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Investigation of a foodborne outbreak at a mass gathering in Petaling District, Selangor, Malaysia

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Objective: On 6 October 2019, Petaling District Health Office received notification of a possible foodborne outbreak involving a mass gathering event. This report presents the processes of diagnosis verification, case identification, determination of associated risk factors and commencement of control measures in managing the outbreak.

Methods: Cases were defined as those who attended the mass gathering event on 6 October 2019, consumed the pre-packaged food and subsequently developed vomiting, abdominal pain, diarrhoea or other symptoms (e.g. fever, nausea and dizziness). Epidemiological, environmental and laboratory investigations were performed. Data were analysed using SPSS software (version 24.0).

Results: A total of 169 cases were identified. The attack rate was 7.2%, and cases ranged in age from 7 to 50 years, with a median of 20 years. A total of 156 (92.3%) cases had vomiting, 137 (81.1%) had abdominal pain and 83 (49.1%) had diarrhoea. Consuming nasi lemak at the mass gathering was found to be significantly associated with developing illness (odds ratio: 9.90, 95% confidence interval: 6.46–15.16). The samples from suspected food, food handlers and the environment were positive for *Bacillus cereus*, *Staphylococcus aureus* or coliforms.

Discussion: The outbreak at this mass gathering was probably caused by food contaminated with *B. cereus* and *S. aureus*. To prevent future outbreaks, we recommend mass gathering events use certified catering services that have adequate food safety training.

An outbreak of food poisoning occurred during a mass gathering held on 6 October 2019 in Petaling District, Selangor, Malaysia. The event was attended by about 20 000 people (politicians, members of the public and students from four public universities). At the event, pre-packaged food was provided by two caterers. The Petaling District Health Office received an initial notification of food poisoning involving attendees of the event from a hospital in Klang District. This report describes the outbreak investigation to identify cases, contaminated food items and the causative pathogen(s), to determine associated risk factors and to describe the prevention and control measures taken by the District Health Office to manage the outbreak.

METHODS

Epidemiological investigation

The case definition was any person who attended the mass gathering event in Petaling District, consumed the pre-packaged food and subsequently developed abdominal pain, diarrhoea, vomiting or other constitutional symptoms (e.g. fever, nausea or dizziness) on 6 October 2019.

Active case finding was conducted by interviewing attendees of the mass gathering on site. Passive case finding was encouraged by alerting all health facilities to report cases related to the outbreak. All cases identified

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were interviewed using a standardized food poisoning questionnaire. Data on sociodemographic characteristics, symptoms of food poisoning, onset of symptoms and food intake history during the event were gathered.

Environmental investigation

An environmental investigation was conducted at the two kitchen facilities involved in preparing the pre-packaged food for the mass gathering. The parameters inspected were environmental hygiene, flow of food preparation including ingredients and their sources, handling of leftover foods and equipment hygiene.

Laboratory investigation

Rectal swabs from cases were taken at random, and environmental samples were collected focusing on suspected food and equipment used during its preparation. Clinical samples were collected in labelled containers with Cary-Blair medium. Vomitus samples were collected in sterile containers. A 250 g sample of each leftover item of food or drink (nasi lemak, bread, rice with chicken, and bottled water) was collected in sterilized sampling bags. Swab samples of food handlers' hands and kitchen utensils (cutting boards, knives, rice cookers and food containers) were collected using 3M quick swabs. All samples were sent to the National Public Health Laboratory within 24 hours of collection for culturing and sensitivity testing.

Analytical epidemiological investigation

An unmatched case–control study was conducted to identify and confirm the food items and risk factors contributing to the outbreak. Convenience sampling at a ratio of 1:0.3 was used, with 169 cases and 47 controls enrolled in the study. A case was defined as described above, while a control was defined as any asymptomatic individual who ate the food items provided during the event. Probability values were obtained using Fisher's exact test.

Data management

Respondents' identities were kept confidential. All data were collected, collated, verified and analysed using SPSS software (version 24.0).

RESULTS

Epidemiological results

Of the 2341 participants who were at risk of consuming the affected food, 169 were identified as cases for an attack rate of 7.2%. Cases' ages ranged from 7 to 50 years, with a median of 20 years. Of the total cases, 161 were detected through active case finding and eight through passive case finding. A total of 156 (92.3%) cases complained of vomiting, 137 (81.1%) had abdominal pain, 83 (49.1%) had diarrhoea and 19 (11.2%) had fever (**Table 1**). All cases sought treatment; 20 were admitted to hospital, and the remaining cases were treated as outpatients. No deaths were reported.

The epidemic curve suggested a point-source outbreak, with a pattern showing a rapid increase, single peak and tapered decline in the number of cases (**Fig. 1**). Exposure time was about 07:00 on 6 October 2019. The onset of the index case was at 08:30, and the last case was at 18:30. The incubation period ranged from 1.5 to 11.5 hours, with a median of 6.5 hours.

Nasi lemak had the highest attack rate, at 89.6% (n = 169). The odds of cases having consumed nasi lemak (odds ratio [OR]: 9.90, 95% confidence interval [CI]: 6.46–15.16) at the mass gathering were significantly higher than the odds of cases having consumed bread (OR: 0.024, 95% CI: 0.010–0.059) or rice with chicken (OR: 0.19, 95% CI: 0.14–0.27). Bottled water also had a high attack rate, at 80.8% (n = 160), but this was probably due to the high overlap of cases who consumed both nasi lemak and bottled water.

Environmental examination

The overall cleanliness rating of facility A was 48.8%. Hazard analysis found poor general cleanliness and hygiene, evidenced by a congested food preparation area and dirty flooring, food preparation surfaces and sink floor. Unsuitable, defective and dirty equipment, such as a dirty chiller with a suboptimal temperature (10 °C), were used during food preparation for the mass gathering. Additionally, the components of the nasi lemak, which included rice, sambal and boiled egg, were cooked using the same pot.

Table 1. **Characteristics and symptoms of cases (*n* = 169) and controls (*n* = 47)**

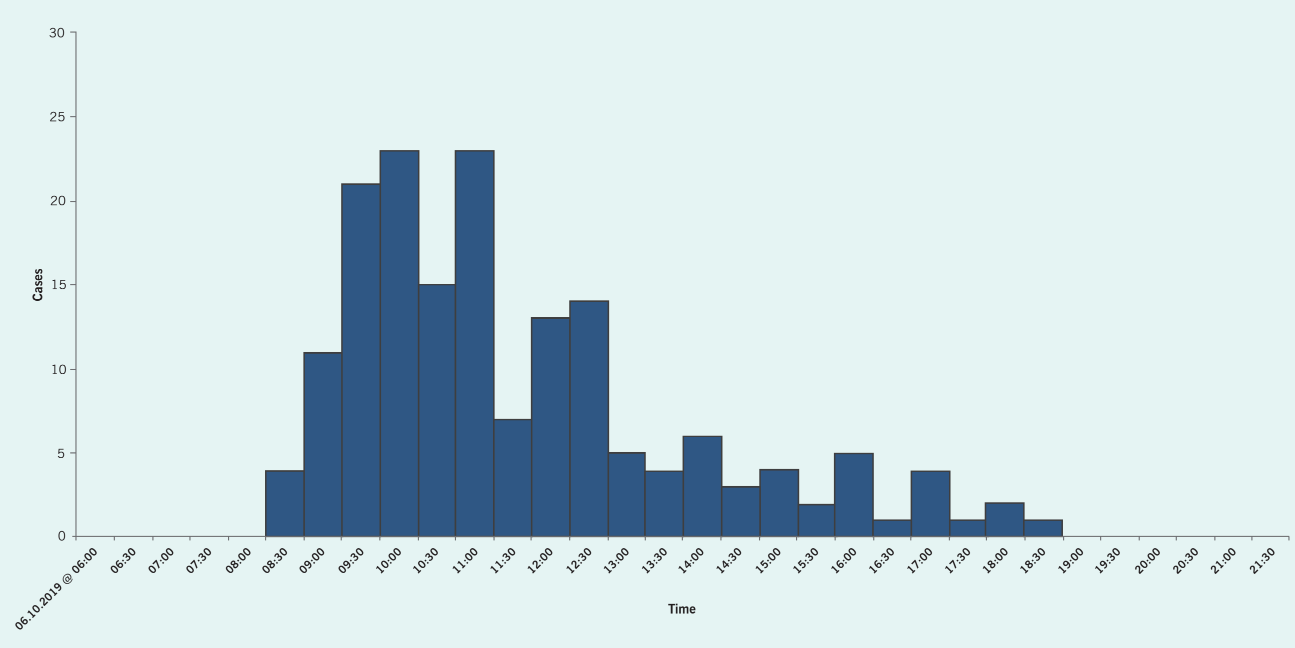
	Cases, *n* (%)	Controls, *n* (%)
Sex		
Male	25 (14.8)	3 (6.4)
Female	144 (85.2)	44 (93.6)
Age group (years)		
≤15	2 (1.2)	0 (0)
16–25	163 (96.4)	47 (100)
26–35	1 (0.6)	0 (0)
36–45	2 (1.2)	0 (0)
46–55	1 (0.6)	0 (0)
Median age (range)	20 (7–50)	21 (19–23)
Affiliation of cases		
University A students	161 (95.3)	47 (100)
General public	6 (3.6)	0 (0)
University B students	2 (1.2)	0 (0)
Symptoms		
Vomiting	156 (92.3)	0 (0)
Abdominal pain	137 (81.1)	0 (0)
Diarrhoea	83 (49.1)	0 (0)
Fever	19 (11.2)	0 (0)

Six food handlers worked at facility A. None had attended a food handling training course or had been vaccinated for typhoid. None had any acute gastroenteritis symptoms at the time of inspection. The preparation of the nasi lemak started 26 hours before consumption and the estimated holding time was up to 20 hours at room temperature.

The overall general cleanliness and hygiene of facility B were satisfactory, with a rating of 86%.

Several control measures were taken to contain and eliminate the outbreak. The caterers' activities at the facilities were suspended temporarily under the legal provisions of Section 18(1)(d) Infectious Disease Control Act 1988, Malaysia (CDC Act 1988: Act 342). This was to ensure that the caterers could take measures to comply with the requirements outlined under the Food and Hygiene Regulation and prevent further outbreaks from occurring before resuming their activities. The caterers and food handlers also underwent food handling and health education, and they were urged to attend a food handling training course and obtain typhoid vaccinations. The organizer of the mass gathering was advised to liaise

Fig. 1. **Epidemic curve of the foodborne outbreak at a mass gathering in Petaling District, Selangor on 6 October 2019**



with the local health district authority before organizing future events, to ensure that preventive measures were taken, including inspection and sampling of food handling facilities.

Laboratory results

A total of 77 samples were taken. None of the 33 rectal swabs or the nine vomitus samples tested positive for microorganisms. All five food samples were positive for at least one microorganism, namely *Bacillus cereus, Staphylococcus aureus* or coliforms. Ten of the 22 environmental samples, and three of the eight hand swabs from the food handlers, tested positive for *B. cereus* and coliforms.

DISCUSSION

The outbreak of food poisoning at this mass gathering was probably caused by *B. cereus* and *S. aureus*. This was consistent with the symptoms and incubation period reported, and was further supported by the laboratory results from samples of suspected foods, kitchen equipment and food handlers, which isolated *B. cereus* and *S. aureus*. The combination of the ubiquitous nature of these organisms and their coexistence in food and the environment is a major concern for food safety. Additionally, *S. aureus* food poisoning resembles that of *B. cereus* in terms of symptoms and incubation period.[1,2] Also, synergism has been observed between *S. aureus* sphingomyelinase and *B. cereus* phosphatidylcholine hydrolase.[2]

The most likely vehicle of the outbreak was the nasi lemak. The odds of its consumption in cases was 9.90 times that of controls, and this result was statistically significant. The other food items, despite being statistically significant, yielded odds of less than 1 (bread and rice with chicken), and the likely causative organisms are not commonly found in bottled water. *B. cereus* is a Gram-positive rod that grows well in both aerobic and anaerobic environments. It produces an emetic toxin leading to the symptoms seen in these cases.[3,4] Plant-based foods – particularly rice, pasta and noodles – are common reservoirs for *B. cereus*.[5,6] Rice is the main ingredient in nasi lemak, enhancing the likelihood of food poisoning by *B. cereus*. The laboratory findings also strengthened the evidence for B. cereus as the causative pathogen because the pathogen was found in samples from the food handlers, food and environment. Low bacterial load could explain the negative clinical samples and the mild symptoms exhibited by the cases.

S. aureus is a Gram-positive, sphere-shaped bacteria that is part of the normal flora of human skin and mucous membranes.[7] Poor hygiene practices by food handlers can increase the possibility of transferring *S. aureus* to prepared food,[7] causing it to release enterotoxins that lead to the symptoms seen in this report.[8] The possibility of *S. aureus* causing the foodborne outbreak was further strengthened by its presence in the tested sample of nasi lemak. Additionally, the prolonged holding time of more than 4 hours increased the multiplication of the microorganisms leading to food poisoning.[8] Poor food safety and hygiene practices have been established as a major factor in foodborne outbreaks in Malaysia and globally.[9,10]

Regarding limitations, since food was only served after the mass gathering event was over, most participants had left the event site before investigation of the foodborne outbreak began. Also, there was no official registry of event participants. This made it difficult to identify and interview participants, and explains the low number of participants in the study and the use of convenience sampling to identify controls.

CONCLUSION

This report highlights the processes undertaken to identify cases and causative pathogens of a foodborne outbreak at a mass gathering, and measures taken to avoid future outbreaks. This study showed that the outbreak was preventable. Recommendations to prevent future outbreaks include that organizers of mass gatherings engage with certified catering services only (e.g. by using the Trust MyCatering initiative established by the Ministry of Health Malaysia, which provides certification to catering operators that comply with food safety requirements);[11] that awareness campaigns, guidelines and policies be established to ensure that organizers of mass gatherings liaise with local health authorities to improve food handling and hygiene practices before events are held; and that stricter enforcement be considered for caterers and organizers that breach food handling and hygiene practices causing foodborne outbreaks.

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Conflicts of interest

The authors declare no conflicts of interest for this publication.

Ethics statement

This study was approved by the Medical Research and Ethics Committee, Ministry of Health Malaysia.

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Epidemiology of coinfection with tuberculosis and HIV in Japan, 2012–2020

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This report examines the characteristics and treatment outcomes of patients with tuberculosis (TB) who are coinfected with HIV in Japan. Active TB cases newly notified to the Japan Tuberculosis Surveillance system during 2012–2020 were analysed retrospectively, during which 379 HIV-positive TB cases were reported. The proportion of HIV-positive cases among those with known HIV status increased, from 1.9% (62/3328) in 2012 to 3.5% (31/877) in 2020. The proportion of those with unknown HIV testing status was consistently high, at approximately 60%, and the proportion of those who did not undergo HIV testing increased significantly, from 21.6% (4601/21 283) in 2012 to 33.7% (4292/12 739) in 2020. The proportion of foreign-born cases more than tripled, from 14.5% (9/62) in 2012 to 45.2% (14/31) in 2020. The TB treatment success rate was higher among HIV-negative than HIV-positive cases (72.7% [3796/5222] versus 60.3% [88/146]), and among Japan-born than foreign-born HIV-positive patients (65.6% [61/93] versus 50.9% [27/53]), owing largely to the high rate of foreign-born cases transferring to care outside Japan. The increasing proportion of HIV positivity among TB cases tested for HIV in this study requires ongoing monitoring, especially among foreign-born persons. However, because the number of reported cases was small, and there was low completeness of reporting of HIV testing data in the TB surveillance system, these results should be interpreted with caution. Encouraging more complete data collection by training public health nurses who complete TB case interviews and ensuring ongoing monitoring of patients with TB/HIV coinfection are recommended.

Tuberculosis (TB) continues to be a leading cause of death for people living with HIV or AIDS, and HIV remains the strongest known risk factor for progression to active TB disease for persons with latent TB infection.[1] In 2019, it was estimated that globally, 8.2% of all people with TB were living with HIV or AIDS.[2]

Japan has a middle-level, nearly low-level, burden of TB, with 12 739 cases newly notified in 2020, giving a notification rate of 10.1 per 100 000 population.[3] In the same year, 750 cases of HIV infection and 345 cases of AIDS were newly reported.[4] The number of new cases of TB, HIV and AIDS has continued to decline; however, there have been increases observed in the burden of these diseases among foreign-born persons. Because recent reports on the epidemiology of TB/HIV coinfection in Japan have been limited to regional analyses[5,6] or hospital-based studies,[7] we analysed national TB surveillance data to examine the characteristics and treatment outcomes of people with TB coinfected with HIV in Japan from 2012 to 2020.

METHODS

This was a cross-sectional study of active TB cases newly notified to the nationwide Japan Tuberculosis Surveillance (JTBS) system between 1 January 2012 and 31 December 2020.

Japan Tuberculosis Surveillance system

The JTBS system was Japan's first nationwide computerized TB surveillance system, introduced in 1987. As TB is a notifiable disease, new cases are notified to public health centres, which are responsible for collecting and entering case data into the system. The specific data items included in the JTBS system can be found else-

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where.[3] The JTBS data are summarized monthly and annually and are made publicly available online (https://jata-ekigaku.jp/english). Mechanisms to ensure data quality include an automatic verification programme and regular meetings attended by hospital and public health centre staff.

HIV status

The information regarding a case's HIV status upon diagnosis of TB is categorized as HIV-positive, HIV-negative, not tested for HIV and unknown HIV testing status. Entering these data is optional, and they are not cross-referenced with any other clinical database.

Country of birth

Information regarding country of birth is reported as Japan-born, foreign-born or unknown. Foreign-born cases are defined as people, including Japanese citizens, who were born outside of Japan.

Treatment outcomes

Prior to 2016, treatment outcomes were evaluated automatically using a computerized algorithm available only for pulmonary TB cases treated with a standard regimen. Since 2016, treatment outcomes have been entered directly by public health centres for all cases of active and latent TB. Therefore, this study examined treatment data from 2016 to 2020. Because the numbers of cases with treatment data available were quite small, statistical testing was not conducted to compare the proportions. One case with an unknown country of birth was excluded from the analysis.

Data analysis and ethics

Trends in the epidemiological and clinical characteristics of TB cases notified in Japan were examined. HIV-positive TB cases, those not tested for HIV and those with unknown HIV testing status were compared. HIV-positive TB cases notified between 2016 and 2019 were analysed by country of birth, and their treatment outcomes were compared with those of HIV-negative TB cases. Trends were tested using the Cochran–Armitage test, and proportions were compared with tests for multiple comparisons, using the Hochberg correction to adjust the P values. R version 3.6.3 (R Development Core Team, Vienna, Austria) was used for all statistical analyses.

RESULTS

General trends, 2012–2020

During the study period, a total of 156 876 TB cases were notified, of which 379 were categorized as HIV-positive, with the number of notifications steadily declining each year (**Fig. 1**). The proportion of HIV-positive cases among all TB cases was consistent at 0.2–0.3%; however, the proportion of HIV-positive cases among those tested for HIV increased significantly, from 1.9% (62/3328) in 2012 to 3.5% (31/877) in 2020 ($P < 0.01$). The proportion of those with unknown HIV testing status was consistently high, at 59.4% in 2020, whereas the proportion of those reported as not being tested for HIV increased significantly, from 21.6% (4601/21 283) in 2012 to 33.7% (4292/12 739) in 2020, although this decrease was not statistically significant ($P < 0.01$). The proportion of foreign-born cases among HIV-positive TB cases more than tripled, from 14.5% (9/62) in 2012 to 45.2% (14/31) in 2020 (**Fig. 2**).

Proportions of cases by HIV status and selected characteristics

Among people with TB, 379 were categorized as HIV-positive, 14 339 were HIV-negative, 43 035 were not tested for HIV and 99 123 had unknown HIV testing status (**Table 1**). The proportion of those tested among the total TB cases was 9.4% (14 718/156 876). The proportion of HIV-positive cases among those tested was significantly higher in males (3.4% [313/9124]) versus 1.2% [66/5594]), highest among those aged 25–64 years old (4.8%; 290/5993) and highest for those whose country of birth was unknown (8.1%; 7/86), followed by those who were foreign-born (7.1%; 107/1505). Among occupational categories, the proportion of HIV-positive cases was highest among service industry workers (6.8%; 38/558), followed by temporary workers (5.1%; 34/666) (**Table 1**).

The proportion of those not tested for HIV was significantly higher in females than males (75.7% [17 406/23 000] versus 73.7% [25 269/34 753]), highest in those aged ≥65 years old (78.7%; 29 116/

Fig. 1. **Number of newly notified TB cases by HIV status and proportion that were HIV-positive, by year, Japan, 2012–2020**

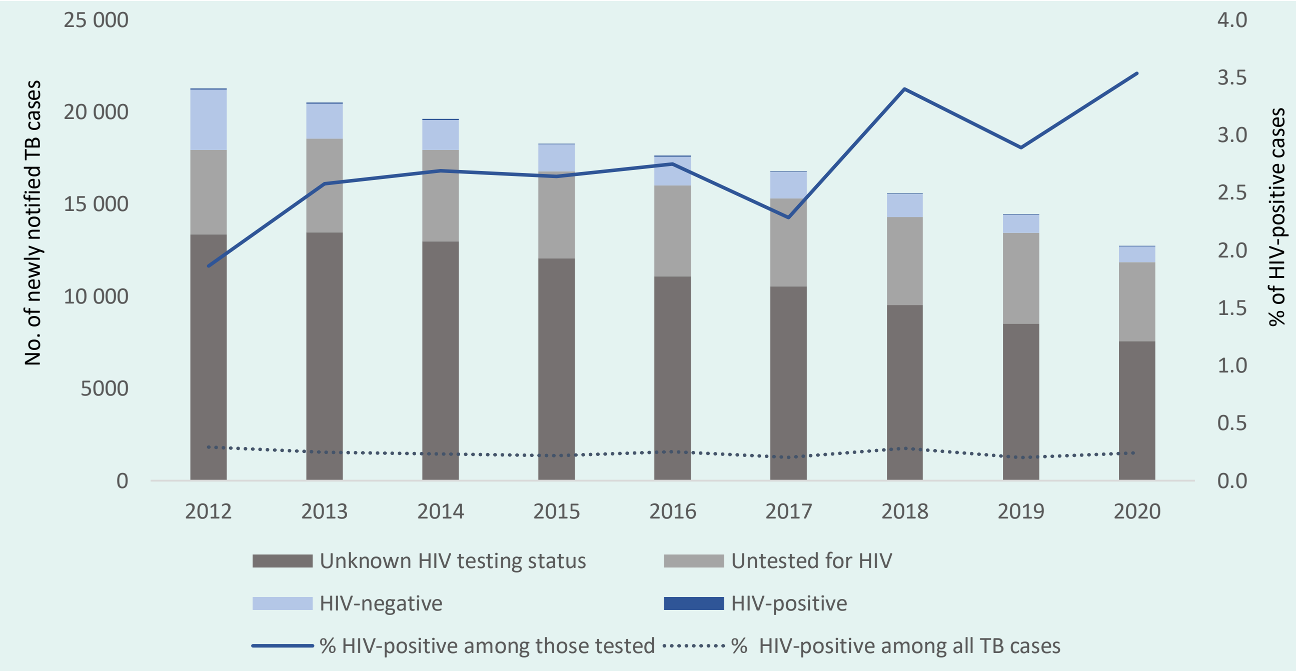
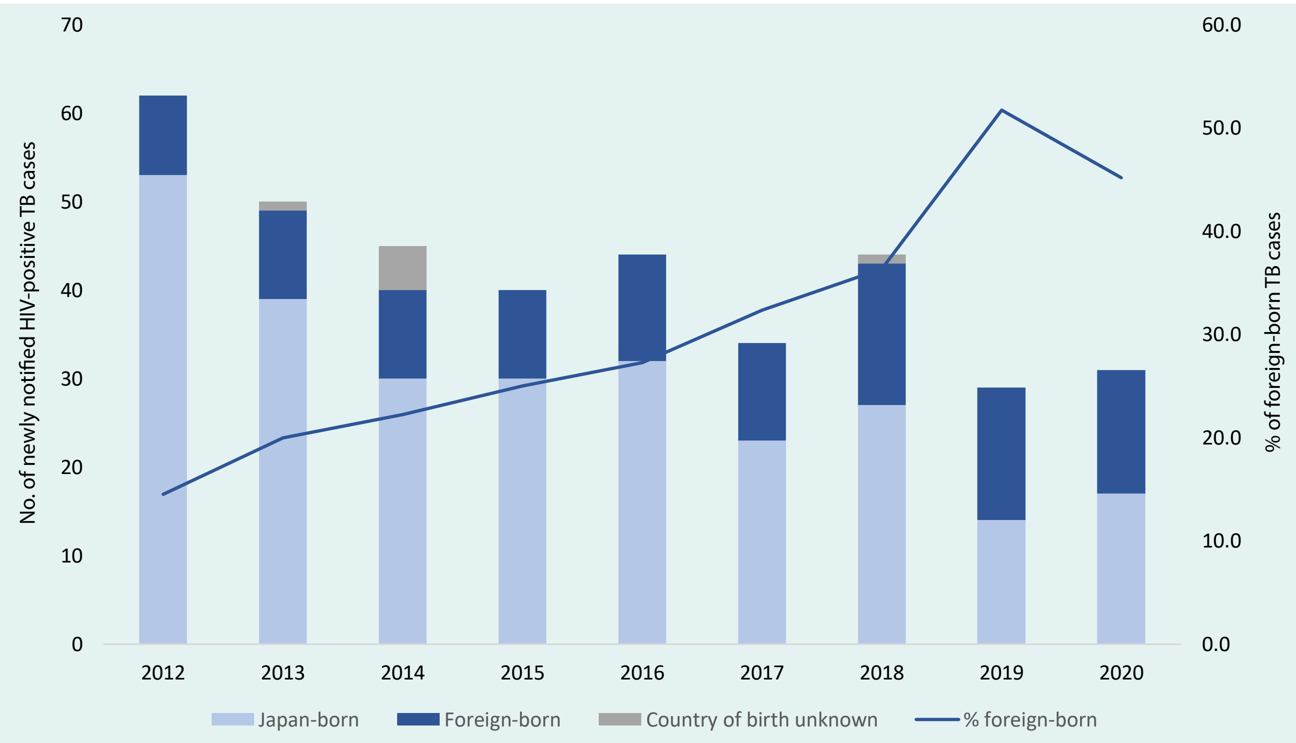


Fig. 2. **Number of newly notified TB cases by country of birth and proportion that were foreign-born, by year, Japan, 2012–2020**



36 988) and highest in those whose country of birth was unknown (88.0%; 632/718), followed by those who were born in Japan (74.9%; 39 215/52 342). Among occupational categories, the proportion of those not tested for HIV was highest among children and infants (i.e. excluding high school and university students) at 83.0% (225/271), followed by unemployed adults (78.0%; 28 971/37 124) (**Table 1**).

The proportion of those with unknown HIV testing status did not significantly differ by sex (63.3% [59 924/94 677] for males versus 63.0% [39 199/62 199] for females); however, it was highest among those aged ≥65 years old (64.2%; 66 295/103 283) and in those whose country of birth was unknown (86.9%; 4752/5470), followed by those who were born in Japan (62.5%; 87 179/139 521). Regarding occupational category, the proportion was highest among those in the category "Other or job unknown", at 69.0% (4351/6303) (**Table 1**).

Demographic characteristics of HIV-positive TB cases by country of birth

The majority of both the Japan-born and foreign-born HIV-positive TB cases were in the two younger age groups (0–24 years and 25–64 years). However, those aged 25–64 years accounted for 85.0% (91/107) of all foreign-born cases compared with 73.6% (195/265) of Japan-born cases. Males comprised 68.2% (73/107) and 88.3% (234/265) of foreign-born and Japan-born cases, respectively. For occupational categories for both Japan-born and foreign-born cases, the highest number of cases was among unemployed adults, followed by other full-time workers, service industry workers and temporary workers. These four occupational categories accounted for 86.8% (230/265) and 80.4% (86/107) of all Japan-born and foreign-born cases, respectively. Among foreign-born cases, high school and university students accounted for another 10.3% (11/107) of cases, but they were not represented in Japan-born cases (**Table 2**).

Treatment outcomes among TB cases by HIV status

The overall treatment success rate among HIV-positive TB cases was lower among foreign-born than Japan-born cases (50.9% [27/53] versus 65.6% [61/93]). Among Japan-born cases, the treatment success rate was lower in HIV-positive than HIV-negative cases (65.6% [61/93] versus 72.2% [3288/4557]), despite a larger proportion of those who were HIV-negative having died (8.6% [8/93] versus 19.0% [865/4557]). The lower treatment success rate among the HIV-positive cases was largely attributable to the higher proportion of those still on treatment (17.2% [16/93] versus 4.1% [185/4557] of HIV-negative cases still on treatment) (**Table 3**).

Among foreign-born cases, again, the treatment success rate was lower among HIV-positive than HIV-negative cases (50.9% [27/53] versus 76.4% [508/665]). This was largely attributable to higher proportions who were still undergoing treatment (11.3% [6/53] versus 5.6% [37/665]), as well as those who had transferred out (28.3% [15/53] versus 14.4% [96/665]) (**Table 3**).

DISCUSSION

Japan has historically had a low HIV prevalence, at less than 0.1 per 1000 population aged 15–49 years,[8] with a concentrated epidemic among men who have sex with men (MSM);[9] therefore, TB/HIV comorbidity has had less public health importance in Japan compared with other similarly industrialized countries. However, this study has shown an increasing proportion of HIV positivity among TB cases who were tested for HIV, which was 3.5% of those notified in 2020. This positivity rate is higher than in the United Kingdom of Great Britain and Northern Ireland (2.8% in 2018), but lower than in the United States of America (4.7% in 2019).[2]

The overall increase in HIV positivity in Japan may be due to the increase in the number of foreign-born persons with HIV who are in Japan: HIV positivity increased by 46%, from 91 cases in 2000 to 133 cases in 2019.[4] There have also been changes in the countries of birth of foreign-born persons with HIV in Japan between 2008 and 2013, with numbers decreasing from countries in the World Health Organization's South-East Asia Region and increasing from countries in the Western Pacific Region, where the estimated number of people living with HIV has increased in recent years.[8,10] Issues associated with diagnosing HIV among foreign-born persons in Japan suggest that cases may be underreported. One study estimated that approximately 50% of HIV cases among foreign-born persons in Japan are currently diagnosed,[11] as opposed to approximately 80%

Table 1. **Number and proportion of TB cases by selected characteristics and HIV status, Japan, 2012–2020**

Characteristic	Notified TB cases							
	TOTAL	No. HIV-positive	No. HIV-negative	No. untested for HIV	No. HIV testing status unknown	% HIV-positive	% untested for HIV	% HIV testing status unknown
Total	156 876	379	14 339	43 035	99 123	2.6	74.5	63.2
Sex								
Male	94 677	313	8811	25 629	59 924	3.4	73.7	63.3
Female	62 199	66	5528	17 406	39 199	1.2	75.7	63.0
Age group (years)								
0–24	7059	17	836	2039	4167	2.0	70.5	59.0
25–64	46 534	290	5703	11 880	28 661	4.8	66.5	61.6
≥65	103 283	72	7800	29 116	66 295	0.9	78.7	64.2
Country of birth								
Japan-born	139 521	265	12 862	39 215	87 179	2.0	74.9	62.5
Foreign-born	11 885	107	1398	3188	7192	7.1	67.9	60.5
Unknown	5470	7	79	632	4752	8.1	88.0	86.9
Occupational category								
Health-care worker	4526	15	478	1259	2774	3.0	71.9	61.3
Service industry worker	3916	38	520	1102	2256	6.8	66.4	57.6
Other full-time worker	22 524	98	2741	5884	13 801	3.5	67.5	61.3
Temporary worker	5256	34	632	1303	3287	5.1	66.2	62.5
Self-employed	6154	20	656	1714	3764	3.0	71.7	61.2
Unemployed								
Adults	103 310	152	8001	28 971	66 186	1.9	78.0	64.1
High school and university students	4360	11	636	1265	2448	1.7	66.2	56.1
Children and infants	527	1	45	225	256	2.2	83.0	48.6
Other or job unknown	6303	10	630	1312	4351	1.6	67.2	69.0

among those born in Japan.[9] This estimate, along with delays in seeking HIV care among foreign-born cases[8,10] and the findings of this study, suggest that Japan could potentially be facing a large pool of foreign-born persons at risk of TB/HIV coinfection.

A low HIV testing rate (9.4%) was observed among TB cases in this study. Although HIV testing is recommended for all people with TB in Japan,[12] and questions about comorbidities are asked during the TB case interview, anecdotal evidence suggests that in practice, public health nurses are reluctant to counsel TB cases about HIV and offer testing. Because approximately 70% of Japan's TB cases are aged ≥65 years, they are not perceived to be at risk of HIV infection or AIDS. Therefore, the question may seem unnecessary. Despite HIV testing being provided free of charge and anonymously at public health centres, low uptake has been reported in Japan[13,14] among younger populations and among MSM, who are considered to be more knowledgeable and conscious about the risk of HIV infection.[15] The number of HIV tests conducted at these centres has also gradually decreased, from about 146 000 tests in 2008 to 105 000 tests in 2019.[4] The proportion of adult males who have ever had an HIV test in Japan is around 10%,[16] much lower than in the United States (41.3%),[17] Canada (40.4%)[18] and England (32.4%).[19] Inconvenience, social stigma against homosexuality and discrimination against MSM and people living with HIV or AIDS are some reasons for the low uptake of testing,[9] and these may prevent the active promotion of HIV counselling and testing, even to those considered to be at high risk. It is necessary for public

Table 2. **Demographic characteristics of HIV-positive TB cases, by country of birth, Japan, 2012–2020 (*N* = 379)**

Characteristic	Country of birth: Japan (*n* = 265)	Foreign country (*n* = 107)	Unknown (*n* = 7)
Sex			
Male	234	73	6
Female	31	34	1
Age group (years)			
0-24	3	14	0
25-64	195	91	4
≥65	67	2	3
Occupational category			
Health-care worker	13	2	0
Service industry worker	26	12	0
Other full-time worker	67	29	2
Temporary worker	18	16	0
Self-employed	17	3	0
Unemployed			
Adults	119	29	4
High school and university students	0	11	0
Children and infants	0	1	0
Other or job unknown	5	4	1

health centres to have staff who are adequately trained and have counselling skills to communicate with patients with TB about HIV and AIDS in multiple languages.

Treatment success differed by HIV status and country of birth. Treatment success was lower for Japan-born HIV-positive TB cases, at 65.6%, compared with Japan-born HIV-negative cases, at 72.2%, largely due to the high proportion of HIV-positive TB cases who were still undergoing treatment. Since treatment outcomes are entered into the JTBS system after 1 year of surveillance, it is possible that the final treatment outcomes of TB cases with HIV coinfection are not captured, especially as their treatment may have been prolonged due to complications.

Among foreign-born patients with TB, treatment success for HIV-positive patients, at 50.9%, was lower than that for HIV-negative cases, at 76.4%. Cases not in the category of treatment success include those still undergoing treatment and those who have transferred out of the system, for example, to return to their home country for treatment. Although there are various public subsidies for antiretroviral therapy in Japan, it is not completely free, and the process of applying for these subsidies can be complicated for people born outside of Japan. Thus the financial burden of antiretroviral therapy, coupled with psychological stress owing to difficulties in communication and cultural differences,

Table 3. **Treatment outcomes for TB cases by country of birth and HIV status, Japan, 2016–2019**

Treatment outcome	Country of birth: Japan, *n* (%)		Foreign country, *n* (%)	
	HIV-positive	HIV-negative	HIV-positive	HIV-negative
Success	61 (65.6)	3288 (72.2)	27 (50.9)	508 (76.4)
Cured	17 (18.3)	815 (17.9)	7 (13.2)	161 (24.2)
Treatment completed	44 (47.3)	2473 (54.3)	20 (37.7)	347 (52.2)
Died	8 (8.6)	865 (19.0)	3 (5.7)	14 (2.1)
Failure	0 (0.0)	4 (0.1)	0 (0.0)	1 (0.2)
Lost to follow-up	4 (4.3)	89 (2.0)	1 (1.9)	7 (1.1)
Transferred out	2 (2.2)	122 (2.7)	15 (28.3)	96 (14.4)
Treatment ongoing	16 (17.2)	185 (4.1)	6 (11.3)	37 (5.6)
Unknown	2 (2.2)	4 (0.1)	1 (1.9)	2 (0.3)
Total	**93 (100.0)**	**4557 (100.0)**	**53 (100.0)**	**665 (100.0)**

have encouraged people who are HIV-positive, and also prompted physicians to persuade them, to return to their countries of birth to continue treatment.[20,21] To prevent disruption of treatment and poor treatment outcomes, social protection measures are urgently required to ensure that foreign-born TB patients receive appropriate care and treatment in Japan; additionally, cross-border referral mechanisms are also needed.

Limitations

Our study had several limitations. First, entering whether a person is living with HIV into the JTBS system is optional. Therefore, public health nurses who interview patients with TB are not obligated to ask for that information. Second, when HIV status is recorded, it is self-reported and not verified or linked to other clinical databases. Therefore, it is possible that the HIV positivity rate reported among TB cases is an underestimation of the true occurrence in Japan. Also, because there are no data in Japan about the uptake of HIV testing stratified by sociodemographic characteristics, it is difficult to assess whether the increase in HIV positivity among those tested was due to a real increase in the number of HIV-positive TB cases or if HIV testing was more focused on high-risk groups.[22]

CONCLUSIONS

The increasing proportion of HIV positivity among TB patients tested for HIV shown in this study requires ongoing monitoring, especially among foreign-born persons. However, as the number of reported cases was small, and the data on HIV testing reported in the JTB system were not complete, these results need to be interpreted with caution. Encouraging more complete data collection by training the public health nurses who complete TB case interviews, as well as ensuring there is ongoing monitoring of patients with TB/HIV coinfection is recommended.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

The study protocol was approved by the Institutional Review Board of the Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association (reference no. RIT/IRB 2021-5). Informed consent was deemed unnecessary by the review board, as the surveillance data did not contain personal identifiers.

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Progress and strength of response against non-communicable diseases in the US-affiliated Pacific Island jurisdictions, 2010-2021

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Objective: To determine the effectiveness of the response to the 2010 declared regional noncommunicable diseases (NCDs) emergency in nine US-affiliated Pacific Island jurisdictions.

Methods: Vital statistics and risk prevalence surveys were retrospectively reviewed using 14 standardized NCD risk, prevalence and death rate indicators to measure changes in health status over time. NCD risk and prevalence change scores were derived from subsets of these indicators, and NCD composite death rates were examined. An NCD strength-of-intervention score derived from a standardized regional monitoring tool provided measures for assessing responses aimed at curbing risk factors, prevalence and death rates. Associations between the strength-of-intervention score and changes in health status were examined.

Results: Pairs of values were available for 97 of 126 individual comparisons for 14 core indicators in nine jurisdictions. The composite mean prevalence of all risk factors across the jurisdictions between baseline and follow-up (26.7% versus 24.3%, P=0.34) and the composite mean diabetes and hypertension prevalence (28.3% versus 28.2%, P=0.98) were unchanged, while NCD death rates increased (483.0 versus 521.9 per 100 000 per year, P<0.01). The composite strength-of-intervention score for the region was 37.2%. Higher strength-of-intervention scores were associated with improvements in health indicators.

Discussion: Despite some improvements in selected NCD indicators at the jurisdiction level, there was no significant overall change in the prevalence of risk factors, diabetes and hypertension, and death rates have continued to increase since the NCD emergency declaration. However, the adoption of public sector NCD interventions was associated with improvements in health indicators.

Globally, the Pacific Islands are largely considered to be among the regions most severely affected by noncommunicable diseases (NCDs).[1–5] In the Pacific, NCDs are fuelled by several behavioural risk factors, including substantial rates of tobacco use and problem alcohol drinking, and (especially) patterns of diet and physical activity that result in a high prevalence of obesity.[6–9] In 2010, the Pacific Islands Health Officers Association (PIHOA), comprising the heads of health in the US-affiliated Pacific Islands (USAPI) – American Samoa, Commonwealth of the Northern Mariana Islands, Guam, Republic of Palau, Republic of the Marshall Islands, and four states of the Federated States of Micronesia (Chuuk, Kosrae, Pohnpei and Yap) – issued a regional declaration of health emergency for NCDs. The declaration called for an intensified response, guided by data.[10] Shortly after the declaration, PIHOA convened technical working groups to develop a framework for tracking the progress of the NCD emergency, and for monitoring the response to NCDs and the impact of the declaration. With this effort, the USAPI became the first international group to recognize and organize a systematic response to NCDs. The surveillance framework includes the following indicators with standardized data definitions: youth and adult tobacco smoking and tobacco chewing; youth alcohol use and adult binge drinking; youth and adult overweight and obesity; adult diabetes and hypertension prevalence; and cause-specific death rates for cancer, cardiovascular disease, chronic lung disease and diabetes (Unpublished document: USAPI NCD Core Monitoring

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& Surveillance Framework. Honolulu, Hawaii: Pacific Islands Health Officers Association; 2012. Available on request). In contrast with infectious disease surveillance, which largely depends on tracking incident cases, NCD surveillance depends on conducting periodic, population-based surveys. These must have consistent survey questions, physical measurement methods, age groups and sampling across jurisdictions and over time. Although difficult to deploy repeatedly and consistently, population-based surveys give a much clearer picture than institution-based incidence data of the burden of NCDs in populations. The use of a predetermined, balanced set of risk, disease prevalence and death indicators across multiple jurisdictions for the past decade is a major strength of this surveillance system. The framework aligns closely with the subsequently released World Health Organization (WHO) monitoring framework, although the USAPI framework measures not just the core indicators recommended by WHO but also youth risk factors.[11]

The USAPI framework called for monitoring the uptake of a specific suite of NCD policy measures developed by a Pacific-wide technical working group, the Pacific Monitoring Alliance for NCD Action (MANA). The MANA coordination team includes NCD policy experts from the Pacific Community (SPC), WHO, PIHOA and the Pacific Centre for Prevention of Obesity at Fiji National University. Indicator definitions and assessment criteria were developed, refined and piloted by the coordination team, and endorsed by the Pacific Heads of Health and Pacific Health Ministers groups in 2017, with the inaugural assessment report released in 2018. Progress is tracked via annual country-based assessments and reported on a MANA dashboard, which is updated every 1–3 years by each member jurisdiction, with assistance from MANA technical partners.

The MANA dashboard comprises 31 NCD interventions covering six categories including preventive policies for tobacco, policies for alcohol, policies for food environments and physical activity, health services system changes, leadership and governance structures, and surveillance and monitoring systems.[12,13] The use of predefined measures for both health status and response across multiple jurisdictions presents an opportunity to systematically examine progress in the fight against NCDs.

In this report, we examine progress in the USAPI jurisdictions by examining the change in health status indicators in the USAPI framework in the 10 years since the emergency declaration. We also look at the strength of the response against NCDs in the USAPI (reflected as intervention scores derived from the MANA dashboards from USAPI jurisdictions) and examine the relationship between the strength of intervention and changes in population health status.

METHODS

In this study, risk, disease prevalence and death rates were collected for each USAPI jurisdiction using historical sources dating back to 2000. Sources included surveys from the WHO STEPwise Approach to NCD Risk Factor Surveillance (STEPS); customized, PIHOA-facilitated, community-based hybrid NCD adult surveys; US Centers for Disease Control and Prevention (CDC) Behavioral Risk Factor Surveillance System surveys; CDC Youth Risk Behavior Surveillance surveys; PIHOA-facilitated, customized Rapid High School Youth Surveys; the US National Center for Health Statistics mortality databases in the three US territories (Guam, the Commonwealth of the Northern Mariana Islands and American Samoa); and jurisdiction vital statistics office databases for non-territory USAPI (the Freely Associated States of Palau, Marshall Islands and the four states of the Federated States of Micronesia). Convenience surveys were excluded. Prevalence estimates were compared from surveys that used consistent sampling, collection methods and survey questions as set forth in the USAPI NCD Core Surveillance Framework and Data Dictionary.

NCD premature mortality rates were 5-year running averages, for those aged 30–69 years, age-adjusted to the WHO 2000–2025 standard population.[14] Prevalence of overweight or obesity, diabetes and hypertension were reported only from studies that included physical measurements of height, weight, blood pressure and fasting blood sugars, omitting those that relied solely on self-reported disease status.

The date of the PIHOA emergency declaration, May 2010, was considered the reference date for baseline measures. For each jurisdiction, the earliest available data point between 2010 and 2013 was used as the baseline value for each indicator, whereas the most recent available data point from 2015 to the present was considered to represent "recent status". If no baseline data point was available between 2010 and 2013, we used data from surveys conducted before 2010.

A composite indicator (the NCD risk and disease prevalence change score) was calculated as the average change from baseline in the prevalence of all risk factors, diabetes and hypertension. In addition, category-specific change scores were produced by averaging the change in prevalence for all indicators within each of the following categories: tobacco, alcohol, nutrition and physical activity, and diabetes and hypertension. A composite NCD death rate indicator was calculated as the sum of death rates for cardiovascular disease, cancer, diabetes and chronic lung disease. These composite indicators were used to assess overall changes from baseline for each category, by jurisdiction and for the region as a whole (e.g. the average of all baseline tobacco use prevalence values for youth and adults across the region was compared with the average of values at follow-up, to assess overall tobacco trends). The scores were not adjusted for the differing population sizes of the jurisdictions; they represent the average of changes that each individual jurisdiction has managed to achieve, and do not measure the true changes in prevalence of the USAPI population as a whole. Only data points having both baseline and follow-up values were included in composite indicator calculations. Confidence intervals (CI) for NCD risk and disease prevalence change score results were calculated using t-tests at a 95% confidence level. Changes in death rates were assessed using Z-scores.

The strength of the NCD response was gauged using strength-of-intervention scores derived from the MANA dashboard. Each intervention item in the dashboard was awarded between 0 and 5 points, based on the strength of the intervention. Intervention scores were calculated as the current percentage of maximum possible points awarded for a group of response items, and were stratified by intervention category and by jurisdiction.

Intervention scores range from 0% (no actions taken) to 100% (all recommended interventions are implemented). For example, the regional tobacco intervention score is the sum of the points for all tobacco items across all nine jurisdictions, divided by the number of points possible × 100%, whereas the overall intervention score is the sum of the points for all intervention items across all nine jurisdictions divided by the number of points possible × 100%.

The relation between strength-of-intervention and change in health status indicators was explored using linear regression, with the intervention score for each category of intervention (tobacco, alcohol, nutrition or physical activity, and health services) as the independent variable. The log of the relative change from baseline of the corresponding health status indicators (i.e. for tobacco, alcohol, overweight or obesity, and NCD death rates) was used as the dependent variable (with tobacco intervention items linked to tobacco indicators, alcohol items to alcohol indicators, nutrition or physical activity items linked to overweight and obesity indicators, and clinical health services linked to NCD death rates). For example, if baseline versus recent cigarette use prevalence is 50% versus 30%, the relative change is (0.30 – 0.50) / 0.50 = –0.40.

The relationship between average intervention scores across all intervention categories (as the independent variable) and the log of the relative change of all health status indicators (as the dependent variable) was used to provide an overall picture of how well the nine jurisdictions were doing relative to one another. Log transformation of the relative change in health status indicators was employed to address skewness of the outcome data (skewness value = 3.69 for relative change in health status indicators versus –0.41 for log transformed data).

RESULTS

Risk factors and disease prevalence, and their changes from baseline varied considerably across jurisdictions (**Tables 1, 2**). The NCD risk and disease prevalence change scores for each indicator category (95% CI) were as follows: alcohol –4.2% (–7.7, –0.7), tobacco –2.4% (–5.3, 0.0), overweight and obesity +1.5% (–4.5, +7.4), and diabetes and hypertension –0.4% (–5.1, +4.3). Negative scores indicate improvement and positive scores worsening of health status over time.

Death rates also varied substantially across jurisdictions (**Table 3**). Composite premature NCD death rates (including deaths from cardiovascular disease, cancer,

Table 1. **Alcohol, tobacco and overweight and obesity prevalence data points for youth and adults for the US-affiliated Pacific Islands, 2010–2021**

USAPI		Alcohol consumption							
		Youth				Adult			
		Baseline % (*n*)	Recent % (*n*)	Change, %	*P*	Baseline % (*n*)	Recent % (*n*)	Change, %	*P*
American Samoa		22.8[a] (2577)	23.1[b] (1940)	+0.3	0.81	27.9[c] (843)	13.0[d] (741)	–14.9	< 0.01
CNMI		41.4[e] (2291)	23.3[f] (1621)	–18.1	< 0.01	–	23.0[g] (1089)	–	–
FSM	Chuuk	17.4[h] (943)	13.1[i] (1280)	–4.3	< 0.01	10.9[j] (2034)	13.0[k] (2046)	+2.1	0.04
	Kosrae	25.6[l] (551)	13.2[m] (479)	–12.4	< 0.01	18.7[n] (412)	21.0[o] (599)	+2.3	0.37
	Pohnpei	30.3[p] (2386)	37.3[q] (1726)	+7.0	< 0.01	26.0[r] (2227)	26.1[s] (1139)	+0.1	0.95
	Yap	–	45.5[t] (699)	–	–	29.9[u] (4271)	–	–	–
Guam		24.7[v] (1385)	18.2[w] (980)	–6.5	< 0.01	18.3[x] (501)	17.9[y] (1534)	–0.4	0.83
RMI		40.8[z] (1381)	–	–	–	–	15.4[aa] (2693)	–	–
Palau		43.4[bb] (875)	37.4[cc] (434)	–6.0	0.04	–	27.3[dd] (1404)	–	–
Alcohol change score		**Percentage (95% confidence interval)**							
		–4.2 (–7.7, –0.7)							

		Smoking tobacco							
		Youth				Adult			
		Baseline % (*n*)	Recent % (*n*)	Change, %	*P*	Baseline % (*n*)	Recent % (*n*)	Change, %	*P*
American Samoa		16.4[a] (2653)	21.7[b] (2091)	+5.3	< 0.01	39.4[c] (2044)	23.9[d] (744)	–15.5	< 0.01
CNMI		23.9[e] (2186)	12.4[f] (1808)	–11.5	< 0.01	28.6[ee] (1429)	25.2[g] (1089)	–3.4	0.06
FSM	Chuuk	19.3[h] (942)	17.4[i] (1284)	–1.9	0.25	33.1[j] (2034)	32.3[k] (2046)	–0.8	0.59
	Kosrae	27.8[l] (551)	25.6[m] (480)	–2.2	0.26	20.4[n] (412)	18.7[o] (604)	–1.7	0.50
	Pohnpei	21.7[p] (2386)	30.6[q] (1726)	+8.9	< 0.1	29.2[r] (2227)	21.3[s] (1134)	–7.9	< 0.01
	Yap	–	39.0[t] (699)	–	–	18.3[u] (4274)	–	–	–
Guam		21.9[v] (1460)	13.3[w] (1079)	–8.6	< 0.01	30.5[x] (501)	21.9[y] (1561)	–8.6	< 0.01
RMI		31.7[z] (1381)	30.7[ff] (2056)	–1.0	0.53	24.6[gg] (2998)	23.3[aa] (2677)	–1.3	0.01
Palau		47.0[bb] (869)	46.8[cc] (427)	–0.2	0.95	16.7[hh] (2184)	16.6[dd] (1404)	–0.1	0.94

		Chewing tobacco							
		Youth				Adult			
		Baseline % (*n*)	Recent % (*n*)	Change, %	*P*	Baseline % (*n*)	Recent % (*n*)	Change, %	*P*
American Samoa		6.1[a] (2653)	–	–	–	–	–	–	–
CNMI		35.2[e] (2186)	15.2[f] (1857)	–20.0	< 0.01	21.2[ee] (1429)	16.7[g] (1089)	–4.5	< 0.01
FSM	Chuuk	24.8[h] (947)	19.2[i] (1278)	–5.6	< 0.01	22.5[j] (2034)	15.3[k] (2047)	–7.2	< 0.01
	Kosrae	30.8[l] (550)	27.6[m] (480)	–3.2	0.26	25.7[n] (412)	28.5[o] (601)	+2.8	0.32
	Pohnpei	21.2[p] (2386)	22.4[q] (1726)	+1.2	0.36	26.1[r] (2227)	48.3[s] (1121)	+22.2	< 0.01
	Yap	–	60.7[t] (699)	–	–	83.3[u] (3543)	–	–	–
Guam		14.0[v] (1460)	13.5[w] (1181)	–0.5	0.71	8.5[x] (501)	4.6[y] (1562)	–3.9	< 0.01
RMI		31.1[z] (1381)	37.4[ff] (2056)	+6.3	< 0.01	–	22.8[aa] (2390)	–	–
Palau		32.5[bb] (869)	27.7[cc] (560)	–4.8	0.05	48.8[hh] (2184)	45.8[dd] (1404)	–3.0	0.08
Tobacco change score		**Percentage (95% confidence interval)**							
		–2.4 (–5.3, 0.0)							

		Overweight and obesity							
		Youth				Adult			
		Baseline % (*n*)	Recent % (*n*)	Change, %	*P*	Baseline % (*n*)	Recent % (*n*)	Change, %	*P*
American Samoa		–	–	–	–	93.1[c] (1995)	94.7[d] (699)	+1.6	0.14
CNMI		–	–	–	–	–	63.9[g] (1032)	–	–
FSM	Chuuk	46.8[h] (957)	44.6[i] (1283)	–2.2	0.30	67.8[j] (2034)	63.1[k] (1332)	–4.7	< 0.01
	Kosrae	36.9[l] (529)	36.3[m] (479)	–0.6	0.84	–	52.6[o] (576)	–	–
	Pohnpei	27.4[p] (2386)	42.4[q] (1720)	+15.0	< 0.01	59.9[r] (2227)	80.4[s] (1130)	+20.5	< 0.01
	Yap	29.8[u] (610)	33.4[t] (699)	+3.6	0.16	70.7[u] (4191)	–	–	
Guam		43.0[ii] (6434)	45.0[jj] (7706)	+2.0	0.02	–	–	–	–
RMI		–	26.5[ff] (2056)	–	–	68.5[gg] (1610)	72.8[aa] (2570)	+4.3	< 0.01
Palau		65.0[bb]	44.7[cc]	–20.3	< 0.01	75.7[hh] (2133)	72.5[dd] (1143)	–3.2	0.04
Overweight and obesity change score		**Percentage (95% confidence interval)**							
		+1.5 (–4.5, +7.4)							

Change scores represent the average per jurisdiction change from baseline of risk factors for alcohol, tobacco and overweight and obesity. They are not adjusted for differing population sizes and are not an estimate of prevalence changes in the USAPI population as a whole. Average values do not include missing values and their pairs (e.g. Yap baseline and recent youth drinking, American Samoa baseline and recent youth chewing tobacco, and Marshall Islands baseline and recent overweight and obesity).

CNMI: Commonwealth of the Northern Mariana Islands; FSM: Federated States of Micronesia; RMI: Republic of the Marshall Islands; USAPI: US-affiliated Pacific Islands.

See additional notes following Table 3.

Table 2. Diabetes and hypertension prevalence data points for adults for the US-affiliated Pacific Islands, 2010–2021

USAPI		Adult diabetes prevalence			
		Baseline % (*n*)	Recent % (*n*)	Change, %	*P*
American Samoa		47.3[kk] (342)	45.4 (746)	–1.9	0.55
CNMI		–	–	–	–
FSM	Chuuk	35.4[j] (2034)	–	–	–
	Kosrae	–	29.4[o] (603)	–	–
	Pohnpei	24.7[r] (2227)	23.5[s] (1146)	–1.2	0.44
	Yap	–	–	–	–
Guam		–	–	–	–
RMI		20.7[gg] (878)	25.3[aa] (2559)	+4.6	< 0.01
Palau		20.6[hh] (1895)	22.2[dd] (1335)	+1.6	0.27

		Adult hypertension prevalence			
		Baseline % (*n*)	Recent % (*n*)	Change, %	*P*
American Samoa		34.2[c] (2050)	39.7[d] (725)	+5.5	0.01
CNMI		–	56.0[q] (1063)	–	–
FSM	Chuuk	11.9[j] (2034)	12.4[k] (1357)	+0.5	0.66
	Kosrae	–	27.0[o] (610)	–	–
	Pohnpei	22.9[r] (2227)	21.6[s] (1143)	–1.3	0.39
	Yap	30.9[u] (4285)	–	–	–
Guam		–	–	–	–
RMI		11.6[gg] (1670)	19.2[aa] (2657)	+7.6	< 0.01
Palau		51.6[hh] (2173)	33.0[dd] (1377)	–18.6	< 0.01
Diabetes and hypertension change score			**Percentage (95% confidence interval)**		
			–0.4 (–5.1, +4.3)		

Change scores represent the average per jurisdiction change from baseline of diabetes and hypertension prevalence. They are not adjusted for differing population sizes and are not an estimate of prevalence changes in the USAPI population as a whole. Average values do not include missing values and their pairs.

CNMI: Commonwealth of the Northern Mariana Islands; FSM: Federated States of Micronesia; RMI: Republic of the Marshall Islands; USAPI: US-affiliated Pacific Islands.

See additional notes following Table 3.

Table 3. **Noncommunicable disease premature death rates for the US-affiliated Pacific Islands, 2010–2021[mm]**

		Diabetes			Cardiovascular disease			Cancer			Chronic lung disease			Total		
		Baseline	Recent	*P*	Baseline	Recent	*P*	Baseline	Recent	*P*	Baseline	Recent	*P*	Baseline	Recent	*P*
American Samoa		107.4[nn]	100.4[oo]	0.64	243.4[nn]	237.0[oo]	0.76	110.7[nn]	118.6[oo]	0.59	22.8[nn]	20.6[oo]	0.73	484.3[nn]	476.6[oo]	0.68
CNMI		48.8[nn]	41.4[oo]	0.35	164.1[nn]	146.8[oo]	0.24	93.3[nn]	101.3[oo]	0.49	33.4[nn]	7.0[oo]	0.69	339.6[nn]	296.5[oo]	< 0.01
FSM	Chuuk	162.0[pp]	193.2[oo]	0.14	216.6[pp]	252.6[oo]	0.14	78.6[pp]	198.2[oo]	< 0.01	23.8[pp]	18.2[oo]	0.45	481.0[pp]	662.2[oo]	< 0.01
	Kosrae	364.1[pp]	327.6[oo]	0.64	292.0[pp]	335.4[oo]	0.56	170.8[pp]	153.7[oo]	0.75	32.0[pp]	45.1[oo]	0.62	858.9[pp]	861.8[oo]	0.97
	Pohnpei	172.0[pp]	186.0[oo]	0.55	251.0[pp]	338.0[oo]	< 0.01	127.0[pp]	135.2[oo]	0.68	72.0[pp]	65.7[oo]	0.66	622.0[pp]	724.9[oo]	< 0.01
	Yap	76.0[pp]	82.2[qq]	0.81	140.2[pp]	159.2[qq]	0.59	306.5[pp]	283.0[qq]	0.64	60.4[pp]	15.0[qq]	0.01	583.1[pp]	539.4[qq]	0.32
Guam		39.9[nn]	36.0[oo]	0.39	223.1[nn]	243.3[oo]	0.07	111.1[nn]	134.3[oo]	< 0.01	15.7[nn]	9.7[oo]	0.02	389.8[nn]	423.3[oo]	< 0.01
RMI		428.0[rr]	404.0[qq]	0.42	139.0[rr]	211.0[qq]	< 0.01	121.0[rr]	129.9[qq]	0.59	11.0[rr]	17.0[qq]	0.27	699.0[rr]	761.0[qq]	< 0.01
Palau		94.0[ss]	65.2[oo]	0.13	266.0[ss]	274.5[oo]	0.80	233.0[ss]	204.7[oo]	0.36	29.0[ss]	32.8[oo]	0.85	622.0[ss]	577.2[oo]	0.23
All USAPI		**381.6**	**368.4**	**0.42**	**717.3**	**791.4**	**< 0.01**	**406.8**	**476.3**	**< 0.01**	**86.7**	**59.9**	**< 0.01**	**483.0**	**521.9**	**< 0.01**

CNMI: Commonwealth of the Northern Mariana Islands; FSM: Federated States of Micronesia; RMI: Republic of the Marshall Islands; USAPI: US-affiliated Pacific Islands.

Notes for Tables 1–3:

[a] 2011 American Samoa Youth Risk Behavior Survey (high school, grades 9–12)
[b] 2015 American Samoa Youth Risk Behavior Survey (high school, grades 9–12)
[c] 2004 American Samoa NCD STEPs Survey (25–64 years)
[d] 2018 American Samoa Hybrid NCD Survey (25–64 years)
[e] 2011 CNMI Youth Risk Behavior Survey (high school, grades 9–12)
[f] 2017 CNMI Youth Risk Behavior Survey (high school, grades 9–12)
[g] 2016 CNMI Hybrid NCD Survey (≥18 years)
[h] 2017 Chuuk Rapid Youth Survey (high school, grades 9–12)
[i] 2019 Chuuk Rapid Youth Survey (high school, grades 9–12)
[j] 2006 Chuuk Behavioral Risk Factor Surveillance System Survey (18–64 years)
[k] 2016 Chuuk NCD STEPs Survey (18–64 years)
[l] 2015 Kosrae Rapid Youth Survey (high school, grades 9–12)
[m] 2019 Kosrae Rapid Youth Survey (high school, grades 9–12)
[n] 2012 Kosrae Behavioral Risk Factor Surveillance Survey (≥18 years)
[o] 2019 Kosrae Hybrid NCD Survey (≥18 years)
[p] 2015 Pohnpei Rapid Youth Survey (high school, grades 9–12)
[q] 2017 Pohnpei Rapid Youth Survey (high school, grades 9–12)
[r] 2008 Pohnpei NCD STEPs Survey, as reported in Pohnpei State Department of Health Year 2015 NCD Profile (25–64 years)
[s] 2019 Pohnpei Hybrid NCD Survey (≥18 years, but values in table were for adults 25–64 years only)
[t] 2016 Yap Rapid Youth Survey (high school, grades 9–12)
[u] 2013 Yap Community Health Assessment Survey (youth items 15–18 years; adult items ≥18 years)
[v] 2011 Guam Youth Risk Behavior Survey (high school, grades 9–12)
[w] 2017 Guam Youth Risk Behavior Survey (high school, grades 9–12)
[x] 2011 Guam Behavioral Risk Factor Surveillance Survey (≥18 years)
[y] 2017 Guam Behavioral Risk Factor Surveillance Survey (≥18 years)
[z] 2011 RMI Youth Risk Behavior Survey (high school, grades 9–12)
[aa] 2018 RMI Hybrid NCD Survey (18–64 years)
[bb] 2011 Palau Youth Risk Behavior Survey (high school, grades 9–12)
[cc] 2015 Palau Youth Risk Behavior Survey (high school, grades 9–12)
[dd] 2017 Palau Hybrid NCD Survey (25–64 years)
[ee] 2011 CNMI Behavioral Health Survey (≥18 years)
[ff] 2016 RMI Joint Global Youth Tobacco & Rapid Youth Survey (high school, grades 9–12)
[gg] 2002 RMI NCD STEPs Survey (18–64 years)
[hh] 2012 Palau NCD STEPs Survey (25–64 years)
[ii] 2015 Guam School BMI Survey (results from grades 9–12 presented)
[jj] 2019 Guam School BMI Survey (results from grades 9–12 presented)
[kk] 2004 American Samoa NCD STEPs Survey (25–64 years; cut off for diabetes set at ≥110 mg/dL)
[ll] 2018 American Samoa Hybrid NCD Survey (25–64 years; cut off for diabetes set at ≥110 mg/dL)
[mm] Death rates – per 100 000 residents per year – are for those aged 30–69 years, age-adjusted (to the WHO 2000–2025 standard population) five-year running averages. USAPI totals are weighted by the population size of those aged 30–69 years for each jurisdiction
[nn] Running average, 2006–2010
[oo] Running average, 2013–2017
[pp] Running average, 2007–2011
[qq] Running average, 2014–2018
[rr] Running average, 2011–2015
[ss] Running average, 2008–2012

diabetes and chronic lung disease) for the region as a whole increased from a baseline of 483.0 to 521.9 per 100 000 residents aged 30–69 years ($P < 0.01$).

Baseline versus recent death rates

Table 4 shows MANA intervention scores for tobacco, alcohol, overweight or obesity, and health services intervention categories by jurisdiction. The average overall NCD strength-of-intervention score for the region was 37.2%. There was considerable variation in the strength of intervention by category, from 24.9% for nutrition or physical activity to 48.1% for tobacco. The average composite strength-of-intervention score across intervention categories by jurisdiction also varied considerably, from 25.0% for the Republic of the Marshall Islands to 54.8% in Guam.

Log linear regression showed an overall negative relationship between response scores and the log

Table 4. **Strength of noncommunicable disease interventions in the USAPI, 2020**

Response category	Interventions	American Samoa	CNMI	Chuuk (FSM)	Kosrae (FSM)	Pohnpei (FSM)	Yap (FSM)	Guam	RMI	Palau	Total points	Points possible	Intervention score by category (%)
Tobacco	Tobacco excise taxes	4	4	3	3	3	3	3	1	5	29	45	
	Smoke-free environments	5	4	1	4	5	1	5	4	4	33	45	
	Tobacco health warnings	0	2	1	1	1	1	3	2	0	11	45	
	Tobacco advertising, promotion and sponsorship	2	1	1	4	5	1	2	4	5	25	45	48.1
	Tobacco sales and licensing	5	5	0	3	1	0	4	0	5	23	45	
	Tobacco industry interference	0	0	1	1	1	1	0	0	0	4	45	
	Enforcement of laws and regulations related to tobacco	1	3	2	2	2	2	3	0	1	18	27	
Alcohol	Alcohol licensing to restrict sales	5	5	3	3	4	3	5	4	5	37	45	
	Restrict alcohol advertising	0	0	0	0	5	0	2	0	0	7	45	
	Alcohol taxation	2	2	2	2	2	2	2	1	2	17	45	46.4
	Drinking and driving penalties	3	3	2	2	2	2	4	3	4	25	45	
	Enforcement of laws and regulations related to alcohol	1	3	0	0	0	0	3	0	1	10	27	
Nutrition & physical activity	Reducing salt consumption	0	1	5	0	1	5	4	0	3	19	45	
	Eliminating trans-fats	1	1	0	0	0	0	1	1	1	5	45	
	Restricting unhealthy food marketing to children	1	0	0	0	1	0	1	0	1	4	45	
	Food fiscal policies	0	0	3	2	3	3	0	3	0	14	45	
	Healthy food policies in schools	4	2	0	1	1	0	5	1	1	15	45	
	Food-based dietary guidelines	1	1	2	2	2	2	4	3	1	18	45	24.9
	Restrict marketing of breast milk substitutes	0	0	0	0	0	0	0	0	5	5	45	
	Baby-friendly hospitals	2	1	2	0	3	2	0	1	1	12	45	
	Maternity leave and breastfeeding	0	1	1	1	0	1	1	0	1	6	45	
	Compulsory physical education in school curriculum	5	1	1	0	1	1	3	0	1	13	45	
	Enforcement of laws and regulations related to nutrition & physical activity	1	3	0	0	0	0	3	0	1	8	27	
Health services	National guidelines for care of main NCDs	4	1	2	1	1	2	4	2	0	17	45	
	Essential drugs	2	5	2	4	4	2	2	1	0	22	45	47.4
	Smoking cessation availability	3	4	3	2	3	3	4	0	3	25	45	
	Total points	**50**	**53**	**37**	**38**	**51**	**37**	**68**	**31**	**51**	**422**	**1116**	
	Points possible	**124**	**124**	**124**	**124**	**124**	**124**	**124**	**124**	**124**	**1116**		
	Intervention score by jurisdiction (%)	**40.3**	**42.7**	**29.8**	**30.6**	**41.1**	**29.8**	**54.8**	**25.0**	**41.1**	**Average intervention score = 37.2%**		

CNMI: Commonwealth of the Northern Mariana Islands; FSM: Federated States of Micronesia; NCD: noncommunicable disease; RMI: Republic of the Marshall Islands; USAPI: US-affiliated Pacific Islands.

Strength of intervention: Not present = 0 points; under development = 1 point; present but low strength = 2 points; present with medium strength = 3 points; present with higher strength = 4 points; present with highest strength = 5 points. Response scores are calculated as number of points awarded in the category, divided by the total points possible × 100%.

Notes: The original MANA dashboard has 31 indicators grouped into categories for governance, monitoring systems, health service systems, tobacco, alcohol, nutrition and physical activity. For this report, we omitted indicators for governance and monitoring systems, and used the remaining 26 that corresponded directly to intervention categories that match groups of health status indicators in the USAPI NCD Monitoring & Surveillance Framework (i.e. MANA tobacco items for tobacco indicators; alcohol items for alcohol indicators; physical activity and nutrition items for overweight and obesity indicators; and health service items for death rates – since health services are deemed to have the greatest potential impact on NCD death rates in the short-to-medium term). Responses for the NCD interventions in the MANA dashboard are graded using a "traffic light" rating scheme: red denotes that no policy or action has been taken; amber denotes that policy or action is under development; and green denotes that policy or action is in place. When a policy or action is in place, the strength of the actions is assessed using a star system (0–3 stars).[12] For the purposes of this report, the traffic light codes for each intervention were assigned a numerical point score ranging from 0 to 5, with 5 points indicating the strongest response for that intervention. In the MANA dashboard, enforcement of laws and policies related to nutrition, alcohol and tobacco are included as a single item (with higher scores awarded for enforcement of more than one substance). In the present report, enforcement was split into three items: tobacco, alcohol, and nutrition law and policies enforcement. These items were graded on a scale of 0–3: 0 = no enforcement provisions; 1 = enforcement regime under development; 2 = compliance monitoring in place with annual summary reports issued; and 3 = compliance monitoring in place with annual summary reports and evidence of fines or other sanctions given to violators.

of relative changes in health status indicators, with an R^2 of 0.063 and regression line slope of –0.0024 (P = 0.01) (**Fig. 1**). This suggests an average improvement in related health status indicators of 2.7% for every 10% increase in the corresponding response index. Log linear regression also showed a negative relationship between average response scores by jurisdiction and the log of relative changes in health status indicators by jurisdiction (regression line slope = –0.0044; P = 0.02) (**Fig. 2**).

DISCUSSION

Through collective action, USAPI countries and territories have defined a consensus set of core NCD response measures and health status indicators, permitting a concerted approach to addressing the NCD crisis and to monitoring progress in the region.

This study shows that, since the NCD emergency declaration in 2010, there was no change in the composite mean prevalence of all risk factors across the USAPI jurisdictions between baseline and follow-up and the composite mean diabetes and hypertension prevalence, whereas NCD death rates significantly increased. There were some improvements in the prevalence of alcohol and tobacco use, and increases in obesity prevalence and NCD death rates. Given these results, it will be difficult to meet the United Nations Sustainable Development Goal 3.4: "By 2030, reduce by one third premature mortality from non-communicable diseases".[15] NCD prevalence and death rates are largely the result of long-standing behaviours and they change relatively slowly in response to policy measures (although improvements in health services can improve death rates more rapidly). In contrast, risk factor prevalence changes more rapidly in response to effective policy measures; thus, the decline in some risk factors could presage future improvements in disease prevalence and mortality as their benefits accrue over time. The only jurisdiction to show a decrease in NCD death rates, the Northern Mariana Islands, has one of the highest intervention scores.

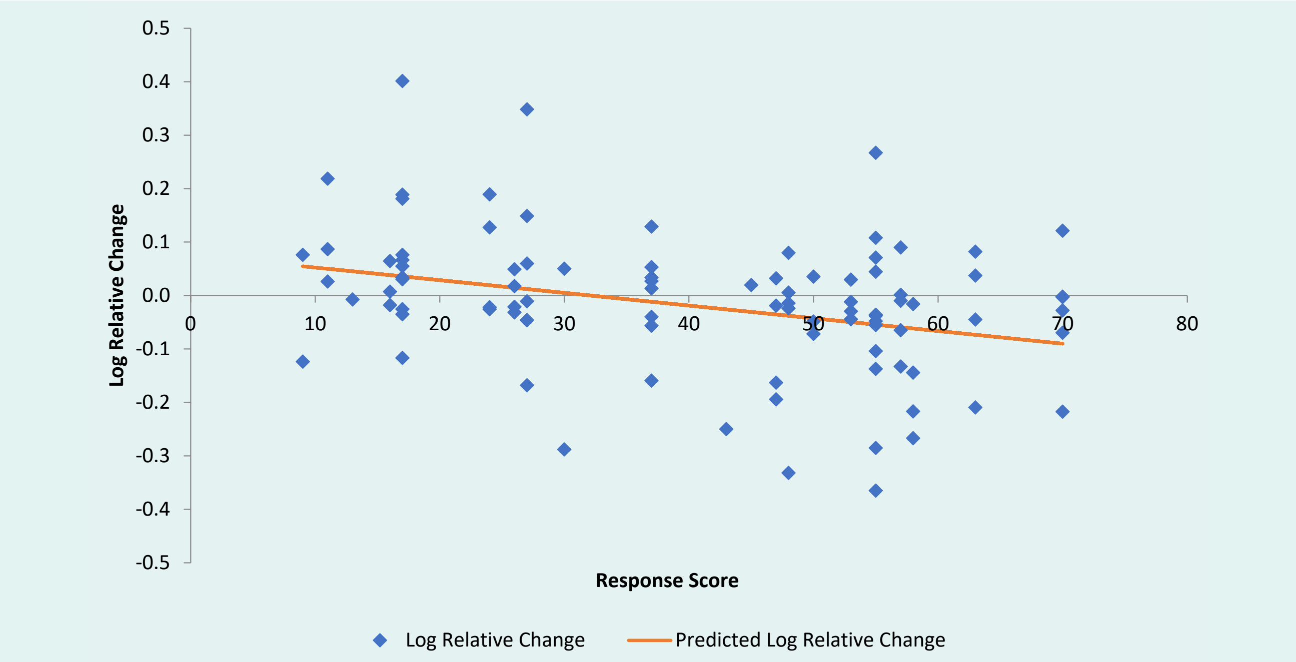
Across all jurisdictions, the strength of response score was 43%, indicating that many evidence-based interventions have not yet been implemented; most of these interventions are the province of policy-makers outside the health sector. As noted by others, strengthened multisectoral commitment is therefore a key to success.[16]

Our conclusions are subject to several limitations. First, various data points for either baseline or recent core health status indicators were not available for some jurisdictions. Timely, routine surveillance activities (youth school-based surveys, adult community-based surveys and analysis of vital statistics data) based on jurisdiction-level NCD monitoring and surveillance plans are needed to fill these gaps and provide a more complete picture of the ongoing NCD emergency. Second, although we would have liked to use 2010 baseline values and recent data points for each indicator, the collection years and time span between the baseline and recent data points vary among indicators and jurisdictions, introducing some uncertainty in assessing progress.

Deficiencies in the completeness and accuracy of mortality reporting that have been observed in the region may also have affected our findings, while out-migration from several of the jurisdictions since censuses were last conducted (between 2010 and 2015) may also have affected mortality rate estimates.[17] In addition, it would be useful to track the exact dates of initiation of interventions. However, some interventions (e.g. tobacco and alcohol tax increases) are introduced in phases and implementation times for others are unclear. Finally, the numerical scoring of ordinal values used in the NCD intervention scores may compromise precision in these measures (since the expected impact from each additional point within an intervention and the expected impact of each point from one intervention to the next may not be constant).

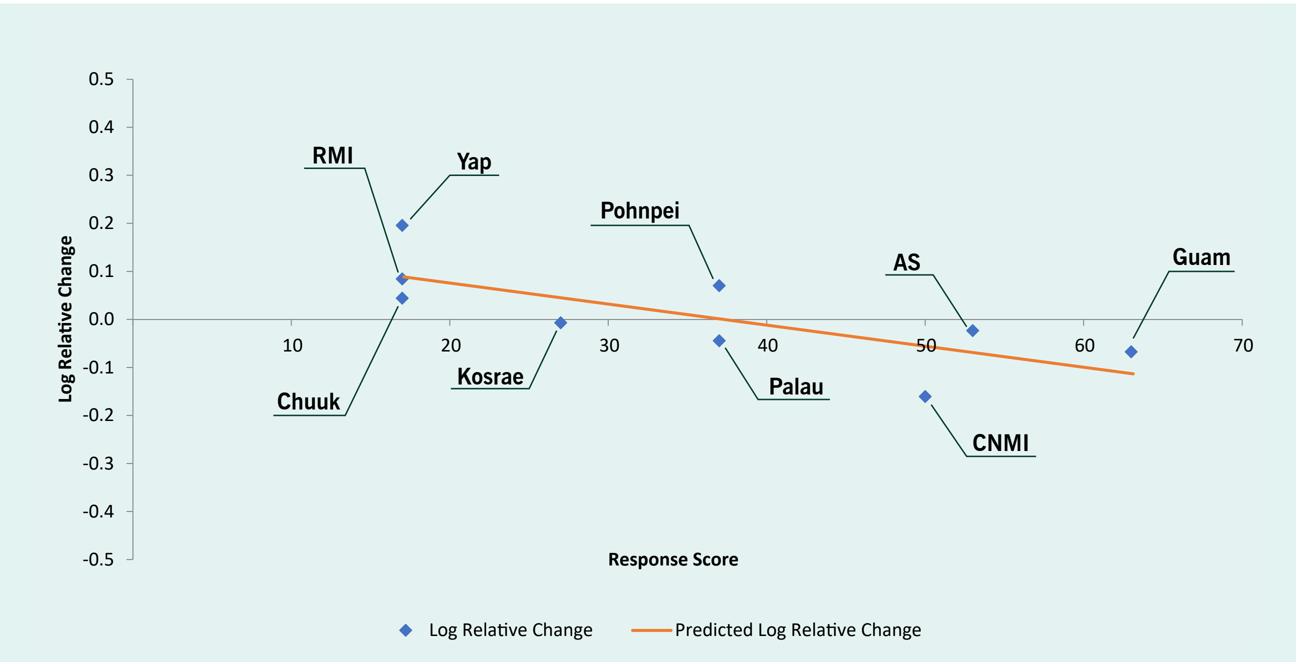
In summary, declaring a regional emergency for NCDs in USAPI has stimulated the development of standardized frameworks for NCD surveillance and response. Although surveillance for NCDs is challenging and additional investments are needed to address gaps and assure rigorous conduct of surveys, existing data do yield a detailed picture of progress over the past 10 years. Some progress has been made towards better control of alcohol and tobacco, but there is little change in other measures of health. The evidence supports the effectiveness of policy and health system interventions in the context of the Pacific Islands; however, many of the recommended NCD interventions have not been adopted, especially in the most affected areas (geographical and risk factors). A renewed commitment to adopt these measures is needed to decisively turn the tide of NCDs in the region.

Fig. 1. **Noncommunicable disease intervention scores versus change in corresponding health indicators, US-affiliated Pacific Islands, 2010–2020**



Data points are the log of the relative changes in health indicators versus corresponding composite intervention indicators at the jurisdiction level (i.e. each tobacco indicator versus the jurisdiction's tobacco intervention score, alcohol indicators versus the jurisdiction's alcohol intervention score, etc.).

Fig. 2. **Composite jurisdiction noncommunicable disease intervention scores versus relative change in health indicators, US-affiliated Pacific Islands, 2010–2020**



Data points are the overall intervention indicator for each jurisdiction versus the log of the average of relative changes for all measured health indicators.

AS: American Samoa; CNMI: Commonwealth of the Northern Mariana Islands; RMI: Republic of the Marshall Islands.

Public health implications

Agreement across countries and territories on a core set of predefined NCD-related response measures and health status indicators enables a systematic approach to monitoring the response to the NCD crisis and resulting changes in population health status. The provision of such high-quality feedback is useful for strategic planning and evaluation for public health practitioners, technical assistance agencies and policy-makers. The discrete groupings and modest population sizes within multiple jurisdictions and the ability to track the impact of interventions make the USAPI an attractive setting for testing innovative approaches to the NCD crisis.

Conflicts of interest

None of the authors has a conflict of interest wherein any author, our institutions or WPSAR reviewers or editors have financial or personal relationships that might influence (bias) their actions.

Ethics statement

The work and results reported in this paper were a product of routine surveillance activities. No information identifiable to specific people is included. Ethics committee approval was not necessary.

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An outbreak of type B botulism in southern Viet Nam, 2020

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Objective: To investigate the cause of a botulism outbreak in several provinces in Viet Nam in 2020.

Methods: An initial investigation was conducted to confirm the outbreak and to form hypotheses about the potential causes, followed by a case–control assessment of the plausible causative food item. Collected food samples were tested to identify the pathogen, and mouse bioassays were performed. Control measures were introduced to stop the outbreak and to prevent similar events in the future.

Results: Twelve people in six southern provinces of Viet Nam were identified as having symptoms of botulism, of whom 11 were in critical condition requiring breathing support. A history of foods eaten in the 4 days before illness onset indicated that all the cases had eaten a tinned vegetarian pâté, and a case–control assessment showed that this was significantly associated with the outbreak, with an odds ratio of 35.2 (95% confidence interval: 3.4–∞). *Clostridium botulinum* type B was detected in three of eight pâté samples collected from the houses of cases. In the mouse bioassay for the toxicity of the pâté samples, all the mice died with clinical symptoms of botulism.

Discussion: A tinned vegetarian pâté was the plausible cause of a botulism outbreak in Viet Nam in 2020. Revision of food safety regulations to improve quality control of tinned foods to prevent future outbreaks is recommended.

Botulism is a life-threatening condition caused by botulinal neurotoxins (BoNTs). The typical symptoms are neurological, including blurred vision, slurred speech, difficulty swallowing and muscle weakness.[1] The mortality rate may be up to 60% without adequate medical intervention.[1] BoNTs are produced by *Clostridium botulinum*, a Gram-positive, rod-shaped, anaerobic, spore-forming, motile bacterium.[2] Of the eight types of BoNT (A–H), A, B, E and F are associated with human botulism.[1] *C. botulinum* spores grow and produce toxins in foods in an anaerobic, non-acidic environment with low sugar and salt. The spores are highly resistant to heat (several hours at 100 °C), desiccation, ultraviolet light and alcohol.[1] *C. botulinum* is present in the environment, with type A or B spores being found primarily in terrestrial vegetables and type E commonly found in fish and aquatic products.[3]

Several outbreaks of botulism have been reported globally, due to consumption of a wide range of foods. In Egypt, a type E botulism outbreak was reported in 1991 in 91 patients, with 19 fatalities, related to consumption of a fermented grey mullet fish (faseikh).[4] In Finland, an outbreak of BoNT type E in 1997 was linked to consumption of hot-smoked Canadian whitefish.[5] Tinned bamboo shoots were found to be the cause of three outbreaks of botulism in Thailand, comprising nine cases in 1998,[6] 19 cases in 1997–1998[7] and up to 209 cases in 2006.[8] In Taiwan (China), two outbreaks have been recorded, one caused by type A botulism in nine patients who consumed preserved peanuts in 1986[9] and another caused by type B botulism in five cases related to consumption of fermented food in 2006.[10] In China, two type A BoNT outbreaks were caused by consumption of smoked ribs by two patients in 2013[11] and of vacuum-packaged salted fish and ham in four cases in 2021.[12] Liquid herbal tea was found to be the main source of a type A botulism outbreak in two elderly people in the United States in 2017.[13]

No outbreaks of botulism had been reported in Viet Nam before the recent outbreak in the southern provinces in July 2020.[14] An initial case series from this outbreak, which comprised the first six cases in a hospital in Ho Chi Minh City, linked cases to consumption of a tinned vegetarian pâté. In addition, the Institute of Public Health

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(IPH) within the Ministry of Health, located in Ho Chi Minh City, received notification of several suspected cases from this and two other hospitals via a hotline. The aim of this study was therefore to investigate the source of the botulism outbreak by examining food consumption histories and pathogens from collected samples to provide information for preventing future foodborne outbreaks.

METHODS

The investigation was conducted in three stages: 1) an initial investigation to confirm the outbreak; 2) an epidemiological investigation to identify foods possibly implicated in the outbreak, including a case–control assessment of the implicated food product; and 3) a laboratory investigation to identify the pathogen. Environmental studies and investigations at food facilities related to the outbreak were conducted by a different institution, and the results were not shared with our investigation team.

Initial investigation

At the end of July 2020, seven patients with severe neurological symptoms were transferred from four provincial hospitals to two central hospitals in Ho Chi Minh City. Initial diagnosis of the six initial cases suggested a potential outbreak of botulism intoxication.[14] A full investigation of all cases in the southern provinces was conducted by the rapid outbreak response team of the IPH. Although cases were also recorded in northern provinces, they were not included in this investigation because of limited resources.

Details of the cases in all hospitals in the southern provinces were collected to confirm whether an outbreak of food poisoning had occurred. The team examined hospital case reports, consulted physicians who treated the patients and interviewed the patients or their caregivers. To avoid missing new cases, the IPH also notified all central hospitals in Ho Chi Minh City to report all suspected cases to IPH between 1 August and 30 September 2020.

The case definition used for the outbreak was any individual admitted to any central hospital in Ho Chi Minh City between July and September 2020 who was diagnosed with botulism intoxication or any individual with three or more of the following symptoms: limb weakness, bilateral ptosis, dysphagia, difficulty breathing, dysarthria, descending paralysis and double and blurred vision, during the same period who was not admitted to hospital. Age, sex, symptoms, date of onset and history of foods consumed during the 4 days before the date of onset were recorded for each patient.

The incubation period was calculated as the time between consumption of the pâté and the onset of symptoms. For patients who ate the pâté more than once during the 4 days before onset of symptoms, the incubation period was calculated as the time between the first and last consumption of the pâté and the onset of symptoms.

Case–control assessment

After the initial investigation, a case–control assessment was conducted to confirm epidemiologically that the implicated food item was the source of the outbreak. The cases were those from the initial investigation, and controls were defined as people who had shared at least one meal with a case in the 4 days before the onset of illness in that case, who showed none of the above symptoms of botulism intoxication.

A structured questionnaire was used to interview the cases and controls, which included age, sex and history of food consumption (including names of foods and quantity ingested) within 4 days of the onset of any symptom. Controls were asked only about their exposure to the implicated food. Odds ratios (ORs) were calculated by exact logistic regression, and P values were calculated for exposure to the implicated food only with Fisher's exact test.

Laboratory investigation

Vegetarian pâté samples from opened tins that had been consumed by patients within 4 days of symptom onset and samples from three unopened tins were collected from household members and sent to the IPH for examination. Patient specimens (faeces and stomach fluid) collected in hospital at admission were also examined.

Testing for *C. botulinum* and botulinal toxin was conducted according to standard methods.[15] Briefly, 1 g of pâté sample was added to 15 mL of cooked meat broth in a tube (Becton Dickinson, Sparks, MD, USA). After 5 days of incubation at 35 °C, enrichment cultures were examined for turbidity, gas production, digestion of meat particles, odour and Gram stain. The enrichment culture was also inoculated onto anaerobic egg yolk agar (HiMedia, India) and incubated at 35 °C for 48 hours. A single pearly zone colony was selected and inoculated into trypticase peptone glucose yeast extract broth (HiMedia). After incubation for 5 days at 26 °C, the culture in broth was used for further detection of toxin in a mouse bioassay. The culture was diluted 1:5, 1:10 and 1:100 in gelatin phosphate buffer (HiMedia), and mice weighing 15–20 g were injected intraperitoneally with 0.5 mL of each dilution of test sample. All the mice were observed periodically for symptoms of botulism for 48 hours. Typically, signs of botulism in mice begin within the first 24 hours with ruffling of fur, followed in sequence by laboured breathing, weakness of limbs and total paralysis with gasping for breath, followed by death due to respiratory failure. *C. botulinum* isolates carrying botulinum neurotoxin A, B, E and F genes were identified in a polymerase chain reaction (PCR) assay, as reported previously.[16]

RESULTS

Initial investigation

Twelve cases of botulism were linked to the outbreak between 24 July and 15 September 2020, 11 of which were treated in intensive care units in three central hospitals; the other case was not admitted to hospital. The cases ranged in age from 20 to 64 years (median, 38 years). Eight of the 12 were female and reported eating a vegetarian diet. The cases were from six southern provinces, with five cases from two families (two cases in Khanh Hoa province and three in Long An province), three cases among roommates in Dong Nai province and four unlinked cases from Vung Tau (n = 2), Ho Chi Minh City and Binh Duong (**Table 1**).

The three most common symptoms were limb weakness (10/12), bilateral ptosis (9/12) and dysarthria (8/12). All 11 hospitalized patients required ventilator support. No deaths were reported (**Table 1**). The four most serious cases were treated with botulinum antitoxins provided by the World Health Organization; however, we were unable to evaluate the effectiveness of botulinum antitoxin treatment.

All 12 cases reported having eaten the same brand of tinned vegetarian pâté in the 4 days before symptom onset. All but one case reported having eaten at least 1.5 spoonfuls. The ingredients of the pâté were mushrooms (such as shiitake, wood ear, chicken drumstick, oatmeal and straw mushrooms), soya bean and nuts (cashew, almond and walnut). All other foods reported in the food histories were consumed by 17–42% of cases (**Table 2**). The incubation period ranged from 11 to 222 hours (median, 73 hours) (**Fig. 1**).

Case–control assessment

All 12 cases and nine controls were included in the case–control assessment of the implicated food product. As most of the cases were vegetarians, their meals were usually different from those of other household members; thus, it was difficult to find controls who had shared meals with the cases. The nine controls identified had all shared a meal with the cases in the 4 days before symptom onset and were relatives (children, spouses, parents or grandparents) or roommates (**Table 3**). Controls were not obtained for six cases who ate meals different from those of other household members.

As the only food item consumed by all cases was a tinned vegetarian pâté, the case–control analysis included only the pâté. Only two controls reported having eaten the pâté, giving an OR of 35.2 (95% confidence interval [CI]: 3.4–∞). The OR for consuming more than one spoonful of pâté was 12.5 (95% CI: 0.84–∞); however, this association was not statistically significant.

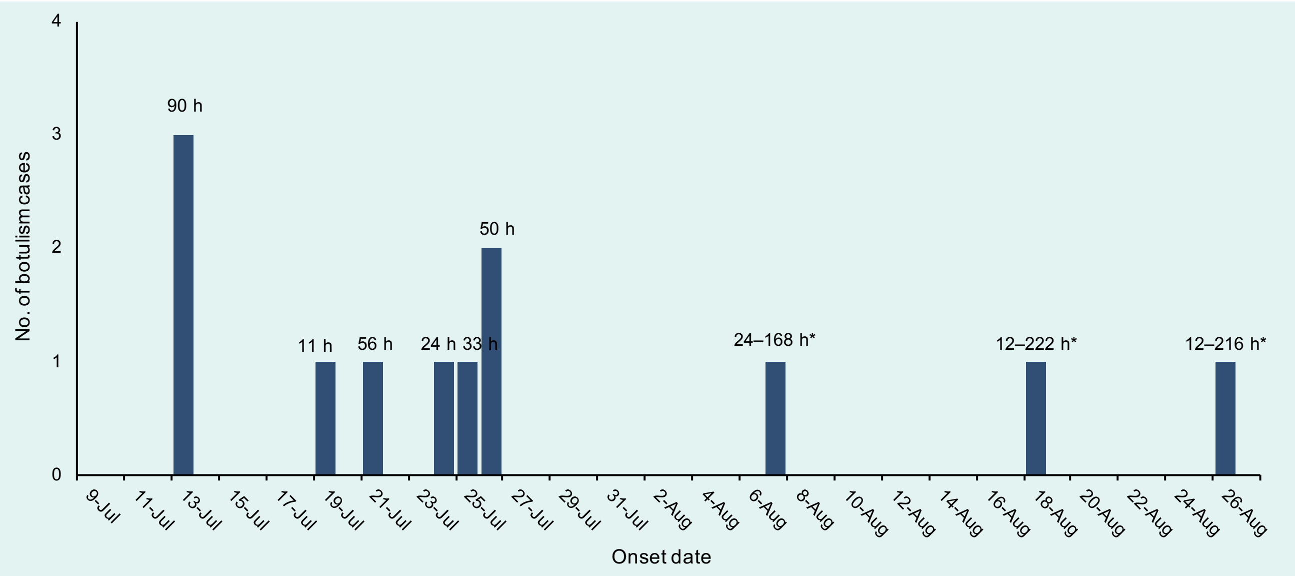
Laboratory investigation

Eight pâté samples, three from unopened tins and five from opened tins and consumed by the cases, and specimens from four patients were collected (**Table 4**). Three of five opened pâté samples were positive for BoNT type B *C. botulinum* by PCR test. None of the unopened tinned pâté samples was positive for BoNT. In the mouse bioassay, all mice died with clinical symptoms of botulism after exposure to the three pâté samples positive for *C. botulinum*. The four specimens from cases were all negative for *C. botulinum*. Six cases had consumed pâté from the three opened tins that were positive for *C. botulinum*: three in Dong Nai province, one in Ho Chi Minh City and two in Khanh Hoa province.

Table 1. **Characteristics of cases and controls in the botulism outbreak investigation, southern Viet Nam, 2020**

Characteristic	Cases (n = 12)		Controls (n = 9)	
	n	**%**	***n***	**%**
Age (years), median (min–max)	38 (20–64)		27 (18–56)	
Sex				
Female	8	67	8	89
Male	4	33	1	11
Vegetarian diet	8	67	3	33
Home province				
Long An	3	25	0	0
Dong Nai	3	25	2	22
Khanh Hoa	2	17	0	0
Vung Tau	2	17	5	56
Ho Chi Minh City	1	8	2	22
Binh Duong	1	8	0	0
Symptoms				
Limb weakness	10	83	-	-
Bilateral ptosis	9	75	-	-
Dysarthria	8	67	-	-
Vomiting	6	50	-	-
Difficulty breathing	5	42	-	-
Hospitalized	11	92	-	-
Required ventilator	11	92	-	-
Relationship to case patients				
Roommate	-	-	2	22
Child	-	-	3	33
Spouse	-	-	2	22
Parent or grandparent	-	-	2	22

Fig. 1. **Epidemic curve and incubation period after consumption of the implicated food of 12 cases of botulism, southern Viet Nam, 2020**



* Range for incubation period of cases that consumed the vegetarian pâté more than once during the 4 days before symptom onset.

Table 2. **Food consumption of 12 cases of botulism in the 4 days before onset of symptoms – southern Viet Nam, 2020**

Food	*n*	%
Vegetarian pâté	12	100
Bread	5	42
Steamed rice	5	42
Pickled vegetables	5	42
Vegetable soup	3	25
Steamed vegetables	3	25
Tofu	3	25
Sweet taro	3	25
Potato	3	25
Bamboo shoot	3	25
Noodle	2	17
Snail	2	17
Cumulative intake of vegetarian pâté (spoonfuls)		
≤ 1	1	8
1.5	6	50
2	3	25
> 2	2	17

Table 3. **Odds ratios (ORs) and 95% confidence intervals (CIs) for case and control consumption of vegetarian pâté – southern Viet Nam, 2020**

Pâté consumption	Case (*n* = 12)	Control (*n* = 9)	OR (95% CI)
Pâté eaten			
Yes	12	2	35.2 (3.4–∞)
No	0	7	
Cumulative amount of pâté eaten			
> 1 coffee spoon	11	0	12.5 (0.84–∞)
≤ 1 coffee spoon	1	2	

DISCUSSION

This outbreak of botulism comprised 12 cases in six southern provinces of Viet Nam in 2020. No deaths were recorded, probably due to timely treatment of all patients and to administration of botulinum antitoxins provided by the World Health Organization to the four most serious cases. In addition, the strain identified was BoNT type B, which is less likely to be fatal than other types, such as BoNT types A and E.[1]

The most plausible source of this outbreak was a tinned vegetarian pâté. All the cases reported having eaten the same brand of the pâté, and the case–control assessment found that consumption of the pâté was significantly associated with the outbreak, with an OR of 35.2. The incubation period was estimated to be 11–222 hours (median, 73 hours), consistent with foodborne botulism, which can occur between 2 hours to 8 days after exposure (usually 12–72 hours).[1] In the laboratory investigation, positive results for

Table 4. **Results of testing of food and patient samples – southern Viet Nam, 2020**

Substrate	Type of sample	Culture	PCR	Toxicity testing in mice
Vegetarian pâté 1	2 jars, 450 g (unopened)	-	N/A	N/A
Vegetarian pâté 2	1 jar, 200 g (unopened)	-	N/A	N/A
Vegetarian pâté 3	1 jar, 450 g (unopened)	-	N/A	N/A
Vegetarian pâté 4	1 jar, 200 g (used)	+	Type B	Died, typical symptoms
Vegetarian pâté 5	1 jar, 200 g (used)	+	Type B	Died, typical symptoms
Vegetarian pâté 6	1 jar (used)	-	N/A	N/A
Vegetarian pâté 7	1 jar (used)	-	N/A	N/A
Vegetarian pâté 8	1 jar (used)	+	Type B	Died, typical symptoms
Gastric fluid		-	N/A	N/A
Gastric fluid		-	N/A	N/A
Gastric fluid		-	N/A	N/A
Faeces		-	N/A	N/A

C. botulinum type B were found in three opened pâté tins. The finding that all four patient specimens were negative for *C. botulinum* may be explained by the fact that the adult gastrointestinal tract is not a natural habitat for *C. botulinum*. Detection of BoNTs in patient specimens was also hindered by lack of reagents for additional testing.

After identification of the contaminated pâté as the cause of this outbreak, the information was widely spread through all media channels, and the population was advised not to eat the product; furthermore, all stocks of the product were recalled. The outbreak was successfully controlled, as no additional cases were identified at the national level.

As the pâté implicated in this outbreak was distributed nationally, cases occurred throughout the country. The ingredients of the pâté – mushrooms, soya beans and nuts – are common environments for C. botulism types A and B.[1] A limitation of this investigation was the inability to determine at which step(s) of the pâté production process the contamination was introduced, as the environmental investigation was conducted by another team, and our investigation team could not inspect the canning company. Foods may be contaminated with *C. botulinum* at all steps of the production process, including cultivation, harvesting, processing and after processing. Contamination often occurs during growth in an environment with a high incidence of spores.[17] *C. botulinum* is common in soil and organic fertilizers, usually at low concentrations.[1] In a survey in China, up to 25 000 *C. botulinum* spores were found per kg of soil and 2100 type B spores per kg of mushrooms.[17]

As *C. botulinum* is ubiquitous in the environment, viable *C. botulinum* or *C. botulinum* spores can occur in food. Botulism occurs only when *C. botulinum* in foods has enough nutritional requirements and anaerobic conditions for growth and production of toxins, such as in tinned foods. Although the optimum temperature for the growth and production of toxins is 35–40 °C, BoNTs can be produced at 3 °C.[1,18] The normal temperature in a refrigerator compartment, which is usually set at 4.4 °C (40 °F) or less, may not be low enough to inhibit the growth of *C. botulinum*. The growth of *C. botulinum* in tinned foods can nevertheless be controlled by several methods, such as low pH, low water activity, high salt concentration and other food preservatives.[16]

The limitations of this outbreak investigation are that it was restricted to the southern provinces of Viet Nam and did not include cases linked to consumption of the vegetarian pâté in the northern provinces Lack of access to the results of the environmental investigation also limited our study. The availability of reagent kits for detection of BoNTs has been a challenge for all laboratories in Viet Nam. In this study, we attempted to cultivate *C. botulinum* from samples and then used PCR to determine BoNT type, in addition to performing mouse bioassays. Another limitation of the response to this outbreak is that botulism is not covered in the national surveillance system, and no outbreaks of botulism had been seen previously.

In conclusion, this outbreak highlights the risk of botulism from tinned foods, especially once they are opened. Strengthening of regulation of the production of processed foods and public education on food safety at home are recommended to prevent future foodborne outbreaks. Although botulism is rare, preparation of reagent kits for early detection of BoNTs and a standard response protocol to ensure prompt investigation and implementation of control measures should be considered.

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Conflicts of interest

None

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The ongoing value of first few X studies for COVID-19 in the Western Pacific Region

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Studies of the first few "X" (FFX) – formerly known as "First Few 100" – cases involve rapid collection of data and specimens from the cases of a novel pathogen or emerging variants and their close contacts. Collection of standardized high-quality clinical, epidemiological, virological and serological data in FFX studies can provide insight into transmission dynamics, severity, risk factors for severe disease and the clinical spectrum of disease. These data can be used in risk assessment and modelling studies, to forecast potential impact and guide preparedness planning and public health interventions.

Independent studies of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), have provided insights into key transmissibility and severity parameters.[1] Although these studies are valuable in contributing to the growing body of scientific evidence on COVID-19 epidemiology, there is need for a greater number of harmonized studies (e.g. FFX studies) that can be rapidly implemented in early epidemic phases.[2]

In early January 2020, the World Health Organization (WHO) adapted and added to existing pandemic influenza and Middle East respiratory syndrome coronavirus (MERS-CoV) protocols for COVID-19 and rebranded them as UNITY studies – a global sero-epidemiological standardization initiative. UNITY protocols aim to increase evidence-based knowledge for action, and are an invaluable tool for improving equity by providing harmonized and fit-for-purpose protocols for all income and resource settings.[3] UNITY studies allow for timely comparison and aggregate analysis of data across countries and regions, to contextualize data to different settings and offer a depth of understanding that is not readily available using other platforms.

WHO solicited interest in implementing these protocols during the COVID-19 pandemic from partners to address knowledge gaps and inform public health response measures.[4] Despite being in an unprecedented pandemic, many countries were able to leverage existing infrastructure to implement UNITY studies. Insights from participating countries are centrally reported to WHO headquarters and regional offices, and include contributions from 98 WHO Member States (including Australia, Mongolia, the Philippines and Singapore in the Western Pacific Region).[4,5]

More in-depth understanding of the epidemiology of COVID-19 gained through such studies can be used to inform adaptive and ongoing control strategies. For example, in early 2020, a study aligned with FFX and UNITY conducted in China showed that most secondary cases were probably infected around the time of symptom onset of the primary cases.[6] This highlighted the need for household infection control measures, given that immediate intervention by local health authorities following symptom onset of the primary case is difficult to achieve. Data from another aligned study conducted in the United Kingdom of Great Britain and Northern Ireland

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(United Kingdom) established a sensitive and specific symptom profile of COVID-19, including the reporting of anosmia in patients. This symptom was later added to the United Kingdom's COVID-19 symptom list.[7] There is also continuing uncertainty about the role of children in spreading COVID-19 and the extent of true asymptomatic and pre-symptomatic transmission. Although the spread appears to be influenced by social settings and household structures, public health interventions (e.g. test, trace and isolate; spontaneous and imposed behavioural and distancing measures and mobility restrictions; communication campaigns; and varying degrees of community engagement and cohesion in response) have led to differing rates of transmission within and between countries. FFX studies can provide opportunities to explore transmission dynamics and severity during all epidemic phases, provided that contacts of cases can still be traced.

FFX and other UNITY studies are well placed to provide information on SARS-CoV-2 variants such as alpha, beta and delta, which are marked by different biological characteristics to those previously observed in epidemiological studies.[8] Pooling of data from FFX studies may help us to understand how SARS-CoV-2 could behave in the Western Pacific, particularly in settings that have not yet experienced uncontrolled epidemics and in populations with low vaccination coverage or low levels of natural immunity. Areas with limited resources to conduct intensive surveillance studies would benefit from globally standardized data collection and analysis to assist with more nuanced planning for future outbreaks.

FFX studies provide a platform to compare epidemiology between waves and jurisdictions and can be used to inform targeted and context-specific public health interventions. For example, Australia and Singapore – countries in the Western Pacific – experienced subsequent waves of epidemic activity that exhibited different epidemiological patterns to earlier waves. The first wave in Australia predominantly featured cases acquired overseas or their close contacts, whereas the second wave was amplified in aged-care and health-care setting outbreaks that led to community transmission.[9] Singapore's initial epidemic was characterized by outbreaks in migrant workers residing in dormitories, with low-level community transmission. In late 2021, Singapore experienced an epidemic wave of the delta variant with widespread community transmission.[10] In both settings, culturally and linguistically diverse communities and workers who were unable to work from home have been disproportionately infected.[9,10]

Existing FFX study populations can be expanded into longitudinal cohorts with extended follow-up to address questions regarding persistence of immunity following both natural and vaccine-induced immunity, and its effectiveness in preventing infection and disease upon re-exposure. These data will be critical in informing future control measures, particularly with the emergence of new variants and the commencement of vaccination campaigns.

For maximum utility, countries should exercise or pilot these studies in advance of future outbreaks – for example, at the beginning of influenza seasons – to facilitate timely implementation during emergencies. Piloting will allow countries to consider data collection and management, laboratory testing and capacity, ethics and governance approvals, identify a suitable workforce and develop workflows in advance of outbreaks, to ensure that they are effective.

Piloting should also consider developing scalable, feasible and culturally appropriate methods for collecting data and specimens, to improve equity and health outcomes for the vulnerable and those at greater risk of disease. These methods should be developed with communities for communities.[11] Historical evidence shows that previous pandemics have disproportionately impacted First Nations peoples.[12–15] Adapting FFX and UNITY studies within a First Nations context can lead to a deeper understanding of the experience of families, explore household transmission in different types of households and improve understanding of how studies can be operationalized to inform culturally appropriate and safe disease control strategies.

FFX studies and the broader suite of UNITY studies remain incredibly useful in the current regional and global context, and they could provide ongoing robust and comparable evidence of COVID-19 epidemiology in low- and middle-income countries as the pandemic evolves. Investing in UNITY studies, readiness and preparedness planning will better support the ongoing COVID-19 response and help to ensure research equity and improve capacity to respond rapidly to future emerging pathogens.

Pandemic-ready, flexible systems are paramount to support an equitable, proportionate and informed emergency public health response.

Conflicts of interest

All authors declare no conflicts of interest.

Ethics statement

Ethics approval was not required for this perspective piece.

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COVID-19 outbreak at an aged-care facility in Selangor, Malaysia, March–April 2020

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Objective: Aged-care facilities are high-risk settings for coronavirus disease 2019 (COVID-19) outbreaks because residents have risk factors such as advanced age and multiple comorbidities. This report details a COVID-19 outbreak at an aged-care facility in Selangor, Malaysia during March–April 2020.

Methods: Epidemiological and environmental data were gathered via telephone interviews and field investigations. Swab samples were taken from all residents and staff for laboratory investigation. Possible contributing factors to the outbreak were explored.

Results: There were a total of 18 individuals at the institution: nine elderly residents and nine staff. The attack rate was 66.67% (6/9) among the elderly residents and 55.56% (5/9) among the staff. The most common symptoms reported were fever, cough, shortness of breath and diarrhoea. The fatality rate among COVID-19 cases was 18.18% (2/11). Both fatal cases occurred in people of advanced age (86 and 92 years old), who had comorbidities and had fever at presentation. The factors contributing to the outbreak included a delay in isolating symptomatic residents, the use of common facilities, caregivers providing support to more than one resident and a lack of natural ventilation.

Discussion: Prevention and control measures must be aggressively implemented in high-risk sites to significantly reduce the risk of morbidity and mortality during COVID-19 outbreaks. Specific guidelines should be developed detailing the management of outbreaks in institutions such as aged-care facilities.

As of 2 January 2022, there were approximately 289 million confirmed cases of coronavirus disease 2019 (COVID-19) globally, with over 5.4 million deaths.[1] Malaysia recorded its first confirmed COVID-19 case on 2 January 2020, and by 6 July 2020, a total of 8476 confirmed cases of COVID-19 were recorded, with 121 deaths. During that period, three clusters involving aged-care facilities were reported in Selangor state, resulting in 44 infections and five deaths.[2] The first COVID-19 case that resulted in death involving a resident of an aged-care facility in the Klang district was notified to the Klang District Health Office on 27 March 2020 from a university hospital.

This report details the investigation and measures taken at this aged-care facility in Klang during the outbreak. The aims were (i) to verify the outbreak and cluster; (ii) to identify cases and describe the outbreak in terms of persons, place and time; (iii) to ascertain the outbreak source, classify at-risk groups and risk factors for disease transmission; and (iv) to implement infection prevention and control measures at the facility.

METHODS

The aged-care facility is privately owned, and it opened in Klang district, Selangor, in December 2019. There are nine staff and nine elderly residents. At the time of the outbreak, all residents had pre-existing comorbidities, including hypertension, diabetes mellitus and cardiovascular disease. Three of the residents required special aids for activities of daily living, which included the use of wheelchairs and specially designed beds.

A suspected case was defined as a person who met the clinical or epidemiological criteria. Clinical criteria were acute respiratory symptoms with at least one of the following: shortness of breath or cough or sore throat and/or fever beginning sometime between 9 March and 7 April 2020 (28 days = 2 incubation periods). Epidemiological criteria included residing or working at the facility anytime within the 14 days prior to symptom onset or from 9 March to 7 April. A confirmed case was an individual with laboratory confirmation of SARS-CoV-2 infection.

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Telephone investigations were conducted with the staff of the facility to gain information about residents and staff. All residents and staff were screened as part of active case detection on 30 March. The information collected included demographic data, clinical symptoms and details of close contacts. Oropharyngeal or nasopharyngeal swab samples were taken and analysed by reverse transcription–polymerase chain reaction at the National Public Health Laboratory in Sungai Buloh. Repeat swab samples were also taken at the university hospital and were analysed at the hospital's laboratory. A field assessment, which investigated the physical aspects of the facility and residents' social interactions and activities, was conducted at the institution to ascertain possible contributing factors to the outbreak.

RESULTS

Epidemiology

On the day of mass screening at the facility, four individuals had already been admitted to the university hospital (one staff member and three elderly residents, one of whom had died). Swab samples were taken from the remaining staff and residents at the facility (a total of 14 individuals). The demographic and clinical details of each resident and staff member are outlined in **Table 1**.

The attack rate was 66.67% (6/9) among the residents and 55.56% (5/9) among the staff. The fatality rate among cases who tested positive for COVID-19 was 18.18% (2/11). The most common symptoms reported were fever, cough, shortness of breath and diarrhoea. The onset of symptoms for the index case was on 23 March, and onset for the last case was on 2 April. All confirmed cases were admitted to the university hospital ward for treatment and isolation. The three elderly residents with negative COVID-19 results were admitted to the university hospital ward for close monitoring and quarantine. Common features among both cases who died were advanced age (86 and 92 years old), the presence of comorbidities, fever at presentation and admission to the ward within 2 days after symptom onset.

The epidemic curve shows a point source outbreak (**Fig. 1**). The index case was a 92-year-old female with symptoms of fever, shortness of breath and diarrhoea. She had been to hospital previously for anaemia from 7–17 March. She was then discharged to the facility, where she developed symptoms of fever and diarrhoea on 23 March. She was readmitted to hospital on 25 March, but she developed shortness of breath and died 3 days later (**Table 1**).

The last case involved a 33-year-old female staff member with onset of fever and sore throat on 2 April. All residents and staff of the facility were at the facility during the outbreak period, which may have led to cross-infection during care work, therapy sessions and daily activities.

Laboratory investigation

There were 14 swab samples taken at the facility on 30 March, three of which tested positive for COVID-19. Fifteen swab samples were taken at the university hospital between 27 March and 7 April (**Table 1**). In total, there were 11 positive cases.

Environmental investigation

The facility is a two-storey bungalow with five bedrooms and four bathrooms, with a total area of about 353 m^2 (3800 square feet). There were three double-occupant rooms and two four-occupant rooms for the residents. All rooms had two occupants, except one double room with only one occupant. Common areas included a lounge, a dining room and a kitchen. Outside of the building is an open space used for physical activities. Air conditioning is used constantly at the facility, and windows generally remain closed. Activities conducted individually included personal care, regular health check-ups and physiotherapy sessions. However, caregivers and the physiotherapist attended to multiple residents. Group activities included meal times, exercise and social activities.

The facility's management staff implemented twice-daily general cleaning and disinfection when the Malaysian government enacted the first Movement Control Order on 18 March 2020. Based on observations and interviews, staff used personal protective equipment inconsistently throughout the outbreak. In general, the level of cleanliness was satisfactory, and measures for physical distancing were in place.

Infection prevention and control

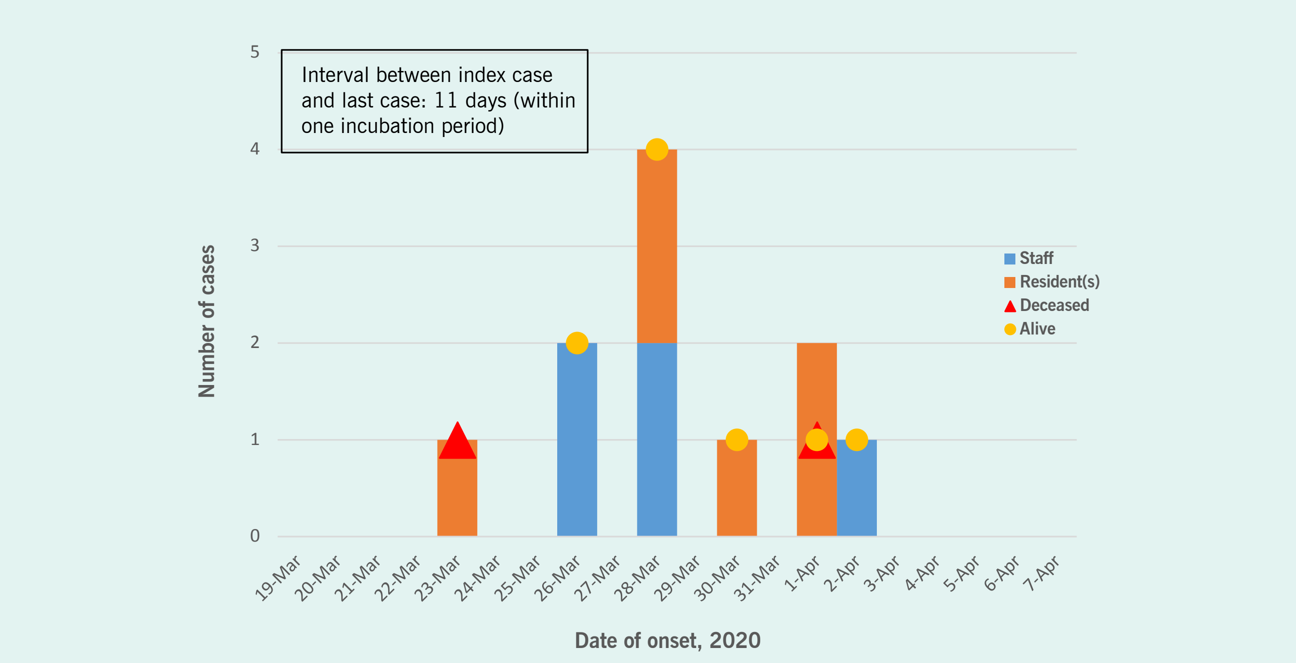
Health education was delivered to the facility's management about infection prevention and control measures for

Table 1. **Demographic information and COVID-19 disease course among residents and staff at an aged-care facility, Klang district, Selangor, Malaysia, 2020**

Age	Sex	Ethnicity	Comorbidity	Symptoms	Symptom onset date	Sample dates and results		Admission date	Outcome
						Care facility	University hospital		
Staff									
35	Male	Pakistani	–	Cough, myalgia	26.03.2020	30.03.2020 Positive	03.04.2020 Positive	04.04.2020	General ward
Unknown	Female	Indian	–	Fever, cough	28.03.2020	30.03.2020 Positive	01.04.2020 Positive	01.04.2020	General ward
36	Female	Chinese	–	Fever, myalgia	28.03.2020	–	29.03.2020 Positive	29.03.2020	General ward
33	Female	Chinese	–	Fever, cough, sore throat	02.04.2020	30.03.2020 Negative	03.04.2020 Negative, 07.04.2020 Positive	08.04.2020	General ward
26	Female	Indian	–	Asymptomatic	–	30.03.2020 Negative	03.04.2020 Positive	04.04.2020	General ward
20	Female	Unknown	–	None	–	30.03.2020 Negative	–	–	Home quarantine
30	Female	Malay	–	None	–	30.03.2020 Negative	–	–	Home quarantine
33	Male	Chinese	–	None	–	30.03.2020 Negative	–	–	Home quarantine
36	Male	Chinese	–	None	–	30.03.2020 Negative	–	–	Home quarantine
Residents									
92	Female	Chinese	Hypertension, CVD	Fever, shortness of breath, diarrhoea	23.03.2020	–	27.03.2020 Positive	25.03.2020	Deceased (28.03.2020)
85	Female	Chinese	DM, hypertension	Fever, cough	28.03.2020	–	29.03.2020 Positive	29.03.2020	General ward
92	Female	Chinese	DM, hypertension	Cough, shortness of breath	28.03.2020	–	29.03.2020 Positive	29.03.2020	General ward
85	Female	Chinese	DM, hypertension, CKD	Cough, diarrhoea	30.03.2020	30.03.2020 Positive	05.04.2020 Positive	05.04.2020	General ward
86	Male	Chinese	Hypertension, CVD	Fever, cough	01.04.2020	30.03.2020 Negative	01.04.2020 Positive	01.04.2020	Deceased (16.04.2020)
85	Female	Chinese	DM	Asymptomatic	–	30.03.2020 Negative	05.04.2020 Positive	05.04.2020	General ward
67	Male	Chinese	DM, hypertension, prostate disease, CVD	None	–	30.03.2020 Negative	05.04.2020 Negative	05.04.2020	General ward
84	Male	Chinese	DM	None	–	30.03.2020 Negative	05.04.2020 Negative	05.04.2020	General ward
85	Female	Chinese	DM, hypertension, CKD	None	–	30.03.2020 Negative	05.04.2020 Negative	05.04.2020	General ward

CKD: chronic kidney disease; CVD: cardiovascular disease; DM: diabetes mellitus.
Dashes indicate that the category is not applicable.

Fig. 1. **Epidemic curve of the COVID-19 outbreak at an aged-care facility, Klang district, Selangor, Malaysia, 2020**



For asymptomatic cases, symptom onset was presumed to be 5 days prior to notification date.

COVID-19 outbreaks on 30 March. Total disinfection of the facility was carried out by the municipality on 6 April. The facility was temporarily closed and all residents and staff were issued quarantine orders in an effort to break the chain of transmission and assist in contact tracing. All remaining residents were pre-emptively admitted to hospital on 6 April for close monitoring and quarantine (prior to the release of swab test results).

DISCUSSION

The index case of this outbreak was an elderly resident with symptom onset on 23 March 2020. She exhibited symptoms of fever and diarrhoea at the beginning of the infectious period, which subsequently led to hospital admission. The source of her infection was believed to be nosocomial, and infection was believed to have occurred during her previous hospital admission in early March. The week that she stayed at the aged-care facility between the two hospital admissions provided ample opportunity for transmission to take place. The onset of the last case was on 2 April (within one incubation period of the index case); this case had symptoms of fever, cough and sore throat. The time of onset showed that the outbreak was limited because no new cases were reported that exceeded one incubation period.

A few mechanisms may have prompted SARS-CoV-2 transmission at the facility. First, SARS-CoV-2 is transmissible even while a case is asymptomatic or presymptomatic.[3] This phenomenon has complicated efforts to isolate infected individuals. Evidence shows that asymptomatic individuals may be infectious as early as 12.3 days (95% confidence interval: 5.9–17 days) before symptom onset.[4] Second, the residents' demographic factors, such as older age and the presence of comorbidities, predisposed them to greater risk of severe infection, with complications and death.[5] Third, the shared use of rooms and bathrooms, group activities and social interactions at the facility may have precipitated the spread of infection among the residents. Fourth, the facility was fully air-conditioned, which hindered natural ventilation, thus predisposing residents and staff to the spread of airborne infection.[6]

Based on the experiences in this outbreak, we have outlined a few recommendations for improvements to outbreak prevention and control measures in similar facilities. First, upon receiving an outbreak notification, a rapid assessment team should conduct a thorough risk assessment of the facility and its occupants (both residents and staff). Second, a high index of suspicion should be adopted to identify symptomatic positive cases early and isolate them from the rest of the residents and staff.

Third, hospital admission should be considered early for elderly residents because they are at great risk for rapid, unpredictable deterioration from SARS-CoV-2 infection. Fourth, repeat testing should be considered in view of the possibility of continuous exposure to asymptomatic cases. Finally, the use of natural ventilation should be encouraged, especially during the day, and windows and doors should be regularly opened at the facility.

Among the limitations of this outbreak investigation were the small sample size and lack of completeness in patient data because they were gathered through telephone interviews with third parties, that is, management staff. Additionally, an outbreak transmission tree could be established through molecular sequencing to better explain the chronology of the outbreak.

Conclusions

COVID-19 outbreaks at aged-care facilities are serious events, as residents are at high risk of morbidity and mortality. In the outbreak at the aged-care facility in Klang district, health authorities took appropriate measures by conducting mass screening at the facility and isolating elderly residents in the hospital. Specific guidelines for managing institutional COVID-19 outbreaks, such as those occurring at aged-care facilities, should be prepared by ministries of health and other appropriate agencies.

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Conflicts of interest

None declared.

Ethics statement

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Nosocomial outbreak of coronavirus disease in two general wards during the initial wave of the pandemic in 2020, Tokyo, Japan

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Objective: Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first reported in China and subsequently spread worldwide. In Japan, many clusters occurred during the first wave in 2020. We describe the investigation of an early outbreak in a Tokyo hospital.

Methods: A COVID-19 outbreak occurred in two wards of the hospital from April to early May 2020. Confirmed cases were individuals with laboratory-confirmed SARS-CoV-2 infection linked to Wards A and B, and contacts were patients or workers in Wards A or B 2 weeks before the index cases developed symptoms. All contacts were tested, and cases were interviewed to determine the likely route of infection and inform the development of countermeasures to curb transmission.

Results: There were 518 contacts, comprising 472 health-care workers (HCWs) and 46 patients, of whom 517 were tested. SARS-CoV-2 infection was confirmed in 42 individuals (30 HCWs and 12 patients). The proportions of SARS-CoV-2 infections in HCWs were highest among surgeons, nurses, nursing assistants and medical assistants. Several HCWs in these groups reported being in close proximity to one another while not wearing medical masks. Among HCWs, infection was thought to be associated with the use of a small break room and conference room.

Discussion: Nosocomial SARS-CoV-2 infections occurred in two wards of a Tokyo hospital, affecting HCWs and patients. Not wearing masks was considered a key risk factor for infection during this outbreak; masks are now a mandated countermeasure to prevent the spread of SARS-CoV-2 infection in hospital settings.

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first reported in Wuhan City, China, in December 2019 and rapidly spread worldwide.[1] Nosocomial SARS-CoV-2 outbreaks have been reported in several countries, including Australia,[2] China,[3,4] Germany[5] and Japan.[6-8]

On 7 April 2020, a patient who had previously been admitted to a Tokyo hospital due to an exacerbation of chronic heart failure developed a fever and dyspnoea 10 days after discharge and was subsequently diagnosed with COVID-19. At the same time, a member of the cleaning staff from the same ward as the patient (Ward A) was referred to the emergency department with fever and dyspnoea and was subsequently diagnosed with COVID-19. On 14 April 2020, two patients, a nurse and a nursing assistant in Ward B became febrile. The two health-care workers (HCWs) were also diagnosed with COVID-19.

This report summarizes the outbreak investigation conducted into the COVID-19 cases in Wards A and B by the hospital infection control team and public health centre staff during the early stages of the COVID-19 pandemic, a period of low community transmission in Tokyo.

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METHODS

Setting

The hospital in Tokyo is a tertiary care facility with 765 beds and 39 subspecialties, including an infectious diseases department. Ward A is a general ward for patients with heart or renal disease, and Ward B is a general ward for surgery, gynaecology and gastrointestinal disease patients. During the 3 months preceding April 2020, the occupancy rate in the hospital's 719 general beds, including 32 intensive care unit beds, ranged from 80% to 85%.

Outbreak investigation and laboratory methods

Confirmed cases were defined as individuals with a positive SARS-CoV-2 result from real-time reverse transcription polymerase chain reaction (RT-PCR) testing of a nasopharyngeal sample or sputum sample, regardless of whether they were symptomatic, as per the World Health Organization's interim guidance for COVID-19 surveillance.[9] A cluster was defined as more than two epidemiologically linked cases, such as people who were on the same ward at the same time.

The two clusters of COVID-19 in Wards A and B were reported to the public health centre on 20 April 2020, and the hospital and public health centre requested assistance in investigating the outbreak from the Ministry of Health, Labour and Welfare in Japan. The assistance provided by the Ministry included developing infection prevention and control measures and interviewing hospital staff to assess their use of personal protective equipment, the break room and conference room; the nursing system – for example, how many patients each nurse was responsible for and how teams of nurses worked; and frequency of patient contact among HCWs. Interviews were conducted by an experienced interviewer, but the interviewer did not use a standardized questionnaire.

As the source of the virus within the hospital was unclear and there was a possibility of additional undetected cases, we used a broad definition of a contact. A contact was defined as an individual who was hospitalized or worked in Ward A or B 2 weeks before the index cases developed symptoms. This group included discharged patients from both wards and patients who had been transferred from Ward A or B to other wards.

All contacts were tested using RT-PCR. A nasopharyngeal swab or sputum sample was collected from all contacts initially, and if the first test result was negative, contacts were retested if they developed new or persistent symptoms. If a HCW tested positive, all HCWs using the same break room or conference room were considered contacts and tested. If a contact tested positive, all patients in the same room as a patient and all HCWs who had had contact with the patient were also considered contacts and tested.

Patients in Wards A and B were observed for symptoms for 14 days after outbreak control measures were implemented, and HCWs were followed up for 14 days from their final exposure to an index case or cluster.

RESULTS

Outbreak description

From 7 April to 3 May 2020, the time from the first case until the last contact was tested, 518 contacts were identified (472 HCWs and 46 patients). The HCWs included 107 doctors, 62 nurses and 303 other medical personnel. All but one contact (471 HCWs and 46 patients) underwent RT-PCR testing. **Table 1** summarizes the outbreak investigation of the HCWs.

A total of 42 people had positive RT-PCR tests: 30 HCWs and 12 patients. Of the 30 positive HCWs, 12 were symptomatic (nine from Ward A or B and three who reported having contact in the break room with workers from Ward A or B who tested positive) and 18 were asymptomatic. Of the 12 positive patients, 10 were symptomatic and two were asymptomatic. The SARS-CoV-2 infection rate among surgeons in Ward B was 30.4% (7/23), for nursing assistants the rate was 17.2% (5/29), for nurses in Ward A it was 11.8% (4/34), for nurses in Ward B it was 14.3% (4/28) and among clerks it was 9.7% (3/31), compared with rates of 0–5% among the other occupational groups, which included, for example, pharmacists, laboratory technicians and cleaning staff (**Table 1**). The epidemic curve of symptomatic cases suggests that the outbreak started in Ward A and spread to Ward B within a week (**Fig. 1**).

At interview, some surgeons reported not wearing masks during their biweekly conferences in a small conference room and other HCWs reported using the small break room without masks.

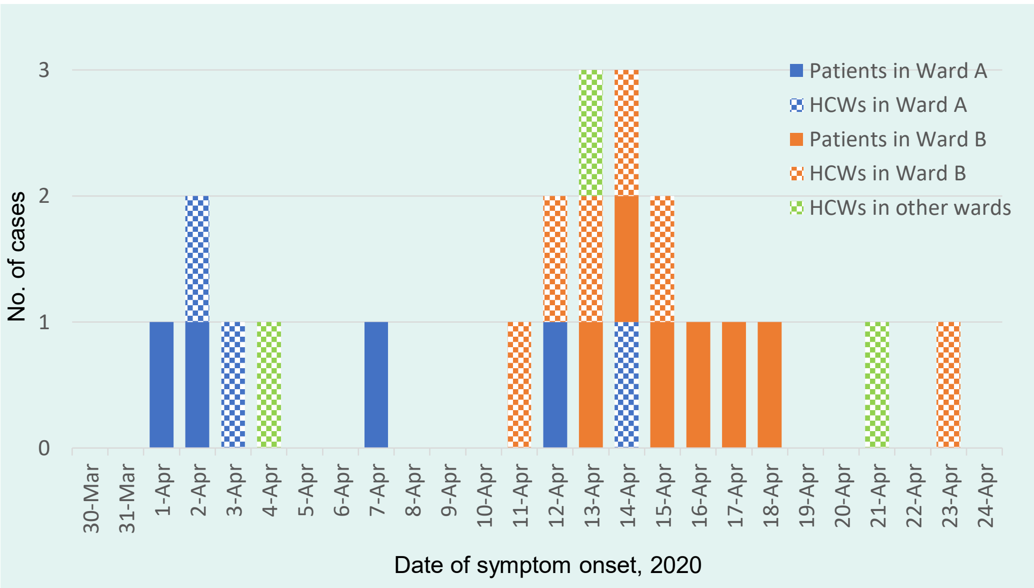
Table 1. **Number and proportion of health-care workers by test result in the investigation of a COVID-19 outbreak in two wards of a Tokyo hospital, Japan, 2020**

Working ward and occupation	Health-care workers					
	Total no.	No. defined as contacts	No. tested	No. positive tests		Positive test (%)
				Symptomatic	Asymptomatic	
Ward A						
Nurse	34	34	34	0	4	11.8
Doctor						
Cardiologist	14	14	14	0	0	0
Nephrologist	9	9	9	0	0	0
Cardiac surgeon	3	3	3	0	0	0
Other doctor	9	9	9	0	0	0
Ward B						
Nurse	28	28	28	4	0	14.3
Doctor						
Surgeon	23	23	23	1	6	30.4
Gynaecologist	22	22	22	0	1	4.5
Gastroenterologist	20	20	20	0	1	5.0
Other doctor	7	7	7	0	0	0
Unspecified ward[a]						
Nursing assistant	29	29	29	3	2	17.2
Clerk	32	32	31	1	2	9.7
Medical worker	81	76	76	2	0	2.6
Radiology technologist	51	49	49	0	1	2.0
Other occupations[b]	155	117	117	1	1	1.7
Total	**517**	**472**	**471**	**12**	**18**	**6.4**

[a] This category includes those who worked on all hospital wards – that is, they worked on either or both wards A and B – and those who tested positive during contact tracing.

[b] Workers in this category included pharmacists, rehabilitation therapists, laboratory technicians and cleaning staff.

Fig. 1. **Epidemic curve of confirmed symptomatic cases of COVID-19, by date of symptom onset during an outbreak in two wards in a Tokyo hospital, Japan, 2020 (n = 22)**



HCW: health-care worker

Outbreak management

After the two clusters of COVID-19 were recognized in the two wards, new admissions were stopped on Ward A on 14 April 2020, in Ward B on 16 April 2020 and hospital-wide on 21 April 2020. All patients who met discharge criteria, except those in Wards A and B, were discharged. On 18 April 2020, all medical services were suspended, including at the tertiary care centre. However, 24-hour emergency services for patients not requiring admission, the perinatal medical centre and psychiatric emergency centre remained open. Visits by family members had been restricted from early March 2020 (i.e. they were limited to family members who had been asymptomatic within the previous 2 weeks, a maximum of 15 minutes per visit, and only one visitor per patient), and visits were completely banned after 27 April 2020. All COVID-19 cases in the hospital were transferred to a dedicated ward, and patients from Wards A and B with negative RT-PCR results were isolated in Ward A. Environmental cleaning was conducted in all wards.

Break room use by HCWs was modified so that fewer people used the rooms; HCWs were advised not to sit facing each other; and partitions were provided for when they had to face each other. Before starting work each day, staff were asked about symptoms and had their temperature checked. The infection control team provided education to HCWs about control measures. These measures were implemented for approximately 1 month, and there were no new laboratory-confirmed cases after 28 April 2020. The hospital resumed regular services on 18 May 2020, with a dedicated ward for patients suspected to have COVID-19 (i.e. patients with acute respiratory failure or fever of unknown origin).

DISCUSSION

This report describes a COVID-19 outbreak in a tertiary care hospital in Tokyo during the first phase of the pandemic. Clusters of cases were reported from two general wards, with the infection spreading among HCWs. The source of SARS-CoV-2 infection in each ward was not identified.

The infection rate of SARS-CoV-2 for HCWs was highest among surgeons, nurses and clerks. Several surgeons reported holding twice-weekly conferences in the small conference room, and nurses reported using a small break room, both of which may have contributed to transmission, as has been reported previously.[2] There were 18 asymptomatic cases in HCWs who also may have contributed to the spread of COVID-19 in the hospital while they were unknowingly infectious,[10-12] especially among those who gathered in close proximity without wearing a medical mask. Appropriate mask use by HCWs can prevent the spread of SARS-CoV-2 in hospitals and allow for better infection control.[13–15] Although self-quarantine, universal mask use and physical distancing are now standard practice,[4,16] these were not universal during the early phase of the pandemic. It is also possible that some infections in HCWs might not have been transmitted in the hospital but may have been community-acquired, although the rate of community-acquired infection was relatively low at the time.

This study has some limitations. A standardized questionnaire was not used during interviews with contacts; therefore, the data collected did not allow for robust analysis of the use of break rooms and conference rooms; personal protective equipment, such as gloves and gowns; handwashing; the performance of medical procedures for inpatient care; and the extent and timing of exposure to infected patients. Also, the approximately 2-week delay in collecting information is likely to have resulted in some recall bias. Contact tracing was limited to the hospital setting, and there was no contact tracing among outpatients or visitors. However, we consider it unlikely that SARS-CoV-2 infections were introduced by outpatients or visitors because outpatients usually do not enter the wards and there were restrictions on visitors. Finally, we were unable to standardize the timing of testing after exposure and the retest protocol for contacts who were negative on initial testing, and this could have resulted in false-negative cases.

In summary, this outbreak investigation documents nosocomial SARS-CoV-2 infection among HCWs and patients that occurred in two hospital wards during the initial wave of the COVID-19 pandemic in 2020 in an area with a low rate of community-acquired infection and before vaccines were available. Extensive contact tracing was conducted with high testing coverage only of contacts within the hospital setting. Because nosocomial infections can spread from asymptomatic or presymptomatic individuals to unmasked HCWs, stringent infection prevention and control measures are required to prevent hospital-based outbreaks; these measures include wearing masks and avoiding close contact when not wearing medical masks in small rooms.

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Ethics statement

This COVID-19 outbreak investigation was conducted according to the policy for active surveillance issued by the Ministry of Health, Labour and Welfare in Japan. The institutional ethical review board at the hospital approved this project (trial registration no. 02-028; registered on 25 June 2020).

Conflicts of interest

None declared.

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Integration of publicly available case-based data for real-time coronavirus disease 2019 risk assessment, Japan

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In response to the outbreak of coronavirus disease 2019 (COVID-19) in Japan, a national COVID-19 cluster taskforce (comprising governmental and nongovernmental experts) was established to support the country's Ministry of Health, Labour and Welfare in conducting daily risk assessment. The assessment was carried out using established infectious disease surveillance systems; however, in the initial stages of the pandemic these were not sufficient for real-time risk assessment owing to limited accessibility, delay in data entry and inadequate case information. Also, local governments were publishing anonymized data on confirmed COVID-19 cases on their official websites as daily press releases. We developed a unique database for nationwide real-time risk assessment that included these case lists from local government websites and integrated all case data into a standardized format. The database was updated daily and checked systematically to ensure comprehensiveness and quality. Between 15 January 2020 and 15 June 2021, 776 459 cases were logged in the database, allowing for analysis of real-time risk from the pandemic. This semi-automated database was used in daily risk assessments, and to evaluate and update control measures to prevent community transmission of COVID-19 in Japan. The data were reported almost every week to the Japanese Government Advisory Panel on COVID-19 for public health responses.

The establishment of reliable and real-time epidemiological data on emerging and re-emerging infectious diseases is crucial for understanding transmission patterns and assessing the impact of public health intervention to mitigate outbreaks.[1] However, during public health emergencies, routine surveillance channels can be overwhelmed; thus, real-time assessment may be hampered by insufficient information.[2]

In 1981, the Government of Japan established a laboratory-based surveillance system for infectious diseases. In 1999, this was expanded to include a system for patient reporting, and the Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases (hereafter, the Infectious Diseases Control Law) was enacted.[3] Collected data were integrated into this national surveillance system: the National Epidemiological Surveillance of Infectious Diseases (NESID) programme.[3] To respond to emerging or re-emerging diseases not defined in the surveillance system, surveillance of "undiagnosed serious infectious illness" is included in NESID to promote early detection of pathogens during public health emergencies.[4] This surveillance system was used to detect and monitor coronavirus disease 2019 (COVID-19) cases[5] even before COVID-19 was labelled as a "designated infectious disease" in Japan by cabinet order on 28 January 2020.[6] The designation mandated that health-care providers report all confirmed cases to public health centres in their local jurisdictions under

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the Infectious Diseases Control Law.[3] Thereafter, the collected data were confirmed by local governments and ultimately reported to the Ministry of Health, Labour and Welfare (MHLW).

The government also established the national COVID-19 cluster taskforce (comprising governmental and nongovernmental experts) on 25 February 2020, to support the MHLW's efforts.[7] The taskforce members analysed current case and cluster data, conducted daily risk assessments and provided technical advice for public health decision-making. The surveillance data from NESID were initially used for this analysis; however, the data were not available to nongovernmental experts owing to privacy issues. Also, the surveillance data were inadequate for timely analyses of community transmission of this emerging infection because they were not designed to report cases on a day-to-day basis. The standard surveillance process involves health-care facilities that diagnose cases sending case information to the public health centre in their jurisdiction via fax for registration; at the health centre, the data are manually entered into the system for further verification and reporting.[3] As the COVID-19 case numbers grew, the reporting process became overwhelmed, leading to significant delays in reporting to public health authorities. Also, the standard reporting form did not include variables essential for risk analysis of COVID-19 transmission, such as history of contact with confirmed cases, being in a possible spreading event or travel history from an epidemic area or country. To alleviate these issues, the MHLW asked local governments to send daily case information in a spreadsheet directly to the MHLW via email.[8]

This updated surveillance process also had reporting delays and discrepancies between the number of cases reported by local governments and those reported by the MHLW as the pandemic unfolded throughout Japan. The reporting delay by local governments to the MHLW could exceed 1 week in some instances. Data entry errors such as spelling and typographical errors were also recognized. These shortcomings made it difficult for the national COVID-19 cluster taskforce to analyse the epidemiological situation and conduct real-time risk assessment to inform decision-making.

Therefore, another system of data collection was urgently needed to collect and integrate case information for more accurate situation analysis and rapid risk assessment to bolster public health decision-making. In this report, we describe the development of such a database that supported real-time risk assessment and its impact on policies for managing the COVID-19 pandemic.

DATABASE DEVELOPMENT

The new database used publicly available data from daily press releases published on local government websites.[9] Each local government releases anonymized individual case data and aggregated daily case numbers on their website. Although the Cabinet Secretariat (https://cio.go.jp/policy-opendata) recommended that local governments share data with the public in a universal format (e.g. a file of comma-separated values) in line with the five-star open data model,[10] the press release format was not standardized or consistent across local governments, especially during the early phase of the pandemic. Some press releases were published as PDF files or embedded directly in the HTML, whereas others described cases in text not in tables. Therefore, the case information needed to be converted and integrated into a standardized data format within a single database.

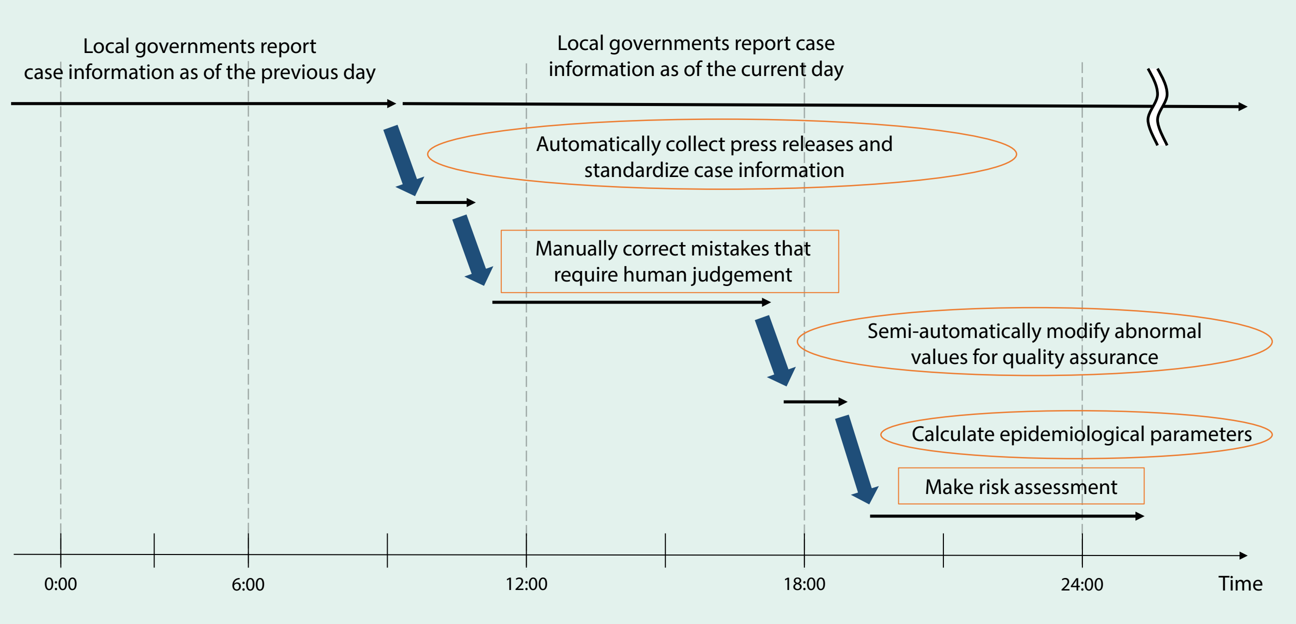
Initially, we extracted the case information manually from each local government website with support from volunteers; however, this was labour-intensive and required significant resources. Subsequently, we developed a programme written in Python programming language[11] to automate extraction of information directly from the websites and its conversion to tabular form.

The database contained the following variables for each case: official reporting date, reporting prefecture, prefectural case identification number, reporting municipality, municipal case identification number, age, sex, occupation, residence (limited to prefecture and municipality), onset date, confirmation date, presence of symptoms at the time of confirmation, history of overseas travel, history of domestic travel and epidemiological link with other confirmed cases.

DATABASE MANAGEMENT

Initially, quality assurance of the data was performed manually, with an algorithm developed in Python to detect possible data errors, including abnormal values,

Fig. 1. **Daily operating procedures of the COVID-19 database, Japan**



missing data, inconsistencies in Japanese characters (Kanji) and categorical variables (e.g. occupation and place of residence). These errors were corrected daily. We developed a standard operating procedure for updating case information without errors (**Fig. 1**). The database automatically collected press releases from websites in the morning, then a manual verification process was used to ensure the data entry was correct. Next, we semi-automatically modified abnormal values before calculating epidemiological parameters, which were then used by the cluster taskforce for their risk assessment. Close collaboration with data users, such as governmental officers and experts, allowed their feedback to improve database development and maintenance.

RESULTS

The database included 776 459 cases from 15 January 2020 to 15 June 2021 (**Table 1**), from which daily epidemic curves and geographical maps were created.[12] Epidemiological information on the first few hundred cases was derived from the database.[13] Further epidemiological parameters (e.g. effective reproduction number, proportion of unlinked cases, age and sex distribution, symptom onset and confirmation delay) were derived from the database for real-time risk assessment. An analysis of clusters in the early phase showed that most cases were younger and either pre-symptomatic or asymptomatic.[14]

Epidemiological analysis and real-time risk assessment results based on this database have been presented to the Japanese Government Advisory Panel on COVID-19 to evaluate the effectiveness of public health measures against COVID-19. The government's COVID-19 dashboard (https://covid19.mhlw.go.jp), which uses data not accessible to the public, was also refined to be used for the visualization of epidemiological data in parallel with our database. Because our database and the government's database were not cross-checked or merged, the Advisory Panel analysed data summaries from both databases to identify discrepancies between them and improve their quality. Furthermore, comparing analyses from both datasets provided a multifaceted perspective to help experts conduct risk assessments.

DISCUSSION

The development of a reliable database during a public health emergency is challenging. High numbers of cases can overwhelm pre-existing surveillance systems, necessitating an alternative system. Basic demographic information derived from a reliable database is required for real-time risk assessment and policy-making. We successfully developed an integrated database platform

Table 1. **List of variables included in the COVID-19 database from 15 January 2020 through 15 June 2021 (N = 776 459), Japan**

Variables	Description	Coverage, *n* (%)
Reporting prefecture	Name of the prefecture where the case was reported	776 459 (100)
Case identification number by prefecture	Serial number of the case in the reporting prefecture	720 726 (92.8)
Reporting municipality	Name of the municipality where the case was reported	275 149 (35.4)
Case ID by municipality	Serial number of the case in the reporting municipality	263 564 (33.9)
Age	Age stratum by decade	668 250 (86.1)
Sex	Male or female	662 444 (85.3)
Occupation	Case's occupation type: health-care professional, public servant, office worker, corporate executive, educational professional, self-employment, unemployment, other	386 874 (49.8)
Residential prefecture	Name of the prefecture where the case resides	692 084 (89.1)
Residential municipality	Name of the municipality where the case resides	506 075 (65.2)
Onset date	Date of illness onset	402 855 (51.9)[a]
Date of confirmation	Date that SARS-CoV-2 infection was confirmed	540 027 (69.5)
Date of official announcement	Date the case was announced by the prefecture or municipality	776 024 (99.9)
Presence of symptoms at the time of confirmation	Whether the case had any symptoms when SARS-CoV-2 infection was confirmed	416 837 (53.7)
History of overseas travel	Whether the case had a history of overseas travel before the infection was confirmed	474 (0.1)
History of domestic travel	Whether the case had a history of domestic travel before the infection was confirmed	13 558 (1.7)
Epidemiological link	Whether the case had a history of close contact with other positive cases or a history of staying in a clustered location known to be associated with more than one infected case before the infection was confirmed	326 693 (42.1)
Re-positive	If an infected person tested positive again after testing negative	353 (0.05)

[a] These calculations included asymptomatic cases. If asymptomatic cases were excluded (N = 710 553), the coverage of onset date would be 56.3% (*n* = 400 350).

that collected press release information from local government websites. Similar processes have been used in other Asian countries and regions, such as Taiwan (China), Hong Kong Special Administrative Region (China) and Singapore, where data from government-issued press releases on new COVID-19 cases have been used for studies to investigate transmission patterns or to evaluate interventions.[15,16] Our database was used for conducting research activities, and also served as a real-time monitoring tool to support public health decision-making in the outbreak setting.

Balancing privacy protection with the need for granular personal data for public health analyses during health emergencies has been controversial. Using press release data that do not include identifying information (as per local government policy) allowed for the sharing of outputs with nongovernmental officers with minimal risk to private information. The database provided consistent reporting of cases nationally, which in turn allowed for information to be shared among local governments, particularly where cases had travelled to multiple prefectures.

One of the limitations of this database is that the reporting format for some variables differed across local governments and phases. Also, some variables were partially or entirely missing from the data recorded by some local governments,[9] and local reporting forms were sometimes reformatted without notification, requiring updating of the database processes; hence, it was difficult to share consistent coding scripts for collecting information. Furthermore, the quality of the data from each local government varied depending on workload, especially for data on epidemiological links from active surveillance at public health centres. Detailed clinical data and disease outcomes were not publicly available.

Despite the limitations, this semi-automated database based on publicly available data was useful for monitoring pandemic trends, conducting real-time risk assessment and assessing the impacts of public health policies. No additional cost for computing resources or software was required apart from a few personal computers to manage our database; also, abstracting sufficient data from open-source data was technically straightforward. Therefore, our method could be adapted for use in resource-constrained settings and could serve as a meaningful model for other countries to create similar databases during public health emergencies. Based on this experience, we recommend that countries develop legislation and establish systems that can extract and store anonymized case information from publicly provided information to supplement routine surveillance systems.

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Conflicts of interest

Mariko Kanamori was a Research Fellow of the Japan Society for the Promotion of Science. The other authors declare no conflicts of interest.

Ethics approval

This study was exempt from institutional review board approval because it involved secondary analysis of publicly available, de-identified data.

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Early COVID-19 response in two small island developing states: Maldives and Trinidad and Tobago

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Problem: Coronavirus disease 2019 (COVID-19) was declared a pandemic on 11 March 2020. Severe illness requires intensive care facilities, which are limited in smaller, resource-constrained settings.

Context: Maldives and Trinidad and Tobago are small island developing states with comparable climates. Similar to island nations in the Western Pacific Region, they are prone to natural disasters and so engage in planning and preparedness activities on an ongoing basis. This paper describes the initial measures taken by both countries during the first wave of COVID-19, from March to May 2020.

Action: In both countries, multisectoral high-level leadership allowed for timely and decisive actions. Early school closures, early border closures and early lockdowns were enforced. Mandatory mask wearing and physical distancing were instituted. Cases and contacts were isolated in facilities away from public sector hospitals, and isolation was implemented at the government's expense. Volunteers were trained to manage dedicated hotlines. Additionally, the governments held daily press briefings.

Outcome: During the first wave, Maldives contained its epidemic to one geographical cluster; Trinidad and Tobago successfully avoided community spread, thus averting an overwhelmed health system.

Discussion: Diligent contact tracing with quarantine implemented at the government's expense successfully minimized spread in both countries. Small countries need volunteers to help with activities such as contact tracing, and recruiting and training volunteers before a health emergency occurs is key. Lessons learned from the experience of Maldives and Trinidad and Tobago could serve as a model for other small island developing states, including those in the Western Pacific Region.

PROBLEM

The World Health Organization (WHO) declared coronavirus disease 2019 (COVID-19) a pandemic on 11 March 2020.[1] Severe COVID-19 may require intensive care, which is limited in smaller, resource-poor nations. This paper describes how two small island nations managed the first wave of the pandemic. Their handling of the pandemic during the first 3 months contained the spread. The lessons learned from their experience may assist small island developing states (SIDS) in WHO's Western Pacific Region.

Context

Maldives and Trinidad and Tobago are SIDS.[2] Maldives has a population of 437 535 persons living on 187 islands in the Indian Ocean[3] and has a human development index score of 0.719.[4] Total health expenditures are 9.0% of gross domestic product.[5] Trinidad and Tobago, in the Atlantic Ocean, has a population of 1.4 million persons and is also high on the human development index, with a score of 0.799.[4] Total health expenditures are 7.0% of gross domestic product.[5] These countries were chosen for this study because they are small island states with relatively high scores on the human development index. They have similar climates, and both countries have experienced natural disasters and are engaged in ongoing planning and preparedness activities. They are similar to SIDS in the Western Pacific Region, such as Fiji,[6] in that tourism is a major income generator for Maldives and to a lesser extent for Trinidad and Tobago, and both depend on imports for many items.

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This paper describes the initial measures taken by Maldives and Trinidad and Tobago during their first waves of COVID-19 (from 7 March in Maldives and 12 March in Trinidad and Tobago to 31 May 2020) that helped keep their health systems from being overwhelmed. The descriptive reports on which this paper is based were made at each country's government briefings.

The first case of COVID-19 in Maldives was detected at a tourist resort on 7 March 2020; by 14 April, there were 20 confirmed imported cases, with 56 suspected cases in isolation and 152 contacts under quarantine. The first local case detected on 15 April in the capital, Malé, prompted a lockdown of the greater Malé area. Cases increased during the following weeks, and by 31 May 2020, there were 1730 cases, 127 recoveries, 12 hospitalizations and 5 deaths.[7]

Trinidad and Tobago reported its first confirmed case of COVID-19 on 12 March 2020 in a traveller returning from Europe. On 13 March, a second case was confirmed, and by 19 March, nine cases were confirmed. On 21 March, 40 cases were confirmed in a group of 68 returning nationals who were aboard a cruise liner. The first death from COVID-19 in Trinidad and Tobago occurred on 25 March, and by 31 May, there were 117 cases and 8 deaths.[8]

In the early phase, the majority of cases in Maldives occurred among males (>80%; 1412/1730). In Maldives, most cases were aged 21–40 years, while in Trinidad and Tobago, the majority of cases were aged 60–69 years. In Maldives, the majority of cases occurred among foreign migrant workers (65%; 1124/1730), with one third observed among Maldivians. In Trinidad and Tobago, most cases were imported, with 34% (40/117) occurring in one cluster on a cruise liner.

Action

In Maldives, the Health Protection Agency is mandated to safeguard the nation's public health. The Director of Public Health heads the Agency and reports to and advises the Health Minister.

In Trinidad and Tobago, County Medical Officers of Health are the public health officers in charge of each county's surveillance and response activities. They report to the Chief Medical Officer at the Ministry of Health.

Both countries adopted a multisectoral approach. The early actions taken by both countries during their first wave of COVID-19 resulted in Maldives containing the epidemic to one geographical cluster, while Trinidad and Tobago managed to avoid community spread, thus preventing its health system from becoming overwhelmed.

Lessons learned

Multisectoral high-level leadership led to a timely response

In Maldives, the Health Emergency Coordination Committee, activated on 21 January 2020, coordinated the multiagency response. As the situation escalated, response coordination was handed to the National Disaster Management Authority to facilitate multiagency coordination; health emergency operations were relocated to the National Emergency Operations Centre on 1 March 2020. With this change, a national task force was established at the executive level, and the strategic decision-making body was chaired by the President. A national public health emergency was declared on 12 March 2020.

In Trinidad and Tobago, a core team was formed to manage the response, comprising the Minister of Health, the Minister of National Security and the Chief Medical Officer and his team of public health professionals at the ministry and county levels. Communication was at the forefront of the response.

In both countries, communication about the pandemic came from trusted sources. In Maldives, communication was led by the President's office, which held daily press briefings; multiskilled staff from across the government and private sectors facilitated content production and managed communication through mass and social media. At the National Emergency Operations Centre, the call centre was operated by dedicated personnel and a large number of volunteers.

In Trinidad and Tobago, the Minister of Health and the Chief Medical Officer, along with subject matter experts, held daily press briefings that included clinical and epidemiological updates and information about the availability of testing facilities. Potential mental health challenges from job loss, domestic violence and stay-at-home restrictions were addressed by clinical psychologists. A hotline staffed by doctors was established as a resource for the public.

Preparedness activities were initiated early and focused on points of entry

In both countries, preparedness activities were initiated approximately 6 weeks before WHO declared the pandemic. Early interventions focused on points of entry. Trinidad and Tobago began its prevention and response efforts on 23 January 2020, implementing entry and exit screening at airports. In Maldives, the early response focused on the tourism sector and travellers to facilitate early detection, contact tracing and isolation. Although evidence supporting entry and exit screening is sparse, these activities can earn public confidence and raise awareness among the travelling public.[9] In retrospect, the asymptomatic phase of the disease means that such individuals would have been missed during airport screening. Border closures were implemented early in both countries, and as in several countries in the Western Pacific Region, this measure was successful in limiting the entry of the virus and keeping case numbers low.

Public health and social measures were initiated early and adjusted as needed

Cinemas and educational institutions were closed when there were 13 cases in Maldives and 5 in Trinidad and Tobago. Borders were closed when Maldives reached 14 cases and Trinidad and Tobago reached 10. Lockdown of non-essential services occurred on 15 April in Maldives and on 29 March in Trinidad and Tobago. Lockdown in the latter included the closure of restaurants and a rapid scaling down of public gatherings from 25 to 5 persons; residents were permitted to visit only supermarkets, pharmacies and hardware stores (**Table 1**; **Figs. 1** and **2**). In Maldives, lockdown measures were eased on 28 May, but physical distancing and mask wearing were made mandatory for essential services and their providers (**Table 1**; **Fig. 1**). In Trinidad and Tobago, face masks became mandatory in public places on 5 April, based on international guidance.[10] On 11 May, lockdown measures were eased with a "no mask, no service" rule in effect (**Table 1**; **Fig. 2**).

In Maldives, in the early stages of the pandemic, community-based interventions and health risk communication did not have the expected impact on physical distancing despite the closure of educational institutions and some workplaces on 22 March because the contact tracing of the first community case identified more than 100 close contacts.[11] This led to enforced movement restrictions and scaling up of risk communications. As a result, within 3 weeks of lockdown and enforcement, contact bubbles were reduced to eight persons per case. This contrasts with Trinidad and Tobago where enforcement of public health measures accompanied lockdown early in the epidemic (18 days after the first case), with citizens allowed outside only to visit supermarkets, pharmacies and hardware stores. Community spread was not reported in Trinidad and Tobago at that time.

Multiagency action supported contact tracing in the containment phase

Surveillance with contact tracing and case investigation was supported by rapid response teams in Maldives and by county office staff in Trinidad and Tobago. In both countries, additional health-care workers, volunteers and students were recruited and trained for contact tracing. Contact tracing was prioritized in Maldives, with near-universal contact tracing within 48 hours of case detection and cases isolated within 2 days. Multiagency action supported by information technology allowed for speedy implementation of containment activities. The use of volunteers in both countries suggests that volunteers should be recruited and trained before a health emergency occurs.[12]

Isolation at state expense likely delayed community transmission

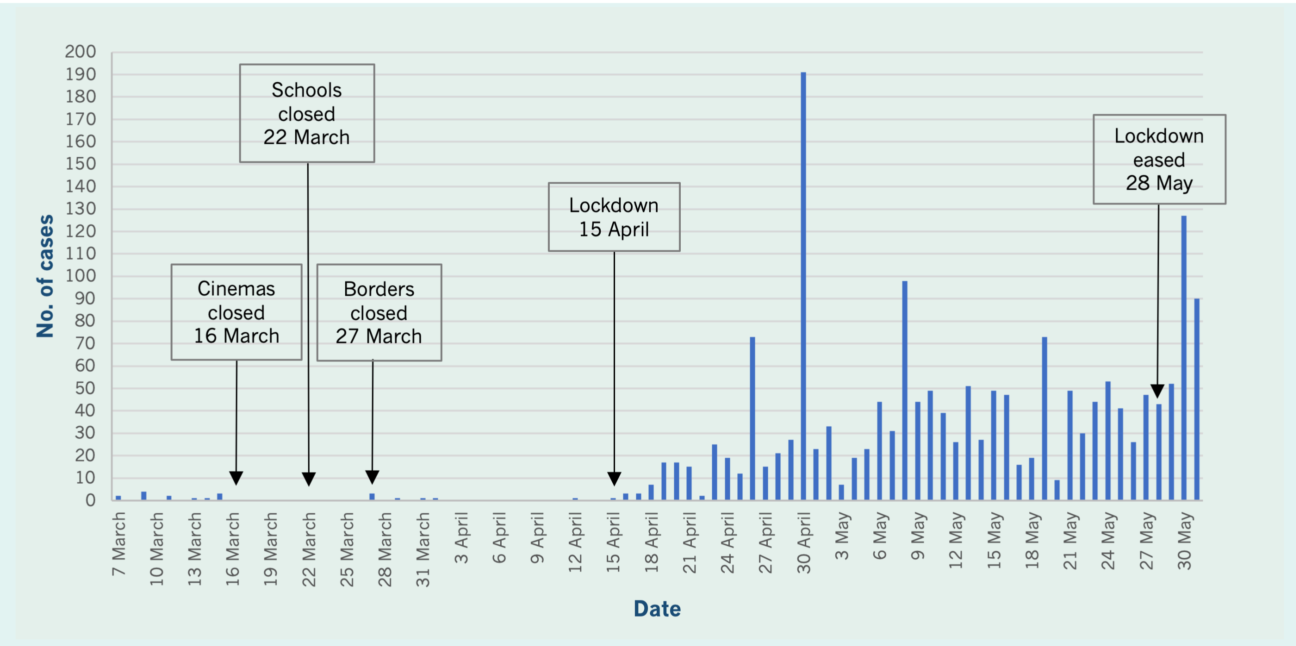
In Trinidad and Tobago, patients were isolated in facilities away from public sector hospitals and private nursing homes, and the government established two facilities with intensive care units (ICUs) and resources for high-dependency care. Health workers caring for patients were housed separately. Suspected cases were isolated in facilities at the government's expense. Discharge from quarantine required two negative test results 24 hours apart.

In Maldives, an ICU ward at the national referral hospital was designated to care for severe cases. One private hospital was commissioned to manage severe cases while work progressed to establish a separate hospital facility for these cases. Quarantine and isolation facilities were established at resort islands managed by the National Emergency Operations Centre. Suspected cases

Table 1. **Timeline of public health and social measures and number of cases of COVID-19, Maldives and Trinidad and Tobago, March–May 2020**

Measures	Maldives		Trinidad and Tobago	
	Date	No. of cases	Date	No. of cases
First case detected	7 March (imported)	1	12 March (imported)	1
Closure of cinemas	16 March	13	16 March	5
Closure of all educational institutions	22 March	13	16 March	5
Borders closed	27 March (suspension of on-arrival visas)	14	22 March (closure includes returning nationals)	10 (plus 40 on a cruise ship)
Lockdown of non-essential businesses and services, with enforcement	15 April	21	29 March	38 (plus 40 on a cruise ship)
Easing of phase 1 lockdown	28 May	1528	11 May	116

Fig. 1. **Epidemic curve of COVID-19, Maldives, 7 March to 31 May 2020**



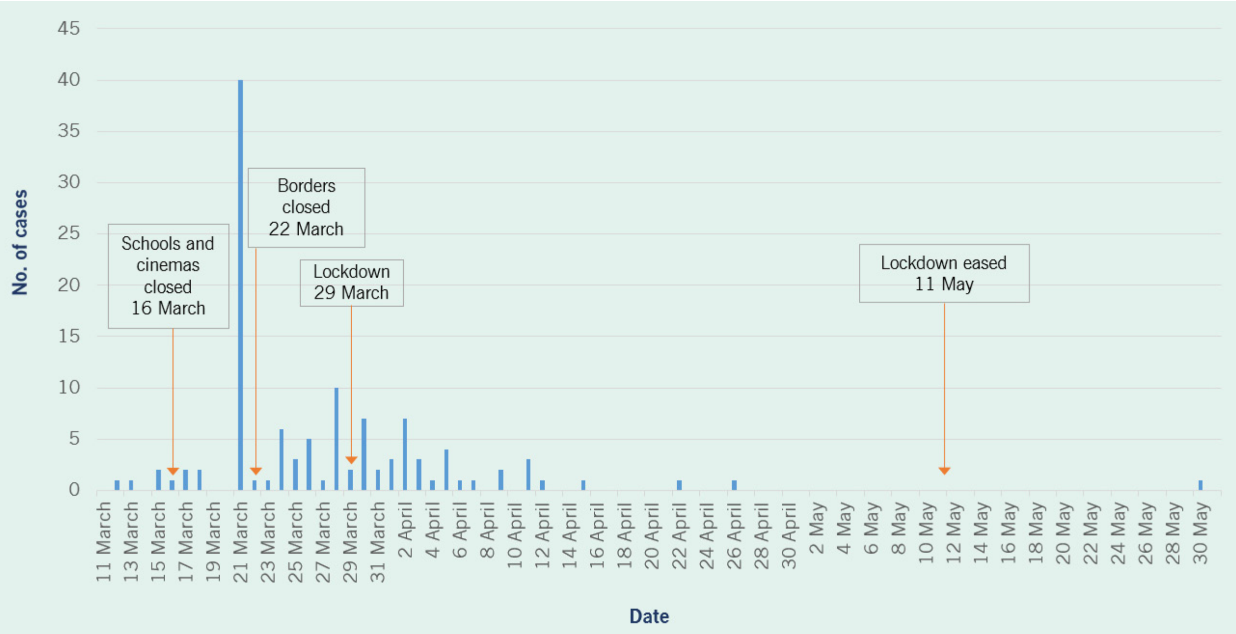
in the community were isolated for monitoring in specially designated facilities. Suspected cases were provided with food and essential commodities and supported by the Maldives Red Crescent.

In both countries, isolation of suspected cases in specially designated facilities at the government's expense, rather than at home, likely contributed to containment of the outbreaks.[13]

Laboratory testing supported the response

In Maldives, strengthening laboratory capacity required activating the emergency contingency budget and mobilizing aid resources to obtain materials for testing. The capacity for polymerase chain reaction testing was increased from 200 tests per day to 1000 tests per day in May 2020. Laboratories in the private sector and the forensic laboratory at Maldives Police Services were mo-

Fig. 2. **Epidemic curve of COVID-19, Trinidad and Tobago, 11 March to 31 May 2020**



bilized. Genomic sequencing is available through regional reference laboratories.

Trinidad and Tobago followed WHO protocols[14] for laboratory testing in April 2020: testing was widened to include frontline personnel in public sector facilities and elderly care facilities, and sentinel surveillance for influenza-like symptoms was implemented. During the initial phases, genomic sequencing was locally available only through the University of the West Indies St Augustine Medical School.

Box 1 highlights key lessons learned during the early response in both countries.

DISCUSSION

Prompt action was critical to contain the COVID-19 pandemic early in both countries. Keeping the numbers low is important for nations with limited resources and less sophisticated health-care systems to buy time until vaccines and medications become available.

Since the first wave of COVID-19 (March to May 2020), both countries have experienced further waves. As of the time of writing, Maldives experienced its latest surge in September 2021, and Trinidad and Tobago is in its fourth wave, with a surge in cases. Trinidad and Tobago was under a prolonged state of emergency from

Box 1. **Lessons learned**

- Early lockdown requires enforcement if it is to be effective at preventing and containing the spread of disease.
- Strong health communication is essential: communities need to be made aware of the rationale for a lockdown and should be engaged in the response to the pandemic.
- Allowing people to isolate in a facility at the government's expense appeared to contain the spread during the first wave of COVID-19.
- Small countries may lack the human resources necessary to carry out sustained public health activities, such as contact tracing, implementing a rapid response and staffing hotlines. Volunteers are a useful resource for these public health activities; potential volunteer pools should be identified.
- Taking a regional approach to guarantee laboratory access and vaccine procurement would ensure equitable access for smaller nations.

16 May to 17 November 2021. From 4 October, fully vaccinated persons were once again allowed to visit cinemas and gyms, and schools reopened to fully vaccinated students who were in their last 4 years of secondary school. In Maldives, school reopening has been staggered, with older students returning first, such as those sitting examinations.

In Trinidad and Tobago, vaccination began in February 2021 with donated vaccines and the prioritization of health-care workers. In April 2021, those aged ≥60 years and those with comorbidities were prioritized, and by August 2021, vaccination was open to all persons aged ≥12 years, including persons from migrant communities. Trinidad and Tobago has achieved 46.3% full vaccination coverage of its eligible population.

In Maldives, vaccination commenced in February 2021 for those aged ≥65 years, persons with comorbidities and frontline workers (including foreign migrant workers). By April 2021, vaccination was available to everyone aged ≥18 years, including foreign migrants. Maldives has achieved 67.5% full vaccination coverage of its eligible population.

The responses of both countries during their first waves served to limit spread and prevent their health systems from being overwhelmed. Lessons may also be derived from the management of the pandemic in the Pacific Island SIDS that closed their borders early. Leaders in the Pacific Islands Forum invoked the Biketawa Declaration to mount a collective response to the pandemic. Additionally, a Pacific action COVID-19 preparedness and response plan was developed to reduce transmission and to manage cases. The plan included activities such as screening passengers at major checkpoints, implementing 14-day quarantine for contacts and closing entry to non-residents. It also included the sharing of resources among islands. The Pacific Humanitarian Pathway on COVID-19 is the Region's mechanism for enabling the political commitment to expedite assistance and foster cooperation among member countries. It also facilitates the provision of medical and humanitarian assistance from regional, international and development partners in a timely and equitable manner.[15,16]

In conclusion, ongoing planning and preparedness, multisectoral collaboration, and community engagement and participation are critical to ensuring a successful response to an outbreak such as COVID-19.[17,18]

Conflicts of interest

The authors declare no conflicts of interest.

Ethics approval

Ethical approval was not required as this paper contains no identifiable patient data.

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None.

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COVID-19 patients with negative results on initial screening: Experience of Brunei Darussalam

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In any infectious disease outbreak, early diagnosis, isolation of cases and quarantine of contacts are central to disease containment. In Brunei Darussalam, suspected cases of coronavirus disease 2019 (COVID-19) were quarantined either at home or at designated centres and were tested immediately for severe acute respiratory syndrome coronavirus 2. We report on 10 cases of COVID-19 that initially tested negative for COVID-19 and were positive on re-testing after becoming symptomatic. These cases comprised 3.8% of the 266 total confirmed COVID-19 cases in Brunei Darussalam as of 9 July 2021, when this study was conducted. All the cases were in quarantine at home and were tested early during their quarantine period. Since then, home quarantine has been replaced by quarantine at designated centres only, with testing on the 12th day of quarantine.

The pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues, and, as of 2 November 2021, the cumulative number of cases reported globally was over 246 million and the cumulative number of deaths nearly 5 million.[1] In any infectious disease outbreak, early diagnosis, contact tracing and effective quarantine and isolation are central to disease containment.[2–4] The reverse transcription polymerase chain reaction (RT-PCR) assay is currently the most reliable test for diagnosis of COVID-19 during the symptomatic phase;[4] however, testing a patient too early after infection can lead to false-negative results.[5,6]

On 9 July 2021, when this study was conducted, there were 266 confirmed COVID-19 cases in Brunei Darussalam: 8 patients remained in the National Isolation Centre, 255 patients recovered and 3 died.[7] According to the World Health Organization (WHO), Brunei Darussalam remained at national transmission assessment stage 1, with only imported cases, from 6 May 2020 to 7 August 2021, when locally transmitted cases again began to be reported.[7,8] Suspected cases were defined according to the WHO definition,[9] and incoming travellers were placed in quarantine, either at home or at designated quarantine centres. Testing was conducted only with RT-PCR immediately upon commencement of quarantine.

We report 10 confirmed COVID-19 cases that initially tested negative in quarantine and the impact of this finding on our protocols during the first month of the COVID-19 outbreak in Brunei Darussalam.

METHODS

A descriptive study was conducted of data retrieved from a prospectively maintained Excel® database that was created to monitor COVID-19 patients. COVID-19 cases (n=12) with initial negative tests within 14 days (the maximum incubation period of SARS-CoV-2) of diagnosis of COVID-19 were included. Two patients were excluded, as the initial negative tests were performed >14 days (24 and 36 days) before the day of diagnosis.

The data extracted for analyses were age, sex, number and dates of RT-PCR tests before admission,

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symptoms, disease category, outcomes and possible source of infection.

Ethics statement

This study was conducted in accordance with the provisions of the Declaration of Helsinki.

RESULTS

Cases

Ten (3.8%) suspected cases (median age, 41.5 years; range, 28–72; 4 males and 6 females) had a negative COVID-19 test before testing positive (**Table 1**), with a median of 5 days (range, 1–10) between the negative and positive tests (**Table 1**). All 10 cases were initially tested because they were contacts of confirmed COVID-19 cases, and all were quarantining at home.

Cases 1–7 were in a family cluster (cluster A) of 15 confirmed COVID-19 cases. Three cases within this cluster had returned from vacations on three separate flights, two flights arriving 5 and 16 days after the first flight. The index case in this cluster was the spouse of case 5, who returned home on the first flight and developed symptoms soon after arrival. She had been symptomatic for 3 days before being tested and was confirmed positive for SARS-CoV-2. All the subsequent cases that tested negative before testing positive, except case 5, developed symptoms during home quarantine after an initial negative test. Case 5 was retested at the request of the family, and, although remaining asymptomatic, also retested positive. Case 7 (spouse of case 6) had two negative tests: initially as a contact of the index case and then when case 6 retested positive. She tested positive on the third test, conducted after the onset of symptoms.

Case 8 (cluster B, 25 cases) was a contact of her spouse and daughter, who had tested positive for SARS-CoV-2 earlier. She later developed symptoms and retested positive 7 days after her initial negative test. Her spouse had contracted the infection from a friend.

Case 9 (cluster C, 7 cases) was a contact of a sibling who had returned from travel. The second test was conducted because of persistent symptoms.

Case 10 (cluster D, 14 cases) was a contact of her spouse, who contracted the infection from a work colleague. Two days after an initial negative test, case 10 was retested because of persistent symptoms and tested positive.

All the cases except case 3 were categorized as mild. Two cases (cases 8 and 9) were hospitalized twice when they retested positive after discharge.

Impact on protocols

Two notable changes were made to the COVID-19 protocols in Brunei Darussalam during this period. First, home quarantine was abolished for incoming travellers within 1 month of the outbreak on 20 March 2020. Second, the testing schedule during quarantine was revised for local suspected cases from immediate testing only to testing on the 4th day of quarantine.

DISCUSSION

In our study, 3.8% of COVID-19 cases in Brunei Darussalam as of 9 July 2021 initially tested negative. Initial negatives or delayed positives are a concern if they are missed cases that become vehicles for continued COVID-19 spread.[10] Fortunately, these 10 cases were under the mandatory 14-day quarantine and had repeat tests, usually because of development of symptoms. No additional transmission was linked to these 10 cases.

Our experience confirms that testing early, especially during the pre-symptomatic phase, can lead to false-negative results.[11,12] Therefore, our testing protocol was revised several times, from immediate testing of cases with initial negative results to the current (as of December 2020) testing on the 12th day of quarantine. Cases are still tested if they become symptomatic or if symptoms persist. Incoming travellers are tested according to a schedule based on the countries to which they had travelled (travel passes A, B and C). Testing can be done immediately or 1 day after arrival from countries listed for travel pass A under certain conditions (pre-travel approved entry permit, COVID-19 testing within 72 hours of arrival, payment for post-arrival RT-PCR and a health tracking application installed on mobile phone), on the 5th day of quarantine for travel pass B and on the 12th day of quarantine for travel pass C.

Home quarantine for returned travellers presented some difficulty in monitoring without personnel on site or a remote monitoring system. All patients were given an information leaflet and a designated number to call if required, for example if they developed symptoms. It is possible that some patients may not call the number, because of unawareness, having misplaced the information leaflet or choosing not to inform the authorities of the progress of their illness. There were also logistical issues for those who required retesting, because of lack of personnel for testing in home quarantine. Quarantine in designated centres was found to be preferable, as COVID-19 is easier to monitor in known locations, of which there are only a few. In home quarantine, quarantine regulations may not be adhered to strictly, and continued transmission can occur.

Our findings show that the pandemic situation is fluid and that protocols and processes must therefore be revised continually. This is particularly important as the pandemic is complicated by SARS-CoV-2 variants of concern. Missed cases are the driver of continued disease transmission. At the time this study was conducted, Brunei Darussalam had remained at WHO stage 1 of transmission (imported cases only) for over one year,[7,8] and we have continued to maintain all preventive and monitoring measures while simultaneously adjusting our protocols and processes. Our findings can be generalized to other settings, especially those in which containment is still possible.

In conclusion, our experience highlights the importance of monitoring people in quarantine and revising protocols to control outbreak situations. Undetected and missed cases can lead to continued disease transmission. Since home quarantine was abolished and testing of those in quarantine was delayed to later in the quarantine period, we have not registered any further COVID-19 cases with initial negative tests. The lessons learnt can be applied in other countries and to outbreaks of other infectious diseases.

Conflicts of interest

None.

Funding

None.

Table 1. **Characteristics and outcomes of cases with initial negative tests before testing positive for COVID-19**

Case (cluster)	Age/sex	Number of initial negative tests for SARS-CoV-2	Number of days between index positive confirmation and testing	Number of days between negative test and positive test	Indication for repeat testing (days after initial test)	Disease severity	Possible source of infection
1 (A)	45/F	1	1	3	Symptoms (3)	Mild	All cases were contacts of the index case (spouse of case 5) who had returned from an overseas trip
2 (A)	33/M	1	1	4	Symptoms (3)	Mild	
3 (A)	50/F	1	1	4	Symptoms (4)	Moderate	
4 (A)	51/F	1	1	4	Symptoms (4)	Mild	
5 (A)	72/M	1	0	6	Asymptomatic, family request	Mild	
6 (A)	43/M	1	0	6	Symptoms (5)	Mild	
7 (A)	36/F	2	1	7 10	Spouse (case 6) tested positive Symptoms (7)	Mild	
8 (B)	40/F	1	0	7	Symptoms (7)	Mild	Contact of two confirmed cases: spouse (admitted 7 days earlier) and daughter (admitted 5 days earlier)
9 (C)	28/M	1	0	8	Symptoms (4)	Mild	Sibling was a confirmed case
10 (D)	39/F	1	2	1	Persistent symptoms (1)	Mild	Contact of two confirmed cases: spouse (admitted 3 days earlier) and son (admitted 2 days earlier)

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Epidemiological characteristics of the SARS-CoV-2 Theta variant (P.3) in the Central Visayas region, Philippines, 30 October 2020–16 February 2021

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The Theta variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported in the Central Visayas region, Philippines, in January 2021. The World Health Organization (WHO) designated the Theta variant as a variant of interest on 24 March 2021,[1] given that it contains the mutations E484K, which has been associated with antigenic escape; N501Y, associated with increased transmissibility; and other mutations of concern found in existing variants of concern (Tablizo FA, Kim KM, Lapid CM, Castro MJR, Yangzon MSL, Maralit BA, et al. Philippine Genome Center, unpublished data, 2021). This report is the first to describe the epidemiological profile of this variant.

Surveillance for pathogens in the Philippines is coordinated at the national level by the Department of Health Epidemiology Bureau and at the regional level by Regional Epidemiology and Surveillance Units (Regional Units); surveillance at the local level is conducted by City and Municipal Epidemiology and Surveillance Units. Regional Units identify candidates for sequencing among SARS-CoV-2 specimens that are positive by nucleic acid amplification test and send these samples to the Philippine Genome Center for whole-genome sequencing (WGS). The criteria for sample selection established by the Central Visayas Regional Unit include specimens from cases with known travel history from countries with variants of concern or interest, specimens that are part of large clusters of positive coronavirus 2019 (COVID-19) cases and specimens that have a volume >500 μL and a cycle threshold value <30 (Central Visayas Center for Health Development, unpublished guidance: collection and testing guidelines for genomic sequencing, 2021). To meet the national capacity for WGS, which is about 750 samples weekly,[2] the Epidemiology Bureau further narrows down samples for WGS.

As of 10 June 2021, 950 samples, one sample per case, had been sent for WGS from the Central Visayas region, and 321 (33.8%) had been sequenced. The samples were collected from 30 October 2020 to 16 February 2021. The WGS results were provided to the Central Visayas Regional Unit between 12 February and 12 March 2021.

Cases were followed up for 60 days post-diagnosis to determine whether they resolved through clinical recovery or death; clinical recovery was defined as the date when a case was discharged from a hospital or isolation facility following SARS-CoV-2 infection. Outcomes were ascertained based on standard discharge and recovery criteria as reported by City and Municipal Surveillance Units or local health facilities.[3]

Cases were excluded from the analysis if they had any of the four variants of concern identified as of June 2021 – that is, Alpha, Beta, Gamma or Delta – as these are known to be associated with higher transmissibility and mortality. Some specimens were from cases in the same outbreak cluster or shared the same home address and date of specimen collection; therefore, all statistical analyses considered clustering at this level. The risk ratio (RR) for COVID-19 hospitalization was calculated using a log-binomial generalized estimating equation with an

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independent working correlation structure and robust sandwich variance estimator.[4] Median recovery times were calculated from Kaplan–Meier survival curves. The hazard ratios (HRs) for recovery were estimated using a shared frailty model, which is an extension of the Cox proportional hazards model that accounts for clustering, and the proportional hazards assumption was checked using Schoenfeld residuals.[4] For both RR and HR, the models were adjusted for morbidity, week of specimen collection of first positive test, age, sex and province. Finally, because contact tracing is done by City and Municipal Surveillance Units, two major cities provided a copy of their database to the Regional Unit. For cases with the Theta variant in those cities, close contacts were counted and cross-referenced with the Regional Unit's confirmed COVID-19 line list to determine which close contacts had tested positive. The secondary attack rate was calculated as the number of positive close contacts divided by the total number of close contacts. All analyses were conducted using Stata version 17 (StataCorp, College Station, TX, USA).

Of the 321 cases with WGS results, four had the variant of concern and were excluded; thus, the final sample size was 317 cases, comprising 2.6% of the 12 136 cases confirmed by nucleic acid amplification tests during the specimen collection period. The Theta variant was detected in 68 (21.5%) of the samples. For all cases, most specimens (200/317; 63.1%) and almost all specimens from Theta variant cases (64/68; 94.1%) were collected during the first 2 weeks of February (**Table 1**). Additionally, most specimens were collected from cases in Cebu province, including from the independent cities of Cebu City, Lapu-Lapu City and Mandaue City (191 [60.3%] of specimens overall and 48/68 [70.6%] among Theta variant cases). The median age of all cases was 33 years (interquartile range [IQR]: 21–46), and 142 (44.8%) cases occurred among women. The age and sex distributions were similar between cases with the Theta and non-Theta variants (**Table 1**).

Hospitalization was required for 18 of the 68 cases with the Theta variant (26.5%) compared with 77 of the 249 non-Theta variant cases (30.9%) (data not shown). The risk for hospitalization was not significantly associated with having the Theta variant (crude RR: 0.86; 95% confidence interval [CI]: 0.48–1.51; adjusted RR: 0.76; 95% CI: 0.40–1.47) (data not shown). The median time to recovery was similar, at 17 days, and the HR for recovery also was not associated with the Theta variant (crude HR: 1.00; 95% CI: 0.70–1.44; adjusted HR: 0.92; 95% CI: 0.65–1.30) (data not shown). Three cases died, none of whom had the Theta variant.

Nineteen clusters were identified from two major cities, with the index case having the Theta variant. The

Table 1. **Comparison of Theta variant and non-Theta variant SARS-CoV-2 cases in the Central Visayas region, Philippines, 30 October 2020–16 February 2021**

Characteristic	Severe acute respiratory syndrome coronavirus 2		
	All[a] (*N* = 317)	Theta variant (*N* = 68)	Non-Theta variant (*N* = 249)
Female, *n* (%)	142 (44.8)	30 (44.1)	112 (45.0)
Age (years), median (IQR)	33 (21–46)	34.5 (20.5–42)	33 (21–49)
Age group (years), *n* (%)			
0–17	69 (21.8)	15 (22.1)	54 (21.7)
18–44	161 (50.8)	39 (57.3)	122 (49.0)
45–60	53 (16.7)	8 (11.8)	45 (18.1)
>60	34 (10.7)	6 (8.8)	28 (11.2)
In Cebu province, *n* (%)[b]	191 (60.3)	48 (70.6)	143 (57.4)
Specimens collected during the first 2 weeks of February 2021, n (%)[c]	200 (63.1)	64 (94.1)	136 (54.6)

IQR: interquartile range.

[a] Excludes four sequenced samples with variants of concern.

[b] A full provincial breakdown is not available due to small sample sizes from some provinces (<5 cases); counts from Cebu province include the independent cities of Cebu City, Lapu-Lapu City and Mandaue City.

[c] Other dates of specimen collection are not available due to small sample sizes in some months (<5 cases).

median number of close contacts was 8 (IQR: 5–13). There were 182 close contacts, 81 of whom tested positive. Therefore, the overall secondary attack rate for cases infected with the Theta variant was 44.5%.

These preliminary results, showing that the Theta variant did not seem to be associated with more severe disease, were similar to findings on the Iota variant (B.1.526) in New York, which also contained the E484K mutation.[5] Additionally, while the secondary attack rate was more than twice as high as the 16.6% previously reported,[6] the number of clusters examined was too few to draw any definitive conclusions. Since March 2021, most of the country's biosurveillance capacity has been dedicated to testing samples from the National Capital Region and from repatriated Filipinos.[7] Further investments to expand biosurveillance capacity, as well as to facilitate timelier linkages of genomic, epidemiological and clinical data, may be needed to further understand the epidemiological profile of the Theta variant. Nonetheless, our results can contribute to the evidence base used by WHO and countries affected by the Theta variant to clarify its status as a variant of interest.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

This analysis received institutional review board exemption from the Ateneo de Manila University Research Ethics Committee (protocol no.: AdMUREC_21_011).

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