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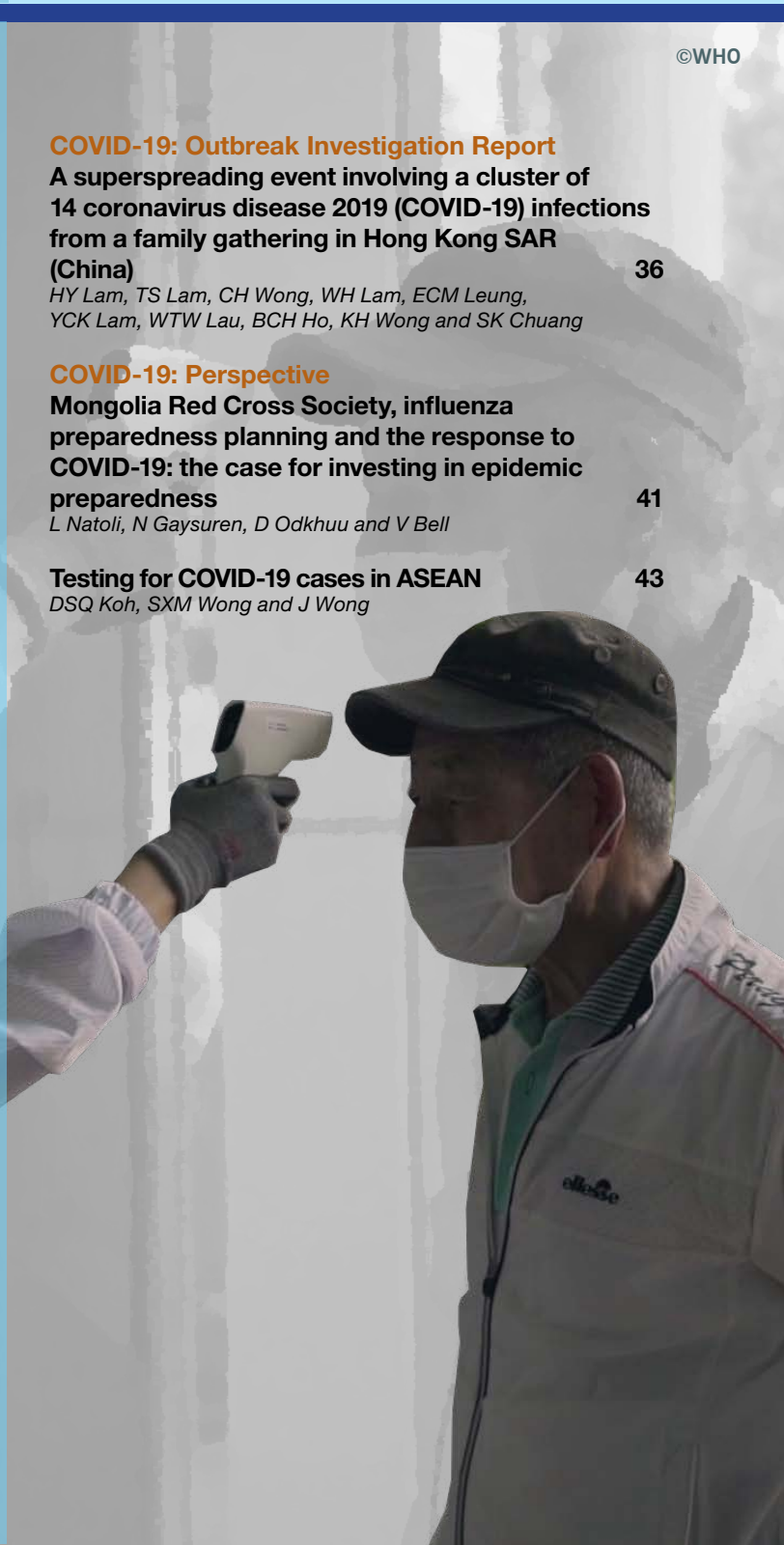

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An accidental household outbreak of paliperidone palmitate poisoning via pancake consumption in Lianyungang, China

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Introduction: At 11:20 on 26 May 2018, a physician from Lianyungang No. 1 People's Hospital, China, reported that six family members were being treated in the hospital with symptoms from an unknown cause.

Methods: A case series for a food poisoning investigation and an environmental survey were conducted. The patients and their relatives were interviewed in person with a questionnaire contained on a digital tablet, and an investigation of the patients' home was conducted in the presence of police officers. Probable case and confirmed case were defined to serve as a basis for identifying additional cases. Confirmed cases were defined as those probable cases in which blood, stool or vomitus specimens tested positive for paliperidone palmitate and/or its metabolites. A descriptive analysis was performed. Follow-up by telephone was conducted four months later.

Results: There were six probable cases. The median age was 35 years (range: 5–76 years). The attack rate was 100% (n = 6/6) of persons who consumed a family dinner, and the hospitalization rate was also 100% (n = 6/6). The median period between exposure and symptom onset was two hours. The main symptoms included vomiting, nausea, drowsiness, dizziness and severe abdominal pain for adults, and vomiting and severe lethargy for children. An 8-year-old girl further showed changes in the ST segment of her electrocardiogram, and a 5-year-old boy showed QT prolongation. The poisoning substance was suspected to be paliperidone palmitate based on the patients' symptoms and epidemiological findings.

Discussion: We investigated the household food poisoning outbreak through epidemiological analysis and an environmental investigation and determined that it was caused by paliperidone palmitate. The source of the paliperidone palmitate was found to be aluminium containers, taken home by the eldest son who worked at a pharmaceutical company. The containers were sent to a drug disposal centre, and the pharmaceutical company was required to enhance the regulation on the pharmaceutical waste materials to prevent drug poisoning events. By the end of September 2018, the six patients recovered and were released from the hospital, and they did not show any clinical sequelae in four follow-up visits.

At 11:20 on 26 May 2018, the staff at the Haizhou District Health Bureau received a call from a doctor in the Health Department informing them that six patients with symptoms from an unknown origin were being treated at the Liayungang No. 1 People's Hospital, China. At that time, three epidemiologists and two laboratory personnel from the Lianyungang Municipal and Haizhou District Centers for Disease Control and Prevention were sent to that hospital to open an investigation.

METHODS

Epidemiological, laboratory and environmental investigations were conducted.

Epidemiological investigation

A case series for a food poisoning investigation and an environmental survey were conducted in accordance with Chinese technical guidelines for epidemiological investigations of food safety incidents.[1]

We interviewed the patients and their relatives in person with a questionnaire contained on a digital tablet. The questionnaire included demographic information, clinical symptoms and treatments, and dietary exposure information over the previous 72 hours. Blood specimens and food samples were collected.

Probable cases were defined as members of the family who ate leftover fish, dry lettuce with sauce, scal-

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lion pancakes and rice porridge for dinner on 25 May 2018, and presented with acute gastroenteritis with at least one of the symptoms: vomiting, malaise and severe abdominal pain. Confirmed cases were defined as those who met the case definition for the probable cases, and whose blood, stool or vomitus specimens tested positive for paliperidone palmitate or its metabolites.

Statistical analysis

We entered the data into a computerized database. The descriptive analysis included the distribution of onset dates and the process used to make the food. In addition, the attack rate (the number of cases divided by the number of family members who ate the scallion pancakes) and the hospitalized rate (the number of hospitalized cases divided by the number of cases) were calculated.

Laboratory investigation

Blood specimens were collected from probable cases and sent to the municipal and provincial Center for Disease Control and Prevention laboratories and the pharmaceutical company laboratory. The dry lettuce (no other dishes from the meal were available) was collected (about 200 g) and sent to the Lianyungang Municipal Center for Disease Control and Prevention to test for pathogenic organisms.

Ethical approval

This outbreak investigation was conducted by public health agencies as a part of their legally authorized mandate. It was, therefore, considered research with minimal risk and was exempted from ethical approval by institutional review boards.

RESULTS

Case characteristics

The six patients being treated in hospital were members of a family that lived in Taiping Village, Haizhou District, Lianyungang, China. They included a 76-year-old man, a 63-year-old woman, a 35-year-old man, a 35-year-old woman, an 8-year-old girl and a 5-year-old boy.

The family's dinner on 25 May 2018 included leftover fish from lunch, dry lettuce with commercially produced soybean sauce, homemade scallion pancakes and rice porridge (**Table 1**). The six patients ate dinner between 18:00 and 18:30. The eldest son went out for a haircut after dinner. Upon returning to the house, he found the five other members of his family in a lethargic state. He called emergency services, and ambulances soon arrived, taking the patients to the Emergency Department of Lianyungang No. 1 People's Hospital for treatment.

Epidemiologic and clinical profiles

There were six probable cases. The first case displayed symptoms, at 20:10 on 25 May 2018; the five remaining cases displayed symptoms by 20:30. The median incubation period was two hours. The attack rate was 100% (n = 6/6) as shown in **Fig. 1**, and the hospitalized rate was 100% (n = 6/6).

All four adult case patients reported dizziness, drowsiness, malaise, nausea, severe abdominal pain and vomiting. Coffee-ground vomitus was not reported, indicating that gastric bleeding had not occurred. The main symptoms and signs exhibited by both children included contracted pupils, severe lethargy (one child was in a coma for two days, and the other for four days), tachycardia and vomiting, but they were otherwise haemodynamically stable. The girl showed ST segment changes in her electrocardiogram, and the boy displayed prolongation of the interval between the Q wave and the T wave (QTc prolongation).

Laboratory

Blood specimens of all six case patients were collected and sent to the municipal and provincial Center for Disease Control and Prevention laboratories, but those laboratories did not have the capacity to test for paliperidone (as suspected from environmental investigation, see below). The dry lettuce tested negative for pathogenic organisms. Stool and vomitus specimens were not collected.

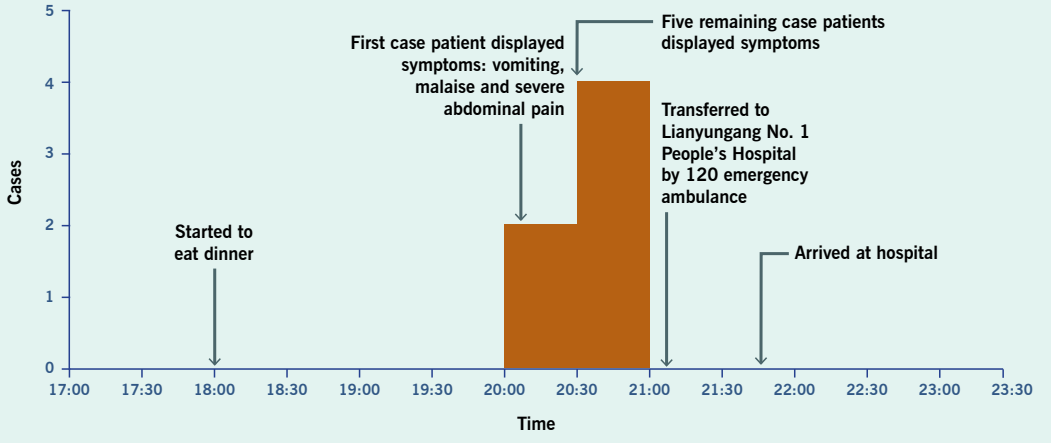
Treatments

At 21:44 of 25 May 2018, the six patients arrived at Lianyungang No. 1 People's Hospital by ambulance. The four adults were quickly transferred to the Emergency Department, and the two children were transferred to the Paediatrics Department. All six case patients were admitted to intensive care units and received supportive

Table 1. **Types and approximate portions of food consumed by patients at dinner (18:00) on 25 May 2018**

Sex	Age (years)	Dinner foods			
		Leftover fish from lunch (mouthfuls)	Dry lettuce with commercially produced soybean sauce (mouthfuls)	Pancake (g)	Rice porridge (bowls)
female	63	3	3	50	1
male	35	2	4	50	1
male	76	4	2	100	1
female	8	0	2	100	1
male	5	0	1	150	1

Fig. 1. **Distribution of six food poisoning cases in Taiping Village, Haizhou District, Lianyungang, China, on 25 May 2018**



treatment with gastric lavage for presumed poisoning, followed by intravenous fluid infusion. They received diuretics to facilitate excretion of the paliperidone palmitate and its metabolites once they were in a stable condition, and after environmental investigation and according to the product prescription by Janssen Pharmaceutica N.V. The median length of hospital stay was 13 days (range: 12-15 days). Four follow-up visits were conducted by the end of September 2018; all six discharged patients reported no clinical sequelae.

Food-making process investigation

Epidemiologists spoke with the 63-year-old's niece, who reported that the grandmother had mixed a handful of white, tasteless "starch" from an aluminium container into the flour when making scallion pancakes on the afternoon of 25 May 2018. The epidemiologists visited the family home to investigate on the morning of 27 May 2018. Two aluminium containers with lids were found in the kitchen; there was a white substance at the bottom of each aluminium container. The containers were labelled "paliperidone palmitate". These aluminium containers had been abandoned in a warehouse of a pharmaceutical company in Lianyungang, China, after most of the powder stored in the containers had been used. The grandmother's eldest son worked for the company and had taken two aluminium containers from the warehouse, without permission, to use for storing items.

On the morning of 27 May 2018, the grandmother described her food-making process to the epidemiologists. She told them that she took some white powder from an aluminium container that her son had brought home from the pharmaceutical company. She said he had told her that the white powder left in containers might be "starch". She used a sieve over a flour-mixing basin to sift any impurities from what she thought was starch on the afternoon of 25 May 2018, then mixed the filtered white powder with water in a bowl. Because paliperidone

palmitate is insoluble in water, the grandmother threw the contents of the bowl, including possibly 20 g of powder, on the ground. But there was still a little of what she believed to be starch (potentially 5 g) sprinkled into the flour-mixing basin during the sifting (**Fig. 2**). Finally, she used the flour-mixing basin to mix the wheat flour (about 500 g), and baked the scallion pancakes as a staple food for dinner.

Control measures

The following public health control measures were implemented following the food poisoning outbreak and discovery:

1. Police officers sealed the aluminium containers and other related articles for safekeeping in the patients' home, and then transferred them to the drug disposal centre for future elimination at the Lianyungang Public Security Bureau. None of the contaminated scallion pancakes remained.

2. Clinicians were informed of the discovery of paliperidone palmitate in the patients' food, to inform treatment decisions"

3. The local Food and Drug Administration immediately launched an investigation into the food poisoning outbreak. It required the pharmaceutical company implicated to strictly enforce regulations on the destruction of expired materials or medicines in pharmaceutical production and storage and to standardize and update protocols for destroying those wastes to prevent drug poisoning events.

DISCUSSION

We describe a household food poisoning outbreak caused by paliperidone palmitate that accidentally contaminated flour that was incorporated into scallion pancakes consumed by a family in Taiping Village, Haizhou District, Lianyungang, China, on 25 May 2018.

Although we could not confirm it by laboratory testing, the epidemiologic and environmental investigation support the conclusion that the patients were poisoned with paliperidone palmitate, used in preparing the pancakes consumed by the family admitted to the Emergency Department.

Paliperidone palmitate is an antipsychotic medication used for the acute treatment and maintenance of schizophrenia cases. Previously reported adverse events include dizziness and vomiting, which were very similar to symptoms of the six patients, except for severe abdominal pain in this event.[2–13]

The half-life of paliperidone palmitate is 25–49 days after a single oral dose of 25–125 mg, according to the product prescription by Janssen Pharmaceutica N.V.

In this outbreak, the young girl showed ST segment changes in her electrocardiogram, and the young boy displayed prolongation of the interval between the Q wave and the T wave (QTc prolongation). Some studies have shown that prolongation of the QT intervals remains a concern with the use of antipsychotics.[14] While others have reported no evidence of clinically significant QTc prolongation with paliperidone palmitate at doses up to 100 mg equivalent.

When four follow-up visits for the discharged patients were conducted by the end of September 2018, all six discharged patients reported no clinical sequelae.

Limitations

The laboratories did not have the capability to test for paliperidone palmitate.

CONCLUSION

We reported a household food poisoning outbreak that is suspected to have been caused by paliperidone palmitate that was accidentally incorporated into scallion pancakes, according to the clinical symptoms of six patients and the epidemiological findings.

It is suggested that the pharmaceutical company strictly enforce regulations on the destruction and disposal of pharmaceutical waste and expired materials. In addition, it is suggested the people not take home unknown and/or abandoned commodities and not to eat unknown food in order to prevent the food-related poisoning events.

Acknowledgements

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Fig. 2. **The insoluble "starch" solution was thrown away on the ground after sifting**

Conflict of interest

The authors declare no conflicts of interest.

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Prevalence of chronic hepatitis B in Oro Province, Papua New Guinea

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Chronic hepatitis B (CHB) affects over 250 million people worldwide. In Papua New Guinea, the prevalence of CHB has been estimated to be over 8%, and it is a leading cause of death. To address this problem, an alliance was formed between the government of Oro Province, a large private employer and an Australian nongovernmental organization, which established a CHB test and treatment programme. Between 2014 and 2019, rapid hepatitis B surface antigen testing was performed on 4068 individuals in Oro Province. The crude prevalence rate was 12.98% and was significantly higher in males (15.26%) than females (10.94%) ($P < 0.001$). The rate was 4.72% among children aged 10 years and under, 12.81% among women of childbearing age (19–35 years) and 18.48% among health-care workers. These results indicate that the rates of vaccination at birth and later among women of childbearing age and health-care workers must be improved to prevent transmission of CHB.

Hepatitis B is a leading cause of morbidity and mortality worldwide; it is responsible for about 900 000 deaths annually, and nearly 300 million people suffer from chronic hepatitis B (CHB).[1] The prevalence of CHB in Papua New Guinea (PNG) has been estimated to be 14.6%;[2] however, numerous barriers hinder accurate country-wide accounting, as over 80% of the 8 million inhabitants of PNG live in geographically remote areas with limited access to health services, and strong beliefs in traditional healing foster a distrust of western medicine. CHB is a major cause of morbidity and mortality in PNG and the leading cause of cirrhosis and hepatocellular carcinoma.[3] Complications of liver cirrhosis, including ascites and variceal bleeding, are reported by local physicians as among the most common reasons for hospital admission. As a result, population-wide screening is critical, with follow-up vaccination of those who are hepatitis B surface antigen (HBsAg) negative and treatment for those who test positive.

Volunteers from Hepatitis B Free (HBF), an Australian non-profit organization, were invited by community leaders and provincial health officials in Oro Province in PNG to address the gap in vaccination against hepatitis B in remote villages. In 2013, HBF donated rapid test kits for HBsAg and began testing and vaccinating individuals in remote communities. Volunteers from HBF travel regularly to PNG and have established a formal partnership with the Oro provincial government, the provincial health department, Popondetta General Hospital and a private company, New Britain Palm Oil Ltd. The company is a large employer in Oro Province and provides health care to employees and families as well as to local non-affiliated patients through a network of health clinics and aid posts. In 2019, tenofovir disoproxil fumarate (TDF), a drug with proven efficacy against CHB, was approved for use by the national Government, and the first patients have been started on TDF according to WHO treatment guidelines,[4] while population screening continues in government hospitals, outreach health fairs and company-operated clinics.

This report describes surveillance of the large cohort of patients who have been tested since 2014.

METHODS

Ethical approval for the hepatitis B testing and treatment programme was obtained from the Medical Research Advisory Committee of PNG (MRAC No. 18–13). All people

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attending routine visits to clinics, at community health fairs and during clinical evaluation of symptoms such as abdominal pain were considered eligible and were screened for HBsAg during the period May 2014–October 2019. They were informed of the reason for screening by a health-care worker fluent in their native language and were given the opportunity to ask questions and refuse testing. Those who tested positive were counselled about the risk of transmission, precautions to take and future treatment options and were referred to hepatitis clinics for evaluation. A WHO pre-approved rapid HBsAg test, SD Bioline (Abbott Corp., USA), was used. The reported sensitivity and specificity of this test are 100% and 98.7%, respectively.[5] Univariate analyses for gender and HBsAg positivity were performed with χ^2 tests, and $P = 0.05$ was considered significant. Subgroup analyses were performed after stratification by age, gender and population.

RESULTS

Between 2014 and the end of 2019, 4068 tests were performed. The refusal rate could not be calculated precisely but is estimated to be <10%. The overall prevalence of HBsAg positivity was 12.98% (**Table 1**). Males were more likely than females to have positive results (X^2 1, $n = 4068$) = 16.75, $P < 0.001$. The 36–49 years age group had the highest prevalence (16.90%), and that of men in this age range was 21.90%. The rate was 3.29% among children under 5 years, 4.72% for those under 10 years and 7.06% for those aged 5–15 years. The prevalence among women of prime childbearing age (19–35 years) was 12.81%, while that among women aged 36–49 years was 11.41%, and the rate among girls aged 11–18 years was 6.55%. Of the 92 health-care workers tested, 17 had positive results (18.48%) (**Fig. 1**).

Of 4068 individuals tested, only 1134 had either documentation of vaccination or could recall that they had been vaccinated. In this group of 1134, 256 (11.29%) were HBsAg positive. Among children under 5 years, 118 were known to have been vaccinated, but 5 (4.31%) were HBsAg positive.

DISCUSSION

Our results show high rates of CHB in Oro Province, despite recent efforts to increase vaccination and public awareness. The overall prevalence of 12.98% is lower than previous estimates (14.6%).[6] As seen elsewhere,[7] we found higher rates among men than women, with the highest prevalence among men aged 36–49 years (21.90%).

The three-dose HBV vaccine was included in the national immunization schedule in 1989, and vaccination at birth was added in 1992.[8] A nationwide, four-stage cross-sectional cluster survey among 2109 children aged 4–6 years during 2012–2013 showed an HBV seroprevalence of 2.3%, which is higher than the WHO Western Pacific regional goal of <1% for children under 5 years.[9] In our study, the prevalence was 3.29% among children under 5 years and 4.72% in children under 10 years, which are also higher than the WHO goal. The coverage of vaccination against HBV at birth in PNG is only 31% because of factors such as lack of vaccine and of adequate refrigeration.[9] As many women give birth at home without a skilled attendant, timely delivery of a birth dose is difficult. Another study concluded that lack of knowledge about the birth dose among health workers contributed to delay in giving the vaccine.[10]

The high prevalence of HBV among adolescent girls, women of childbearing age and health-care workers indicates that testing and vaccination should be improved. Health-care workers are a priority, as they are at risk for both infection and transmission to patients. Universal testing of pregnant women is essential, and antenatal treatment for CHB with new protocols should be considered in order to decrease the risk of vertical transmission.

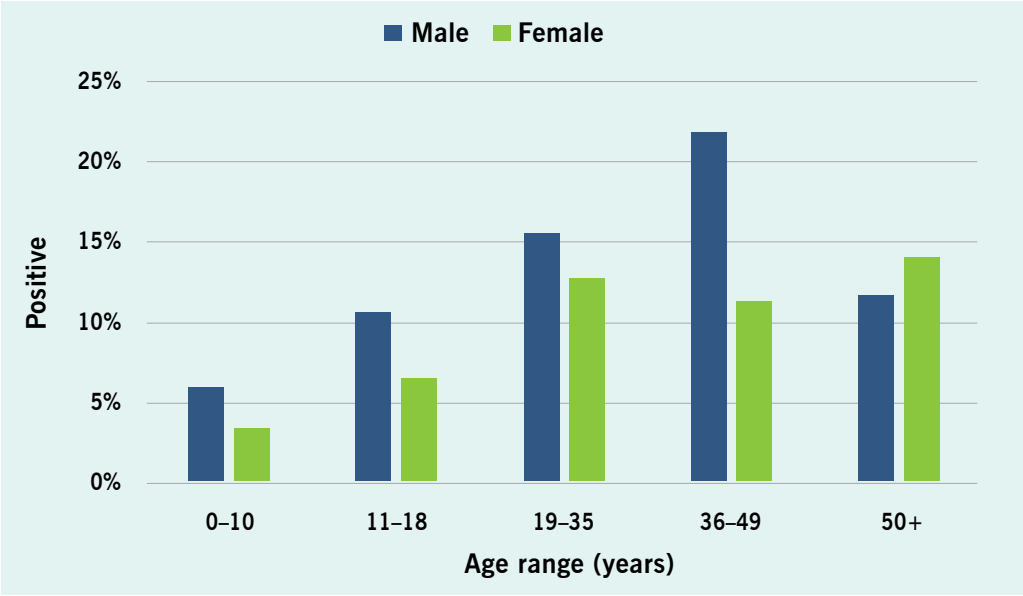
Other high-risk groups, including people with HIV and tuberculosis, are not routinely screened for HBV. The prevalence of HIV infection is 0.9% in the general adult population and higher in high-risk groups.[3] It is presumed that co-infection with HBV is significant, but testing is often not performed because of lack of availability of rapid testing kits.

It is unclear why CHB appeared to be so prevalent (11.29%) among people who reported previous vaccination. Some may have received fewer than the recommended three doses, mis-reported the type of vaccine administered or were vaccinated when they were already infected but did not know their status. Some may have become infected despite having been vaccinated.

Table 1. **Numbers and percentages of persons positive for hepatitis B surface antibody, by age and gender**

Age range (years)	Positivity				Total (%)
	Males		Females		
	Total (no.)	Positive (no. (%))	Total (no.)	Positive (no. (%))	
0–10	233	14 (6.01)	233	8 (3.43)	4.72
11–18	131	14 (10.69)	229	15 (6.55)	8.06
19–35	934	146 (15.63)	1132	145 (12.81)	14.09
36–49	452	99 (21.90)	412	47 (11.41)	16.90
≥50	170	20 (11.76)	142	20 (14.08)	12.82
Total	1920	293 (15.26)	2148	235 (10.94)	12.98

Fig. 1. **Proportions of persons positive for hepatitis B surface antigen, by age and gender**



The strengths of this study include the large cohort, the inclusion of individuals in remote areas and use of a sensitive rapid test kit. The limitations include opportunistic testing, possible recall bias of vaccination status and lack of data on co-infection with HIV, hepatitis C virus or tuberculosis. The refusal rate was difficult to calculate; if it was high, the representativeness of the sample would have been biased. As testing was limited to a single province, the results cannot be generalized to the national population.

An antiviral medication, TDF, has been approved for use in PNG. The first patients were started on treatment in Oro Province in November 2019 through the consortium described above. Travel restrictions due to COVID-19 and lack of reagents have slowed the required pre-treatment evaluations, and, thus far, only 20 patients are currently on medication. Consideration should be given to extending treatment to HBV-positive pregnant women. Public education, community HBsAg screening and birth-dose vaccination, which have been prioritized in Oro Province, must be implemented nationwide to achieve the WHO goal of elimination of hepatitis B by 2030.

CONCLUSIONS

We found high rates of CHB in the general population, especially among children under 5 years, women of child-bearing age and health-care workers. The data should assist local and national stakeholders in designing policies and guidelines for therapy and for the prevention of CHB, including vaccination of newborns and at-risk groups, and consideration of prophylactic treatment of HBsAg-positive pregnant women to prevent vertical transmission of hepatitis B. The results should be used to inform policy-makers, mobilize resources and encourage funding from internal and external organizations to reduce the burden of CHB in PNG.

Conflicts of interests

None of the authors report a conflict of interest.

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Epidemiology of tuberculosis in the Western Pacific Region: Progress towards the 2020 milestones of the End TB Strategy

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Since 2015, the End TB Strategy and the Regional Framework for Action on Implementation of the End TB Strategy in the Western Pacific 2016–2020 have guided national tuberculosis (TB) responses in countries and areas of the Region. This paper provides an overview of the TB epidemiological situation in the Western Pacific Region and of progress towards the 2020 milestones of the Strategy. A descriptive analysis was conducted of TB surveillance and programme data reported to WHO and estimates of the TB burden generated by WHO for the period 2000–2018. An estimated 1.8 million people developed TB and 90 000 people died from it in the Region in 2018. Since 2015, the estimated TB incidence rate and the estimated number of TB deaths in the Region decreased by 3% and 10%, with annual reduction rates of 1.0% and 3.4%, respectively. With current efforts, the Region is unlikely to achieve the 2020 milestones and other targets of the Strategy. Major challenges include: (1) wide variation in the geographical distribution and rate of TB incidence among countries; (2) a substantial proportion (23%) of TB cases that remain unreached, undiagnosed or unreported; (3) insufficient coverage of drug susceptibility testing (51%) for bacteriologically confirmed cases and limited use of WHO-recommended rapid diagnostics (11 countries reported <60% coverage); (4) suboptimal treatment outcomes of TB (60% of countries reported <85% success), of TB/HIV co-infection (79%) and of multidrug- or rifampicin-resistant TB (59%); (5) limited coverage of TB preventive treatment among people living with HIV (39%) and child contacts (12%); and (6) substantial proportions (35–70%) of TB-affected families facing catastrophic costs. For the Region to stay on track to achieve the End TB Strategy targets, an accelerated multisectoral response to TB is required in every country.

Tuberculosis (TB) continues to be a global public health problem, which disproportionately affects poor and marginalized populations who often have limited health care access. Despite the continued global effort to end TB, the disease continues to be the leading infectious killer on the planet. In 2018, an estimated 10 million people fell ill with TB and 1.5 million died from the disease.[1] Geographically, over 85% of TB cases in 2018 occurred in three WHO regions: 44% in South-East Asia, 24% in Africa and 18% in the Western Pacific.[1] In total, 30 countries with high burdens of TB accounted for 87% of the world's cases.[1]

In 2014, the Sixty-seventh World Health Assembly endorsed a global strategy, now commonly known as the End TB Strategy,[2] and targets for TB prevention, care and control after 2015. The Strategy set the ambitious target of ending TB by 2035, by reducing the incidence rate by 90% and the number of deaths by 95% from those in 2015. Interim 2020 milestones were defined as reductions of 20% of the incidence rate and 35% in the number of deaths, in addition to eliminating catastrophic costs incurred by TB.[2] Since 2014, two global high-level meetings (the WHO Global Ministerial Conference on "ending TB in the sustainable development era", held in Moscow, Russian Federation, in 2017, and the first high-level meeting on TB at the United Nations General Assembly, in New York in 2018) created unprecedented political momentum to accelerate the global TB response.[3] The world is, however, unlikely to achieve the 2020 milestones, with only a 6.3% reduction in TB incidence and a 5.2% reduction in TB deaths reported between 2015 and 2018.[4] In addition, there is grave concern that the COVID-19 pandemic will set back the modest gains made to date.[5]

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The WHO Western Pacific Region is home to 1.9 billion people in 37 countries and areas. The Region is diverse, comprising large countries with populations of more than 1 billion people and small Pacific island countries with a few thousand residents, as well as countries with high and intermediate TB burdens and others in the pre-elimination stage. The Regional Framework for Action on Implementation of the End TB Strategy in the Western Pacific 2016–2020 has guided national TB responses in countries and areas of the Region by proposing actions for national TB programmes.[6,7] This paper provides an overview of the epidemiology of TB in the Region and of progress towards the 2020 interim milestones of the End TB Strategy and the Regional Framework.

METHODS

We conducted a descriptive analysis of TB surveillance and programme data reported by countries and areas to WHO, and TB burden estimates generated by WHO for the Western Pacific Region, for the period 2000–2018. Countries and areas report data on TB to WHO annually via an electronic platform. The data are then verified and published in WHO's Global TB Reports, in which WHO-generated estimates are also published. A full description of WHO's data collection methods is available in the Global TB Report 2019;[1] the methods used to estimate TB incidence and mortality are provided in an online technical appendix.[8] We used the definitions of cases and treatment outcome given in the WHO reporting framework for TB.[8] All data sets are available from the WHO global TB database.[4] In 2019, data for 2018 were reported to WHO by 35 countries and areas in the Region, accounting for 99.9% of the regional population.

We reviewed trends in TB incidence and mortality, case notifications, indicators of collaborative TB/HIV activities and treatment outcomes. In addition to regional analyses, we also reviewed national data from the seven countries with high burdens of TB in the Region (Cambodia, China, the Lao People's Democratic Republic, Mongolia, Papua New Guinea, the Philippines and Viet Nam), which have more than 95% of the Region's cases.

The cascade of care for TB, drug-resistant TB (DR-TB) and TB/HIV co-infection was assessed to identify and quantify gaps in care delivery. For DR-TB, the estimated number of incident multidrug- or rifampicin-resistant TB (MDR/RR-TB) cases, the case detection rate (the number of laboratory-confirmed MDR/RR-TB cases divided by the estimated number of incident cases) and the treatment enrolment rate (the number of cases enrolled in second-line treatment divided by the number of laboratory-confirmed cases) were provided for countries with the highest estimated numbers of MDR/RR-TB incidence. Indicators of TB prevention and catastrophic costs due to TB were assessed where data were available. Catastrophic costs for TB-affected families are defined as total costs (comprising direct medical and non-medical costs plus income losses) that represent 20% or more of annual household income. We also developed a colour-coded scorecard to summarize indicators of implementation of the End TB Strategy for each country in the Region. In this paper, "range" refers to the 95% uncertainty interval. All analyses were conducted with the statistical software package R 3.6.1 (Comprehensive R Archive Network at https://cran.r-project.org/).

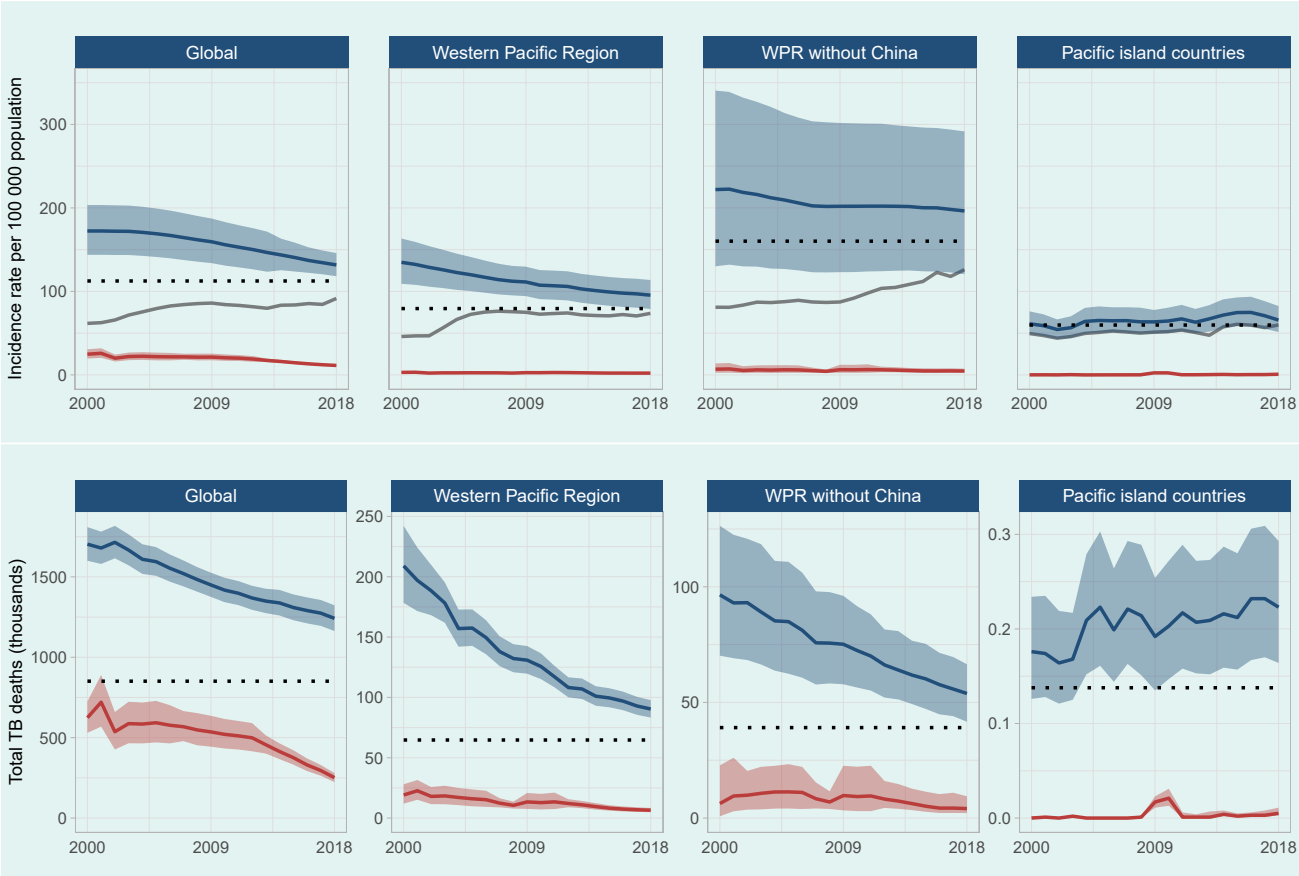
Ethical clearance was not required, as this report was part of a regular evaluation of programme performance.

RESULTS

Estimates of TB burden

Since 2000, the estimated incidence of TB in the Region has decreased steadily, from 135 (range, 109–163) per 100 000 population (2.3 [range, 1.7–2.8] million cases) to 96 (range, 79–114) per 100 000 population (1.8 [range, 1.5–2.2] million cases) in 2018. The estimated number of TB deaths more than halved in the same period, from 209 000 (range, 178 000–242 000) (12 [range, 10–14] deaths per 100 000 population) in 2000 to 90 000 (4.7 [4.3–5.1] deaths per 100 000 population) in 2018 (**Fig. 1**). Since 2015, when the End TB Strategy and the Regional Framework: 2016–2020 were endorsed, the estimated incidence rate and number of TB deaths have decreased by 3% and 10%, with annual reductions of 1.0% and 3.4%, respectively. The estimated TB incidence and mortality rates among people living with HIV (PLHIV) have both remained low in the Region (2.1 [range, 1.5–2.8] and 0.34 [range, 0.25–0.43] per 100 000 population in 2018, respectively).

Fig. 1. **Trends in estimated TB incidence and total TB deaths at global and regional levels, 2000–2018**



Estimated incidence and numbers of deaths are shown in blue and those among HIV-positive people in red. The horizontal dashed lines show the 2020 milestones of the End TB Strategy. Shaded areas represent uncertainty intervals. The grey solid lines show notifications of new and release TB cases for comparison with estimates of the totl incidence rate.

WPR: Western Pacific Region.

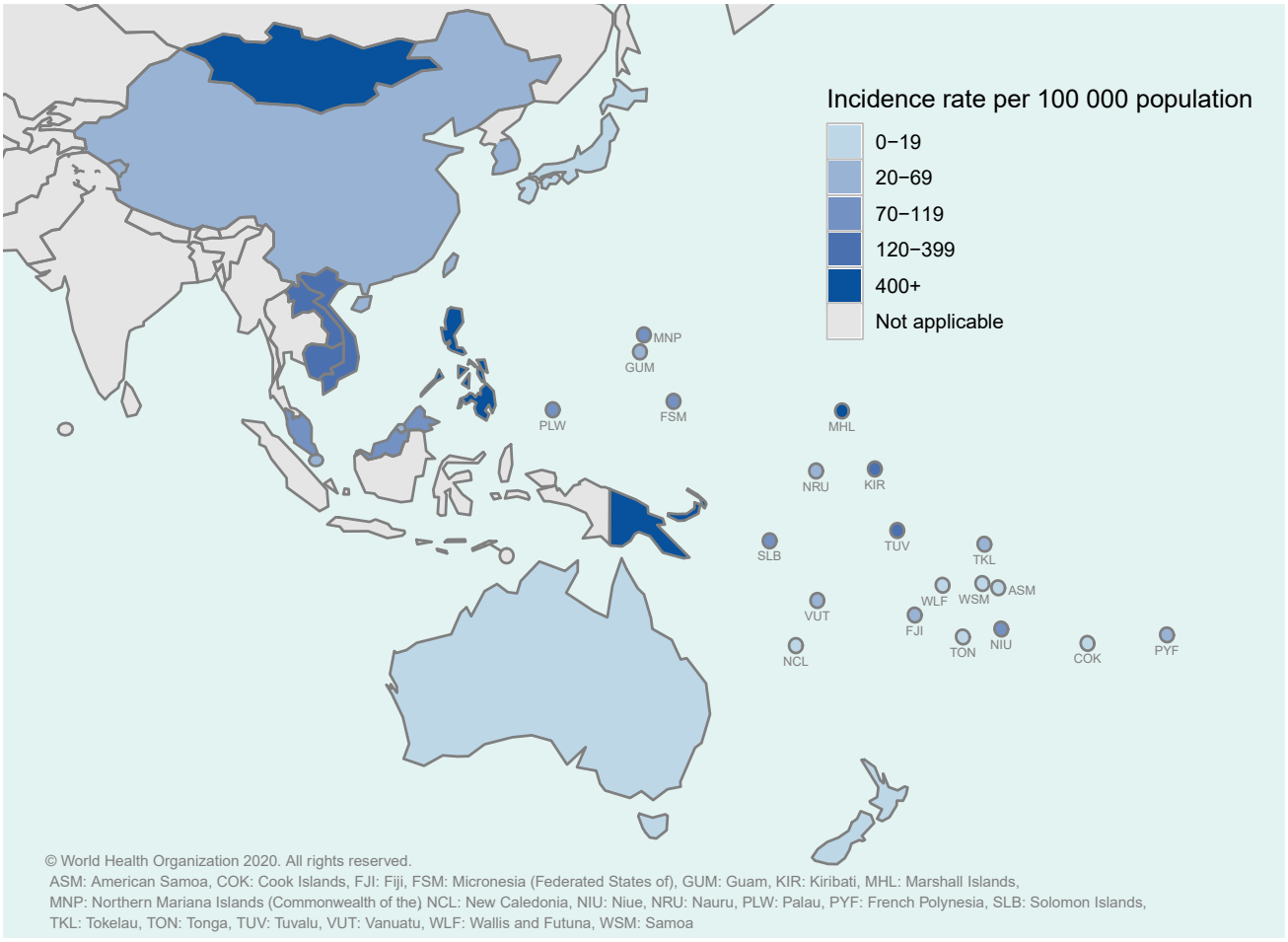
The decreasing trends in TB incidence and mortality observed in the Region are broadly in line with global trends and are driven mainly by improvements in TB control in China. When data from China are excluded, the estimated TB incidence rate in 2018 doubles to 196 (range, 121–292) cases per 100 000 population. The estimated TB incidence rate was lower in the subregion of the Pacific island countries than in other parts of the Region, but there has been no decrease in incidence since 2000, the rate ranging from 54 (range, 43–66) per 100 000 population in 2002 to 75 (range, 58–94) per 100 000 population in 2016.

The estimated incidence of TB varies widely among countries in the Region (**Fig. 2**). In 2018, nearly 80% of all estimated TB cases occurred in just two countries, China (47% or 866 000 [range, 740 000–1 000 000] cases) and the Philippines (32% or 591 000 [range, 332 000–924 000] cases). A further 9% (174 000 [range, 111 000–251 000] cases) occurred in Viet Nam. In 2018, six countries had an estimated TB incidence rate of more than 300 cases per 100 000 population. The highest incidence rate was recorded in the Philippines (554 [range, 311–866] cases per 100 000), followed by the Marshall Islands (434 [range, 332–549] cases per 100 000), Papua New Guinea (432 [range, 352–521] cases per 100 000), Mongolia (428 [range, 220–703] cases per 100 000), Kiribati (349 [267–441] cases per 100 000) and Cambodia (302 [range, 169–473] cases per 100 000) (**Fig. 3**). Six countries and areas, American Samoa, Australia, Cook Islands, New Zealand, Samoa and Wallis and Futuna, had an estimated TB incidence rate of <10 cases per 100 000 population in 2018.

TB case notifications

The number of case notifications in the Region rose sharply between 2000 and 2007, mainly reflecting increased reporting from China, but has since remained stable, with 1 416 729 new and relapse cases noti-

Fig. 2. **Estimated TB incidence rates per 100 000 population in countries and areas in the Western Pacific Region, 2018**



ASM: American Samoa, COK: Cook Islands, FJI: Fiji, FSM: Micronesia (Federated States of), GUM: Guam, KIR: Kiribati, MHL: Marshall Islands, MNP: Northern Mariana Islands (Commonwealth of the) NCL: New Caledonia, NIU: Niue, NRU: Nauru, PLW: Palau, PYF: French Polynesia, SLB: Solomon Islands, TKL: Tokelau, TON: Tonga, TUV: Tuvalu, VUT: Vanuatu, WLF: Wallis and Futuna, WSM: Samoa

Fig. 3. **Estimated numbers of incident TB cases and TB incidence rates per 100 000 population in countries and areas in the Western Pacific Region, 2018**

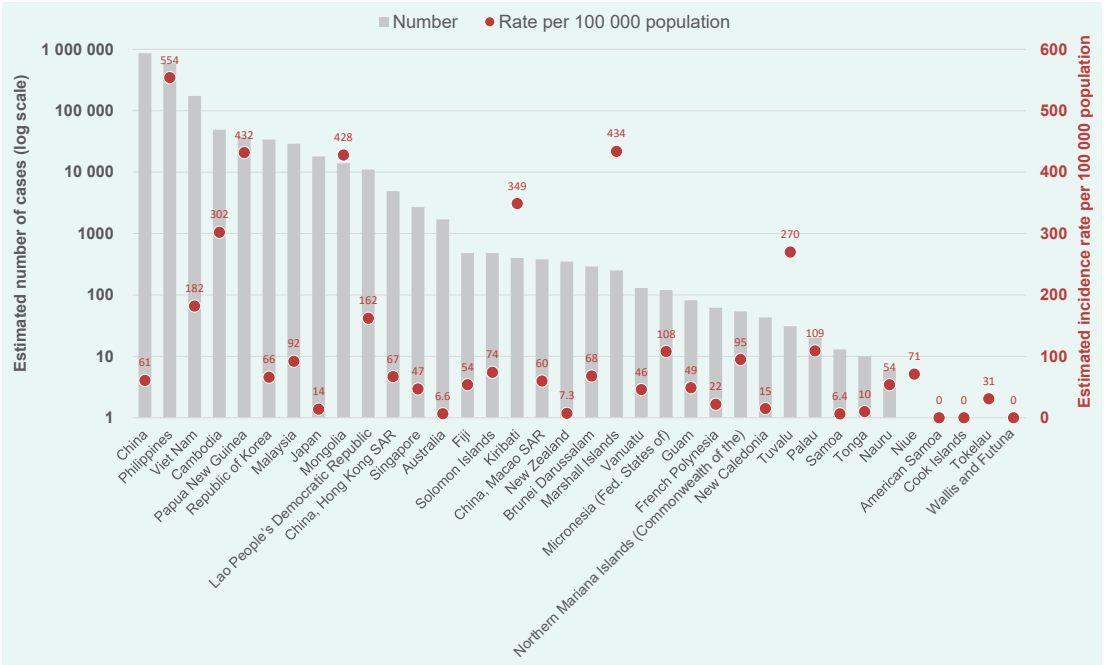


Fig. 4. **Case notifications of all forms of TB in the Western Pacific Region and in the seven focus countries, 2000–2018**

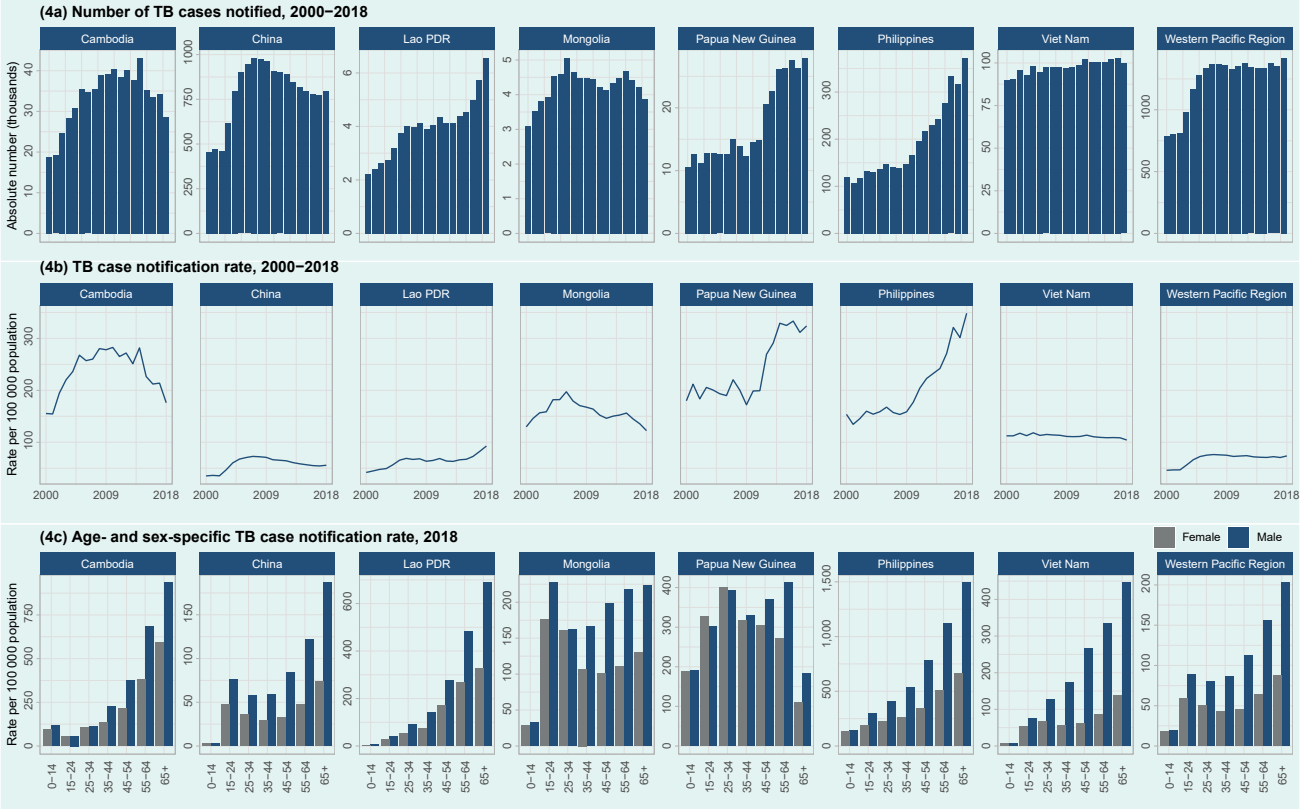


Fig. 4a and 4b show both total numbers of new and relapse cases and cases with an unknown TB treatment history. Fig. 4c presents total numbers of new and relapse cases.

PDR, People's Democratic Republic.

fied in 2018 (a case notification rate of 74 per 100 000 population) (**Fig. 4a**). Trends in case notification from countries vary widely. During the past decade in the seven focus countries, decreasing case notification rates were observed in Cambodia, China and Mongolia, and increasing rates were reported in the Lao People's Democratic Republic, Papua New Guinea and the Philippines (**Fig. 4b**).

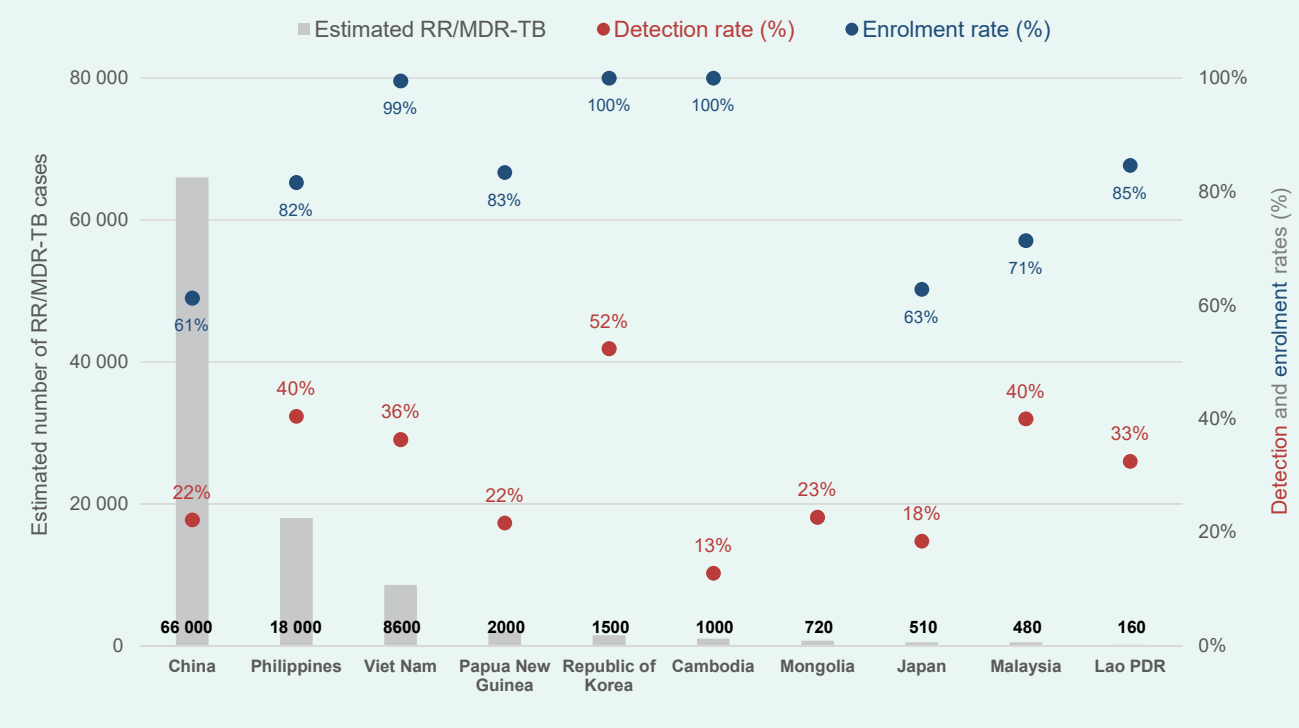
In the Region, the highest TB notification rate was for males aged ≥65 years (202 cases per 100 000 population), with a general tendency to higher case notification rates for older age groups (**Fig. 4c**). The exceptions were Mongolia and Papua New Guinea, where the proportions of younger people (0–24 years) among total cases were still high (32% and 46%, respectively), suggesting high rates of transmission in the general community. The male-to-female ratio of TB cases was high in adults (from 1.5 in those aged 15–24 years to 2.5 in those aged 45–54 years), with the largest differences being observed in older groups.

Drug-resistant TB

Between 2015 and 2018, the numbers of laboratory-confirmed MDR/RR-TB cases and of patients enrolled in second-line treatment increased by 50% and 47%, respectively. During the same period, drug susceptibility testing (DST) coverage of bacteriologically confirmed cases rose from 28% in 2015 to 51% in 2018 but still remains far below the 100% target.

China had the highest estimated number of MDR/RR-TB cases (66 000 [range, 50 000–85 000]) in 2018, followed by the Philippines (n = 18 000 [range, 7700–32 000]), Viet Nam (n = 8600 [range, 5400–13 000]), Papua New Guinea (n = 2000 [range, 1200–2900]), the Republic of Korea (n = 1500 [range, 1300–1700]), Cambodia (n = 1000 [range, 460–1900]), Mongolia (n = 720 [range, 340–1200]), Japan (n = 510 [range, 220–930]), Malaysia (n = 480 [range, 360–620]) and the Lao People's Democratic Republic (n = 160 [range, 65–280]) (**Fig. 5**). These 10 countries accounted for

Fig. 5. **Estimated numbers of MDR/RR-TB incidence and detection and treatment enrolment rates for MDR/RR-TB in the 10 most-affected countries in the Western Pacific Region, 2018**



"Case detection rate" is defined as the number of laboratory-confirmed MDR/RR-TB cases divided by the estimated number of incident MDR/RR-TB cases. "Treatment enrolment rate" is defined as the number of cases enrolled in second-line treatment divided by the number of laboratory-confirmed cases.

PDR, People's Democratic Republic.

more than 99% of the total estimated MDR/RR-TB case load in 2018 (n = 99 000). Importantly, case detection rates remained low in all these countries, ranging from 13% in Cambodia to 52% in the Republic of Korea. The rates of enrolment in treatment after diagnosis were excellent in Cambodia (100%), the Republic of Korea (100%) and Viet Nam (99%) but suboptimal in China (61%), Japan (63%) and Malaysia (71%).

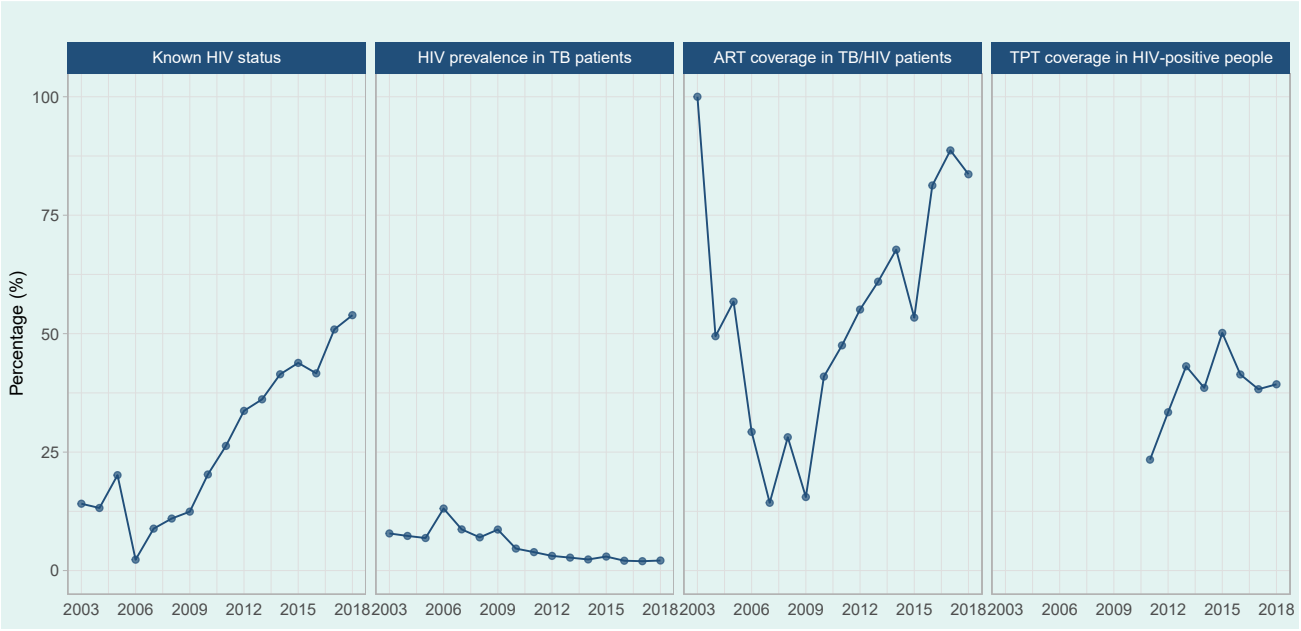
Indicators of collaborative TB/HIV activities

Key indicators for TB-HIV care and collaborative activities have improved over time (**Fig. 6**). The proportion of TB cases with known HIV status increased substantially, from 12% in 2009 to 54% in 2018, although the proportion remains well below the target of 100% and the global average of 64%. The HIV prevalence among tested TB cases fell from a high of 13% in 2006 to <3% in 2016, which has been maintained, reflecting more comprehensive screening. The proportion of TB/HIV co-infected patients receiving antiretroviral therapy (ART) has increased over time, reaching 84% in 2018 (based on reporting from 13 countries); however, this is also below the 100% target and does not include delays in initiation, as many countries still do not meet this reporting requirement. Coverage of TB preventive treatment (TPT) in PLHIV remains at <50% (based on reports from only eight countries).

Treatment outcomes

A TB treatment success rate (new and relapse cases) of >90% has been maintained at regional level for over a decade (**Fig. 7**). The rate is due mainly to high treatment success rates in a few countries with large TB caseloads, including China (93%) and Viet Nam (92%), which tends to hide poor rates in many smaller countries. Overall, 20 of 32 reporting countries and areas (>60%) had treatment success rates of <85%, and success rates of <70% were reported by countries and areas such as Hong Kong SAR (China) and Japan, where TB predominantly affects the elderly, but also in some Pacific island countries such as Papua New Guinea and Tuvalu, which have younger populations. The treatment outcomes of patients with TB/HIV co-infection and MDR/RR-TB remain suboptimal in most countries and

Fig. 6. **Trends in key indicators of collaborative TB/HIV activities in the Western Pacific Region, 2003–2018**

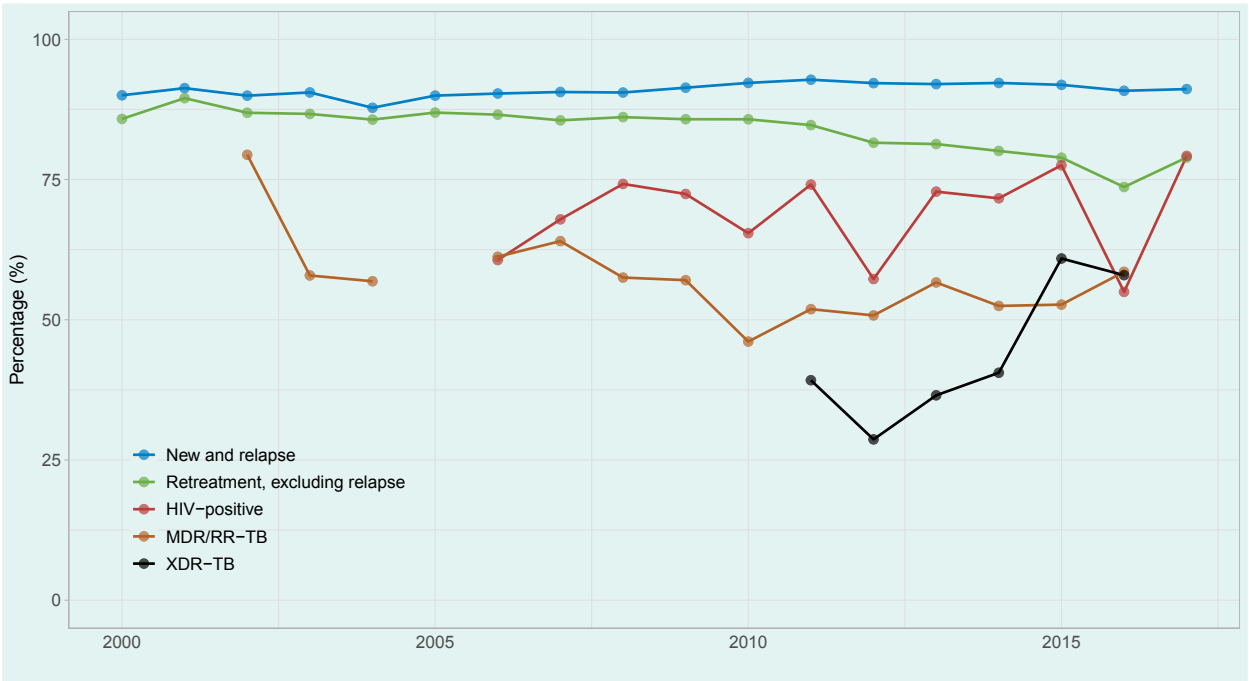


ART: antiretroviral therapy; TB: tuberculosis; TPT: TB preventive treatment.

TPT: TB preventive treatment

"Known HIV status" is calculated as the number of patients with new and relapse TB patients and documented HIV status divided by the number of patients with new and relapse TB notified in the same year, expressed as a percentage. "HIV prevalence in TB patients" is the proportion of TB patients tested for HIV whose results were positive.

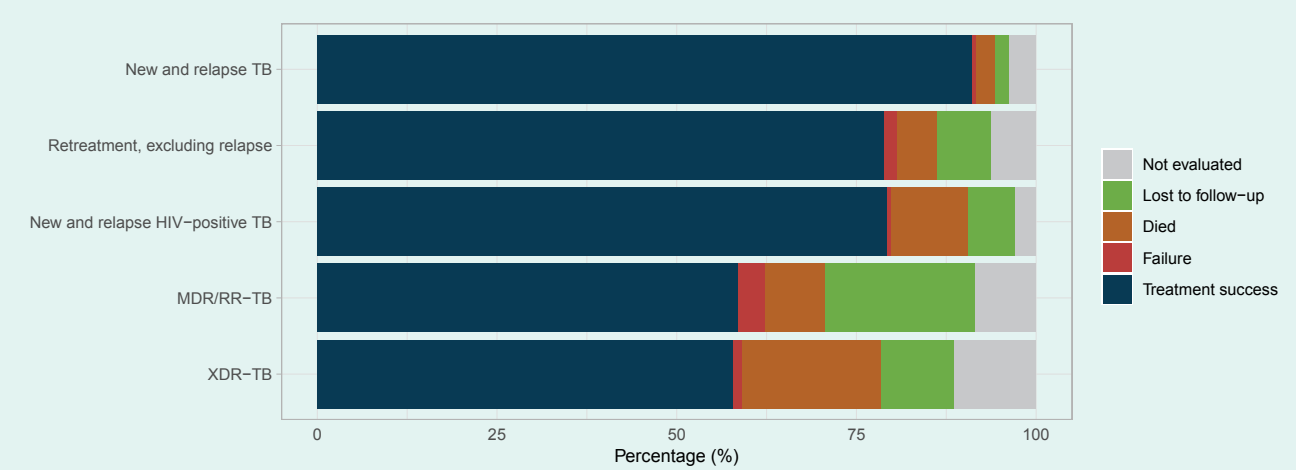
Fig. 7. **Trends in TB treatment success rates for different patient categories in the Western Pacific Region, 2000–2017**



As treatment outcomes for cases of drug-susceptible TB are reported to WHO 1 year after notification, data for 2017 were the latest available at the time this report was written.

As treatment outcomes for cases of MDR/RR-TB and extensively drug-resistant (XDR) TB are reported to WHO 2 years after notification, data for 2017 were not available at the time this report was written.

Fig. 8. **TB treatment outcomes by patient category in the Western Pacific Region, 2018**



Data from 2016 were used for MDR/RR-TB and XDR-TB and from 2017 for the other types of TB.

at regional level (**Fig. 8**), the proportions being 79% and 59%, respectively, in 2018 (reflecting the 2017 and the 2016 patient cohorts, respectively).

TB care cascade

Fig. 9 shows gaps in the cascade of care for TB, DR-TB and TB/HIV co-infection in the Western Pacific Region. Of an estimated 1.8 million (range, 1.5–2.2 million) incident cases of TB in 2018, 5.4% (n = 99 228) were estimated to be MDR/RR-TB and 2.2% (n = 40 638) to be co-infected with HIV. Gaps in the TB care cascade in the Region remain substantial, especially for DR-TB and TB/HIV. Treatment coverage was relatively high for TB, at 77.2% (range, 64.9–93.4%), but low for TB/HIV co-infection (38.9%, range [29.6–53.6%]) and MDR/RR-TB (27.2%, range [19.3–40.2%]). Major gaps between the numbers of notified and confirmed MDR/RR-TB cases and patients enrolled in second-line TB treatment and in initiation of ART among HIV-positive TB patients are of particular concern. The proportions of estimated incident TB cases successfully treated for TB, MDR/RR-TB and TB/HIV co-infection were 66.4%, 8.6% and 23.7%, respectively.

TB prevention

TPT coverage among PLHIV remained low, at 39%, in 2018. This figure is based on reports from eight countries, and coverage in non-reporting countries may be even lower. TPT coverage of children under 5 years who were household contacts of a bacteriologically confirmed case of pulmonary TB was estimated to be very low (12%) from data for 14 countries.

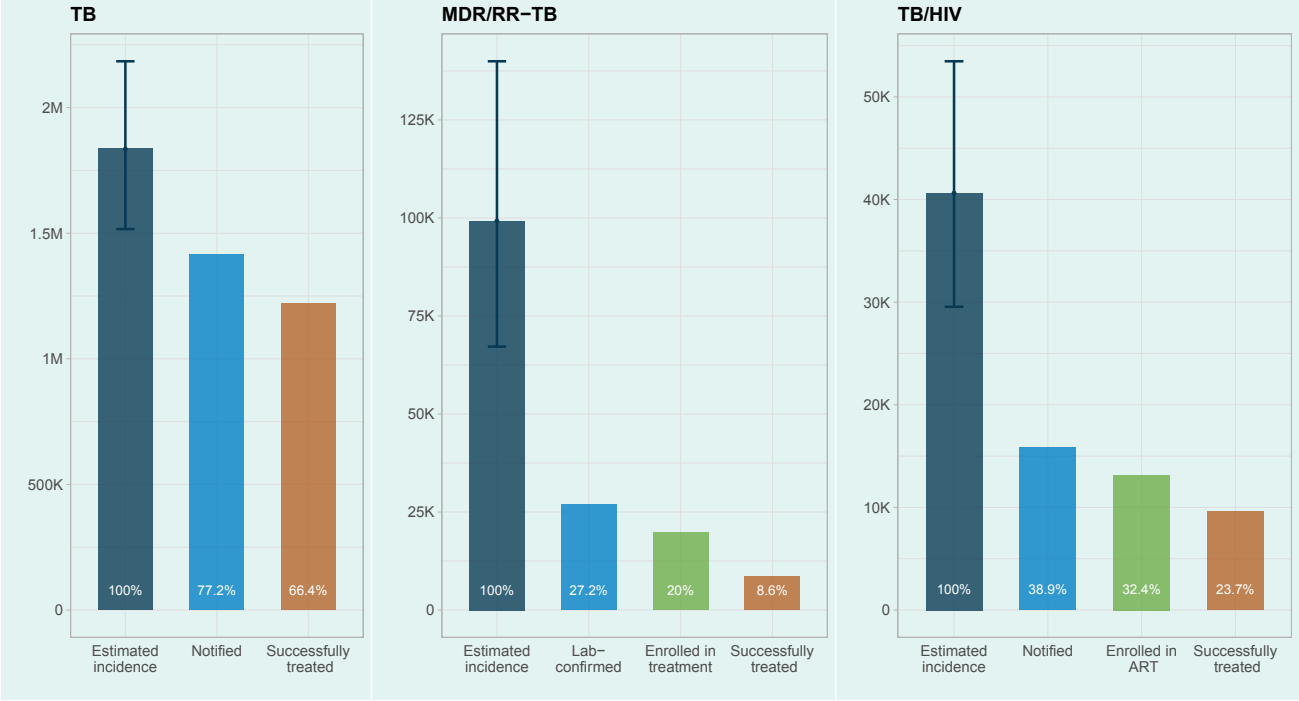
Patient costs due to TB

Eight countries in the Region have conducted national TB patient cost surveys and have established a baseline from which to monitor progress towards elimination of catastrophic costs due to TB. In the surveys, 35–70% of TB-affected families reported facing catastrophic costs.

Proposed "top-10" indicator scorecard

Table 1 represents a proposed colour-coded scorecard of the "top-10" TB indicators of programme performance towards the End TB Strategy targets. In 2018, treatment coverage remained low (<60%) in some countries with a high TB burden (Cambodia, Lao People's Democratic Republic, Mongolia and Viet Nam), and low treatment success rates were reported in Japan (68%), Hong Kong SAR (China) (65%) and some Pacific island countries, including Papua New Guinea (68%) and Tuvalu (68%). The proportion of TB patients tested with a WHO-recommended rapid diagnostic test (molecular techniques to detect TB among people with signs or symptoms of TB, such as Xpert MTB/RIF®) at the time of diagnosis remained low in many countries (11 countries reported <60%). DST coverage was extremely low (<5% of bacteriologically confirmed TB cases) in Cambodia, the Philippines, Papua New Guinea and Solomon Islands, while many with successful Xpert MTB/RIF® roll-out programmes reported high coverage.

Fig. 9. **Key gaps in the cascade of care for TB, MDR/RR-TB and TB/HIV co-infection in the Western Pacific Region, 2018**



Data for 2017 were used for successfully treated cases of TB and TB/HIV co-infection and data for 2016 for successfully treated cases of MDR/RR-TB.

Despite a long-standing policy to test all TB patients for HIV infection, the proportion of TB patients of known HIV status remained low in many countries. The case fatality ratios were high in Japan (16%), Lao People's Democratic Republic (22%), Papua New Guinea (13%) and Vanuatu (17%). Contact investigation coverage and treatment coverage for new drugs were among the "top-10" TB indicators; however, data are not available. The 2020 End TB Strategy milestones of reduced TB incidence rate and deaths were achieved by 2018 by only 19% (7/36) and 11% (4/36) of the countries in the Region, respectively.

DISCUSSION

This epidemiological analysis shows regional progress over time in certain programmatic areas, including sustained, good treatment outcomes, improvements in TB/HIV indicators and improved case detection and enrolment of MDR/RR-TB cases. Programmes should continue to extend diagnosis and case finding, enhance service quality and increase resources for TB programmes.

The number of sites in the Region that provide TB diagnoses with Xpert MTB/RIF® increased by 48%, from 1351 in 2015 to 1998 sites in 2018, based on reports from 15 countries and areas.[4] Increased case notification rates were reported in several high-burden countries (Lao People's Democratic Republic, Papua New Guinea and Philippines), which may reflect intensified case detection in these countries. Careful monitoring will be necessary to ensure that the numbers do not decrease over time. The same observation applies to Pacific island nations, such as the Marshall Islands, where active case finding projects may transiently increase the case numbers; if the projects are successful, they should be followed by drastic reductions in case numbers.

Between 2015 and 2019, total funding, both domestic and international, for TB in countries and areas of the Region increased by 67%, from US$ 504 million to US$ 843 million, although the funding gap remains large at US$ 249 million (23%).[3,4] Indications of increased resource allocation and service provision are encouraging, as they may reflect increased political commitment from governments in the Region.

Overall progress in reducing the TB burden in the Western Pacific Region is slow, as little progress has

Table 1. **Proposed scorecard for assessing the "top-10" indicators for monitoring implementation of the End TB Strategy in the Western Pacific Region**

	Top Indicators (%)									% Change from 2015	
	Treatment coverage	Treatment success rate	TB-affected households with catastrophic costs due to TB	TB patients tested using WRD at diagnosis	LTBI treatment coverage (PLHIV)	LTBI treatment coverage (Child contact)	DST coverage for TB patients	Documentation of HIV status	Case fatality ratio	Estimated incidence rate	Estimated deaths
Recommendeed Target†	≥90%	≥90%	0%	≥90%	≥90%	≥90%	100%	100%	≤5%	-20%	-35%
American Samoa*		80					100				
Australia	87	82					93	88	3	10	-3
Brunei Darussalam*	87	75			0	0	100	100	6	15	-4
China	92	93		15			63	60	5	-6	-5
Cook Islands*											
Fiji*	80	81	40	95		100	109	89	9	4	11
Micronesia (Federated States of)*	80	88					86	0	11	-10	-7
Guam*	87	89		69			100	96	8	-9	-7
China, Hong Kong SAR	87	65		32		11	91	78	3	-7	-13
Japan	87	68				62	74	8.3	16	-14	-8
Cambodia	58	94					0	94	7	-18	-9
Kiribati*	80	89		50			100	51	11	-38	1
Republic of Korea	94	83		26		60	84		7	-17	-9
Lao People's Democratic Republic	57	89	63	63		18	52	81	22	-11	-33
China, Macao SAR*	87	82		68		20	99	92	8	-16	-12
Marshall Islands*	170	83		77			100	22	11	45	47
Mongolia	29	91	70	39	0	7.4	79	70	3	0	-1
Northern Mariana Islands (Commonwealth of the)*	87	98		32			100	100	8	65	64
Malaysia	87	81			38	88	78	82	5	3	1
New Caledonia*	87	35		5.4			100	30	8	-36	-34
Niue*	87							0	8		
Nauru*	87	78					0	0	8	-51	-50
New Zealand*	87	82				100	0	0.3	4	1	3
Philippines	63	91	35	36	52	9.4	4	27	5	1	-8
Palau*	87	80		88			100	94	8	20	21
Papua New Guinea	75	68	54		21	27	0	55	13	0	12
French Polynesia*	87	81		63			100	85	8	15	17
Singapore	87	79		60	0	100	98	89	2	5	-11
Solomon Islands*	80	92		27			0	28	11	-14	-7
Tokelau*									11	-85	-84
Tonga*	87	82		89			100	100	8	-37	-36
Tuvalu*	87	68		74			89	100	8	30	35
Viet Nam	57	92	63	20	39	22	84	85	8	-9	-24
Vanuatu*	67	96		46			100	69	17	-27	17
Wallis and Futuna*											
Samoa*	87	57			0		0	100	8	-43	-42
Cutoff values for colour code											
Green	≥85	≥85	≤29	≥80	≥70	≥70	≥80	≥85	≤5	< 0	< 0
Yellow	60-84	75-84	30-59	60-79	50-69	50-69	60-79	75-84	6-9	0-5	0-5
Red	≤59	≤74	≥60	≤59	≤49	≤49	≤59	≤74	≥10	≥6	≥6

† The target levels are for 2025 for the "Top indicators" and for 2020 for "% change from 2015" of estimated incidence and deaths. Targets for contact investigation coverage and treatment coverage for new TB drugs, which are included in the top 10 indicators, are not available in the WHO Global TB database. Detailed definitions of each indicator are provided in the Global TB Report 2019, p. 15.[1]

* Countries estimated to have fewer than 1000 cases, where the percentage change in estimated incidence and deaths may not reflect true trends because of possible large fluctuations.

Pitcairn Islands is excluded from annual collection of data on TB.

DST: drug susceptibility testing; LTBI: latent tuberculosis infection; PLHIV: people living with HIV;

TB: tuberculosis; WRD: WHO-recommended rapid diagnostic test.

been made in some countries. In 2018, the TB incidence rate was 96 per 100 000 population, whereas the 2020 milestone is 79 per 100 000 population, and an estimated 97 000 deaths from TB occurred, whereas the 2020 milestone is 70 200. In view of the current annual reductions in the TB incidence rate (1.0%) and the number of deaths (3.4%), the Region is unlikely to achieve the 2020 milestones and other targets of the End TB Strategy.

Our analyses signal several challenges for the Region: (1) wide variation among countries in the geographical distribution and incidence of TB, including the fact that TB continues to largely affect younger age groups in several countries; (2) a sizeable proportion of TB cases remain unreached, undiagnosed or unreported; (3) insufficient coverage of DST and use of WHO-recommended rapid diagnostic tests; (4) suboptimal TB treatment success rates in some countries and poor

treatment outcomes for PLHIV and patients with DR-TB; (5) limited TPT coverage of PLHIV and child contacts; and (6) a substantial proportion of TB-affected families facing catastrophic costs.

The wide variation in TB epidemiology and contextual factors among countries poses a challenge for mounting a coordinated regional TB response. In countries with a low TB burden, such as Australia and New Zealand, >80% of the cases notified are in foreign-born individuals, and TB is essentially an imported disease.[4] In countries and areas with ageing populations, such as Japan and the Republic of Korea, TB occurs mainly in the elderly, people aged ≥65 years accounting for 66.7% of total case notifications in Japan, 45.4% in the Republic of Korea and 43.7% in Hong Kong SAR (China) in 2018.[4] In lower-income high-burden countries, undernutrition is considered a major risk factor for TB,[1] and high rates of cigarette smoking may contribute to over-representation of TB in men.[9] In Pacific island countries, diabetes is highly prevalent and considered a major driver of the TB epidemic.[10,11] Understanding of population-level risk factors for TB by analysis of routine surveillance data, survey results and facility records is important in order to design targeted interventions. The Western Pacific Region therefore requires a tailored regional strategy to guide the response in various epidemiological and contextual settings, including for small Pacific island countries with unique geographical challenges and high TB incidence rates per capita, such as Kiribati, Marshall Islands and Tuvalu.

TB case notifications are affected by many factors, and careful analysis and interpretation are required to understand the strengths and weaknesses of national TB programmes. Interventions such as community-based active case finding, facility-based systematic screening, increased use of sensitive screening and diagnostic tools and algorithms, improved referral mechanisms and specimen transport, engagement of private and other health sectors and mandatory notification policies can increase case notifications.[12,13] Although decreasing numbers of case notifications may represent a true decrease in TB incidence, they may be due to decreased case finding or reduced TB programme funding and functioning.[12] In the Region, significant funding for TB is provided by the Global Fund to Fight AIDS, Tuberculosis and Malaria. Over time, such funding has supported expansion of TB services and improved TB surveillance in many high-burden countries, including Cambodia, China, the Lao People's Democratic Republic, Mongolia and Papua New Guinea.[14] In the Philippines, over-reliance on chest X-ray for diagnosis resulted in increased case notifications of clinically diagnosed TB in the 2010s. Subsequently, the introduction of a mandatory TB notification policy increased reporting from the private sector, resulting in a sharp rise in case notifications in 2018, although a national survey demonstrated many unidentified cases. (Epidemiological review for tuberculosis in the Philippines. 2019, unpublished). The recent increase in TB case notifications in the Lao People's Democratic Republic can be attributed to intensified case-finding among high-risk populations (Epidemiological review for tuberculosis in Lao People's Democratic Republic. 2019, unpublished), and a decrease in case notifications in Cambodia is probably attributable to reduced community-based case-finding activities because of reduced external funding (Epidemiological review for tuberculosis in Cambodia. 2019, unpublished). Trends in case notification should therefore be considered carefully in relation to any major programmatic changes. In most instances, an emphasis on "finding missing cases" is appropriate. Furthermore, given the geographical variation in TB epidemiology within a country, monitoring and evaluation should be strengthened at subnational level to ensure better-targeted interventions guided by data.[15]

Accurate diagnosis is a fundamental component of TB care. Rapid molecular diagnostics ensure early detection and prompt treatment, while testing for drug resistance is essential to ensure appropriate treatment.[1] As part of TB laboratory-strengthening in the End TB Strategy, countries are encouraged to adopt a policy to use a WHO-recommended rapid diagnostic test as the initial test for all people with presumptive TB and to provide universal access to DST for patients with bacteriologically confirmed TB.[1] In the Region in 2018, only 25% of countries and areas (n = 9/36) had a policy to use a WHO-recommended rapid test at diagnosis, and only 39% (n = 14/36) had a policy of universal access to DST.[4] This explains the insufficient DST coverage and use of WHO-recommended rapid diagnostic tests that we observed. Adoption and implementation of such policies requires substantial investment, with sustainable financing for TB laboratory services. This remains a major challenge, but successful examples exist in other parts of the world[16] to guide implementation. In-depth analysis of national networks for TB diagnosis and specimen transport to understand the levels of underutilization or

access to existing diagnostic tools and investigation of opportunities for collaboration with other public health programmes and the private sector could pave the way for a massive roll-out of WHO-recommended rapid diagnostic tests and expanded DST. This will be essential to close the gap in case detection and improve treatment outcomes for patients with MDR/RR-TB. It could also reduce MDR/RR-TB transmission by prompt initiation of effective treatment. Estimating longer-term population-level benefits of such policies could convince policy-makers to take action.

Treatment outcomes remain a challenge in many countries in the Region, particularly for patients with DR-TB and TB/HIV co-infection. WHO recommends a wide range of interventions to facilitate early diagnosis and optimal treatment, including screening of PLHIV for TB, early initiation of ART, better infection control, provision of TPT, wider use of more effective MDR-TB treatment regimens, active TB drug-safety monitoring and management and more patient-centred models of care.[1] Digital technologies to support adherence to TB medication are becoming increasingly available.[17] Assessing and addressing gaps in such interventions and promoting the uptake of new tools and innovations should help to improve treatment outcomes. Furthermore, risk groups and geographical areas in which poor treatment outcomes are reported should be identified to guide the most appropriate targeted responses. Generally, treatment outcomes vary by geographical areas according to the local TB epidemiology and response.[18] (Epidemiological review for tuberculosis in the Philippines. 2019, unpublished; Epidemiological review for tuberculosis in Lao People's Democratic Republic. 2019, unpublished). In Japan, the overall treatment success rate is low mainly because of a high mortality rate among the elderly, the population most affected by TB.[19] Other countries in which the population is ageing rapidly and the proportion of TB cases among the elderly is increasing may face a similar challenge in the future.[20] Global and regional TB programmes should be ready to address the issue of TB among the elderly on the basis of evidence-based guidance and effective interventions.[21]

TPT is an essential intervention for achieving the goals of the End TB Strategy. The first United Nations high-level meeting on TB, held in 2018, set a new global target, to provide TPT to at least 30 million people in the period 2018–2022, comprising 6 million PLHIV, 4 million children under 5 years who are household contacts of people affected by TB and 20 million other household contacts of TB cases.[1] At the current rate of treatment enrolment, the world will not reach the target for household contacts, and, in May 2020, global TB partners released a joint call to action to scale up access to TPT.[22] In view of the low coverage of TPT in the Region, rapid adoption and implementation of the recently published TPT guidelines[23] is critical. In particular, a systems approach is necessary to make contact investigation and TPT integral parts of primary health care services as an essential public health function.[24]

TB patients continue to bear a heavy financial burden, despite the provision of free TB services in most countries in the Region. National surveys of the cost of TB patients have provided solid evidence that TB-affected families face severe financial hardship, non-medical costs and income loss due to TB are major components, poor households get poorer due to TB and loss of jobs, and households of patients with DR-TB and TB/HIV co-infection face significantly higher costs.[1,25] These results are powerful arguments for initiating policy dialogue with other programmes and sectors and as a basis for policies and strategies to optimize health care delivery and financing and increase social protection for TB patients.[1]

This analysis has several limitations. First, data for several indicators, such as TPT and DST coverage, were not complete, and therefore the regional averages are not always from all countries. Second, regional averages of the indicators and estimated burden are driven largely by the numbers recorded in China and the Philippines, where the numbers of cases are relatively large; therefore, the findings must be interpreted carefully. Third, the number and proportion of successfully treated patients used in the analysis of the care cascade were for patient cohorts in previous years (2017 for TB and TB/HIV, 2016 for DR-TB); therefore, the gaps calculated for 2018 may not be accurate, although we believe them to be very close approximations of the complete data set. Finally, in countries and areas with few cases, the percentage changes in estimated incidence and mortality shown on the scorecard may not reflect true trends because of possible large fluctuations. Despite these limitations, our analysis provides comprehensive, useful insights into the regional TB situation based on

several years of data reported according to adopted, well-established case definitions from nearly all the countries in the Region.

If the Region is to achieve the End TB Strategy targets beyond the interim 2020 milestones, it must overcome several challenges. Some of these challenges lie outside national TB programmes and even the health sector, requiring a multisectoral response.[3] In addition, the COVID-19 pandemic has disrupted health services worldwide and poses a considerable challenge for TB programmes and for TB patients; however, it also provides an opportunity to increase investment in health and to promote multisectoral responses to health system transformation, from which the TB programme can benefit and to which it can contribute. The WHO Regional Office for the Western Pacific will continue to provide data-driven, evidence-based regional guidance and will support Member States on their journey towards ending TB.

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Conflicts of interests

The authors have no conflict of interests.

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Intensified research on tuberculosis in the Western Pacific Region: a bibliometric analysis, 2000–2019

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"Intensified TB research and innovation" is one of the three pillars of the End TB Strategy. To assess achievements and gaps in tuberculosis (TB) research productivity in countries and areas of the Western Pacific Region quantitatively, a bibliometric analysis was carried out by examining trends in the numbers of publications on TB indexed in PubMed between 2000 and 2019 and by comparing them with trends in publications on other selected major infectious diseases for the same period. The number of publications on TB in the Region increased by 3.2 times during the period, from 534 in 2000–2004 to 1714 in 2015–2019, as compared with 2.9 times each for HIV, hepatitis and malaria. The number increased by 46% in 2005–2009, 79% in 2010–2014 and 23% in 2015–2019, as compared with each previous 5-year period. The average annual growth rate between 2000 and 2018 was 8.8%. China accounted for 34.8% of the total number of publications on TB in the Region. Increases in TB research were observed in most countries and areas in the Region, particularly in those with a high TB burden. The number of publications on TB remained low, however, in the Lao People's Democratic Republic, Mongolia and Pacific island countries. Countries are encouraged to implement the set of actions proposed in the Global Strategy for TB Research and Innovation to accelerate progress towards ending TB.

Tuberculosis (TB) remains a major public health issue globally. In 2018, worldwide, an estimated 10 million people contracted TB and 1.5 million died from the disease.[1] Since 2015, the WHO End TB Strategy has guided national TB responses by providing principles and essential programme components in three fundamental pillars.[2] The Strategy set ambitious targets for ending TB: reducing the incidence by 90% and deaths by 95% in 2035, as compared with 2015, and eliminating catastrophic costs for TB-affected households.[2] To reach these targets, new tools and strategies must be developed and introduced, with universal access to and better use of existing technologies.[3] The third pillar of the Strategy, "intensified research and innovation", thus promotes intensification of research on TB at all levels and empowerment of a strong, self-sustained TB research community in low- and middle-income countries with high TB burdens.[4] The Moscow declaration to end TB (2017) and the political declaration of the United Nations high-level meeting on TB (2018) also made bold commitments for action on TB research and innovation.[3] In 2020, WHO Member States adopted the Global Strategy for TB Research and Innovation for action to meet these commitments.[3]

Intensified TB research, unlike routine TB surveillance and programme activities, is difficult to monitor and evaluate quantitatively. Research varies in type, end-point and outcome, from basic scientific research to operational research. Moreover, research is conducted by the entire scientific community, which includes academia and research institutions that are not necessarily linked to national TB programmes. Bibliometric analysis is widely used in the health sciences and public health[5,6] to measure scientific productivity and to assess trends and patterns in research output.[7,8] Bibliometric analyses of research on TB have been reported in several publications, with various objectives.[9–11] Ramos et al.[10] showed increasing research activity in the field of TB during the period 1997–2006 and reported that less research was conducted in countries with the highest estimated numbers of TB cases. Most recently, Nafade et al.[9] found that the annual growth rate of TB publications between 2007 and 2016 was 7.3% globally, with the highest rate (13.1%) in Brazil, the Russian

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Federation, India, China and South Africa (BRICS). No studies are available, however, of regional productivity of research on TB.

The WHO Western Pacific Region (WPR) consists of 37 countries and areas, with a total population of 1.9 billion. The Region is diverse, including only one country with populations of more than 1 billion and small Pacific island countries with a few thousand residents and also countries with high and intermediate TB burdens and others in the pre-elimination stage. The Region accounted for 18% of global TB incidence in 2018.[1] The Regional Framework for Action on Implementation of the End TB Strategy in the Western Pacific 2016–2020,[12] in line with the End TB Strategy, also emphasized the importance of increasing capacity for research on TB for the development, uptake and optimum use of new interventions and proposed actions such as expanding national TB research networks, developing national TB research plans and priorities, building capacity for TB research and increasing TB research funding.

The aims of this analysis were to: (i) examine regional trends in the numbers of publications on TB indexed in PubMed in the past two decades; (ii) to compare the trends with those for other, selected major infectious diseases; and (iii) to assess intensified TB research activity in countries and areas in the Region quantitatively.

METHODS

A bibliometric analysis was performed with the RISmed package[13] in R (CRAN: Comprehensive R Archive Network at https://cran.r-project.org/), which permits extraction of bibliographic content from the United States National Center for Biotechnology Information databases, including PubMed. We extracted metadata from scientific publications indexed in PubMed with a combination of Medical Subject Headings (MeSH) terms for four major infectious diseases, "Tuberculosis", "HIV Infection", "Hepatitis" and "Malaria", and the names of countries and areas in the Western Pacific Region. We then constructed a regional database of the number of publications per year during the period 2000–2019 at 13 September 2020. The four diseases were selected on the basis of the global burden of each as a single infectious disease[14] and regional priorities in "reaching the unreached".[15] We did not include countries and areas for which MeSH terms were not available, which were Cook Islands, Kiribati, Marshall Islands, Nauru, Niue, Commonwealth of the Northern Mariana Islands, Solomon Islands, Tokelau, Tuvalu and Wallis and Futuna. The numbers of publications from Pacific island countries and areas were aggregated in the results because of the small number of publications. Duplicates of publications were removed from the regional aggregate counts. In this paper, the numbers of publications from China excluded those from Hong Kong SAR (China), Macao SAR (China) and Taiwan (China) as they were separately-defined geographical MeSH terms.

We examined trends in the numbers of publications on the four major infectious diseases at regional level over 5-year periods between 2000 and 2019 and computed the percentage increase from the level in 2000–2004, growth rates in each 5-year period and average annual growth rates for the period 2000–2018 (the year 2019 was removed because of the time required to indexing[16]). We further examined trends in the numbers of publications on TB in countries over the 5-year periods between 2000 and 2019 and computed the percentage changes from the level in 2000–2004 and average 5-year growth rates. The proportions of publications on TB from China, other regional high-burden countries and non-high-burden countries were also investigated for the same periods.

Ethics statements

Ethical clearance was not required as this was an analysis of available published research.

RESULTS

The number of publications indexed in PubMed on the four major infectious diseases in countries and areas in the WHO Western Pacific Region has increased by 3.0 times over the past two decades (**Fig. 1**), from 2609 in 2000–2004 to 7770 in 2015–2019 (**Table 1**). During the 5-year periods between 2000 and 2019, articles on HIV were published most often, followed by publications on hepatitis, TB and malaria. In the period 2000–2019, publications on TB accounted for 21% of all publications on the four diseases in the Region, which was less than for HIV (36%) and hepatitis (32%) and more than for malaria (11%) (**Fig. 2**). The proportion of publications on TB varied by country and area, from ≤10% for Papua

Fig. 1. **Numbers of publications on major infectious diseases from the WHO Western Pacific Region indexed in PubMed over 5-year periods, 2000–2019**

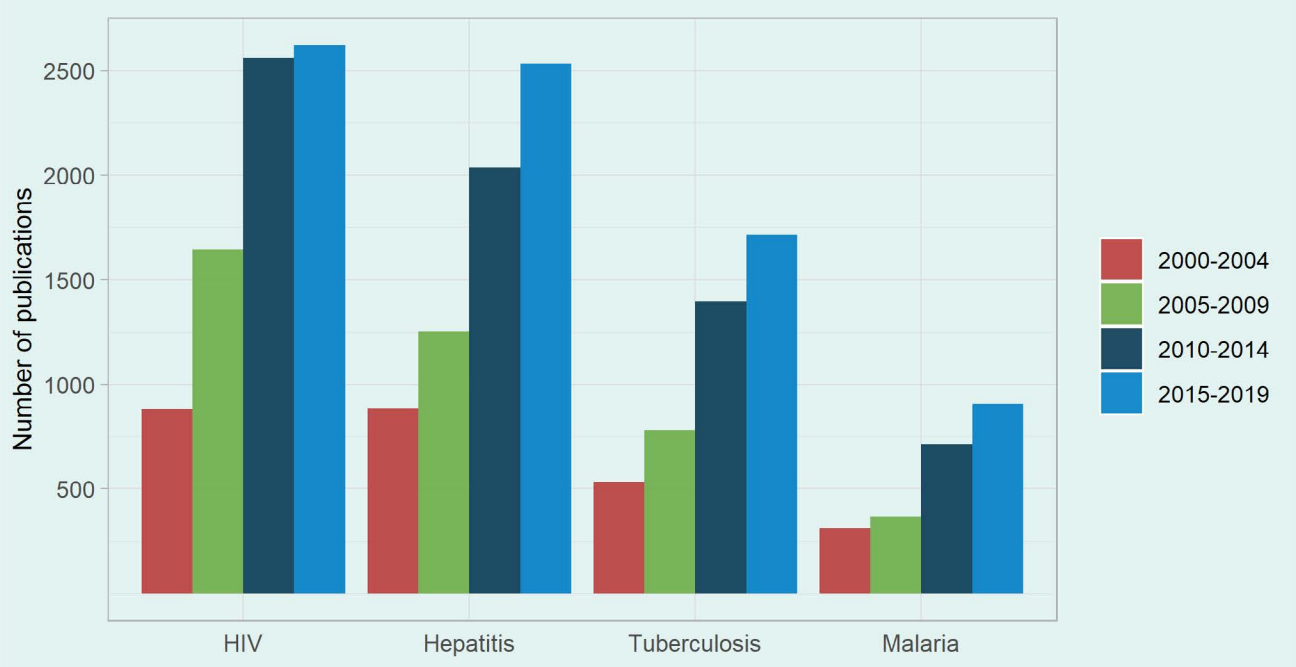


Table 1. **Numbers and growth rates of publications from the WHO Western Pacific Region indexed in PubMed on major infectious diseases over 5-year periods, 2000–2019**

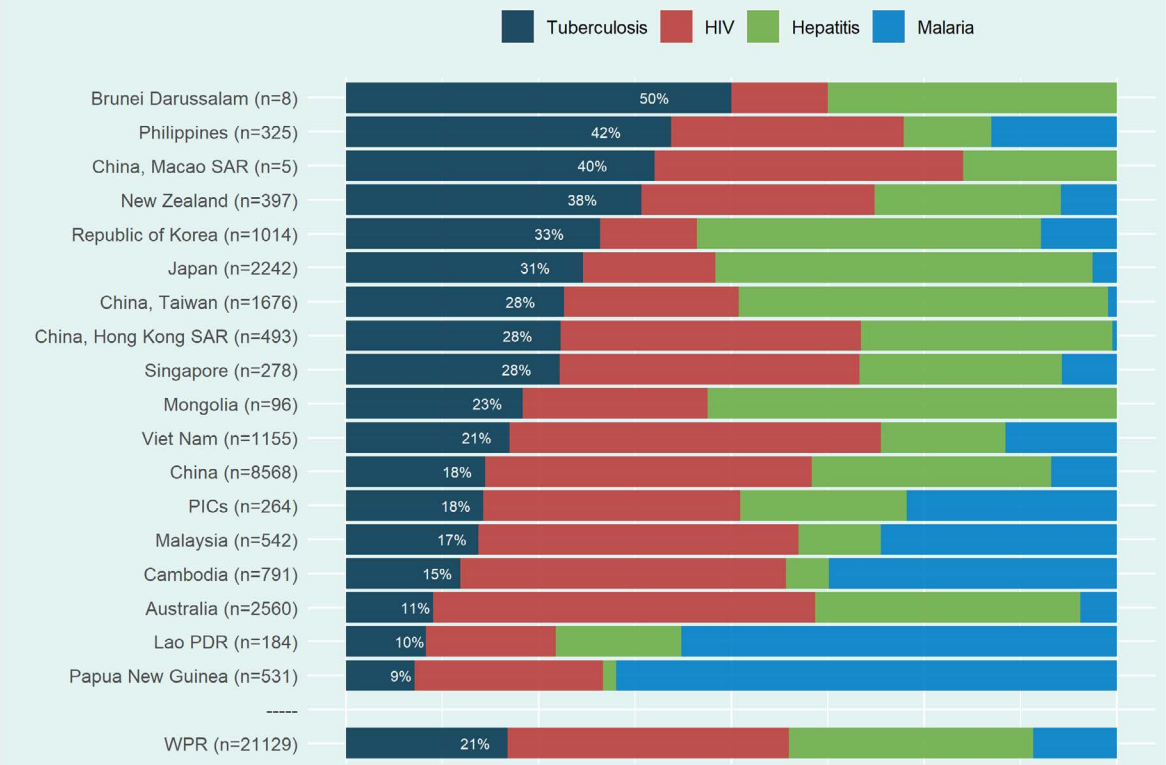
	Number of publications				% increase, compared to the 2000–2004 level			Growth rate compared to the previous 5-year period			Average annual growth rate for 2000–2018
	2000–2004	2005–2009	2010–2014	2015–2019	2005–2009	2010–2014	2015–2019	2005–2009	2010–2014	2015–2019	
HIV	881	1644	2557	2691	187%	290%	297%	87%	56%	2%	10.5%
Hepatitis	883	1254	2035	2530	142%	230%	287%	42%	62%	24%	9.1%
Tuberculosis	534	781	1396	1714	146%	261%	321%	46%	79%	23%	8.8%
Malaria	311	369	714	907	119%	230%	292%	19%	93%	27%	15.6%
Total	**2609**	**4048**	**6702**	**7770**	**155%**	**257%**	**298%**	**55%**	**66%**	**16%**	**9.3%**

New Guinea and the Lao People's Democratic Republic to ≥30% for Japan, New Zealand, the Philippines and the Republic of Korea, excluding Brunei Darussalam and Macao SAR (China), which had fewer than 10 publications (**Fig. 2**).

The number of publications on TB from the Region increased by 3.2 times, from 534 in 2000–2004 to 1714 in 2015–2019 (2.9 times each for HIV, hepatitis and malaria). **Table 1** shows the growth rate in the number of publications on TB in the Region increased by 46% in 2005–2009, 79% in 2010–2014 and 23% in 2015–2019 compared to the previous 5-year period. The average annual growth rate in the number of publications on TB between 2000 and 2018 was 8.8%.

Between 2000 and 2019, there were 4425 publications on TB in the Region (**Table 2**). China accounted for the largest proportion (34.8%), followed by Japan (15.5%), Taiwan (China) (10.7%), the Republic of Korea (7.5%), Australia (6.5%) and Viet Nam (5.5%). These six countries and areas accounted for >80% of all publications on TB in the Region; Pacific island countries accounted for only 1%. The number of publications on

Fig. 2. **Proportions of publications on TB, HIV, hepatitis and malaria from countries and areas in the Western Pacific Region indexed in PubMed, 2000–2019**



PICs, Pacific island countries; PDR, People's Democratic Republic; SAR, Special Administrative Region; WPR, Western Pacific Region.

Table 2. **Numbers of publications on TB from countries and areas in the Western Pacific Region indexed in PubMed over 5-year periods, 2000–2019**

Country and area	Number of publications					% change from 2000–2004 to 2015–2019	Growth rate between 2010–2014 and 2015–2019
	2000–2004	2005–2009	2010–2014	2015–2019	Total (N/%)		
Australia	46	57	94	91	288 (6.5%)	198%	-3%
Brunei Darussalam	0	4	0	0	4 (0.1%)	N/A	N/A
Cambodia	14	28	44	31	117 (2.6%)	221%	-30%
China	94	189	477	782	1542 (34.8%)	832%	64%
China, Hong Kong SAR	42	43	29	23	137 (3.1%)	55%	-21%
China, Macao SAR	0	1	0	1	2 (0.05%)	N/A	N/A
China, Taiwan	41	99	177	157	474 (10.7%)	383%	-11%
Japan	166	174	195	153	688 (15.5%)	92%	-22%
Lao PDR	2	3	8	6	19 (0.4%)	300%	-25%
Malaysia	18	20	27	28	93 (2.1%)	156%	4%
Mongolia	2	7	4	9	22 (0.5%)	450%	125%
New Zealand	25	41	50	36	152 (3.4%)	144%	-28%
Papua New Guinea	0	7	18	22	47 (1.1%)	N/A	22%
Philippines	24	24	39	50	137 (3.1%)	208%	28%
Republic of Korea	0	13	123	198	334 (7.5%)	N/A	61%
Singapore	18	16	18	25	77 (1.7%)	139%	39%
Viet Nam	38	53	70	84	245 (5.5%)	221%	20%
Pacific island countries	4	2	23	18	47 (1.1%)	450%	-22%
Western Pacific Region	**534**	**781**	**1396**	**1714**	**4425 (100%)**	**321%**	**23%**

PDR, People's Democratic Republic; SAR, Special Administrative Region.
N/A = not applicable

Fig. 3. **Number of publications on TB from countries and areas in the Western Pacific Region indexed in PubMed over 5-year periods, 2000–2019**

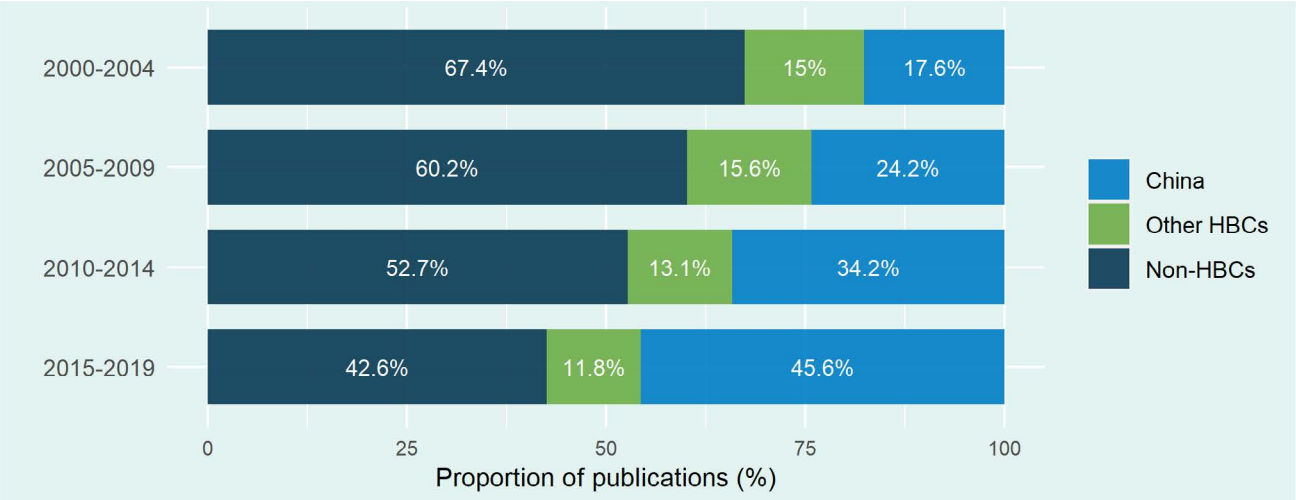
PICs, Pacific island countries; PDR, People's Democratic Republic; SAR, Special Administrative Region; WPR, WHO Western Pacific Region.

TB has tended to increase in most countries and areas in the Region in the past two decades, including in Cambodia, Papua New Guinea, the Philippines and Viet Nam, with the highest percentage increase in China (832%) (**Fig. 3**). The number of publications on TB over the 5-year periods remained at <10 in the Lao People's Democratic Republic and Mongolia, although increasing trends are observed. The percentage of publications on TB from China out of the total number from the Region increased from 17.6% in 2000–2004 to 45.6% in 2015–2019, while those of other high-TB burden countries and of other countries have shrunk (**Fig. 4**).

DISCUSSION

Our analysis demonstrates increasing research on the four major infectious diseases, including TB, in the Western Pacific Region over the past two decades. The importance of intensifying research has been stressed in global and regional strategies, not only for TB[2,12] but also for other communicable disease programmes, including HIV,[17] hepatitis[18] and malaria.[19] It is anticipated that increasing trends in the number of publications reflect accelerated research and innovations to better control and eliminate the diseases.

Fig. 4. **Proportions of publications on TB from China, other high-burden countries and non-high-burden countries/areas in the Western Pacific Region indexed in PubMed over 5-year periods, 2000–2019**



HBC, high-burden country.

Other HBCs: Cambodia, the Lao People's Democratic Republic, Mongolia, Papua New Guinea, the Philippines, Viet Nam.

Non-HBCs: Other countries and areas included in the analysis.

After 2015, when the End TB Strategy was introduced, the 5-year trend in the number of publications on TB continued to grow, demonstrating successful implementation of the third pillar of the Strategy in the Region. The increasing trends observed in low- and middle-income countries with high burdens of TB, such as Cambodia, China, Papua New Guinea, the Philippines and Viet Nam, may be considered to reflect empowered research communities and enhanced research collaboration on TB in these countries. The annual regional growth rate in the number of publications on TB in 2000–2018 was 8.8%, which was slightly higher than the global annual growth rate of 7.3% for 2006–2017.[9]

Government commitment and leadership play pivotal roles in advancing research and innovation for TB, and increasing financial investments is critical. Our analysis showed that China's contribution to regional TB research productivity was remarkable, especially in 2015–2019. China's National TB Strategic Plan 2016–2020 emphasizes the importance of intensified national research and development on TB prevention and care and of promoting international cooperation.[20] Accordingly, the national annual budget allocated for research and surveys on TB in China increased dramatically between 2015 and 2019, by six times, from US$ 5.7 million to US$ 34.3 million.[21] This may be one reason for the substantial increase in the number of publications, with rapid economic development enhancing domestic research capacity.[9,22] Ongoing initiatives to intensify collaboration in research on TB within the BRICS TB Research Network[23] may accelerate this trend in coming years.

Developing national TB research agendas and strategic plans and establishing national TB research networks creates an environment for high-quality TB research and innovation.[3,12] In Viet Nam, where the number of publications on TB has increased continuously over the past two decades, the national TB research agenda is explicitly defined in the National TB Strategic Plan 2015–2020.[24] Furthermore, in 2015, the Ministry of Health formed the Viet Nam Integrated Centre for TB and Lung Disease Research (VICTORY) under the management of the National Lung Hospital and National Tuberculosis Programme, to lead in implementing and coordinating research on TB and other lung diseases and to establish a research network.[12,25] This has fostered collaboration on TB research within and outside the country and also led to institutionalized research within programmes to ensure that research outputs inform policy and practice and improve programme performance.[25,26]

Effective bilateral and multilateral North–South and South–South collaborations among researchers and research institutions in high- and in low- and middle-income countries are essential to promote relevant

research and to cross-fertilize research capacity.[3] Several TB research networks are active in the WHO Western Pacific Region, including the Centre for Research Excellence in Tuberculosis Control in Australia[27] and the Asian Tuberculosis Research and Clinical Trials Integrated Organizational Network among members of the Asia–Pacific Economic Cooperation.[28] National TB research institutions, such as the Research Institute of Tuberculosis in Japan and the Korean Institute of Tuberculosis in Republic of Korea, have long contributed to international research on TB and to capacity-building in the Region. Molton et al.,[29] however, reported less intra-Asian TB research collaboration than in other regions, which they considered a missed opportunity to optimize regional research funding, capacity-building and a region-specific research agenda. Further enhancement of TB research collaboration is desirable in the Region, building on existing networks and initiatives.

Although there is increasing TB research collaboration and productivity in the Region, our analysis indicates that the output remains relatively low in several countries with higher burdens of TB such as Lao People's Democratic Republic and Mongolia as well as in Pacific island countries, where TB incidence per capita can be high. Operational, implementation, health system and social science research on TB to generate context-specific evidence to improve programme performance[3] could be prioritized in those countries, coordinated by national programmes, to gain the immediate benefits of research.

Our study has several limitations. First, we included publications only from the PubMed database and only those found with MeSH terms for both diseases and country names. We thus excluded relevant publications in other databases or not indexed as MeSH terms, regional publications from Asia and Oceania with no country-specific indexing and several Pacific island countries for which MeSH terms were not available. Second, the time required for indexing might have affected the completeness of indexing, especially for 2019, although we ensured that sufficient time (257 days) had elapsed between the end date of 2019 and the date of data extraction. These limitations may have resulted in an underestimate of the number of publications. Lastly, we did not investigate regional trends and patterns by research type and programmatic areas in published articles, which could reveal gaps in evidence for the regional TB response. This was beyond the scope of the present analysis but should be addressed in future studies.

Despite these limitations, the results of our bibliometric analysis indicate contemporary trends in TB research productivity in countries and areas in the Region and highlight achievements and gaps in implementing the third pillar of the End TB Strategy. Countries are encouraged to implement the actions proposed in the Global Strategy for TB Research and Innovation to accelerate progress towards ending TB.[3] The WHO Regional Office for the Western Pacific will continue to play a catalytic role in fostering regional TB research collaboration and providing technical assistance to build research capacity in national TB programmes in the Region.

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Conflicts of interest

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The Pandemic Influenza Preparedness (PIP) Framework: strengthening laboratory and surveillance capacities in the Western Pacific Region, 2014–2017

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The World Health Organization's (WHO) Member States unanimously adopted the Pandemic Influenza Preparedness (PIP) Framework in May 2011.[1] The Framework has two aims: (1) to improve the sharing of influenza viruses with pandemic potential; and (2) to increase the access of developing countries to vaccines and other life-saving products during a pandemic. Implementing the PIP Framework enables Member States to meet their obligations under the International Health Regulations, or IHR (2005),[2] and advance implementation of public health emergency preparedness. The PIP Framework contributes to national and regional preparedness, alert and response priorities across all focus areas of the Asia Pacific Strategy for Emerging Diseases for Public Health Emergencies (APSED) framework.[3]

One key benefit of the PIP Framework is the Partnership Contribution (PIP-PC).[4] Annually, US$28 million is provided to WHO[6] by influenza vaccine, pharmaceutical and diagnostic manufacturers that use the Global Influenza Surveillance and Response System (GISRS) – a network of laboratories conducting surveillance of seasonal, pandemic and zoonotic influenza viruses.[4] PIP-PC funds complement investments from other sources and are used in synergy with national, regional, and global funding to strengthen preparedness capacities globally and in priority countries in the Western Pacific Region. From 2014 to 2017, PIP-PC funds were used according to the first high-level implementation plan (HLIP I) developed by WHO, in consultation with stakeholders, which focused on five areas of work: laboratory and surveillance, burden of disease estimation, regulatory capacity-building, risk communication and planning for deployment of pandemic products.[6] These areas of work where capacity building has been targeted form the foundation for an effective response not only to an influenza pandemic but for novel respiratory viruses (e.g. SARS-CoV-2). While there have been achievements in all five areas of work,[5] this paper provides an overview of implementation achievements in laboratory and surveillance capacities in the Region.

Between 2014 and 2017, in addition to other agencies' contributions for influenza capacity building, US$8.6 million of PIP-PC funds was invested in the Region[5] for improving laboratory and surveillance capacities through detection of respiratory diseases due to a novel virus, monitoring influenza trends including through sentinel surveillance systems and strengthening GISRS and global collaboration through information and virus sharing. Using the country selection criteria established in HLIP I, the WHO Regional Office for the Western Pacific identified five countries to receive PIP-PC funds:[6] Cambodia, Fiji, the Lao People's Democratic Republic, Mongolia and Viet Nam. While other regional and global investments have played a foundational role in establishing these national capacities, PIP-PC investment into national preparedness have supplemented these programs and further strengthened core capacities for pandemic response. By 2017, laboratory and surveillance capacities had improved in these five priority countries as well as in the Region more broadly (**Table 1**). Criteria used to measure improvement were indicators established in HLIP I (e.g. the number

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Table 1. **Changes in the laboratory and surveillance capacities in the five countries[1] prioritized for PIP-PC in WHO's Western Pacific Region, 2014[2]–2017**

Capacity category	Funds spent (million US$)[3]		Capacity (data source)	No. of countries[4] 2014	2017
Detection	$5.1	1.	National event-based surveillance system in place including available protocols, definitions and procedures (country self-report)	1	5
		2.	Rapid Response Team established and trained in the past year (country self-report)	3	5
Monitoring	$1.8	3.	Influenza-like illness surveillance was conducted, samples collected weekly and regularly sent to a laboratory (country self-report)	2	5
		4.	Severe acute respiratory infection surveillance conducted, samples collected weekly and regularly sent to a laboratory (country self-report)	2	4
		5.	Capacity for influenza virus sequencing (country self-report)	2	3
		6.	Influenza surveillance reports with integrated data published in the public domain (country self-report)	2	3
		7.	Consistently[5] reported virological data to WHO FluNET during the influenza season (WHO database)	4	5
		8.	Consistently[5] reported epidemiological data to WHO FluID during the influenza season (WHO database)	0	5
Global collaboration	$1.7	9.	Shared influenza viruses with WHO at least once a year in the last two years (WHO database)	5	5
		10.	Staff trained and certified to ship influenza clinical specimens/virus isolates out of the country (WHO database)	2	4
		11.	Participated yearly and scored 100% in the WHO External Quality Assessment Project for the detection of influenza viruses by real-time polymerase chain reaction in 2014–2017 (WHO database)	5	4

1. Cambodia, Fiji, the Lao People's Democratic Republic, Mongolia and Viet Nam.
2. Funding period not implementation period.
3. Figures extracted from WHO financial management system on 7 March 2018, net of programme support costs.
4. Number of countries receiving PIP-PC funds.
5. Consistently means that a country reports weekly at least 60% of the weeks during the influenza season.

of countries consistently reporting to FluID[7]); some are based on country self-reporting and others are extracted from WHO databases.

All PIP-PC priority countries improved influenza detection capacities through strengthened event-based surveillance (EBS) systems,[8] particularly at the human–animal interface (HAI) (see **Table 1**). All five also established or maintained their rapid response teams. These teams are integral for countries to rapidly identify and control disease outbreaks, as noted by the IHR (2005). Examples of how countries have improved their capacities were recently reported in IHR Joint External Evaluation missions.[9–12] Activities that supported these achievements included provision of technical assistance for influenza surveillance protocols and guidelines and delivery of training programs in field epidemiology, HAI rapid response and surveillance. These programmes have been integral for countries in rapidly identifying and investigating potential outbreaks, highlighting the impact of the investments on broader country-level preparedness and strengthening of core capacities under the IHR (2005) using the Asia Pacific Strategy for Emerging Diseases and Public Health Emergencies (APSED III) as an implementing framework.

All five PIP-PC recipient countries conduct epidemiological and virological surveillance for influenza in either outpatient or inpatient populations (**Table 1**). All five countries have the improved capacity to routinely monitor influenza virological and epidemiological trends; three have published surveillance reports that integrate virological and epidemiological findings. Furthermore, all five countries consistently share influenza viruses/specimens with GISRS and report surveillance data to the WHO reporting platforms FluNet[13] and FluID. To enhance regional information sharing, the WHO Regional Office for the Western Pacific Region launched an online

influenza dashboard that presents consolidated seasonal and avian influenza surveillance data.[14] It provides public access to regularly updated regional influenza activity and provides an opportunity for countries to share important severity assessment evaluations during unusual outbreaks. Combined with virological data, this enables timely global situational monitoring and risk assessment and provides a collateral benefit to partners using GISRS.

Improvements in national influenza laboratory systems assure quality contribution to GISRS, thereby contributing to global preparedness for future influenza pandemics. PIP-PC funds helped support trainings in the five priority countries, and other countries in the Region as needed, on specimen collection and handling, virus isolation, molecular diagnostic techniques, sequencing and bioinformatics and laboratory biosafety and biosecurity. Supplies and equipment were provided to national laboratories to facilitate these capabilities. Regional technical experts routinely provided or sourced expertise to support and mentor influenza laboratory and epidemiology surveillance staff. Countries continue to participate in the WHO External Quality Assessment Project[15] for the detection of influenza viruses by polymerase chain reaction, and the results indicate ongoing capacity-strengthening needs.

There was a marked improvement in preparedness in the PIP priority countries from 2014 to 2017, including enhanced capacities to detect and respond to influenza-related events through improved EBS and laboratory capacities. In addition, improved indicator-based surveillance systems[8] allow estimation of influenza disease burden in support of high-risk group vaccination policies, as well as establishment of thresholds to monitor seasonality and severity. Meanwhile, improved cross-sectoral information sharing between public and animal health authorities facilitates risk assessment for public health action. These gains are attributed to the collective effort and commitment of national authorities, in parallel with investments made by national and international partners, including the PIP-PC funds and APSED III.

Investing in preparedness is an ongoing requirement.[16] There is a need for continuous support in surveillance and laboratory strengthening, particularly for laboratory capacity. Of the 27 countries and areas in the Western Pacific Region, 14 countries report to FluNet, 18 countries report to FluID and 15 countries routinely share influenza viruses with GISRS, so there are still opportunities for improvement. With the end of HLIP I implementation, further improvements in pandemic preparedness can build on the success achieved and the lessons learnt. While HLIP I has a sustainability principle, WHO put in further measures in HLIP II so that procurement and activity implementation is done with sustainability in mind.

In 2018, WHO launched HLIP II, which sets out an ambitious agenda for continuing to strengthen pandemic influenza preparedness capacities in 2018–2023.[17] A sixth area of work focusing on pandemic influenza preparedness planning was introduced to link the other five areas together. It provides an opportunity for capacity building efforts from HLIP I to be linked to the broader development and testing of national pandemic plans and health security strategies through simulation exercises and after-action reviews. In the Western Pacific Region, HLIP II implementation will increase focus on strengthening regional and national capacities in influenza risk, severity assessment and pandemic planning capacities. Following a successful initiation, the PIP Framework remains an effective tool to strengthen regional and country pandemic preparedness, particularly in the surveillance and laboratory area.

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A superspreading event involving a cluster of 14 coronavirus disease 2019 (COVID-19) infections from a family gathering in Hong Kong SAR (China)

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Objectives: An outbreak of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported in Wuhan, China, in December 2019, with subsequent spread around the world. Hong Kong SAR (China) recorded its first confirmed cases on 23 January 2020. In this report, we describe a family cluster of 12 confirmed cases, with two additional confirmed cases from secondary transmission.

Methods: We reported the epidemiological, clinical and laboratory findings of the family cluster, as well as the public health measures instituted.

Results: All 12 confirmed COVID-19 cases were among the 19 attendees of a three-hour Chinese New Year family dinner consisting of hotpot and barbecue dishes. Environmental sampling of the gathering venue was negative. Two additional confirmed cases, who were co-workers of two confirmed cases, were later identified, indicating secondary transmission. Contact tracing, quarantine and environmental disinfection were instituted to contain further spread.

Discussion: Our findings were highly suggestive of a superspreading event during the family gathering. The source was likely one of the cases during the pre-symptomatic phase. The event attested to the high infectivity of SARS-CoV-2 through human-to-human transmission from social activities and argued for the necessity of social distancing in curtailing the disease spread.

An outbreak of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2),[1] was first reported in Wuhan, China, in December 2019. With its spread to other countries and areas, COVID-19 was declared a public health emergency of international concern by the World Health Organization on 30 January 2020.

Current research suggests SARS-CoV-2 to be of zoonotic origin, with the capacity of human-to-human transmission.[2] It is highly infectious,[3,4] and can be transmitted via droplets and contact with contaminated surfaces. Airborne transmission might take place during aerosol-generating procedures.[5] Some experts proposed that certain social activities involving water-vapour generation, such as hotpot meals and saunas, were associated with increased risk of transmission.[6] Transmission from asymptomatic contacts was also reported.[7]

Hong Kong SAR (China), a metropolitan city located on China's southern coast and with intimate economic and social ties with mainland China, reported its first confirmed cases of COVID-19 on 23 January 2020. As of the end February 2020, Hong Kong SAR (China) had recorded 95 confirmed cases of COVID-19. Twenty-six cases were local or possibly a locally acquired infection without identifiable sources. In this report, we described a family cluster of 12 confirmed cases, with two additional confirmed cases from secondary transmission.

METHOD

Case identification

Cases of COVID-19 were identified from notification by medical practitioners in Hong Kong SAR (China) to the Centre for Health Protection (CHP) under the Department of Health or from contact tracing of confirmed cases.

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Epidemiological investigation

For each notification, CHP initiated a case investigation, including source identification, contact tracing and additional case findings. The incubation period of COVID-19 was defined as 1–14 days before symptom onset.[8]

We describe the course of our epidemiological investigation leading to the identification of this family cluster and present the clinical, epidemiological and laboratory findings of the cases.

Environmental investigation

During the investigation, it was noted that all confirmed cases attended a family gathering before symptom onset. A site visit was conducted to the venue of the gathering with environmental swabs collected for examination.

Laboratory investigation

All locally confirmed cases of COVID-19 described in this report were laboratory confirmed by the positive detection of SARS-CoV-2 RNA in the patient's clinical specimens using real-time reverse transcription polymerase chain reaction. The same approach was used for environmental swabs.

Infection control measures

We describe the various infection control measures instituted.

RESULTS

The index case and his family

On 9 February 2020, CHP received notification of a confirmed case of COVID-19 involving a 24-year-old male (Patient 1) who had developed a fever and a productive cough on 30 January 2020. He was admitted to a public hospital on 8 February 2020, and his nasopharyngeal aspirate tested positive for SARS-CoV-2. He did not travel outside Hong Kong SAR (China) during the incubation period. He worked as a sales representative and denied having any contact with confirmed COVID-19 cases.

Contact tracing revealed that his parents and maternal grandmother, who resided with him, also had developed symptoms between 28 and 31 January 2020, respectively. They were admitted for isolation and also tested positive for SARS-CoV-2 (Patients 2 to 4).

In view of the proximity of their symptom onset dates, a common source exposure was suspected. Further enquiry revealed that they attended a Chinese New Year gathering with 15 other relatives on 26 January 2020 (**Fig. 1**). At the time of the investigation, eight of them were found to be symptomatic from 30 January to 8 February 2020, and arrangements were made for hospital admission. Seven tested positive for SARS-CoV-2 (Patients 5 to 11). Two of the attendees (a father and his son) were visitors from Guangdong Province, China, and had already returned home at the time of our investigation. We were later informed by the Health Commission of Guangdong Province that the son had developed a cough and runny nose on 2 February 2020 and had tested positive for SARS-CoV-2 on 10 February (Patient 12). The father reported having had a cough for a few days beginning 20 January 2020, which had subsided during the gathering. His respiratory specimen collected on 9 February was negative for SARS-CoV-2. His serology remained negative for SARS-CoV-2 antibodies.

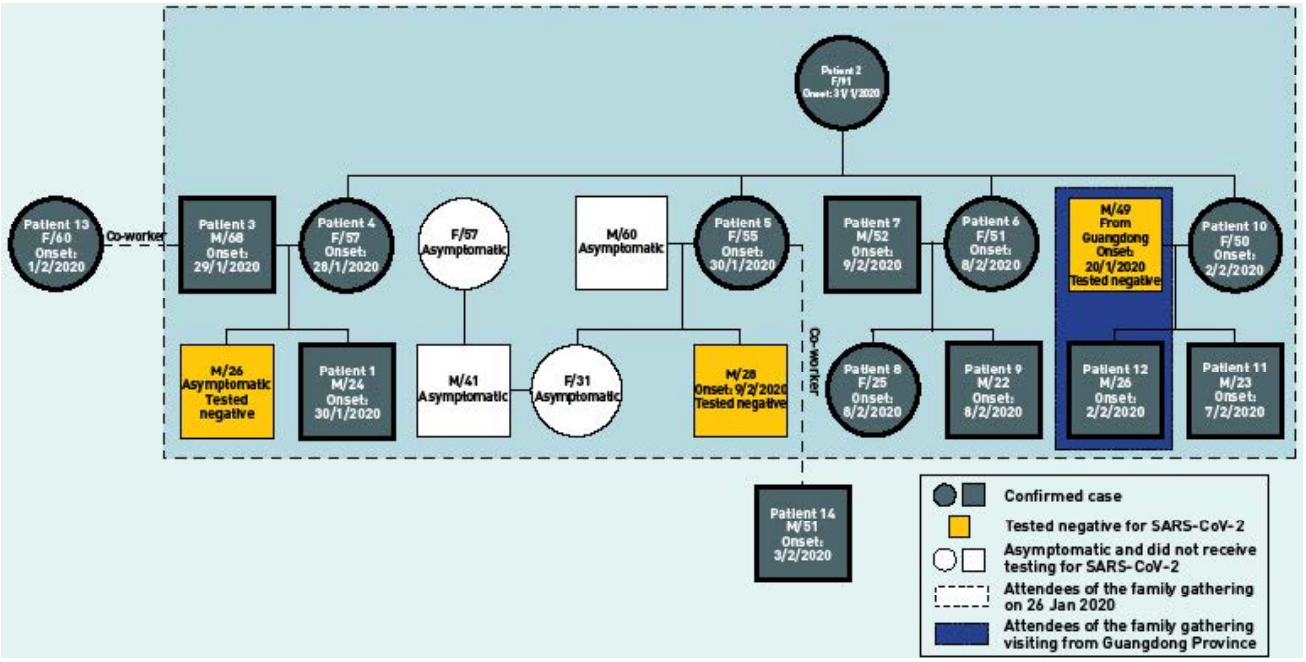
Family gathering

The 19 attendees lived in several different residences, and the family gathering was the only occasion attended by all 12 confirmed cases during their incubation periods. It was held in a commercial party room during the evening and lasted for about three hours. The attendees had an indoor hotpot dinner and a barbeque held at an outdoor area. No game meat or wild poultry was consumed. They also played mah-jong and snooker. None of the attendees were symptomatic during the gathering. Staff of the party room did not enter the room during the gathering, and there were no other patrons that evening. None of the staff and patrons who used the room in the following days reported symptoms.

Environmental investigations

A site visit was conducted at the party room on 9 February 2020. Environmental swabs were taken at 18 high-touch areas, including doorknobs, door handles, table surfaces and edges, and light switches. All tested negative for SARS-CoV-2.

Fig. 1. **The family tree of the cluster**



Additional case finding and infection control measures

Extensive contact tracing was conducted for each individual patient confirmed in Hong Kong SAR (China). All symptomatic contacts were isolated in a public hospital for treatment and SARS-CoV-2 testing. Asymptomatic contacts were quarantined in quarantine facilities or put under medical surveillance, depending on the nature and duration of contact with the patient. Forty-six close contacts and 166 other contacts were identified. Among them, two contacts who were co-workers of Patients 3 and 5 developed symptoms, one on 1 February and the other on 3 February, and tested positive for SARS-CoV-2 (Patients 13 and 14).

Overall, the entire cluster of 14 confirmed cases consisted of seven males and seven females aged 22 to 91 (median: 51). All of them had a record of good health and had no history of travel outside Hong Kong SAR (China) during the incubation period, except Patient 12 who had been visiting from China. They all presented with upper respiratory symptoms and/or fever (**Fig. 2**).

Environmental cleansing and disinfection were arranged for the party room, the residences of the cases and their workplaces. As of the end of February, all cases remained stable, and eight (Patients 1, 3, 4, 5, 9, 10, 12 and 13) were discharged. No further cases related to this cluster were identified.

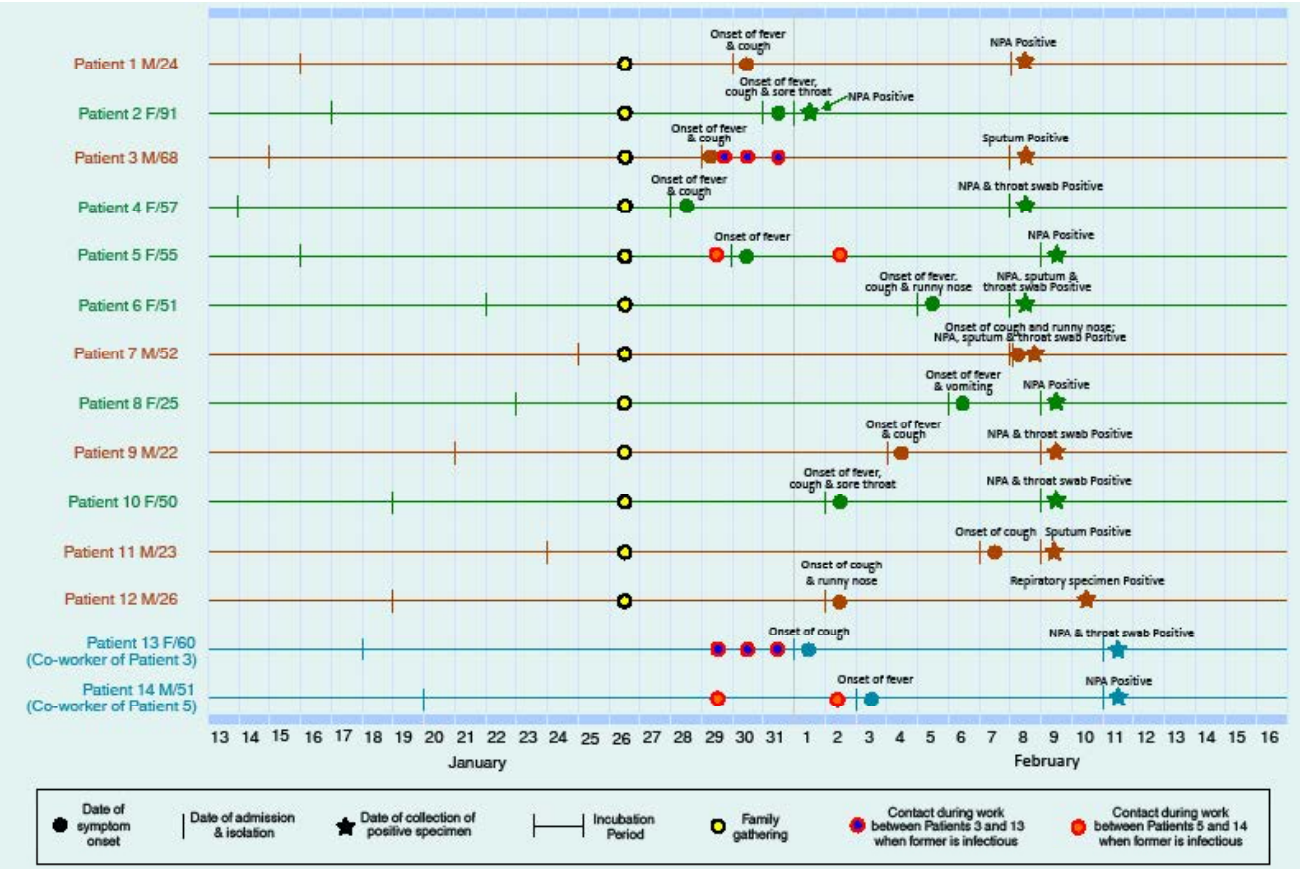
DISCUSSION

This was the largest COVID-19 family cluster recorded in Hong Kong SAR (China) at the time of our reporting. Our epidemiological investigation suggested that primary transmission took place during the family gathering, with secondary transmission leading to the infection of two more cases. As none of the attendees were symptomatic during the gathering, it was likely that pre-symptomatic transmission from one of the attendees had occurred.

Our investigation supported and supplemented the current understanding of the COVID-19 infection. In this cluster, the incubation periods ranged from 2–13 days, which is compatible with the current knowledge. Nevertheless, those with a longer incubation period might represent secondary interfamilial transmission. Our findings also supported human-to-human transmission of SARS-CoV-2. As the family gathering was the only occasion attended by the 12 patients during the incubation periods, it demonstrated the high infectivity of SARS-CoV-2 (as 11 out of 17 susceptible attendees, excluding the potential source, were infected) and its ability to cause a superspreading event.

Environmental factors and behavioural factors have been proposed as risk factors of a superspreading event.[9] For example, one study in Japan demonstrated 18.7 times higher odds for transmission in a closed compared with an open-air environment.[10] In our cluster, part of the

Fig. 2. **Chart illustrating key events of Patients 1 to 14**



NPA = *nasopharyngeal aspirate*

family gathering took place in a party room that was a closed environment. Nevertheless, we were unable to determine the significance of environmental contamination in the transmission chain in this cluster. Moreover, the transmission of SARS-CoV-2 could be enhanced through close and prolonged social contacts without wearing a mask, such as in the family gathering described above.

Although the family gathering involved a hotpot dinner, there was not enough information to support the expert hypothesis that it could enhance SARS-CoV-2 transmission through water-vapour generation.

It is also noted that it took more than one week since symptom onset for most cases in this cluster to receive COVID-19 testing. In fact, several cases had consulted primary care physicians, but they were not tested as tests were only available then in public hospitals and the CHP laboratory. Subsequently, COVID-19 testing had been made available at the primary care level to allow earlier identification of cases in the community.[11]

Our investigation had several strengths. Our immediate investigation allowed identification of the possible sources and the establishment of the transmission chain. Extensive contact tracing allowed swift identification of more confirmed cases and ensured contacts were quarantined and put under medical surveillance. The timely institution of these infection control measures allowed complete case ascertainment in this cluster and shed light on the transmission dynamic of COVID-19.

On the other hand, there were some limitations regarding our investigation. Our environmental investigation was conducted two weeks after the family gathering, which might limit the positive yield of the environmental sampling. Cases who remained asymptomatic might not be identified.

In Hong Kong SAR (China), family gatherings involving relatives from other extended families and friends are quite common during major festivities (e.g. Chinese New Year) and are considered an important local tradition.

These occasions offer good opportunities for superspreading of a highly infectious agent such as SARS-CoV-2.

Social distancing has been advocated as one of the community mitigation measures during influenza pandemics. It entails an increase in physical distances and a reduction of gatherings in dense social settings.[12] With the continuing global spread of COVID-19, apart from advocating personal hygiene and protection, social distancing might be necessary to curtail further disease spread in the community, especially for preventing occurrence of superspreading events.

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Conflicts of interest

No potential conflicts of interest were reported by the authors.

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Mongolia Red Cross Society, influenza preparedness planning and the response to COVID-19: the case for investing in epidemic preparedness

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Globally, seasonal influenza contributes to approximately 291 000 to 645 000 deaths each year.[1] The burden of annual influenza epidemics can be particularly high in low- and middle-income countries[1] such as Mongolia,[2] which experienced a nationwide epidemic of influenza A(H1N1) 2009 in the winter of 2018–2019. The national health system was quickly overwhelmed, prompting the State Emergency Commission to involve key partners – including the Mongolia Red Cross Society (MRCS) and its network of more than 6000 volunteers – to augment the Government's response capacity. This paper describes how the experience of MRCS and subsequent planning for the 2019–2020 influenza season were effectively leveraged during the response to coronavirus disease 2019 (COVID-19).

Over the last decade, MRCS has been engaged by the Government to support the prevention and control of several communicable disease outbreaks; however, MRCS had had little involvement in influenza-related activities since the 2009 H1N1 pandemic. Recognizing the value of preparedness after the winter of 2018–2019, MRCS developed an influenza preparedness plan in advance of the 2019–2020 influenza season. Planning comprised a review of seasonal influenza risk, including risk factors and vulnerability; mapping key stakeholders and relevant policies, plans and capacities; and a literature review to determine the evidence base for community-focused, influenza-related interventions.

Aligned with recommendations of the WHO *Global Influenza Strategy 2019–2030*[3] and structured around the "epidemic response cycle" (preparedness, alert, response and evaluation),[4] the preparedness plan set out actions for MRCS to contribute to mitigating the threat of seasonal influenza, including annual training of volunteers, pre-positioning of health communication materials and hand sanitizer, and strengthening planning and collaboration with local authorities and stakeholders. Volunteer training and activities focused on non-pharmacological interventions – strategies individuals or communities could adopt when well (to reduce exposure to the virus and avoid infection) or unwell (to avoid spreading the infection to others).[5] Prevention messages focused on hand hygiene, cleaning of high-touch surfaces, respiratory etiquette, self-quarantine when feeling unwell and promoting annual influenza vaccination, especially for children aged 2–5 years. Tailored education messages for children were delivered through games, songs and fun activities rather than didactic approaches.

The preparedness plan aimed to strengthen community-centred preparedness for seasonal influenza, as well as to provide the foundation for MRCS to contribute to broader epidemic preparedness. The benefits of this were almost immediate, with MRCS leveraging the plan in the preparedness phase of the national COVID-19 response in January 2020. Many of MRCS's routine influenza prevention messages similarly apply to COVID-19, and they were quickly rebranded for this purpose and incorporated into volunteer training and public communication materials. Relationships established with national and local authorities to address seasonal influenza were swiftly capitalized upon to enable joint planning and information sharing for COVID-19. And continuous reflection and evaluation processes are providing lessons learnt to inform ongoing COVID-19 interventions, as well as preparedness actions for the 2020–2021 influenza season. For example, a public survey to determine communica-

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tion preferences highlighted gaps in the MRCS approach, and it has resulted in greater use of television and radio to better reach herder communities.

The COVID-19 pandemic underscores the importance and value of investing in epidemic preparedness planning well in advance of disease outbreaks. Thus far, Mongolia has effectively contained COVID-19 through a proactive and comprehensive public health response that acknowledges and values the role of the community and community-based organizations in health promotion and disease prevention.[6] As of 30 August 2020, Mongolia had reported 301 cases of COVID-19 and no community transmission.[7] As we have seen with other epidemics,[8] community volunteers working to advance health literacy can play a vital role in epidemic disease prevention, detection and response. However, it takes time and resourcing to train and equip them with the necessary skills and communication materials, and for them to gain the trust and respect of their community peers and build necessary credibility to be listened to when outbreaks occur.[9] Similarly, strong organizational partnerships do not develop overnight, but once in place they can be effectively leveraged when emergencies occur. The partnership between MRCS and the Ministry of Health established through the influenza experience resulted in greater recognition of the organization's epidemic preparedness and response "value add" through its vast volunteer network – and ultimately in MRCS being assigned responsibility for community-level health communication and psychosocial support in the COVID-19 response. To date more than 2000 volunteers have shared prevention messages and provided reassurance and support to more than 290 000 people, and assisted more than 7000 repatriated nationals in home quarantine (which occurs for several weeks following centralized quarantine in government facilities); support to those in home quarantine includes two social welfare checks per week providing social connection and reassurance, practical help (for example, grocery shopping), reinforcement of prevention messages and referral to formal mental health services if needed.

The COVID-19 pandemic is a reminder of the need to intensify and sustain the commitment to public health preparedness.[10] Well-prepared communities, empowered to take action when a threat is detected, are critical to determining if health risks escalate from a local containable outbreak to national and regional threats. The return on investment is incontestable.[11]

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Testing for COVID-19 cases in ASEAN

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How many people actually have coronavirus disease 2019 (COVID-19)? Valid data describing the number and distribution of COVID-19 cases are critical for the design and implementation of containment strategies; however, timely and accurate measurement of disease incidence continues to pose challenges.[1] To obtain an accurate picture of the scale of the outbreak, we reviewed the count of cases and tests, as well as the testing rate and the proportion of positive tests, in Member States of the Association of Southeast Asian Nations (ASEAN). ASEAN is a 10-member grouping of countries with a population of over 650 million people.[2] Cases of COVID-19 within ASEAN were reported first in Thailand and then Singapore in January 2020 and later in other ASEAN countries, with the first death outside China reported in the Philippines. To date, COVID-19 has affected all countries in the ASEAN region, with many imposing community quarantines and all restricting travel to varying degrees.[3]

No country knows the true number of people infected with COVID-19. All that can be ascertained is the status of those who have been tested. The total number of people who have tested positive – the number of confirmed cases – is not the total number of people who have been infected. The number of COVID-19 cases reported in a country is dependent on its surveillance sensitivity and laboratory testing capacity. The criteria for laboratory testing are also important because countries screen and test "suspect cases" based on clinical symptoms and a relevant epidemiological history.[4,5] It is likely that in some ASEAN countries, cases of COVID-19 may be undetected because of restrictive case definitions of suspect cases or limited testing capability to possible issues with case ascertainment in the early phases of ASEAN countries'COVID-19 responses, we reviewed information on testing and cases obtained from ministries of health and online news sources from March–April 2020 (**Table 1**). We provide an overview important testing indicators in ASEAN countries during this phase of the COVID-19 pandemic and discuss the utility of testing coverage, positivity rate and criteria for testing.

One indicator of the reliability of testing data is testing coverage, or the number of tests conducted per 100 000 population. Generally, we would expect that there are two reasons that countries with higher testing coverage have more reliable data on confirmed cases. First, a greater degree of testing provides us with a larger "sample" of people for whom disease status is known. Second, it may be the case that where the capacity for testing is low, tests may be reserved for particularly high-risk groups. Such rationing is one reason that those people tested may not be representative of the wider population. As observed in **Table 1**, all countries increased their testing coverage from March to April 2020, and marked heterogeneity exists across countries. We note that across all countries, the number of cases increased dramatically in March and April 2020. In addition to the expansion of testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19, this pattern of rapid case increase in some countries could also have been reflective of community transmission.

A second indicator we highlight in **Table 1** is the test positivity rate (TPR), defined as the number of confirmed COVID-19 cases per 100 tests. TPR is widely used by malaria surveillance programmes as one of several key indicators of temporal trends in malaria incidence.[6] For COVID-19, WHO interim guidance notes percent positive as an epidemiological factor to be used in risk assessments for countries.[7] We support that this indicator may be of utility with respect to the assessment of COVID-19 in ASEAN country contexts. At the beginning of the outbreak, when the COVID-19 caseload was low, a smaller number of tests was needed to accurately assess the spread of the virus. As the disease spreads, testing coverage needed to expand to provide a reliable picture of the true number of infected people. TPR can also be useful in determining whether or not an apparent

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Table 1. **Confirmed COVID-19 cases and laboratory tests performed in ASEAN countries (March-April 2020)**

Country	Population (millions)	Confirmed cases		No. of individuals tested		Individuals tested per 100 000		Test positivity rate (%)		WHO transmission classification as of 30 Apr
		Early Mar	29 Apr	Early Mar	End Apr	Early Mar	End Apr	Early Mar	End Apr	
Singapore	**5.8**	117	15 641	1300[25F]	99 929[27A]	23	1772	9	16	Clusters of cases
Malaysia	**32**	55	5945	1000[25F]	154 203[29A]	3	489	5.5	4	Clusters of cases
Thailand	**69**	47	2947	3680[3M]	62 018[29A]	5	89	1.3	5	Clusters of cases
Viet Nam	**97**	16	270	N/A	261 004[29A]	0	273	N/A	0	Clusters of cases
Philippines	**109**	3	8212	N/A	88 869[28A]	0	83	N/A	9	Clusters of cases
Indonesia	**273**	2	9771	331[3M]	67 784[29A]	0	18	0.6	14	Community transmission
Cambodia	**16.7**	1	122	227[5M]	11 576[27A]	1	71	0.44	1	Sporadic cases
Myanmar	**54**	0	150	43[5M]	7718[29A]	0	14	0	2	Clusters of cases
Lao People's Democratic Republic	**7.2**	0	19	54[5M]	1796[27A]	1	25	0	1	Sporadic cases
Brunei Darussalam	**0.43**	0	138	32[5M]	13 428[29A]	7	3130	0	1	Sporadic cases

[25F] as of 25 February,[5M] as of 5 March,[28A] as of 28 April,[3M] as of 3 March,[27A] as of 27 April,[29A] as of 29 April

Source: Ministries of health; WHO Coronavirus Disease 2019 (COVID-19) Situation Report – 101, 30 Apr 2020.

Note: All ASEAN countries require a positive polymerase chain reaction test for SARS-CoV-2 to confirm a case.

increase in incidence is a result of better case detection, or a true increase. For example, if incidence is calculated using total population as a denominator and is found to be higher than usual, this could indicate a true increase in incidence. However, if the TPR shows a declining trend, it may suggest that this apparent increase is actually a result of better testing.[8] Here, we observe wide discrepancies across countries, with Viet Nam having a TPR of 0.1%, compared with Singapore having a TPR of 16%. A high TPR could be an indicator of under-detection, as tests may be reserved for those with a high probability of having the disease. Individuals who have the disease but are asymptomatic may not be detected. Broad surveillance strategies should encounter far more people who are not infected than people who are, so the TPR should be lower.

Based on our findings, we make three observations. First, some countries established additional surveillance by performing laboratory tests for SARS-CoV-2 for patients with pneumonia or selected community cases of influenza-like illness.[9]

To get a clearer sense of SARS-CoV-2 transmission intensity, countries need to broaden criteria for testing. Rather than testing solely based on restrictive suspect case definitions, population or clinic-based fever surveillance, along with testing suspect cases, would provide a more accurate understanding of SARS-CoV-2 transmission. This is particularly relevant in view of the varied and non-specific clinical presentation of COVID-19. Both random testing and targeted testing, particularly among individuals in high-risk settings such as health care, have merit and need to be conducted simultaneously.

Second, all cases reported by ASEAN countries in this dataset were diagnosed based on viral detection by polymerase chain reaction tests, which cannot detect resolved infections,[9] and depending on testing criteria, may have missed asymptomatic or mild infections, because such people may not be tested. While acknowledging current limitations and variable test performance characteristics, we recommend large-scale seroprevalence studies as one additional measure to identify the best available estimate of disease burden and to compare with reports from existing surveillance systems. Longitudinal cohort studies that estimate seroprevalence can also assist in estimating trends in disease transmission over time.

Third, as a regional grouping, with significant volumes of travel and trade among Member States,

ASEAN countries have a vested interest in assessing disease burden as they move towards de-escalation of travel restrictions and other restrictions on movement. To increase transparency and build trust, we suggest that countries report not only the number of confirmed cases in their country, but also the number of people tested or tests performed, and the criteria for such testing.

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