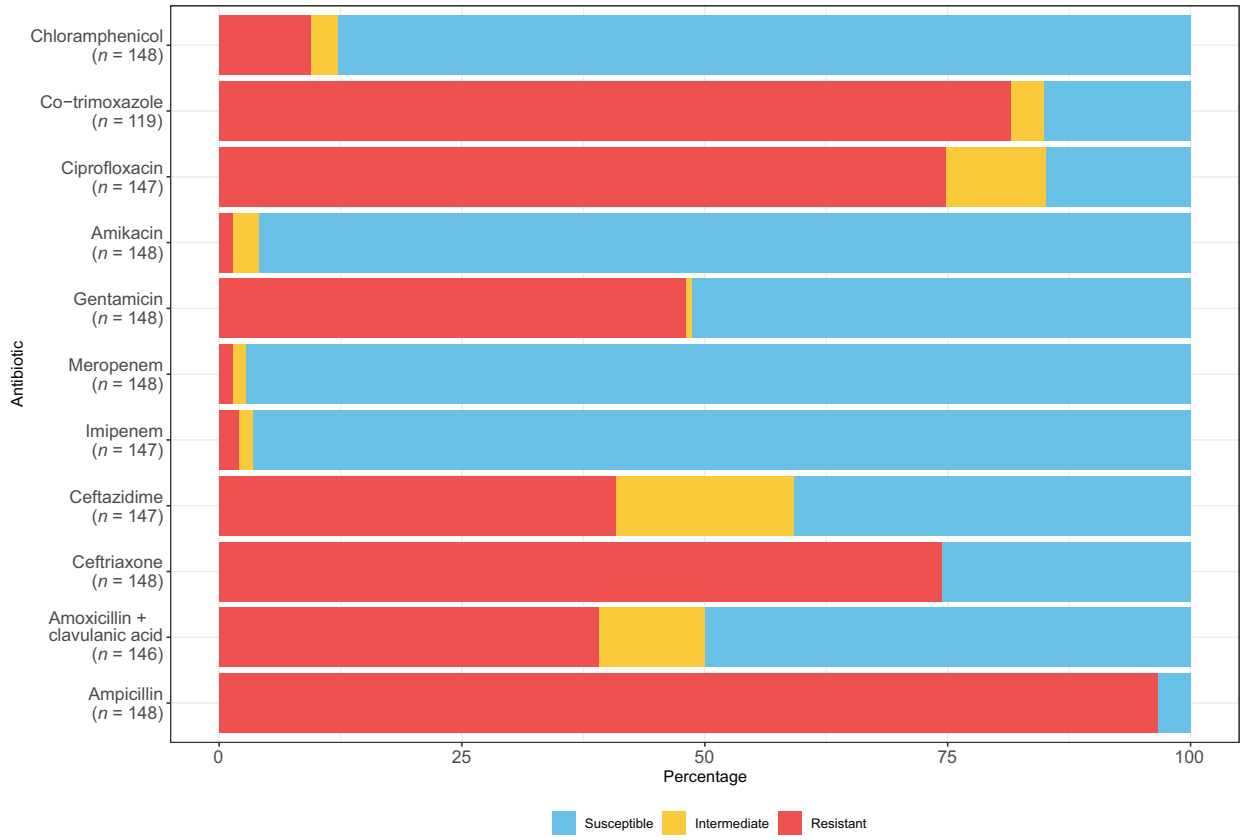
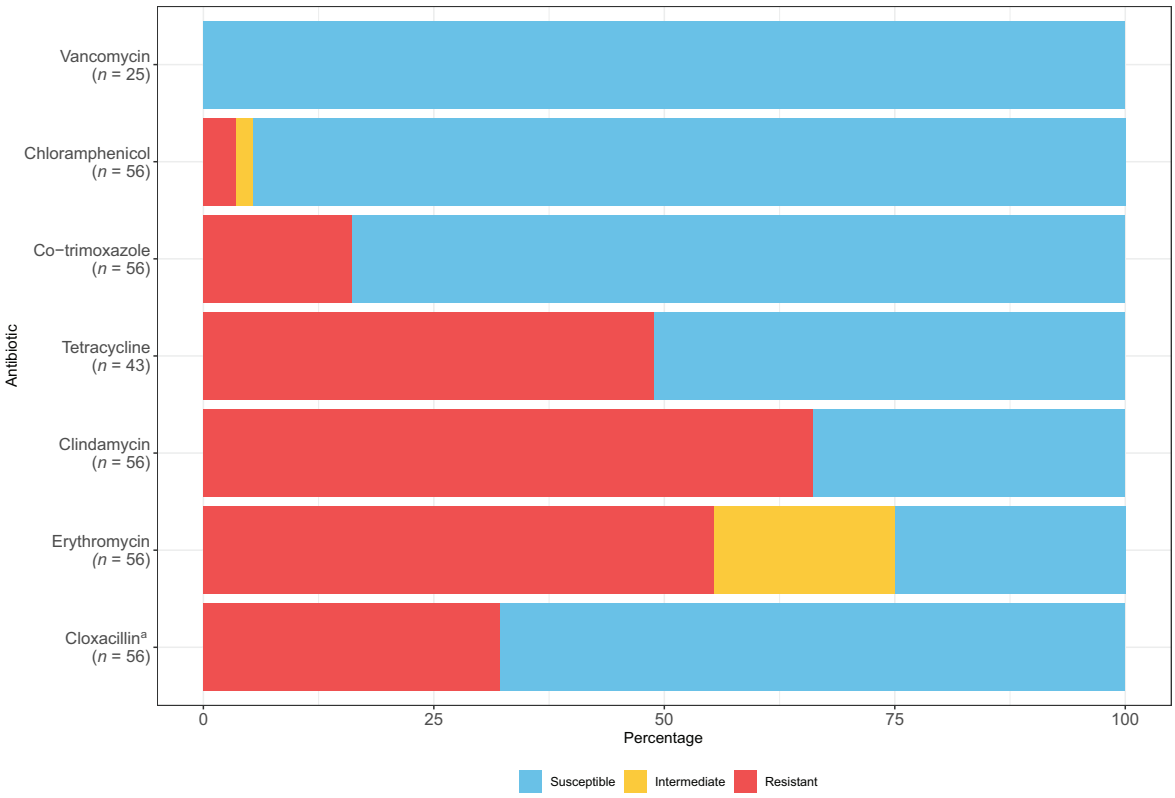


Fig. 2. **Antimicrobial resistance in *Staphylococcus aureus* blood isolates, Battambang, Cambodia, 2020–2022**



[a] Cefoxitin was used as a surrogate agent for methicillin, with cloxacillin as the β-lactam reported to clinicians.

Table 3. **Antimicrobial resistance in *Staphylococcus aureus* blood isolates, stratified by patient's age group, Cambodia, 2020–2022**

Antimicrobial class	Antibiotic	Adult[a]				Paediatric[a]			
		Total	Susceptible	Intermediate	Resistant	Total	Susceptible	Intermediate	Resistant
Glycopeptide	Vancomycin	23	23 (100.0)	0 (0)	0 (0)	2	2 (100.0)	0 (0)	0 (0)
Amphenicols	Chloramphenicol	44	42 (95.5)	1 (2.3)	1 (2.3)	12	11 (91.7)	0 (0)	1 (8.3)
Folate antagonists	Co-trimoxazole	44	36 (81.8)	0 (0)	8 (18.2)	12	11 (91.7)	0 (0)	1 (8.3)
Tetracyclines	Tetracycline	33	16 (48.5)	0 (0)	17 (51.5)	10	6 (60.0)	0 (0)	4 (40.0)
Lincosamides	Clindamycin	44	13 (29.5)	0 (0)	31 (70.5)	12	6 (50.0)	0 (0)	6 (50.0)
Macrolides	Erythromycin	44	10 (22.7)	9 (20.5)	25 (56.8)	12	4 (33.3)	2 (16.7)	6 (50.0)
Penicillins	Cloxacillin[b]	44	26 (59.1)	0 (0)	18 (40.9)	12	12 (100.0)	0 (0)	0 (0)

[a] Values are *n*(%). Adults are those aged ≥18 years. Paediatric cases are those aged <18 years.
[b] Cefoxitin was used as a surrogate disk to report methicillin resistance, with cloxacillin as the β-lactam reported to clinicians.

include good laboratory practice: the hospital laboratory had an established quality management system in place and followed Clinical and Laboratory Standards Institute guidance for AST, including annually updating breakpoints.

Based on the findings, recommendations for further work can be suggested. The national AMR surveillance system should be strengthened to include patient-level data to improve understanding of the impact of resistance on clinical outcomes and to guide targeted interventions. Given the widespread misuse of antibiotics, it will be important to begin to monitor antimicrobial use and its appropriateness, at least at national sentinel sites for AMR surveillance. Surveillance data should be collated regularly and used to inform the development of or changes to treatment guidelines and to optimize empirical therapy. Given the issues around inappropriate antibiotic use in Cambodia, surveillance data should be used to raise public awareness about the seriousness of AMR and to promote the responsible use of antibiotics.

In conclusion, high rates of AMR were demonstrated in *E. coli* and *S. aureus* isolates from patients with bloodstream infections from a Cambodian provincial referral hospital. Further work is required to understand the clinical impacts of this resistance and to identify potential mitigation strategies.

Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

This work was done as part of the activities of Cambodia's national AMR surveillance system. The Cambodia Centre for Disease Control and the National Ethics Committee for Health Research approved the use of the de-identified clinical microbiology data described in this report.

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Horse-racing injuries in children before and after the introduction of safety regulations in Mongolia

Gerelmaa Gunsmaa,[a] Uugantsetseg Gurbazar,[b] Tumen Ulzii Badarch[c] and Masao Ichikawa[a]

Correspondence to Gerelmaa Gunsmaa (email: gunsmaagerelmaa@gmail.com; gusnmaagerelmaa.gt@u.tsukuba.ac.jp)

The aim of this study was to assess the effectiveness of safety regulations governing traditional Mongolian horse racing on the frequency and severity of injuries among child jockeys. Regulations introduced in 2019 mandate the wearing of helmets and protective clothing, prohibit the participation of jockeys aged <7 years, and ban horse racing during the cold season (November–April). National injury surveillance data were used to compare the profile of injuries that occurred among children aged <15 years in the 4-year periods before and after the introduction of the regulations (2015–2018 and 2019–2022) and to investigate whether injuries continued to occur among underage children and during the banned season. The proportion of head injuries among injured children was calculated before and after the regulations were introduced. During the study periods, 6309 animal-riding injuries were recorded among children aged 3–14 years; 2539 occurred before the regulations were introduced and 3770 occurred after. Following the introduction of the regulations, the proportion of injured children aged <7 years decreased slightly. However, during 2019–2022, 294 animal-riding injuries were observed among underage children and 855 during the banned season. The proportion of head injuries among children with animal-riding injuries remained unchanged before and after the regulations were implemented (33.7% and 34.6%, respectively). The regulations have been ineffective. To reduce the burden of injuries among child jockeys, safety regulations need to be enforced throughout the year, and more stringent penalties for noncompliance should be imposed.

Horse racing is deeply rooted in Mongolian culture.[1,2] It has been an integral part of the celebration of key cultural events since the era of the Hun Dynasty,[3] during which time winning horses were revered as treasures.[4] Horse racing remains a beloved sport among Mongolians, and races take place across the country throughout the year. It is one of three traditional sports (alongside wrestling and archery) that form part of Naadam,[5] the country's biggest and most important national festival, which is celebrated in July and is included on the Representative List of the Intangible Cultural Heritage of Humanity of the United Nations Educational, Scientific and Cultural Organization (UNESCO).[6]

Mongolian horse racing has three distinctive characteristics: long distances, natural terrain courses and child jockeys (**Fig. 1**). Race distances typically range from 10 km to 26 km, depending on the age of the horse.[7] For the child jockeys, who may be as young as 5 or 6 years, riding for such long distances over natural terrain is a high-risk activity. Moreover, child jockeys need only to have completed 1 month of training, and many participate in multiple races in a single day. Reportedly, in the first half of 2022, 835 horse races took place involving 33 818 child jockeys; 298 were injured, six seriously, and six lost their lives.[8]

To reduce the risk of injury among child jockeys, the Government of Mongolia introduced safety regulations in January 2019, mandating that all jockeys wear helmets along with gloves, boots and other protective gear during both races and training sessions.[9] The Government also prohibited children aged <7 years from participating in races and banned horse racing during the cold season (November–April).[7,10]

[a] Department of Global Public Health, Institute of Medicine, University of Tsukuba, Tsukuba, Ibaraki, Japan.
[b] Department of Public Health and Traditional Medicine, Darkhan-Uul Medical School, Mongolian National University of Medical Sciences, Darkhan, Mongolia.
[c] Department of Statistics and Surveillance, National Trauma and Orthopedic Research Center, Ulaanbaatar, Mongolia.
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Fig. 1. **Mongolian child jockeys**

Source: [Mongol Magnai horse race has been cancelled] [online newsletter]. Ulaanbaatar: Zuunii Medee; 2021 (in Mongolian). Available from: https://www.zms.mn/a/86097, accessed 9 September 2025.

In this study, national injury surveillance data were used to examine whether these regulations have achieved their goals and whether the requirement to wear a helmet has led to a reduction in head injuries among child jockeys.

METHODS

Study setting

Mongolia has a population of approximately 3.4 million individuals, 32% of whom are children aged <15 years.[11] In 2022, more than 190 000 households engaged in herding activities, managing 71 million livestock, including 4.8 million horses.[12] These animals play a pivotal role in the daily lives and livelihoods of nomads, providing transportation, food, clothing and other necessities.

Data

Data about injuries from riding animals among children aged <15 years were obtained for the period 2015–2022 from the database for National Surveillance on Injury, Mortality and Morbidity, which is maintained by the National Trauma and Orthopaedic Research Center. The national injury surveillance system routinely collects data from the medical records of all injured patients attending any of the more than 600 health facilities across the country, including 17 specialized hospitals, 5 regional hospitals, 22 provincial hospitals, 14 municipal district hospitals, 319 district hospitals and 224 family health centres, as well as private hospitals that provide trauma care. These data include information about patient demographics, injury severity and treatment outcomes. All health facilities must submit electronic records monthly. Injuries are coded according to the 10th revision of the World Health Organization's International Classification of Diseases and Related Health Problems (ICD-10) by the Department of Statistics and Surveillance at the National Trauma and Orthopaedic Research Center.

For the purposes of this study, information was extracted from the surveillance database about the sex and age of patients, the place and date of injury, the affected body parts (e.g. head) and injury severity (i.e. fatal or non-fatal) for children whose injuries were coded as V80.0 (rider or occupant injured by fall from or being thrown from an animal or animal-drawn vehicle in a noncollision accident), V80.1 (rider or occupant injured in a collision with a pedestrian or animal), V80.7 (rider or occupant injured in a collision with other nonmotor vehicle, which includes an animal being ridden), V80.8 (rider or occupant injured in a collision with a fixed or stationary object) or V80.9 (rider or occupant injured in

other and unspecified transport accidents, which include unspecified animal-rider accidents). We excluded V80.2 (those injured in a collision with a pedal cycle), V80.3 (injured in collision with a two- or three-wheeled motor vehicle), V80.4 (collision with a car, pick-up truck, van, heavy transport vehicle or bus), V80.5 (collision with any other specified motor vehicle) and V80.6 (collision with a railway train or railway vehicle) because they are unlikely to be related to horse racing. Head injuries were defined as "injuries to the head", coded as S01–S09 to capture moderate to severe injuries. Head injuries coded as S00 (superficial injury of head) were excluded to ensure only the more severe cases were captured.

Data analysis

The characteristics of children who sustained animal-riding injuries during the 4-year period before the introduction of the safety regulations (January 2015–December 2018) were compared with those during the 4-year period after (January 2019–December 2022) in terms of sex (male vs female), age group (<7, 7–9, 10–12, 13–14 years), month of injury (November–April vs May–October), injury severity (fatal vs non-fatal) and type of injury (ICD-10 classification). To assess whether head injuries decreased after the introduction of the regulations in 2019, the proportion of head injuries among injured children was calculated, overall and by sex and age group, for the same two periods. The analysis was stratified by place of injury to determine whether there were differences in the frequency and type of injuries between urban and rural areas.

RESULTS

Between 2015 and 2022, 6309 injuries related to animal riding occurred among children aged 3–14 years. The majority (95.3%, 6014/6309) were classified as V80.0. Boys accounted for 91.1% (5748/6309) of all recorded injuries; 9.5% (598/6309) occurred in children aged <7 years. Just over half of all injuries (55.5%, 3504/6309) occurred in rural areas, 21.0% (1328/6309) occurred during the banned season and 1.7% (109/6309) of injuries were fatal (**Table 1**).

A total of 2539 injuries occurred during the 4 years before the regulations were implemented, while 3770 occurred in the subsequent 4-year period. While the overall number of injuries increased, the proportion of injured children aged <7 years was lower in the 4-year period following the introduction of regulations in both urban and rural areas (urban areas: 10.8% [118/1095] vs 7.3% [124/1710]; rural areas: 12.9% [186/1444] vs 8.3% [170/2060]). In contrast, the proportion of injuries that occurred during the banned months increased, most noticeably in urban areas (13.9% [152/1095] vs 21.3% [364/1710]). The distribution of injuries by sex, injury severity and ICD-10 classification remained largely unchanged across the two periods (**Table 1**).

The proportion of head injuries among all injuries was higher in rural areas than in urban areas. This proportion did not change markedly between the two study periods; in urban areas, head injuries accounted for 24.0% (259/1095) of injuries before and 25.0% (427/1710) after the regulations, and in rural areas for 41.0% (598/1444) before and 43.0% (876/2060) after (**Table 2**). In both periods, the proportion of head injuries was similar between boys and girls but was higher among younger children.

DISCUSSION

Despite the introduction of horse racing regulations banning the participation of child jockeys aged <7 years and racing during the cold season, in the 4 years after introduction, 294 animal-riding injuries were recorded among underage children. Moreover, 855 children were injured during the banned season, up from 473 in the preceding 4-year period. Furthermore, safety regulations mandating helmet-wearing by child jockeys do not appear to have reduced either the number or the proportion of head injuries among children with animal-riding injuries. These findings are consistent between urban and rural areas but, notably, the number of children who sustained head injuries, especially young children, was much higher in rural areas than in urban areas.

The failure of helmet-wearing regulations to reduce head injuries may be due to a combination of factors. First, compliance with regulations about helmet-wearing is low. According to nationwide inspections conducted in 2020 and 2021, the proportion of 17 450 jockeys wearing helmets during races was 42% (General Agency for Specialised Inspection of Mongolia. Official letter No. 02/356, February 21, 2022. Ulaanbaatar, Mongolia. Not publicly available). A subsequent qualitative study reported that child jockeys often find helmets uncomfortable and

Table 1. **Injuries associated with riding an animal in children aged <15 years before and after the introduction of horse racing safety regulations in 2019 by urban or rural area, Mongolia, 2015–2022**

Characteristic	Urban				Rural				Total			
	Before (2015–2018)		After (2019–2022)		Before (2015–2018)		After (2019–2022)		Before (2015–2018)		After (2019–2022)	
Total no.	1095		1710		1444		2060		2539		3770	
Sex												
Male	996	(91.0)	1568	(91.7)	1291	(89.4)	1893	(91.9)	2287	(90.1)	3461	(91.8)
Female	99	(9.0)	142	(8.3)	153	(10.6)	167	(8.1)	252	(9.9)	703	(9.2)
Age group (years)												
<7 (banned age)	118	(10.8)	124	(7.3)	186	(12.9)	170	(8.3)	304	(11.9)	294	(7.8)
7–9	326	(29.8)	510	(29.8)	466	(32.3)	607	(29.5)	792	(31.2)	1117	(29.6)
10–12	368	(33.6)	695	(40.6)	488	(33.8)	809	(39.3)	856	(33.7)	1504	(39.9)
13–14	283	(25.8)	381	(22.3)	304	(21.1)	474	(23.0)	587	(23.1)	855	(22.7)
Month of injury												
November–April (banned season)	152	(13.9)	364	(21.3)	321	(22.2)	491	(23.8)	473	(18.6)	855	(22.7)
May–October	943	(86.1)	1346	(78.7)	1123	(77.8)	1569	(76.2)	2066	(81.4)	2915	(77.3)
Injury severity												
Fatal	4	(0.4)	5	(0.3)	45	(3.1)	55	(2.7)	49	(1.9)	59	(1.6)
Non-fatal	1091	(99.6)	1705	(99.7)	1399	(96.9)	2005	(97.3)	2490	(98.1)	3710	(98.4)
Injury classification (ICD-10 code)[a]												
V80.0	1094	(99.9)	1699	(99.4)	1319	(91.3)	1902	(92.3)	2413	(95.0)	3601	(95.5)
V80.1	1	(0.1)	0	(0.0)	23	(1.6)	42	(2.0)	24	(0.9)	42	(1.1)
V80.7	0	(0.0)	3	(0.2)	7	(0.5)	15	(0.7)	7	(0.3)	18	(0.5)
V80.8	0	(0.0)	8	(0.5)	35	(2.4)	49	(2.4)	35	(1.4)	57	(1.5)
V80.9	0	(0.0)	0	(0.0)	60	(4.2)	52	(2.5)	60	(2.4)	52	(1.4)

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

Values are *n* (%).

[a] V80.0: injured by fall from or being thrown from animal or animal-drawn vehicle in noncollision accident; V80.1: injured in collision with pedestrian or animal; V80.7: injured in collision with other nonmotor vehicle, which includes an animal being ridden; V80.8: injured in collision with fixed or stationary object; V80.9: injured in other and unspecified transport accidents, which include unspecified animal-rider accidents.

Table 2. **Head injuries as a proportion of all injuries associated with riding an animal among children aged <15 years before and after the introduction of horse racing safety regulations in 2019 by urban or rural area, Mongolia, 2015–2022**

Characteristics	Before (2015–2018)					After (2019–2022)				
	All injuries		Head injuries		% head injuries	All injuries		Head injuries		% head injuries
Urban areas										
Total no.	1095	(100.0)	259	(100.0)	24.0	1710	(100.0)	427	(100.0)	25.0
Sex										
Male	996	(91.0)	237	(92.0)	24.0	1568	(92.0)	395	(93.0)	25.0
Female	99	(9.0)	22	(8.0)	22.0	142	(8.0)	32	(7.0)	23.0
Age group (years)										
<7 (banned age)	118	(10.0)	34	(13.0)	29.0	124	(7.0)	35	(8.2)	28.0
7–9	326	(30.0)	97	(37.0)	30.0	510	(30.0)	156	(37.0)	31.0
10–12	368	(34.0)	82	(32.0)	22.0	695	(41.0)	162	(38.0)	23.0
13–14	283	(26.0)	46	(18.0)	16.0	381	(22.0)	74	(17.0)	19.0
Month of injury										
November–April (banned season)	152	(14.0)	63	(24.0)	42.0	364	(21.0)	110	(26.0)	30.2
May–October	943	(86.0)	196	(76.0)	21.0	1346	(79.0)	317	(74.0)	24.0
Rural areas										
Total no.	1444	(100.0)	598	(100.0)	41.0	2060	(100.0)	876	(100.0)	43.0
Sex										
Male	1291	(89.0)	526	(88.0)	41.0	1893	(92.0)	803	(92.0)	42.0
Female	153	(11.0)	72	(12.0)	47.0	167	(8.0)	73	(8.0)	44.0
Age group (years)										
<7 (banned age)	186	(13.0)	97	(16.0)	52.0	170	(8.0)	85	(10.0)	50.0
7–9	466	(32.0)	186	(31.0)	40.0	607	(29.0)	284	(32.0)	47.0
10–12	488	(34.0)	199	(33.0)	41.0	809	(39.0)	353	(40.0)	44.0
13–14	304	(21.0)	116	(20.0)	38.0	474	(23.0)	154	(18.0)	32.0
Month of injury										
November–April (banned season)	321	(22.0)	152	(25.0)	47.0	491	(24.0)	249	(28.0)	51.0
May–October	1123	(78.0)	446	(75.0)	40.0	1569	(76.0)	627	(72.0)	40.0
Total (urban and rural)	2539	(100.0)	857	(100.0)	33.7	3770	(100.0)	1303	(100.0)	34.6

Values are *n* (%) unless otherwise indicated.

so avoid wearing them.[13] Other possible reasons for low levels of compliance include a reluctance on the part of guardians and race organizers to abide by the regulations, possibly because of a lack of concern about safety and regulatory enforcement. Indeed, many horse races are unregistered,[14] and the fines for violating regulations are low, typically no more than 100 000 Mongolian tugrug (approximately US$ 30).[15] Second, although the new regulations stipulate that helmets must conform to Mongolian standards, we suspect that some child jockeys are wearing non-standard or loose-fitting helmets without chin straps. Considering the hard, rocky natural terrain of the race courses, such helmets are unlikely to afford sufficient protection in the event of a fall.

This study also provides evidence of noncompliance with the regulations about horse racing seasons and the age of child jockeys. Despite the ban on horse races during November–April, in 2022, horse races were held in eight of the country's 21 provinces to celebrate the National Spring Festival (known as Tsagaan Sar) and the Lunar New Year, which in 2022 was at the end of February.[16,17] The increase in horse-related injuries after the introduction of the regulations might have resulted from an increasing number of such horse races due to commercialization of the races. Traditionally, horse racing was part of nomadic herders' culture, with races held a few times a year during the summer festival, and children rode their own family's horses. However, horse racing has now become a business and gambling may be involved. Horses are raised year-round under careful management, and children are employed as jockeys, with horses bred for racing commercially rather than in the traditional way.

Enforcement actions are clearly needed to increase compliance with safety regulations throughout the year, especially in rural areas where head injuries were more prevalent among injuries sustained while riding than they were in urban areas. Additionally, more stringent penalties for noncompliance should be imposed. Such policies have proven effective in other countries. For instance, in 2002, the Government of the United Arab Emirates banned child jockeys aged <15 years from participating in traditional camel races. Strict penalties were imposed on camel owners: a fine of 20 000 dirhams (approximately US$ 5500) was levied for the first offence; a second offence incurred a 1-year suspension from racing; and third and subsequent offences resulted in imprisonment.[18] A single-centre study reported that there were no paediatric patients with injuries related to camel racing after the ban in the United Arab Emirates,[19] although violations of the ban were reported in 2010.[20] Almost concurrent with the 2002 ban, robotic jockeys were developed to replace child jockeys,[21] and these have since become commonplace in camel races across the United Arab Emirates.[22] We believe that switching to robotic jockeys would allow Mongolians to enjoy the ancient tradition of horse racing throughout the year, while protecting the safety and human rights of children.

This study has several limitations. First, ICD-10 codes, notably V80.0, are not specific to injuries incurred while participating in horse racing. However, our findings are not likely to be distorted because it is unlikely that the incidence of riding injuries unrelated to horse racing (e.g. in farming) changed substantially during the study period. Second, surveillance data did not capture injuries incurred during horse racing that were not treated at health-care facilities. Presumably, such injuries were mostly minor and did not require medical treatment. Conceivably, increased helmet-wearing may have reduced the severity of head injuries; had this been the case, we might have expected to see a drop in the proportion of head injuries among injured children after the introduction of regulations. However, we did not, most likely because compliance with helmet-wearing was low (General Agency for Specialised Inspection of Mongolia. Official letter No. 02/356, February 21, 2022. Ulaanbaatar, Mongolia. Not publicly available). Data on helmet use among injured children would have been helpful, as they would have allowed us to assess the relative contributions of not wearing a helmet and the inappropriate use of a helmet to the apparent ineffectiveness of the regulations in reducing head injuries. Finally, as we did not have information about the number of child jockeys who participated in the horse races, we were unable to estimate the incidence of injury per at-risk population during the study period. Nevertheless, we believe that the proportion of head injuries attributed to riding an animal as a percentage of all such injuries should be a sufficiently sound indicator of trends because the overall number of injuries could be considered a proxy for the at-risk population.

In conclusion, we consider the 2019 horse racing regulations to be ineffective. Head injuries did not decrease among children with animal-riding injuries following the introduction of the safety regulations; furthermore, riding

injuries continued to occur among underage children and during the banned season. To reduce the burden of these injuries, year-round enforcement of safety regulations and more stringent penalties for noncompliance are recommended.

Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

This study was approved by the research ethics committees of the National Trauma and Orthopedic Research Center of Mongolia and the Faculty of Medicine at the University of Tsukuba, Japan.

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Trends in and factors associated with late initiation of antiretroviral therapy among newly diagnosed HIV cases, Kampong Thom, Cambodia, 2014–2023

Vathanak Sann,[a] Sengdoeurn Yi,[b] Chanratana Leng,[c] Sophanith Ung[d] and Khemrin Pong[d]

Correspondence to Vathanak Sann (email: vathanaktsmc@gmail.com)

Late initiation of antiretroviral therapy (ART) is associated with worse health outcomes for people living with HIV. In 2019, Cambodia implemented a same-day policy allowing people with HIV to start ART on the day they were diagnosed. Using case data collected by Cambodia's National Center for HIV/AIDS Dermatology and STDs, this study examined trends and factors influencing late ART initiation among newly diagnosed HIV cases attending three clinics in Kampong Thom province from 2014 to 2023. Factors linked to late ART initiation (defined as starting treatment >1 day after diagnosis) were assessed using descriptive statistics and logistic regression. Statistical significance was set at $P < 0.05$. The study included 741 newly diagnosed HIV cases, with a mean age of 45.7 years at diagnosis (standard deviation: 10.2); 57.1% (423) of cases were female and more than 70% (504/704) were employed. In the 5-year period before the implementation of same-day ART initiation (2014–2018), 91% (325/356) of cases had late ART initiation. In the subsequent 5-year period (2019–2023), the proportion of cases with late ART initiation averaged 23%, and in 2023 was just 3%. Late ART initiation was more common at the Baray Santuk clinic (adjusted odds ratio: 3.94, 95% confidence interval: 1.99–7.81, $P < 0.001$), likely due to a lack of staff dedicated to HIV care. The findings demonstrate that same-day ART initiation is feasible in resource-limited settings and that adequate staffing can further improve prompt ART initiation.

HIV remains a significant public health concern worldwide. As of the end of 2023, an estimated 39.9 million individuals were living with HIV, and during 2023, 1.3 million became newly infected.[1] In the Asia-Pacific region alone, in 2023, there were an estimated 6.6 million people living with HIV and around 300 000 new infections.[1,2] The effectiveness of HIV prevention, diagnosis, treatment and care programmes varies considerably across regions, countries and populations.

The World Health Organization (WHO) currently recommends rapid initiation of antiretroviral therapy (ART) for all patients newly diagnosed with HIV, with same-day initiation for those ready to start treatment.[3] The United States Department of Health and Human Services also recommends immediate ART initiation.[4] This approach aims to increase ART uptake, reduce the time to viral suppression and improve virological suppression rates.[5]

As of December 2022, the latest available data showed that an estimated 76 000 people in Cambodia are living with HIV. Since 1991, a total of 65 587 cases of HIV have been reported, of whom 99% have accessed ART. Of those who received ART, 98% achieved viral suppression.[6] In 2019, Cambodia's National Center for HIV/AIDS Dermatology and STDs advised all of its ART sites to implement a same-day policy by offering patients the option of starting ART on the day that their diagnosis of HIV was confirmed. The same-day policy was introduced with the dual aim of improving links to care and reducing the risk of loss to follow up, and enhancing treatment outcomes for people living with HIV.[7]

[a] Baray Santuk Operational District, Kampong Thom Provincial Department of Health, Kampong Thom, Cambodia.
[b] Communicable Disease Control Department, Ministry of Health, Phnom Penh, Cambodia.
[c] National Center for HIV/AIDS Dermatology and STDs, Phnom Penh, Cambodia.
[d] South Asia Field Epidemiology and Technology Network, Cambodia.
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To be eligible to start same-day ART, patients must have a confirmed HIV diagnosis and have completed a clinical readiness assessment. This assessment takes the form of a clinical evaluation by a health-care provider to determine whether the patient is medically stable. It typically includes symptom screening for serious opportunistic infections, a basic physical examination, a review of medical history and a set of baseline laboratory tests, ideally CD4 count, creatinine and haemoglobin levels, and liver function tests. Provided the patient is deemed clinically stable and is free of opportunistic infections, such as tuberculosis or cryptococcal meningitis, ART can be initiated immediately without waiting for blood test results. The new policy was designed to offer a more streamlined approach to providing ART by reducing some of the procedural barriers to initiating treatment.

Since the implementation of the same-day policy in Cambodia, no study has measured its impact on ART initiation rates. This study aims to examine the trends in, and determinants of, late ART initiation among patients newly diagnosed with HIV in Kampong Thom, a province in central Cambodia, using HIV case data routinely collected by the National Center for HIV/AIDS Dermatology and STDs. Kampong Thom province was selected due to its combination of a moderate HIV burden and programmatic relevance. It provides a representative setting in which to assess policy implementation in a semi-rural context where challenges such as delayed diagnosis, stigma and service accessibility remain key barriers to early ART initiation. Findings from this setting may offer insights that are applicable to similar provinces across the country.

METHODS

Study setting

Kampong Thom province has nine districts, and it borders the provinces of Siem Reap, Preah Vihear, Stung Treng, Kratie, Kampong Cham, Kampong Chhnang and Tonle Sap. It is Cambodia's second largest province by area and has a population of around 750 000.

Fig. 1 shows the typical care pathway of HIV patients in Cambodia. Individuals suspected to have HIV are referred to voluntary confidential counselling and testing (VCCT) sites for confirmation of their status. Individuals may be referred from home care or community-based health-care services from programmes such as those aiming at prevention of mother-to-child transmission (PMCT); individuals can also self-refer. Once an HIV diagnosis is confirmed, newly diagnosed cases are referred to an ART clinic for treatment. Kampong Thom has three ART clinics, which are part of a national network of 69 clinics and health facilities that enrol people newly diagnosed with HIV in ART and that contribute data to the country's ART surveillance system.

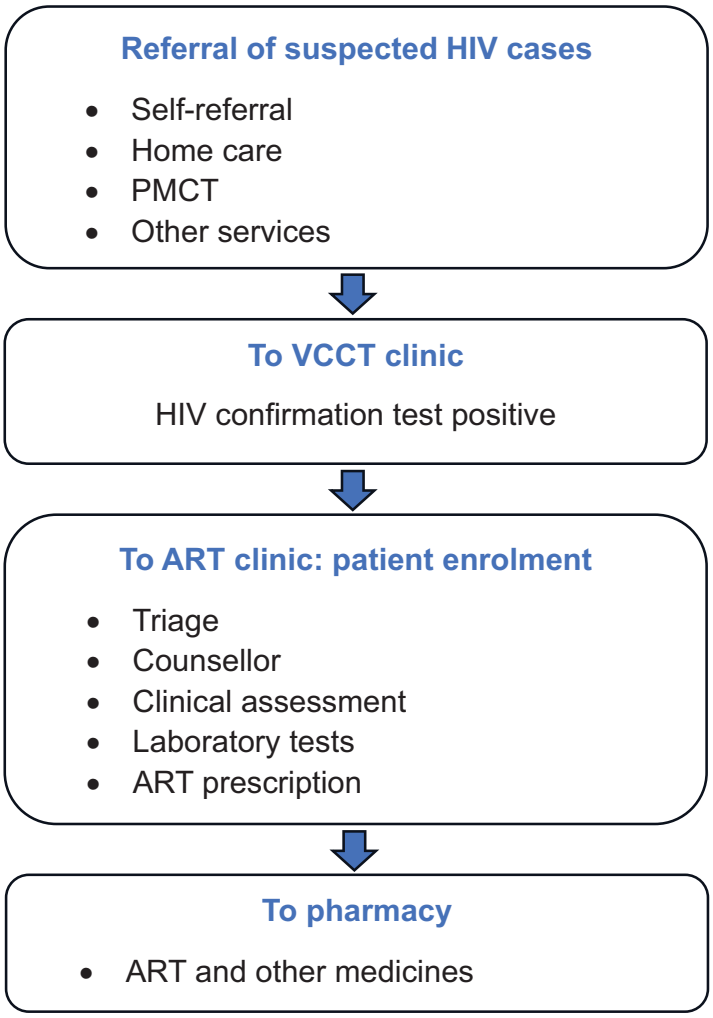
Study design and data collection

This study is a secondary analysis of data collated by the National Center for HIV/AIDS Dermatology and STDs about people living with HIV who enrol in ART at clinics across Cambodia. Data from paper-based forms are entered into the database monthly by data officers at provincial and municipal health departments. Patient-level information captured by the system includes the confirmatory HIV test result and status of ART enrolment, previous and current treatment history, referral route, clinical stage of HIV, other diagnoses and treatment for opportunistic infections, as well as sociodemographic characteristics.

Data from 2014 to 2023 were extracted from the ART database for the three clinics in Kampong Thom province: Baray Santuk, Kampong Thom and Stoung. All newly diagnosed cases who engaged with one of these three ART clinics for treatment during this period were included in the analysis.

For the purposes of this analysis, late ART initiation was represented as a categorical variable (yes or no). Cases were categorized as late ART if they did not receive ART on the same day as they were diagnosed with HIV. Categorical variables were also created to represent patient sociodemographic and clinical characteristics that were considered to be potential risk factors for late ART initiation. The patient's age at HIV diagnosis was grouped into one of four categories: 15–24 years, 25–34 years, 35–49 years and ≥50 years. Disease status was categorized using WHO stages I (infection), II (asymptomatic), III (symptomatic) and IV (AIDS/progression of HIV to AIDS).[8] Other variables for risk factors included sex (male, female), marital status (single, married, divorced/widowed, unknown), employment status (employed, unemployed, unknown), level of educational attainment (none, primary, secondary/higher, unknown), source of referral for VCCT (self-referral, home

Fig. 1. **Pathways to diagnosis and enrolment in ART in Cambodia**



ART: antiretroviral therapy; PMCT: prevention of mother-to-child transmission; VCCT: voluntary confidential counselling and testing.

care/community, PMCT or other) and the ART clinic attended. In addition, cases were categorized according to their risk behaviours for HIV.

Statistical analysis

Socioeconomic and clinical characteristics were summarized in the form of frequency and percentages for categorical variables and mean and standard deviation (SD) for continuous variables. We used univariate logistic regression models to estimate crude odds ratios (ORs) for the association between risk factors and late ART initiation. Multivariate logistic regression with adjusted ORs was used to identify which factors were independently associated with late ART initiation. Univariate and multivariate analyses were restricted to those diagnosed from 2019 onwards to reflect the impact of the introduction of the same-day policy on initiation of ART. A P value of <0.05 was considered to be statistically significant.

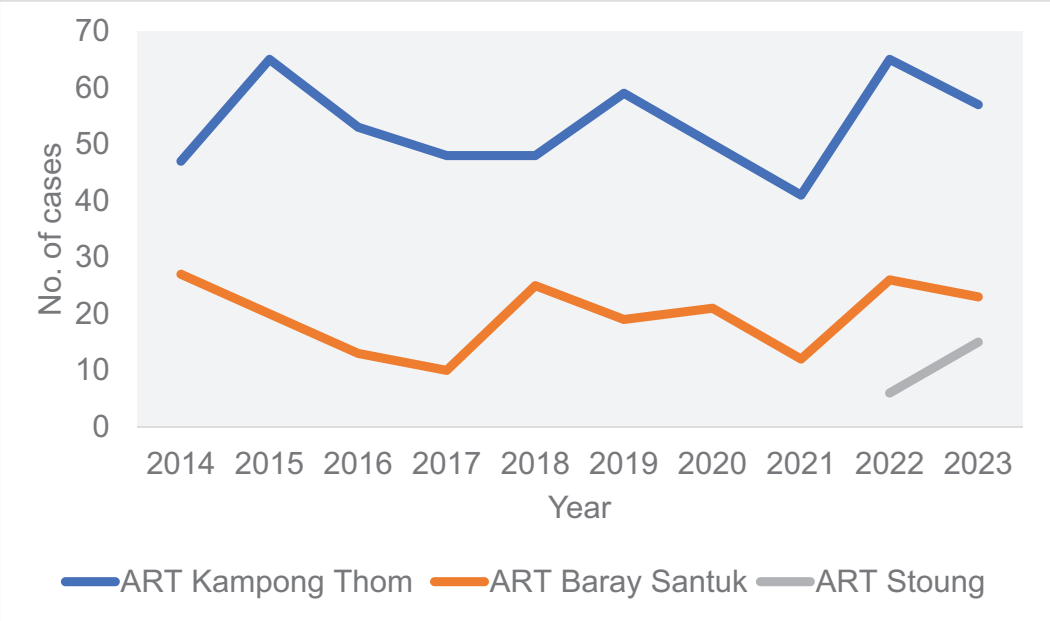
Statistical analyses were conducted using STATA version 17 (StataCorp, College Station, TX, USA).

RESULTS

A total of 741 patients newly diagnosed with HIV attended the three ART clinics in Kampong Thom province between 2014 and 2023. Two thirds of cases (511, 68.9%) were seen at the provincial hospital (ART Kampong Thom) (**Fig. 2**).

Of the 741 patients, 423 (57.1%) were female. The mean age at diagnosis was 45.7 years (SD: 10.2), with

Fig. 2. **Number of newly diagnosed cases of HIV enrolled in the three ART clinics in Kampong Thom, Cambodia, 2014–2023 (*N* = 741)**



ART: antiretroviral therapy.

half falling within the 35–49-year age group (*n* = 408, 55.1%). Among the 591 whose marital status was known, 443 (75.0%) were married; 504 of 704 (71.6%) were employed. Of the 687 cases with data about educational attainment, around half (336, 48.9%) had primary education, and one third (215, 31.3%) had no formal education. Nearly three quarters (514/723, 71.1%) were in WHO stage IV (AIDS/progression of HIV to AIDS) at diagnosis. The majority of patients (602, 81.2%) were not in a high-risk category, and two thirds (470, 63.4%) had referred themselves for HIV diagnosis or confirmation; another third (236, 31.9%) were referred for confirmation by PMCT services (**Table 1**).

Data were not available for all variables; denominators therefore vary across categories such as education level, employment status and WHO stage.

During the study period, the number of patients newly diagnosed with HIV who enrolled at ART clinics remained relatively stable (**Fig. 2**). Around half of enrolments (356, 48.0%) occurred during 2014–2018, and the other half during 2019–2023 (385, 52.0%). Overall, 415 (56.0%) patients experienced late ART initiation (>1 day). Between 2014 and 2018, 325/356 (91.3%) people newly diagnosed with HIV did not start treatment on the same day compared with 90/385 (23.4%) between 2019 and 2023 (**Fig. 3**). The median time to ART initiation for those diagnosed during 2014–2018 was 28 days (range: 0–2016 days); it was 0 days (range: 0–96 days) for those diagnosed during 2019–2023 (**Table 1**). The number and proportion of people with late ART initiation decreased rapidly after 2019, reaching 3% in 2023 (**Fig. 3**).

During the 5 years from 2019 to 2023, females were overrepresented in the group who had delayed ART (65.5% [59/90] vs 34.4% [31/90], $P = 0.095$). Late initiation was more common among those aged 35–49 years than among those aged >50 years (64.4% [58/90] vs 32.2% [29/90], $P = 0.019$), and among those who were employed vs unemployed (75.3% [67/89] vs 24.7% [22/89], $P = 0.048$) (**Table 2**). In multivariate analyses, factors independently associated with an increased likelihood of late ART initiation included receiving care at the Baray Santuk ART clinic (adjusted OR: 3.94, 95% confidence interval [CI]: 1.99–7.81, $P < 0.001$) and year of diagnosis. Late ART initiation was significantly lower in 2023 compared with 2019 (adjusted OR: 0.01, 95% CI: 0.00–0.02, $P < 0.001$).

Table 1. **Sociodemographic and clinical characteristics of patients newly diagnosed with HIV enrolled in three ART clinics in Kampong Thom province, Cambodia, 2014–2023 (*N* = 741)**

Characteristic	Newly diagnosed cases of HIV	
	No.	Percentage
Sex		
Male	318	42.9
Female	423	57.1
Mean (SD) age at diagnosis	45.7 (10.2)	
Age group (years)		
15–24	15	2.0
25–34	71	9.6
35–49	408	55.1
≥50	247	33.3
Marital status		
Single	61	8.2
Married	443	59.8
Divorced/widowed	87	11.8
Unknown	150	20.2
Occupation		
Unemployed	200	27.0
Employed	504	68.0
Unknown	37	5.0
Education level		
No formal education	215	29.0
Primary	336	45.3
Secondary or higher	136	18.4
Unknown	54	7.3
Residence		
Kampong Thom province	678	91.6
Other province	62	8.4
ART site		
Kampong Thom	511	68.9
Baray Santuk	196	26.5
Stoung (commenced in 2022)	34	4.6
WHO stage		
I (infection)	16	2.2
II (asymptomatic)	80	10.8
III (symptomatic)	113	15.2
IV (AIDS/progression to AIDS)	514	69.4
Unknown	18	2.4
Type of patient (by risk behaviour)		
General population	602	81.2
Female entertainment worker	36	4.9
Men who have sex with men	78	10.5

Characteristic	Newly diagnosed cases of HIV	
	No.	Percentage
Other[a]	25	3.4
VCCT referral source		
Self-referral	470	63.4
Home care and community	24	3.2
PMCT	236	31.9
Other[b]	11	1.5
Late ART initiation		
Yes	415	56.0
No	326	44.0
Year of diagnosis		
2014–2018	356	48.0
2019–2023	385	52.0
Median (range) days to ART initiation		
2014–2018	28 (0–2016)	
2019–2023	0 (0–96)	

ART: antiretroviral therapy; PMCT: prevention of mother-to-child transmission; SD: standard deviation; VCCT: voluntary confidential counselling and testing.

[a] This category includes patients notified for testing because they were partners of someone who was HIV-positive, pregnant, used or injected drugs, or transgender.

[b] This category includes referral from a tuberculosis programme or other route.

Fig. 3. **Number and percentage of people newly diagnosed with HIV starting ART late (>1 day after diagnosis) in Kampong Thom province, 2014–2023 (*N* = 741)**

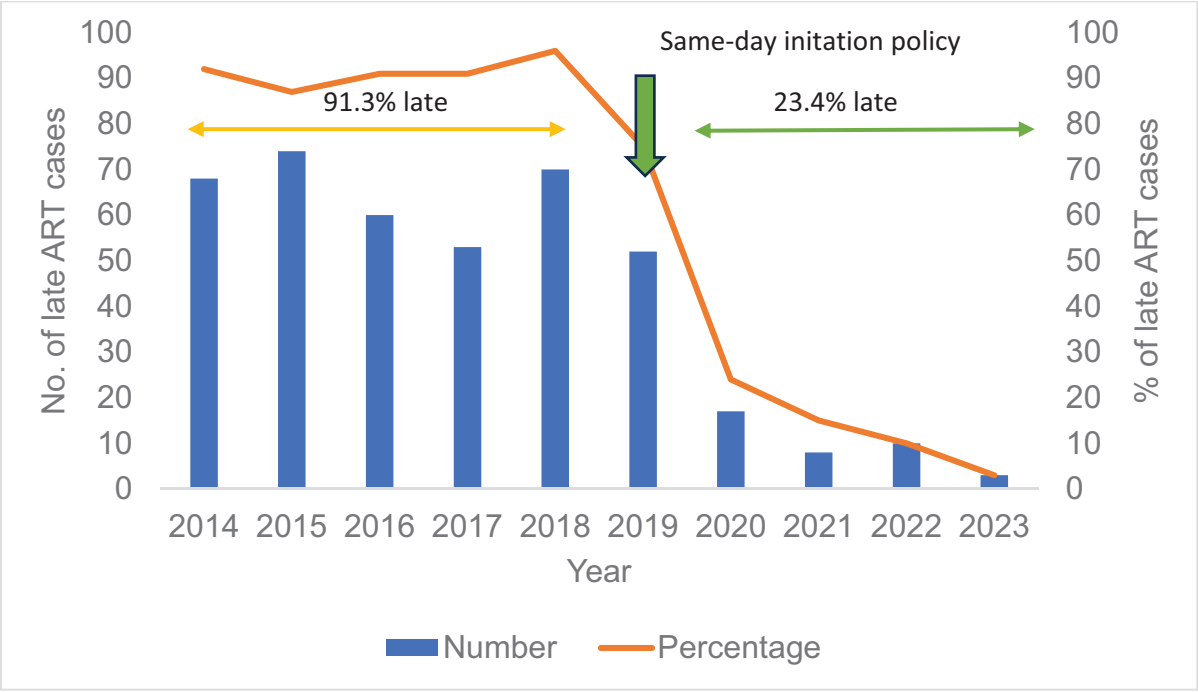


Table 2. **Univariate and multivariate analysis of factors associated with late ART initiation (>1 day after diagnosis) after implementation of the same-day ART policy among patients newly diagnosed with HIV, Kampong Thom province, Cambodia, 2019–2023 (*N* = 385)**

Characteristic	Late ART[a]	Crude OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Sex					
Male	31 (34.4)	1	Reference	1	Reference
Female	59 (65.5)	1.52 (0.93–2.48)	0.095	1.73 (0.85–3.53)	0.128
Age at diagnosis (years)					
15–24	0 (0.0)	–	–	–	–
25–34	3 (3.3)	0.59 (0.16–2.12)	0.427	1.90 (0.26–13.6)	0.520
35–49	58 (64.4)	2.10 (1.27–3.49)	0.004	2.05 (0.98–4.28)	0.056
≥50	29 (32.2)	1	Reference	1	Reference
Marital status					
Single	6 (9.0)	1	Reference	1	Reference
Married	51 (77.2)	1.38 (0.54–3.52)	0.496	1.90 (0.27–3.63)	0.990
Divorced/widowed	9 (13.6)	1.07 (0.34–3.37)	0.899	0.72 (0.16–3.23)	0.670
Occupation					
Unemployed	22 (24.7)	1	Reference	1	Reference
Employed	67 (75.3)	1.72 (1.0–2.95)	0.048	1.61 (0.75–3.46)	0.221
Education level					
No formal education	24 (28.2)	1	Reference	1	Reference
Primary education	47 (55.2)	1.41 (0.80–2.47)	0.226	1.82 (0.80–4.16)	0.151
Secondary or higher	14 (16.4)	0.85 (0.41–1.78)	0.678	1.30 (0.46–3.63)	0.614
Residence					
Kampong Thom	85 (94.4)	0.47 (0.15–1.49)	0.203	0.23 (0.03–1.61)	0.141
Other	5 (5.6)	1	Reference	1	Reference
ART site					
Kampong Thom	49 (54.4)	1	Reference	1	Reference
Baray Santuk[b]	36 (40.0)	2.33 (1.40–3.90)	0.001	3.94 (1.99–7.81)	<0.001
Stoung	5 (5.6)	0.91 (0.33–2.53)	0.870	1.23 (0.36–4.20)	0.737
WHO stage					
I (infection)	0 (0.0)	–	–	–	–
II (asymptomatic)	7 (7.8)	0.59 (0.24–1.41)	0.242	0.65 (0.12–3.25)	0.620
III (symptomatic)	14 (15.5)	0.63 (0.33–1.21)	0.174	0.58 (0.16–2.05)	0.400
IV (AIDS/progression to AIDS)	69 (76.7)	1	Reference	1	Reference
Type of patient (by risk behaviour)					
General population	75 (83.3)	1	Reference	1	Reference
Female entertainment worker	3 (3.3)	0.21 (0.06–0.72)	0.013	0.30 (0.06–1.45)	0.136
Men who have sex with men	9 (10.0)	0.29 (0.14–0.63)	0.002	0.48 (0.18–1.31)	0.156
Other	3 (3.4)	0.31 (0.09–1.07)	0.065	1.18 (0.02–1.62)	0.127
VCCT referral type					
Self-referral	81 (90.0)	0.91 (0.41–1.99)	0.820	1.48 (0.54–4.01)	0.438
Other route	9 (10.0)	1	Reference	1	Reference

Characteristic	Late ART[a]	Crude OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Year confirmed					
2019	52 (57.8)	1	Reference	1	Reference
2020[b]	17 (18.9)	0.10 (0.04–0.22)	<0.001	0.80 (0.03–0.18)	<0.001
2021[b]	8 (8.9)	0.05 (0.02–0.14)	<0.001	0.04 (0.01–0.13)	<0.001
2022[b]	10 (11.1)	0.03 (0.01–0.08)	<0.001	0.02 (0.01–0.07)	<0.001
2023[b]	3 (3.3)	0.01 (0.00–0.03)	<0.001	0.01 (0.00–0.02)	<0.001

CI: confidence interval; OR: odds ratio; VCCT: voluntary confidential counselling and testing.
[a] Values are *n* (%).
[b] Statistically significant factor.

DISCUSSION

Before 2019, less than 10% of people newly diagnosed with HIV in Kampong Thom province started ART on the day their diagnosis was confirmed. This proportion rose dramatically following the introduction of the same-day ART policy in 2019, and by 2023, only 3.2% of people newly diagnosed with HIV had a delayed start to ART. The median time to ART was also significantly reduced by this policy. However, uniformly high rates of same-day initiation were not observed at all three ART sites in the province.

This study highlights the positive impact of implementation of the same-day ART policy in reducing the time to ART in people with HIV, a policy aligned with the objectives of WHO's HIV treatment guidelines, which recommend initiating treatment as soon as possible. Other countries have also experienced improvements in the time-to-ART initiation after changes in policy.[9] In Jamaica, for example, same-day ART initiation increased from 37% to 51% between 2015 and 2019, following the introduction of the Treat All strategy.[10] Our study adds to the evidence that such strategies can be implemented and can successfully increase the proportion of patients newly diagnosed with HIV who start treatment immediately.

The clinical benefits of initiating ART immediately upon diagnosis have been demonstrated by several studies. One study in Rwanda showed that, on average, patients who began ART on the same day as diagnosis achieved better viral suppression than those who started ART 1–7 days or more than 7 days post-enrolment.[11] Other studies have suggested that same-day ART initiation may be associated with a higher loss to follow up, a potentially negative outcome and a finding that underscores the need for enhanced patient support and follow up.[12,13] Thus, the evidence regarding the impact of same-day ART initiation on retention in care is inconsistent: several observational studies have reported that same-day ART initiation may be associated with an increased loss to follow up, but others, particularly randomized controlled trials, have found the opposite – that is, same-day ART can improve engagement and retention in care. This discrepancy has been attributed to differences in study designs and selection biases.[14] The ensuing debate has underscored the need for studies that avoid such pitfalls by beginning follow up at the point of HIV testing and when patients are linked to care, rather than from the point of ART initiation. Although our study was not designed to directly assess the impact of same-day ART on retention outcomes, we adopted this approach and enrolled participants at the time of diagnosis.

Cambodia's success may partly be due to VCCT and ART clinics being located at the same hospital and to VCCT staff actively referring patients to the ART clinics, which make access easier for patients and reduce the likelihood that individuals leave before attending the ART clinic. In this study, late ART initiation was more prevalent among those attending the Baray Santuk ART clinic than those attending the clinic in Kampong Thom. The subsequent review of these findings with HIV programme managers revealed that the Baray Santuk clinic does not have staff who are dedicated to HIV care, whereas the Kampong Thom clinic has multiple staff who are dedicated to delivering this care. Other studies have demonstrated that the success of same-day ART initiation is contingent upon the presence of skilled and committed personnel capable of addressing patients' immediate needs following diagnosis. Insufficient staffing may hinder clinics' ability to successfully implement same-day ART initiation, resulting in delayed ART.[15]

This study has several limitations. First, the surveillance data used in this analysis – which depend on those who collect the data and on those who enter these data at the ART sites – may vary in completeness, consistency and reliability across sites and over time. Second, the lack of complete patient data about clinical parameters, such as CD4 count, viral load, and signs and symptoms, limited our ability to fully characterize patients' health at the time of their HIV diagnosis and thus assess a wider range of factors associated with late ART initiation. Moreover, because longitudinal follow-up data about treatment continuity were not collected, only trends in the timing of ART initiation could be described and conclusions could not be drawn about the comparative retention benefits of early versus delayed ART initiation. Finally, there could have been biases in the recording of the characteristics of the high-risk groups. For example, men who have sex with men and female entertainment workers may not disclose, for example, their sexual orientation or occupation, which means individuals will be misclassified in the analysis.

In conclusion, this study has demonstrated the feasibility of implementing a same-day ART initiation policy, even in a low-resource setting. The introduction of this policy in 2019 led to a significant improvement in the time to treatment for people newly diagnosed with HIV in Kampong Thom province. However, successful implementation depends on having staff dedicated to providing HIV care to ensure that ART can be offered on the same day as diagnosis. Further research is needed to assess the clinical impact of starting treatment on the same day in Kampong Thom, specifically to determine whether patients remain in HIV treatment and care, and whether same-day treatment initiation leads to improved clinical outcomes.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

Ethical clearance was not required because this surveillance report is based on the secondary analysis of routinely collected data. No personally identifying information was collected or reported in this study.

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Assessing progress and challenges towards malaria elimination in Kampong Speu, Cambodia: analysis of *Plasmodium vivax* and mixed infections, 2019–2023

Kanha Ly,[a] Sophanith Ung,[b] Maria Concepcion Roces,[c] Dysoley Lek[d] and Po Ly[d]

Correspondence to Kanha Ly (email: lykanha537@gmail.com)

Malaria is a life-threatening but preventable disease caused by *Plasmodium* parasites transmitted through bites of infected female *Anopheles* mosquitoes. According to the World Health Organization, the Western Pacific Region reported 1.7 million malaria cases in 2023, of which *Plasmodium vivax* accounted for 28.9% of cases and approximately 3500 malaria-related deaths. This reflects a decrease in the incidence of malaria cases and associated mortality compared to 2022, highlighting progress but underscoring persistent challenges. Cambodia, with its goal to eliminate malaria by 2025, continues to face public health challenges, particularly from *P. vivax* and mixed-species infections. This report provides an in-depth epidemiological analysis of malaria cases and radical cure treatment outcomes for *P. vivax* and mixed-species infections in Kampong Speu Province from 2019 to 2023. Data were drawn from Cambodia's national Malaria Information System and radical cure treatment records. The analysis demonstrated a substantial increase in malaria screening, primarily conducted by village malaria workers, while the number of confirmed malaria cases continued to decline. The annual parasite incidence dropped from 23.8 per 1000 at-risk individuals in 2019 to 0.7 per 1000 in 2023. Radical cure treatment completion rates among eligible cases improved from 78% in 2019 to 98% in 2023. Significant progress has been made towards malaria elimination. However, males aged 15–49 years, particularly forest-goers in the Kampong Speu operational district, remain the most at-risk group. In support of malaria elimination, it is recommended to enhance prevention measures, increase screening and ensure 100% radical cure treatment for all eligible cases in high-risk populations.

Malaria is a life-threatening but preventable disease caused by parasites transmitted to humans through the bites of infected female *Anopheles* mosquitoes. Five parasite species cause malaria in humans, with *Plasmodium falciparum* and *Plasmodium vivax* posing the greatest risk.[1] Globally, an estimated 263 million malaria cases were reported in 2023, showing a slight decline from 249 million cases in 2022. The number of malaria-related deaths has trended downward from 864 000 in 2000 to 597 000 in 2023.[1–3] In the World Health Organization (WHO) Western Pacific Region, over 1.7 million cases were recorded in 2023, with *P. vivax* accounting for 28.9% of these cases and approximately 3400 related deaths. This represented an 11% increase in cases and 4% increase in deaths compared to 2020 figures.[1]

The Greater Mekong Subregion aims for zero malaria cases by 2030,[4] aligning with the regional malaria elimination goal. As part of this initiative, Cambodia has set a national goal to eliminate all species of malaria parasites affecting humans by 2025, as outlined in the *Cambodian National Strategic Plan for Malaria Elimination, 2011–2025*.[5] The strategy focuses on universal access to early malaria diagnosis and treatment, and emphasizes the identification and treatment of all malaria cases, particularly among mobile and migrant populations. This strategy includes treating both *P. falciparum* gametocytes and the dormant liver stage of *P. vivax* to prevent relapse and further transmission through radical cure with primaquine. The strategy also includes managing the challenge of glucose-6-phosphate dehydrogenase (G6PD) deficiency,[5] which affects

[a] Kampong Speu Provincial Health Department, Kampong Speu, Cambodia.
[b] South Asia Field Epidemiology and Technology Network, Phnom Penh, Cambodia.
[c] South Asia Field Epidemiology and Technology Network, Manila, Philippines.
[d] National Center for Parasitology, Entomology, and Malaria Control, Phnom Penh, Cambodia.
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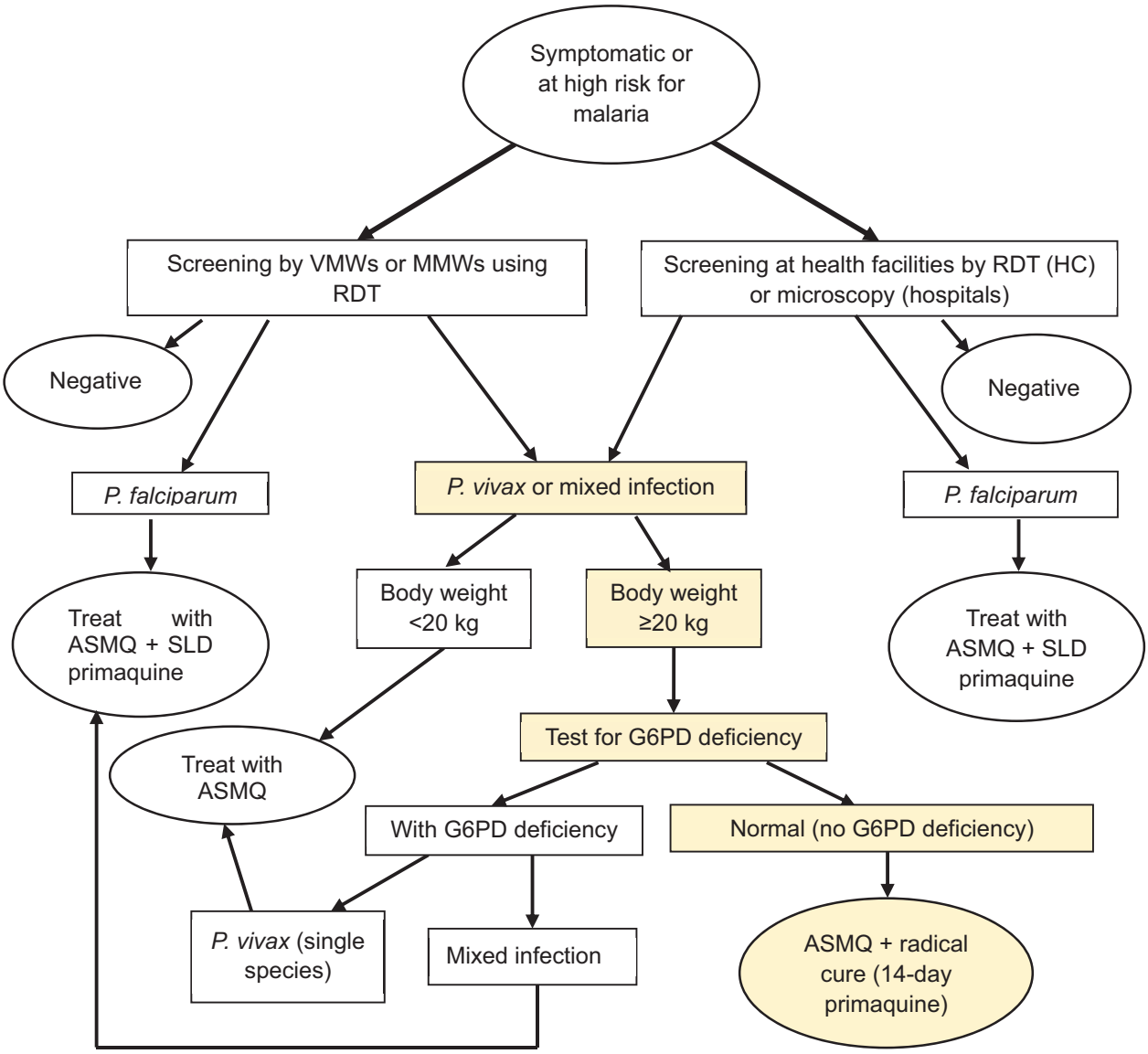
Fig. 1. **Screening, diagnosis and treatment of non-pregnant malaria cases in Cambodia**[a]



ASMQ: artesunate + mefloquine; G6PD: glucose-6-phosphate dehydrogenase; HC: health centre; MMW: mobile malaria worker; P: plasmodium; RDT: rapid diagnostic test; SLD: single low dose; VMW: village malaria worker.

[a] Highlighted boxes indicate the pathway of patients who receive radical cure treatment.

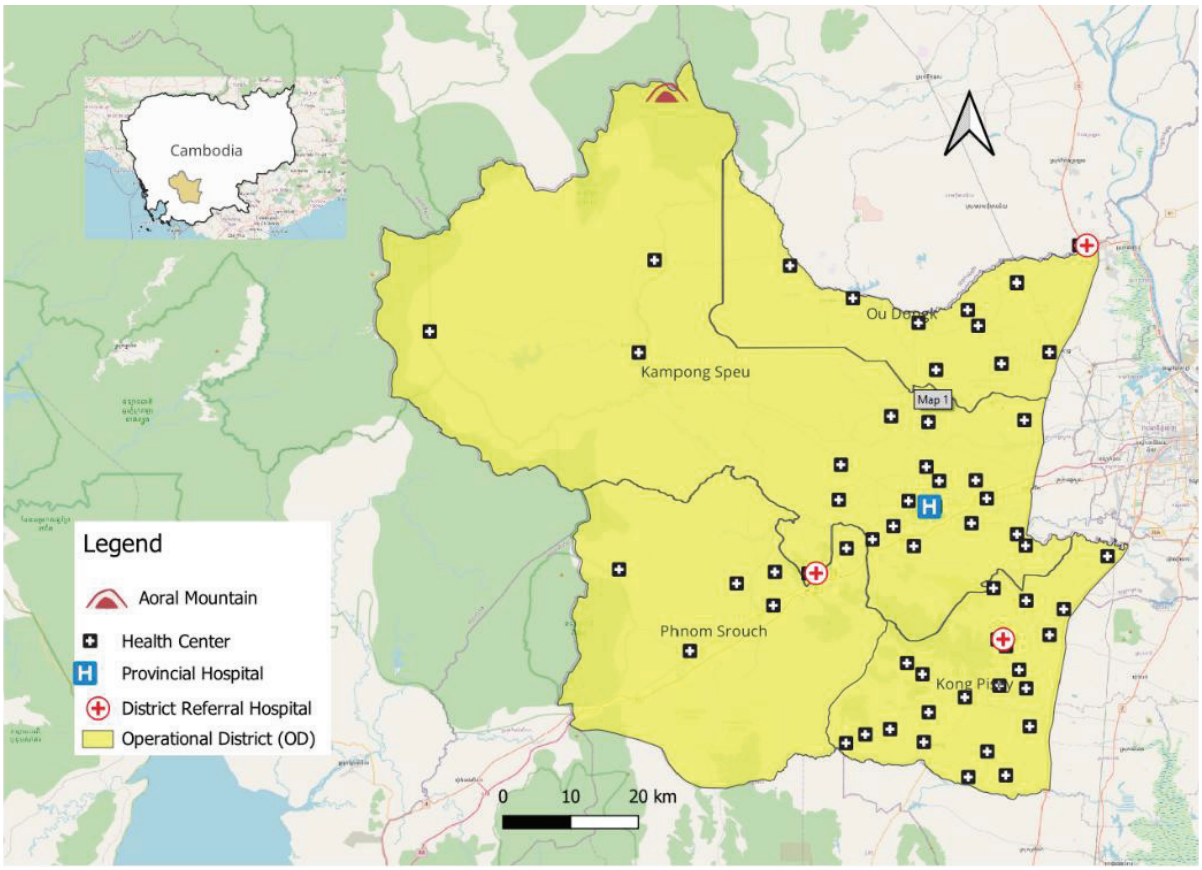
10–19% of Cambodian males and up to 13.8% of females, with regional and ethnic variations.[6]

In 2023, Cambodia reported 1384 malaria cases, comprising 94% *P. vivax*, 2% *P. falciparum* and 3% *Plasmodium malariae* and *Plasmodium knowlesi* cases. *P. vivax* cases decreased by 63% and *P. falciparum* cases by 95% compared to 2022.[7]

In line with Cambodia's 2022 national treatment guidelines for malaria, all cases should be treated with a 3-day artesunate–mefloquine regimen as first-line treatment. Patients with *P. vivax* or mixed infections should receive a 14-day course of primaquine (0.25–0.5 mg/kg/day) as a radical cure, provided they are G6PD-normal and weigh at least 20 kg, while low-dose primaquine is given for *P. falciparum* gametocyte clearance (**Fig. 1**).[8]

Kampong Speu, one of Cambodia's 25 provinces, lies approximately 48 km west of Phnom Penh, with a population of 978 189 in 2024.[9] The province is largely characterized by mountainous and forested areas, with agriculture being a significant industry. It is one of Cambodia's 21 malaria-endemic provinces.[5]

Fig. 2. **Map of Kampong Speu Province, Cambodia, indicating the location of hospitals and medical facilities in four operational districts, 2019–2023**



The Kampong Speu Provincial Health Department oversees four operational districts (ODs) and includes a provincial referral hospital, three district referral hospitals, 59 health centres and four health posts (**Fig. 2**). The provincial malaria programme is supported by 296 village malaria workers (VMWs) and 15 mobile malaria workers who operate at the community level.

This report describes the epidemiological characteristics of patients with *P. vivax* or mixed species malaria in Kampong Speu from 2019 to 2023 and their associated treatment outcomes.

METHODS

This study reports on data from malaria cases in Kampong Speu Province, focusing on cases involving *P. vivax* and mixed infections of *P. vivax* and *P. falciparum*. Data were sourced from the Malaria Information System (MIS) and from aggregated monthly radical cure treatment reports for Kampong Speu, covering the years 2019–2023.

Malaria Information System data

Data from the MIS included comprehensive records collected by VMWs and health facilities (health centres, district and provincial hospitals). The dataset includes the patients' demographic information (age, sex, residential address), body weight and mobility status, the health facility where the patient sought care, the type of test performed, that is, rapid diagnostic test (RDT) and/or microscopy, and corresponding results including malaria species detected (*P. falciparum, P. vivax, P. malariae*, mixed infection), the case notification date, severity classification, treatment administered and the final outcome of the illness.

Radical cure treatment data

Radical cure treatment data were sourced from each OD in Kampong Speu Province. The dataset, provided in Microsoft Excel format (Microsoft Corporation, Redmond, United States of America), aggregated information from

VMWs and health facilities about patients treated for *P. vivax* or mixed infections. Key variables included the following:

- number of confirmed *P. vivax* or mixed species malaria cases;
- number of patients eligible for G6PD testing and associated test results;
- number of patients eligible for radical cure based on G6PD test results;
- number of patients who started radical cure treatment; and
- number of patients who completed the radical cure regimen.

Data cleaning and anonymization

Before analysis, the dataset underwent several preparation steps. Duplicate records were identified using conditional formatting based on name, age, sex and date of notification, and were subsequently removed. Missing values were coded as "99" to enable identification and handling during analysis. The entire dataset was reviewed to detect anomalies, such as out-of-range ages, sex mismatches and incorrect or inconsistent treatment records, through automated filters and a manual review. Records with detected anomalies were then verified and corrected using patient registration log books from VMWs and health facilities. Unverified and inconsistent records were excluded from the dataset before analysis. Finally, patients' names were removed following data cleaning to ensure data anonymization and confidentiality.

Descriptive analysis

Descriptive statistics calculated frequencies and percentages per year, OD, patient demographics, diagnostic test results, treatment received and treatment outcomes.

The annual parasite incidence (API) for Kampong Speu Province and its ODs was determined by dividing the number of *P. vivax* and mixed-infection malaria cases by the at-risk population. The at-risk population was defined as individuals living in: (1) villages with reported malaria cases, indicating confirmed local transmission; and (2) villages located within 5 km of a forest or body of water (for example, a stream). These areas are considered environmentally at risk due to increased exposure to mosquito breeding habitats and higher vector density, even in the absence of confirmed cases.

RESULTS

Screening of individuals and test results

Between 2019 and 2023, the number of individuals tested for malaria saw a significant increase, from 33 574 in 2019 to 116 452 in 2023. Despite a substantial rise in the number of tests conducted, the number of confirmed malaria cases in the province dropped markedly, from 5484 cases in 2019 to 126 cases in 2023 (**Fig. 3**). VMWs played a crucial role in diagnosing malaria cases, identifying 60% (6094/10 094) through RDTs, while the remaining 40% were diagnosed at public health facilities.

Malaria species identification

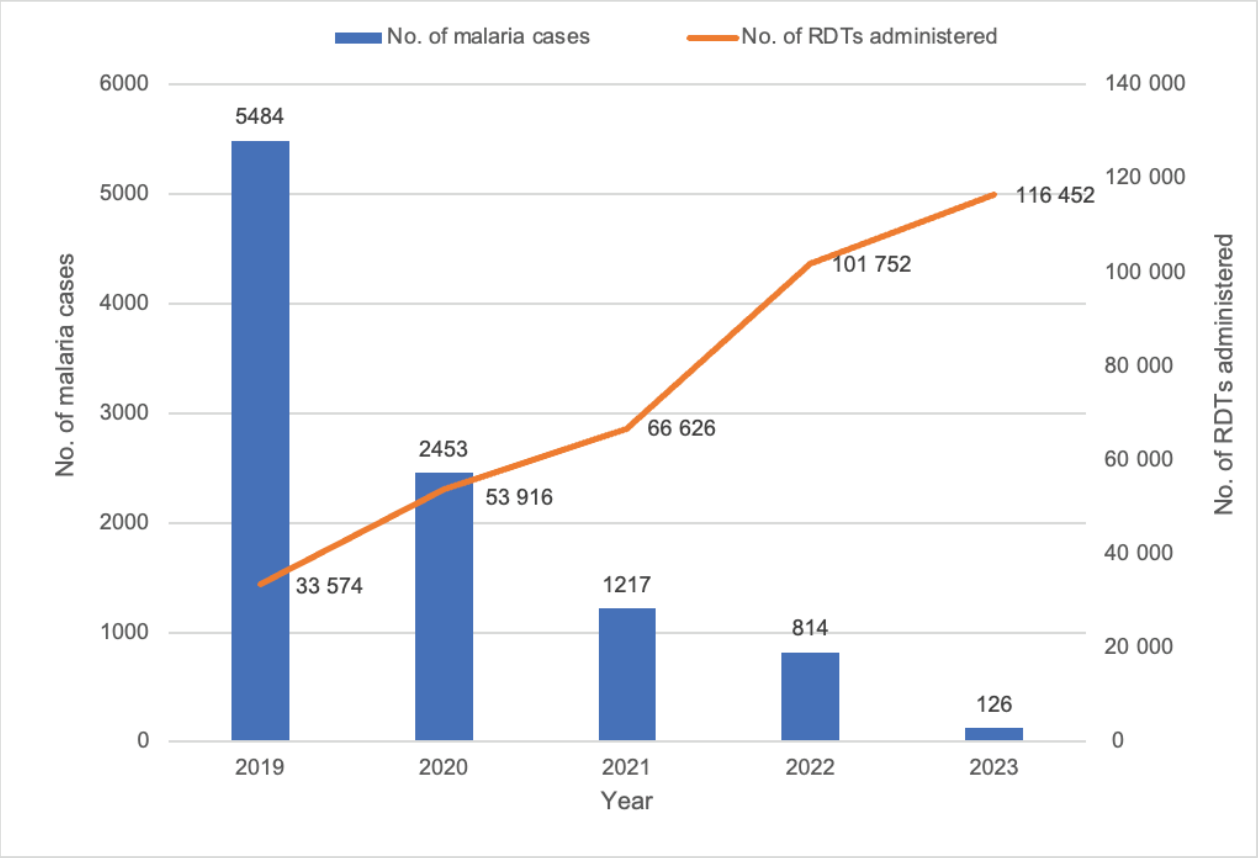
Table 1 presents the type of malaria species identified annually among diagnosed cases in the province from 2019 to 2023. *P. vivax* was the predominant species, accounting for 78.7% (7940/10 094) of cases. Mixed infections comprised 1.5% (148/10 094) of cases, while 19.7% (1993/10 094) were *P. falciparum* and 0.1% (13/10 094) were *P. malariae*.

Profile of malaria cases with *P. vivax* or mixed infections

During the same period, a total of 8088 cases were identified with either *P. vivax* or mixed infections. The age of cases ranged from 1 to 83 years, with the majority (7069, 87.4%) falling within the 15–49-year age group. A significant portion of the overall cases (7253, 89.7%) were male, with a male-to-female ratio of 9:1. Among those with recorded mobile population status, the majority (3474/4892, 71.0%) were non-mobile (**Table 2**).

Cases with severe illness were rare (44, 0.5%). The rest had simple or uncomplicated malaria. No deaths were reported. According to available surveillance data (2021–2023), 59.7% (1177/1970) of cases were classified as relapses based on a history of *P. vivax* infection in the past 12 months.

Fig. 3. **Number of malaria cases identified and number of rapid diagnostic tests administered by year, Kampong Speu Province, Cambodia, 2019–2023**



RDT: rapid diagnostic test.

Table 1. **Total number of types of malaria species identified in Kampong Speu Province, Cambodia, by year, 2019–2023**

Malaria species/year	2019	2020	2021	2022	2023	Total
P. vivax	3992 (73.0)	1982 (80.8)	1095 (90.0)	759 (93.2)	112 (88.9)	7940 (78.7)
Mixed[a]	135 (2.5)	9 (0.4)	–	4 (0.5)	–	148 (1.5)
P. falciparum	1357 (24.7)	462 (18.8)	122 (10.0)	47 (5.8)	5 (4.0)	1993 (19.7)
P. malariae	–	–	–	4 (0.5)	9 (7.1)	13 (0.1)
Total	5484 (100)	2453 (100)	1217 (100)	814 (100)	126 (100)	10 094 (100)

Values are *n* (%); *P: Plasmodium*.

[a] Mixed = *P. vivax* and *P. falciparum* coinfection.

G6PD testing and radical cure treatment

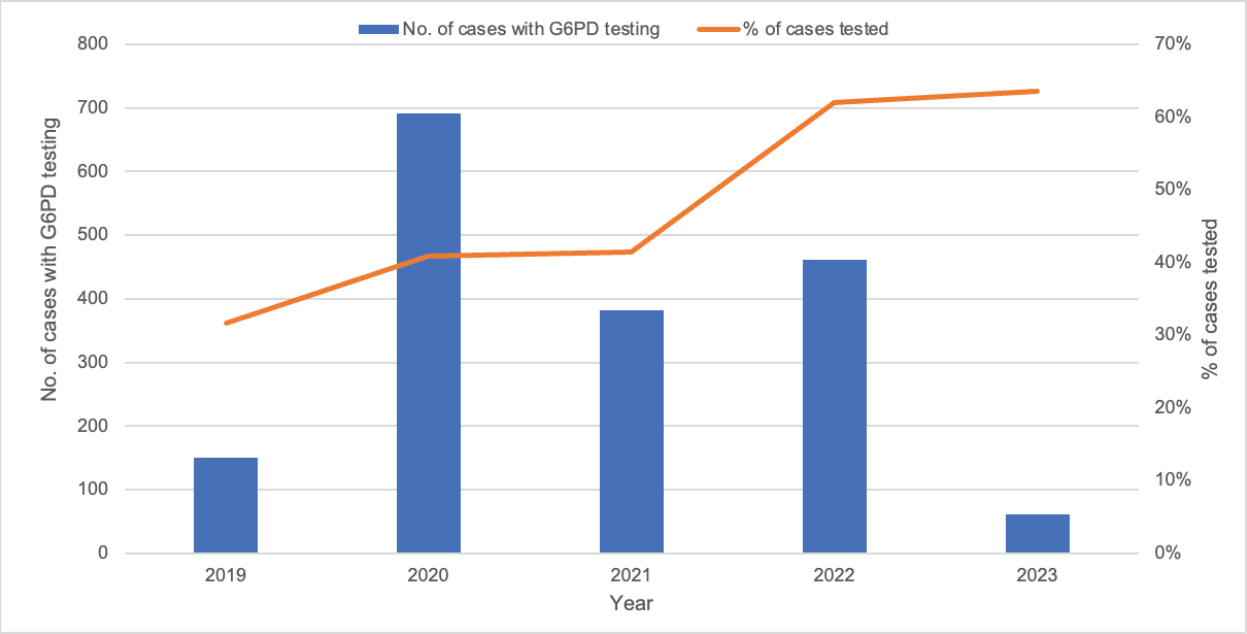
The proportion of eligible malaria cases tested for G6PD deficiency improved from 31.7% (151/476) in 2019 to 63.5% (61/96) in 2023 (**Fig. 4**). The majority (66.4%, 1144/1723) of those tested were not G6PD deficient, making them eligible for radical cure treatment (**Fig. 5**). The completion rate for radical cure treatment increased from 77.0% (67/87) in 2019 to 97.6% (41/42) in 2023 (**Fig. 6**).

Table 2. **Characteristics of malaria cases with *Plasmodium vivax* or mixed infections (*N* = 8088), Kampong Speu Province, 2019–2023**

Characteristics	*n* (%)
Age group (years)	
<5	66 (0.8)
5–14	303 (3.7)
15–49	7069 (87.4)
≥50	650 (8.1)
Sex	
Male	7253 (89.7)
Female	835 (10.3)
Mobility status	
Mobile	1418 (17.5)
Non-mobile	3474 (43.0)
Missing data[a]	3196 (39.5)

[a] Mobility status was not recorded for cases seen at health facilities.

Fig. 4. **Number and percentage of eligible malaria cases tested for G6PD deficiency, Kampong Speu Province, Cambodia, 2019–2023**

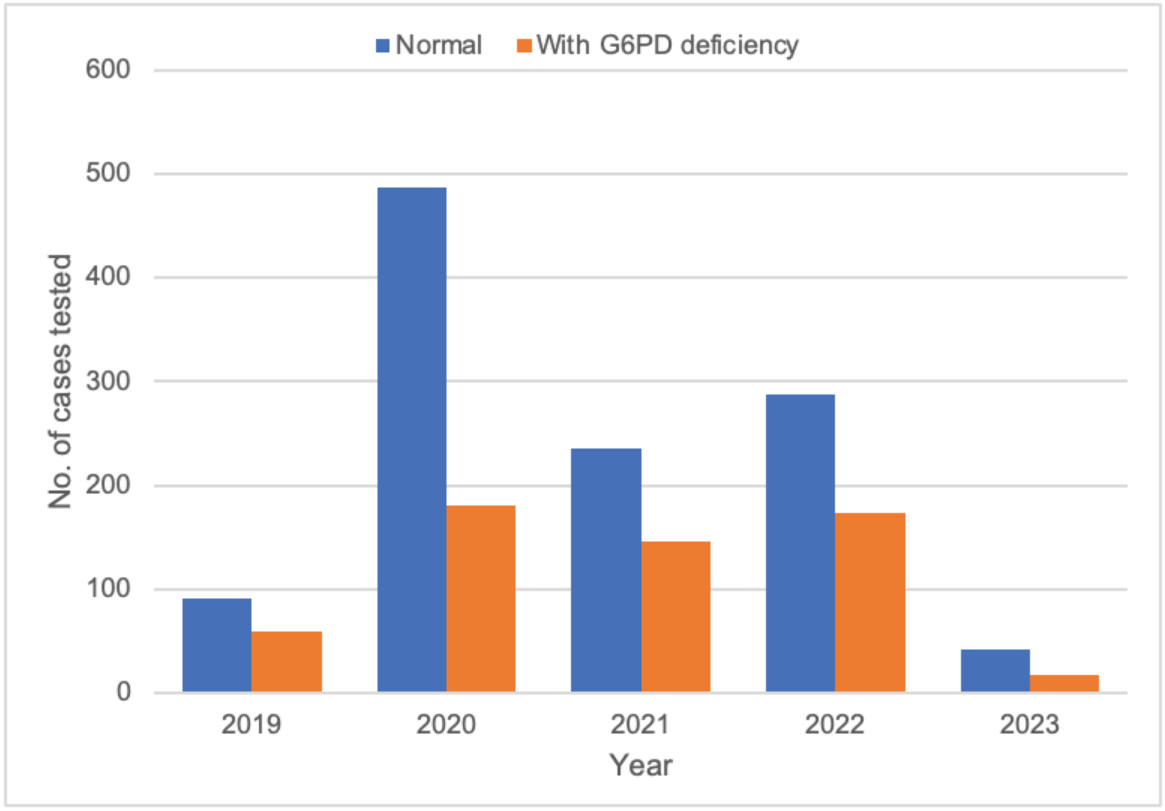


G6PD: glucose-6-phosphate dehydrogenase.

Annual parasite incidence

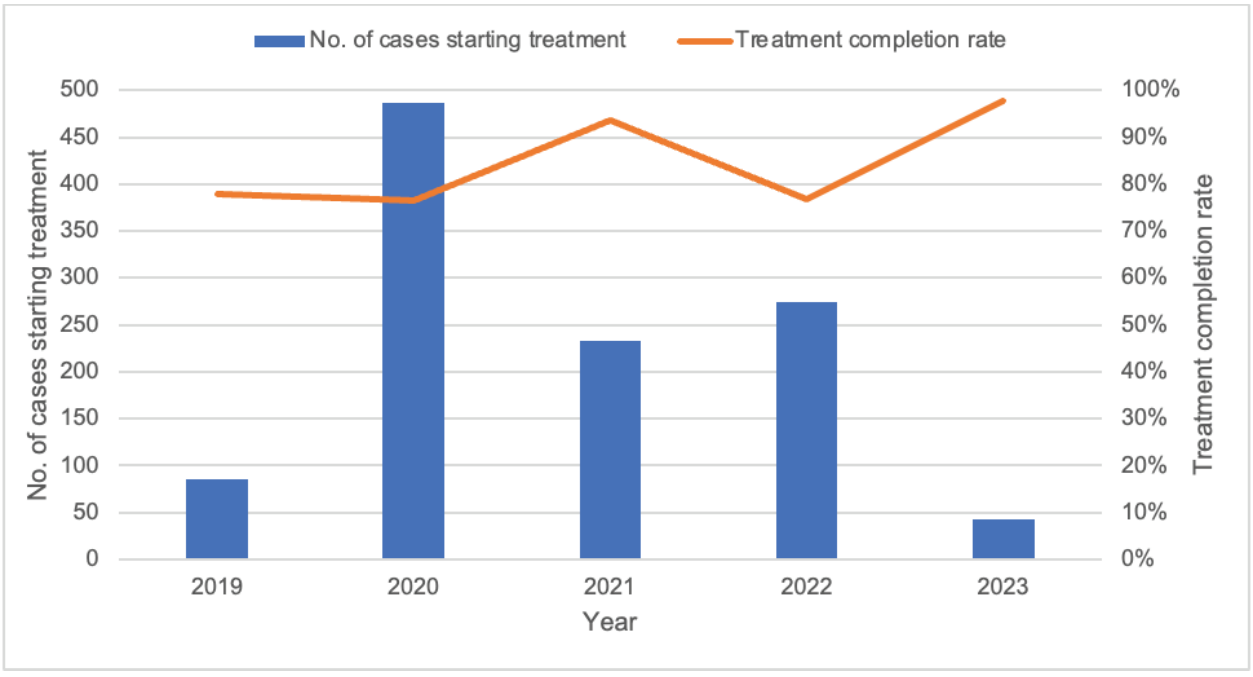
The API of *P. vivax* and mixed-infection cases demonstrated a substantial decrease from 23.8 per 1000 at-risk population in 2019 to 0.7 per 1000 in 2023. While all ODs in the province showed a decreasing API trend, Kampong Speu OD consistently recorded the highest (**Fig. 7**).

Fig. 5. **Number of G6PD deficiency test results compared to normal results by year, Kampong Speu Province, Cambodia, 2019–2023**



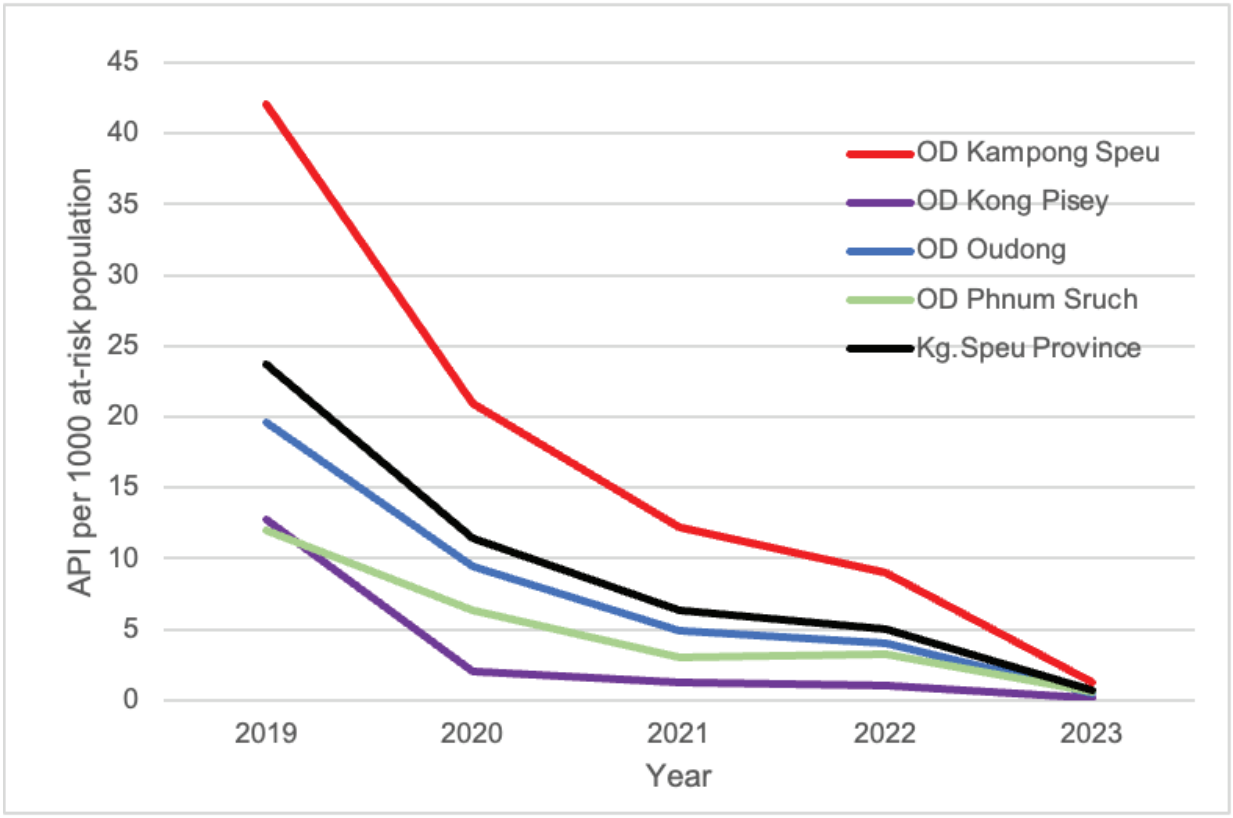
G6PD: glucose-6-phosphate dehydrogenase.

Fig. 6. **Number of cases starting radical cure of malaria species and treatment completion[a] rates by year, Kampong Speu Province, Cambodia, 2019–2023**



[a] Cases who received primaquine for 14 days are considered to have completed treatment.

Fig. 7. **API[a] by operational district, Kampong Speu Province, Cambodia, 2019–2023[b]**



API: annual parasite incidence; OD: operational district.

[a] API = no. of malaria cases/at-risk population.

[b] At-risk populations are the populations of villages with reported local cases or located <5 km from a forest or a body of water, such as a stream.

DISCUSSION

From 2019 to 2023, Kampong Speu Province experienced a consistent decline in malaria API, indicating steady progress towards eliminating malaria by 2025. This notable decrease in API can be attributed to several concerted efforts within the province. Key among these is the scaling up of active malaria screening, primarily carried out by VMWs who play an essential role in early detection and community-level interventions. Additionally, the increased completion rate of radical cure treatments among eligible cases has contributed significantly to this downward API trend by preventing relapse and by reducing transmission potential.

Despite the overall success, males aged 15–49 years continue to represent the most at-risk demographic for malaria in Kampong Speu Province. This aligns with findings from a comprehensive review of Cambodia's malaria surveillance spanning 2006–2019, which identified a similar pattern.[10] The elevated risk among this group can be linked to socioeconomic and occupational factors, as Cambodian men frequently engage in work that requires them to travel and remain in forested areas for multiple days or weeks, such as logging, agriculture and construction.[11] Forested areas show higher exposure to the *Anopheles* mosquito vectors that thrive in such environments, thus increasing the risk of transmission.

Kampong Speu OD has consistently reported the highest API among the four ODs in the province. This could be attributed to its unique geographical and environmental characteristics. The presence of Mount Aoral, the tallest peak in Cambodia, contributes to extensive forest cover in the district. This forested terrain is a known habitat for malaria vectors and serves as a work location for many male residents. The combination of dense forest cover, high human activity within these areas, and limited access to malaria prevention and treatment in forested areas is mainly due to the difficult terrain and the mobile nature of seasonal work such as

logging and foraging. Many people stay in the forest for extended periods, ranging from a few days to several weeks, and only seek care when symptoms appear, often after leaving, leading to delayed diagnosis and ongoing transmission. Mobile malaria workers offer some services, but coverage remains limited.

Limitations

The data collected through the MIS are primarily derived from reports provided by health facilities and community-level health-care workers within Kampong Speu Province. However, this system does not include reports from military health services where malaria testing and treatment are also conducted. As a result, the overall number of reported malaria cases and the API presented in this study may be underestimated.

However, national malaria programme staff we spoke to confirmed that only seven cases of *P. vivax* were reported from the military camps in the province from 2019 to 2023 (personal communication to KL). Therefore, we believe that the trends observed in this report are representative of the malaria trends in the province.

Conclusion

Kampong Speu Province has demonstrated considerable progress in its efforts towards malaria elimination. Continued momentum in achieving full malaria elimination will require enhanced and more focused interventions, particularly targeted at high-risk populations within Kampong Speu OD. Strengthening surveillance, improving access to preventive and curative services and engaging in strategies adapted to vulnerable groups will be crucial in ensuring that the province maintains and accelerates its path towards malaria elimination.

Recommendations

Kampong Speu Province has shown significant progress towards eliminating malaria, but continued efforts are necessary to ensure sustainable results. Key focus areas for future interventions include:

- **Implementing interventions that target high-risk populations.** Develop focused strategies to protect and serve populations at the highest risk of malaria, such as young adult males and forest-goers.
- **Engaging with vulnerable groups.** Foster community engagement and education to raise awareness about malaria prevention, symptoms and treatment in collaboration with local organizations and health workers to reach underserved populations effectively.
- **Strengthening surveillance.** Implement robust surveillance systems to track malaria cases in real time, enabling timely responses and resource allocation.
- **Striving to meet the 1–3–7 target.** Ensure case notification within 1 day from diagnosis, reactive case detection within 3 days of notification of an index case, and foci investigation within 7 days of notification of a case with *P. falciparum* or an indigenous case regardless of the species.
- **Improving access to services.** Determine whether the current prevention measures can be adapted and ensure that diagnostics and treatment are readily available and accessible in clinics, especially in remote areas. Continue to provide radical cure treatment to patients with *P. vivax* or mixed infections, including those with G6PD deficiency, in accordance with the latest treatment guidelines.[8]

By concentrating on these key strategies, Kampong Speu Province can build on its achievements and continue moving towards the goal of malaria elimination. Sustained commitment and innovation will be key to overcoming the remaining challenges.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

Ethical clearance was not required, as this study analysed fully de-identified routine public health surveillance data collected under public health surveillance of a national malaria programme. No personal identification information was collected or reported in this study.[12]

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Tuberculosis trends during the COVID-19 pandemic in Japan: statistical considerations and limitations

Keita Wagatsuma[a,b]

Correspondence to Keita Wagatsuma (email: waga@med.niigata-u.ac.jp)

Dear Editor,

I read with great interest the recent study by Kawatsu and Uchimura on the potential impact of COVID-19 on tuberculosis (TB) trends in Japan.[1] Using national TB surveillance data and time-series regression modelling, they estimated expected TB notifications in the absence of the pandemic. Overall, TB notifications from 2020 to 2022 fell significantly below these expectations, with notable differences by age group and place of birth. In particular, the authors should be congratulated for their effective use of nationwide surveillance data and for demonstrating an apparently good agreement between observed and fitted notifications. I commend this timely analysis but would like to discuss several points regarding the statistical methods and limitations.

First, the study analyses monthly TB notifications from 2017 to 2022, with the forecasting model trained only on the three pre-pandemic years (2017–2019). This is a relatively short baseline for capturing long-term trends and established seasonality. For time-series analysis, larger samples, such as ≥50 observations, are often recommended.[2] Also, the extension of the baseline or the incorporation of earlier historical data could improve forecast stability.

Second, the model specification and evaluation are insufficiently described, hindering the assessment of validity.[3] In time-series model building, choices of statistical models, such as generalized additive models, and the assumed error structure, for instance, normal, quasi-Poisson and/or negative binomial, can materially affect predictive performance. In addition, Japan's TB notifications exhibit a clear annual cycle (summer–autumn peak) and a secular decline, but it is unclear how these components were encoded, for example, with dummies and/or splines. While mean absolute percentage error was reported, multiple metrics, such as root mean squared error and correlation coefficient, would provide a more comprehensive appraisal.

Third, the authors note that observed counts in certain subgroups differed significantly from predictions. The clarification of how significance was assessed, for instance, via prediction intervals or formal tests comparing observed and expected counts, would aid interpretation. This is particularly the case when wide, overlapping forecast confidence intervals across strata make it difficult for readers to appraise uncertainty.

Fourth, additional analytical approaches could complement the modelling strategy. Interrupted time-series analysis can quantify level and slope changes attributable to the pandemic while adjusting for pre-existing trends, seasonality, lags and autocorrelation; such models are widely used to evaluate COVID-19 impacts.[4]

Finally, the limitations of surveillance and the potential for underascertainment during the pandemic warrant emphasis. The analysis is ecological and cannot establish causality because the TB surveillance system is not linked to COVID-19 databases. In Japan, bacteriologically confirmed TB cases declined sharply early in the pandemic, with missed cases most likely being due

[a] Division of International Health (Public Health), Graduate School of Medical and Dental Sciences, Niigata University, Niigata, Japan.
[b] Institute for Research Administration, Niigata University, Niigata, Japan.
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to service disruption and reduced care-seeking.[5] Future studies linking TB and COVID-19 data, and investigating care-seeking behaviour, would help disentangle these effects.

In conclusion, Kawatsu and Uchimura's study provides valuable evidence of the impact of COVID-19 on TB trends in Japan. With regards to the consistency of the results, their graphical presentation of observed and model-predicted counts is especially reassuring. Their conclusions may be further strengthened by addressing the above points. I thank the authors for their important contribution and hope my comments help refine understanding of the complex interplay between the COVID-19 pandemic and TB control.

Conflicts of interest

The author has no conflicts of interest to declare.

Ethics statement

No ethical approval was obtained as this Letter to the Editor was written in response to a previously published article and does not constitute original research.

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