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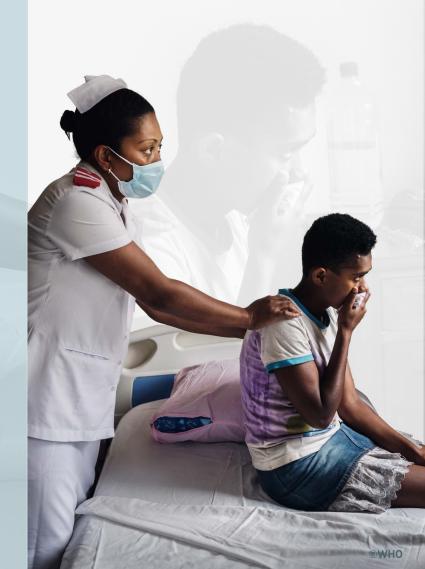
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# Using an online calculator to describe excess mortality in the Philippines during the COVID-19 pandemic

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**Objective:** Excess mortality is an indicator of the impact of the coronavirus disease (COVID-19) pandemic. This study aims to describe excess mortality in the Philippines from January 2020 to December 2021 using an online all-cause mortality and excess mortality calculator.

**Methods:** All-cause mortality datasets from 2015 to 2021 from the Philippine Statistics Authority were obtained and analysed using the World Health Organization Western Pacific Regional Office All-Cause Mortality Calculator. Expected mortality, excess mortality and P-scores were obtained using two models, 5-year averages and negative binomial regression, for total deaths and by administrative region.

Results: Reported national all-cause mortality exceeded the expected mortality in August 2020 and from January to November 2021, peaking in September 2021 at 104 per 100 000. Total excess mortality using negative binomial regression was -13 900 deaths in 2020 and 212 000 deaths in 2021, peaking in September 2021. P-scores were -2% in 2020 and 33% in 2021, again peaking in September 2021 at 114%. Reported COVID-19 deaths accounted for 20% of excess deaths in 2021. In 2020, consistently high P-scores were recorded in the National Capital Region from July to September and in the Bangsamoro Autonomous Region in Muslim Mindanao from June to July. In 2021, most regions recorded high P-scores from June to October.

**Discussion:** Tracking excess mortality using a robust, accessible and standardized online tool provided a comprehensive assessment of the direct and indirect impacts of the COVID-19 pandemic in the Philippines. Furthermore, analysis by administrative region highlighted the key regions disproportionately affected by the pandemic, information that may not have been fully captured from routine COVID-19 surveillance.

he coronavirus disease (COVID-19) pandemic has been ongoing since March 2020 and, as of early January 2023, there have been more than 666 million reported cases and more than 6.7 million reported deaths globally. The numbers of daily or weekly COVID-19 cases and deaths have been used to assess the impact of the pandemic. However, while data on COVID-19-related deaths have been widely reported, the quality, accuracy and timeliness of mortality data can be influenced by country-specific factors such as COVID-19 testing capacity, population and per capita income, and are often under-reported or delayed especially in low-income countries. Therefore, reported COVID-19 mortality data may not reflect the full impact of the pandemic. An assessment by the World Health

Organization (WHO) of 133 countries in 2020 found that almost 40% of the world's deaths were not registered.<sup>6</sup>

One method to standardize estimates of COVID-19 deaths is through measurement of excess mortality, defined as "the increase of all-cause mortality over the mortality expected based on historic trends". P-score is an associated index of excess mortality and represents the percentage of excess deaths relative to the expected deaths. In a 2020 study, excess mortality and P-scores were reported for most countries, particularly those in Central and South America, with global estimates of excess mortality for 2021 of 18.2 million people, more than three times the reported global COVID-19 deaths. Excess mortality and P-scores provide more realistic

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estimates of the true mortality during the COVID-19 pandemic, which includes estimates of underreported COVID-19 deaths as well as indirect deaths, that is, those from other diseases.8,9

The Philippines is an archipelagic lower middleincome country divided into 13 administrative regions (Map 1). Country data on mortality are available from both the Philippine Statistics Authority (PSA) and the Department of Health (DOH). The PSA data are obtained from death certificates, whereas the DOH data are obtained from mortality reports sent to the DOH Epidemiology Bureau. 10 There have been several reports on excess mortality in the Philippines, with low and negative excess mortality reported compared to other countries in the region;<sup>7,11</sup> one study also reported that the excess mortality rate in the Philippines was almost 3.5 times the recorded number of COVID-19 deaths.7

The World Health Organization Western Pacific Regional Office All-Cause Mortality Calculator ("ACM Calculator") is an open-source online tool developed to calculate expected all-cause mortality, excess mortality and P-scores from mortality data. All-cause mortality can also be calculated by age, sex and administrative state or region if the disaggregated mortality data are indexed in the calculator. The results can then be displayed using tables and graphs. The ACM Calculator estimates excess mortality and P-scores using two approaches: historical 5-year averages (5YA) and a non-parametric negative binomial regression (NBR) model.<sup>12</sup>

The aim of this study is to describe excess mortality in the Philippines at national and regional levels during the COVID-19 pandemic (2020 and 2021) using data generated by the ACM Calculator.

# **METHODS**

Mortality data from publicly available PSA reports<sup>13</sup> from 2015 to 2021 were obtained by year, month and region. These data were encoded into a blank template provided by the ACM Calculator website and used to generate the following statistics in the Calculator. 14,15

Expected all-cause mortality and 95% confidence intervals using 5YA. This statistic takes the monthly average and 95% confidence intervals of the reported mortality using data from 2015 to 2019.

Expected all-cause mortality and 95% prediction intervals using NBR. This statistic uses an NBR approach to estimate deaths for 2020 and 2021 using data from 2015 to 2019. This technique is preferred since it allows for overdispersion and can also account for low or zero counts. The mean parameter ( $\lambda t$ ) for the counts is modelled as

$$\log \lambda t = c(t) + trend(t) + Xt\beta$$

where c(t) is the annual cycle in all-cause mortality, modelled as a piecewise cyclic cubic spline function, trend(t) is the non-cyclic cubic spline function of all-cause mortality over time, and Xt is for arbitrary time-varying covariates.

Excess mortality. Excess mortality was calculated using the formula

excess mortality = reported mortality - expected mortality

and values were calculated per region and per month for 2020 and 2021. Excess mortality counts were computed using both 5YA and NBR expected mortality.

P-scores of excess mortality. P-score was calculated using the formula

$$P\text{-score} = \frac{excess\ mortality}{expected\ mortality} \ x\ 100$$

and is expressed as percentages. These values were calculated per region and per month for 2020 and 2021 and were also computed using both 5YA and NBR expected mortality.

Total excess mortality and P-scores were calculated using both 5YA and NBR expected mortality. However, only NBR was used to calculate excess mortality and P-scores per administrative region due to its increased accuracy and adoption by WHO.

Reported COVID-19 deaths per month for 2020 and 2021 were also extracted from the WHO coronavirus (COVID-19) dashboard. 16 The ratio of COVID-19 deaths to excess deaths was calculated using the formula

$$ratio = \frac{COVID-19 \ deaths}{excess \ mortality} \times 100$$

CAR REGION REGION II **REGION II REGION IV-A REGION V REGION IV** REGION **REGION** BARMM REGION XII

Map 1. Administrative map of the Philippines, 2019

BARMM: Bangsamoro Autonomous Region in Muslim Mindanao; CAR: Cordillera Administrative Region; NCR: National Capital Region. Map revised from Dakilang Isagani - Own work.

Source: authors; map adapted from Felipe\_Aira's Municipal and city map of the Philippines (CC BY-SA 4.0. See: https://commons.wikimedia.org/w/index. php?curid=81166427)

All raw data on reported mortality as well as calculated statistics were tabulated. Time-series line graphs for reported mortality, expected mortality and P-scores were generated, and box plots for excess mortality were created. Data entry, cleaning and processing were completed in Microsoft Excel.

# **RESULTS**

In 2020, reported mortality in the Philippines peaked during August at 52 per 100 000 population, with the lowest mortality rate reported in April at 41 per 100 000. In 2021, the peak occurred in September at 104 per 100 000, with the lowest rate observed for December at 44 per 100 000 (Fig. 1). The reported mortality for the Philippines exceeded the upper bound of the expected

mortality in August 2020 and from January to November 2021, while mortality was lower than expected in March and April 2020 and in December 2021 (Fig. 1).

The total excess mortality using the NBR method for the Philippines was -13 900 deaths, or -13 deaths per 100 000 population for 2020, and 212 900 deaths or 193 deaths per 100 000 population for 2021. P-scores were -2% for 2020 and 33% for 2021 (Table 1). The highest excess mortality (56 per 100 000 population) and P-score (114%) were recorded in September 2021. The calculated excess mortality was lower using NBR compared to 5YA across all time points (Table 1).

The ratio of reported COVID-19 deaths to calculated excess mortality was -66% in 2020 and 20% in 2021,

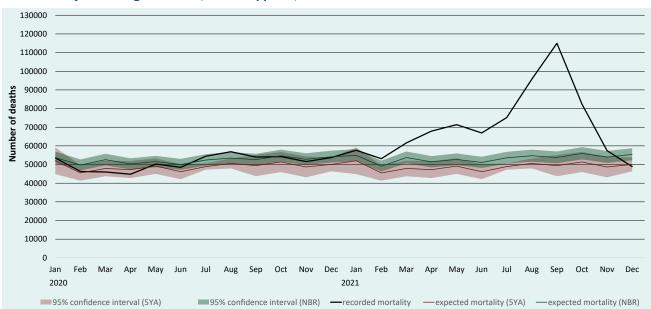


Fig. 1. Number of reported deaths and expected deaths calculated using the negative binomial regression and 5-year average methods, the Philippines, 2020 and 2021

5YA: 5-year average; NBR: negative binomial regression.

the latter suggesting that reported COVID-19 deaths in the country only accounted for about 20% of excess mortality in 2021. Monthly ratios ranged from -360% in October to 142% in September of 2020 (interquartile range = 56%) and from -44% in December to 159% in November of 2021 (interquartile range = 15%) (Fig. 2).

In the analysis by administrative region, only the National Capital Region (NCR) reported positive excess mortality of 14 100 deaths or 105 per 100 000 in 2020, while all administrative regions reported positive excess mortality in 2021 (Table 2). Overall, for both years, NCR had the highest excess mortality, with Region IV-A and Region III ranking second and third, respectively. The regions with the highest excess mortality rates in 2021 were Regions I, III and IV-A, while Bangsamoro Autonomous Region in Muslim Mindanao (BARMM) had the lowest excess mortality (Table 2).

When assessing P-scores per region per month for 2020 and 2021 (Fig. 3; Table 3), the top three highest monthly P-scores occurred in September 2021 from Region I at 183%, Region III at 160% and Region II at 153%. Up until June 2020, most regions had negative P-scores, whereas in June 2020 only three regions had negative P-scores. NCR had high P-scores (that is, greater than the 75th percentile) from July to September 2020, while BARMM had high P-scores in June and July. In 2021, there were high P-scores for most regions

from June to October, while NCR had high P-scores from March to May and from August to September. BARMM consistently had high P-scores from January to September 2021.

# DISCUSSION

By using the ACM Calculator, we showed that the reported all-cause mortality in the Philippines exceeded expectations in July and August 2020, which coincided with the peak of the country's second wave<sup>17</sup> in August 2020. Most months in 2021 recorded a higher mortality rate than expected, which peaked in September. This coincided with the spread of the Delta variant across the Western Pacific Region and throughout the country. 17

As there is a lack of published studies on excess mortality by region for the Philippines, we also calculated excess mortality and P-scores by administrative region. Unlike the results for the Philippines overall, most regions had negative P-scores during July and August 2020. However, the high P-scores in NCR, Region VII and BARMM contributed significantly to the total allcause mortality recorded during those months. BARMM and NCR recorded positive excess mortality and high P-scores consistently from the start of the pandemic despite having highly different local government structures, population demographics, population density and distribution, and even geospatial characteristics. During

Table 1. Reported number of deaths and number, rate and P-score of excess deaths calculated using the negative binomial regression and 5-year average methods, the Philippines, 2020 and 2021

Year and month	Reported mortality <sup>b</sup>	Excess deaths using binomial regre		Excess deaths using 5-year average method				
rear and month	Number (rate per 100 000 population)	Number (rate per 100 000 population) <sup>b</sup>	P-score (%)°	Number (rate per 100 000 population) <sup>b</sup>	P-score (%)°			
2020 total <sup>a</sup>	613 900 (563)	-13 900 (-13)	-2%	27 200 (25)	5%			
January	53 500 (49)	-200 (0)	0%	1500 (1)	3%			
February	46 300 (42)	-3500 (-3)	-7%	800 (1)	2%			
March	46 000 (42)	-6600 (-6)	-12%	-1900 (-2)	-4%			
April	44 800 (41)	-5500 (-5)	-11%	-2500 (-2)	-5%			
May	50 300 (46)	-1300 (-1)	-3%	1100 (1)	2%			
June	48 500 (44)	-1500 (-1)	-3%	2400 (2)	5%			
July	54 400 (50)	2000 (2)	4%	5600 (5)	11%			
August	56 800 (52)	3400 (3)	6%	6300 (6)	12%			
September	54 000 (49)	1400 (1)	3%	4600 (4)	9%			
October	54 200 (50)	-500 (0)	-1%	2900 (3)	6%			
November	51 600 (47)	-1200 (-1)	-2%	2900 (3)	6%			
December	53 700 (49)	-400 (0)	-1%	3700 (3)	7%			
2021 total <sup>a</sup>	853 100 (774)	212 900 (193)	33%	266 400 (242)	45%			
January	57 600 (52)	2700 (2)	5%	5600 (5)	11%			
February	53 100 (48)	4000 (4)	8%	7700 (7)	17%			
March	61 600 (56)	7900 (7)	15%	13 700 (12)	29%			
April	67 900 (62)	16 500 (15)	32%	20 700 (19)	44%			
May	71 400 (65)	18 600 (17)	35%	22 300 (20)	45%			
June	66 900 (61)	15 900 (14)	31%	20 800 (19)	45%			
July	75 200 (68)	21 600 (20)	40%	26 300 (24)	54%			
August	95 700 (87)	41 100 (37)	75%	45 200 (41)	89%			
September	115 000 (104)	61 200 (56)	114%	65 600 (60)	133%			
October	82 400 (75)	26 500 (24)	47%	31 100 (28)	61%			
November	57 400 (52)	3400 (3)	6%	8700 (8)	18%			
December	48 900 (44)	-6500 (-6)	-12%	-1100 (-1)	-2%			

<sup>&</sup>lt;sup>a</sup> Cumulative counts of excess mortality per year may not reflect the sum of values shown due to rounding.

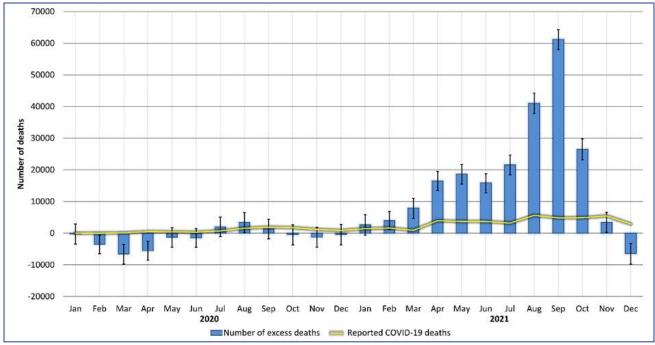
2021, most regions recorded positive excess mortality and P-scores for most months, and all contributed to the higher-than-expected national all-cause mortality rate reported in 2021. This provides further evidence of the country-wide spread of COVID-19 during 2021.

Overcrowding was identified as a factor affecting excess mortality in Chile. 18 In this study, regions with the highest population density (that is, NCR, Region III and Region V-A)<sup>19</sup> also had the highest total excess mortality from 2020 to 2021. A local study showed a strong positive correlation (r = 0.92) between COVID-19 deaths and regional population density, as well as between the number of intensive care unit beds and doctors absent due to being in quarantine (r = 0.92 and 0.85, respectively).<sup>20</sup> Regions III and IV-A border NCR with many workers regularly travelling to NCR from these regions, suggesting labour mobility may have also played a role in excess deaths. However, the above-mentioned local study found low correlation between mobility and COVID-19 deaths.<sup>20</sup> Aron et al. recommended supplementing region-based disaggregation analysis with analyses by age, sex and

b Mortality counts 100 and above were rounded to the nearest 100; mortality counts below 100 were rounded to the nearest 10; rates were rounded to the nearest integer.

<sup>&</sup>lt;sup>c</sup> P-scores were rounded to the nearest integer.

Reported COVID-19 deaths and number of excess deaths calculated using the negative binomial Fig. 2. regression method,<sup>a</sup> the Philippines, 2020 and 2021



<sup>&</sup>lt;sup>a</sup> Error bars represent the 95% prediction intervals.

Table 2. Number of excess deaths calculated using the negative binomial regression method by administrative region, the Philippines, 2020 and 2021

Region  NCR  Region I  Region II  Region III  Region IV-A  Region IV-B  Region V  Region VII  Region VIII  Region VIII  Region X  Region X  Region XI  Region XII  Region XIII	Number of excess deaths (rate per 100 000 population) by year <sup>a</sup>									
Region	2020	2021	2020 and 2021 <sup>b</sup>							
NCR	14 100 (105)	22 500 (161)	36 600							
Region I	-1800 (-33)	16 200 (304)	14 400							
Region II	-3200 (-86)	8900 (240)	5700							
Region III	-6600 (-53)	33 800 (270)	27 200							
Region IV-A	-6200 (-39)	2020 2021 4 100 (105) 22 500 (161) -1800 (-33) 16 200 (304) -3200 (-86) 8900 (240) -6600 (-53) 33 800 (270) -6200 (-39) 39 500 (241) -1900 (-58) 4800 (148) -5200 (-86) 9400 (152) -4100 (-52) 15 800 (198) -900 (-11) 15 500 (192) -2700 (-58) 7200 (150) -2100 (-55) 6900 (182) -2500 (-49) 6300 (124) -1400 (-27) 9000 (167) -1700 (-40) 8700 (174) -1900 (-69) 4200 (152) -90 (-2) 1300 (30)								
Region IV-B	-1900 (-58)	4800 (148)	2900							
Region V	-5200 (-86)	9400 (152)	4200							
Region VI	-4100 (-52)	15 800 (198)	11 600							
Region VII	-900 (-11)	15 500 (192)	14 600							
Region VIII	-2700 (-58)	7200 (150)	4600							
Region IX	-2100 (-55)	6900 (182)	4800							
Region X	-2500 (-49)	6300 (124)	3800							
Region XI	-1400 (-27)	9000 (167)	7600							
Region XII	-1700 (-40)	8700 (174)	7000							
Region XIII	-1900 (-69)	4200 (152)	2300							
BARMM	-90 (-2)	1300 (30)	1200							
CAR	-1200 (-65)	3400 (186)	2200							

BARMM: Bangsamoro Autonomous Region in Muslim Mindanao; CAR: Cordillera Administrative Region; NCR: National Capital Region.

a Mortality counts 100 and above were rounded to the nearest 100; mortality counts below 100 were rounded to the nearest 10; rates were rounded to the nearest integer.

<sup>&</sup>lt;sup>b</sup> Totals of excess mortality for 2020 and 2021 may not reflect the sum of values shown due to rounding.

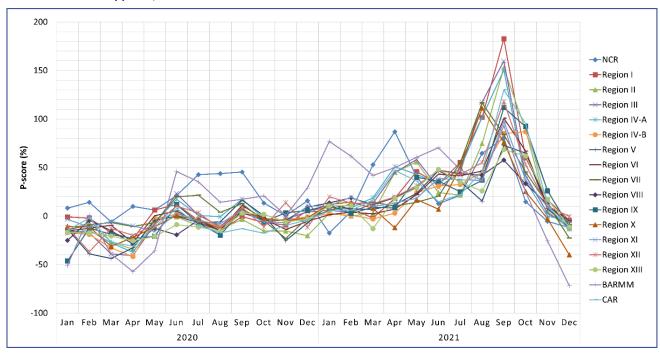


Fig. 3. P-scores<sup>a</sup> calculated using the negative binomial regression method by administrative region and month, the Philippines, 2020 and 2021

BARMM: Bangsamoro Autonomous Region in Muslim Mindanao; CAR: Cordillera Administrative Region; NCR: National Capital Region.

socioeconomic categories (such as inequality and urban density) to reveal "the effectiveness of different types of policy". <sup>21</sup> Nonetheless, an analysis disaggregated by region could contribute to the assessment of the impact of the COVID-19 pandemic, particularly by identifying specific areas that are disproportionately affected.

While this study showed that the patterns of allcause mortality and excess mortality were similar to reported COVID-19 deaths in the Philippines, these reported COVID-19 deaths only accounted for 20% of the excess mortality in 2021. A recent global study estimated this proportion at 29% for the Philippines from 2020 to 2021, compared to around 85% in high-income countries such as Belgium and Sweden.9 The Commission on Population and Development in the Philippines also acknowledged that COVID-19 was a major contributor to excess mortality in 2021.22 Discrepancies in excess deaths versus reported COVID-19 deaths suggest that there may be: (1) underreporting of actual COVID-19 deaths; (2) a large cohort of deaths indirectly caused by the pandemic that are not COVID-19 deaths; or (3) a combination of both. 23-27

Delays in reporting contribute to underreporting of COVID-19 deaths, as can the varying quality, intensity

and timing of testing and location of death. Early in the pandemic, data quality was recognized as a possible factor in underestimating COVID-19 deaths, especially in developing countries.<sup>3</sup> In some states in the United States of America, increases in excess deaths corresponded to increases in testing intensity.<sup>28</sup> In Italy, COVID-19 mortality data did not include deaths at home or in care facilities where COVID-19 testing was not routinely carried out.<sup>27</sup> The Philippines DOH released several advisories which acknowledged delays in reporting of COVID-19 mortality data, citing logistical delays from local government units and health-care providers as well as technical issues with the information system as possible reasons for delayed reporting. 29,30 Often considered the most reliable epidemic indicator internationally, reporting of daily deaths may be unreliable and may peak at times that appear contradictory to patterns of confirmed cases.31

Indirect deaths caused by the pandemic also contribute to the excess mortality counts, <sup>11,32</sup> but the exact proportion of indirect deaths is difficult to ascertain, varying by country, state or even locality. Based on our study, indirect deaths appear to be a significant contributor to excess mortality, possibly responsible for as much as 80% of the excess deaths in 2021. In one

<sup>&</sup>lt;sup>a</sup> P-scores were rounded to the nearest integer.

Table 3. P-scores<sup>a</sup> calculated using the negative binomial regression method by administrative region and month, the Philippines, 2020 and 2021

	P-score (%), 2020											
Region	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
NCR	8	14	-6	10	6	21	43	44	45	13	0	16
Region I	-1	-2	-17	-24	6	12	-5	-15	-1	-7	-9	6
Region II	-15	-7	-27	-34	-2	-1	-10	-14	-3	-15	-15	-20
Region III	-15	-17	-39	-41	-8	23	1	-11	8	-7	-3	4
Region IV-A	-17	-15	-28	-37	-7	17	1	-1	17	-3	-4	-4
Region IV-B	-17	-19	-33	-42	-3	2	-3	-12	3	-3	-4	-1
Region V	-13	-39	-44	-33	-4	0	-7	-6	16	0	-25	-7
Region VI	-15	-13	-10	-28	0	5	-7	-15	11	-3	-14	-6
Region VII	-14	-9	-7	-11	-7	20	21	4	13	-5	-23	-2
Region VIII	-25	-4	-15	-29	-13	-19	-4	-15	3	-4	-5	9
Region IX	-46	-12	-19	-23	-21	12	-7	-20	6	-6	3	6
Region X	-11	-11	-31	-22	-11	0	-4	-13	6	-3	-5	-2
Region XI	-3	-11	-6	-10	-16	3	-5	-8	6	-6	-7	10
Region XII	-12	-37	-13	-20	-9	10	3	-13	9	-11	14	-12
Region XIII	-17	-17	-21	-25	-21	-9	-11	-15	3	2	-6	-3
BARMM	-51	1	-39	-57	-36	46	35	14	17	21	1	29
CAR	-15	-2	-27	-31	-11	8	-9	-17	-13	-18	-10	-4
					P-score (%	6), 2021						
Region	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
NCR	-17	5	53	87	40	13	21	65	80	15	-5	-12
Region I	9	7	-2	18	46	33	55	102	183	60	17	-4
Region II	3	0	3	45	56	24	22	75	153	88	5	-13
Region III	6	4	13	45	58	29	45	117	160	42	3	-11
Region IV-A	6	8	19	51	43	33	49	102	151	36	0	-5
Region IV-B	2	1	-3	3	24	31	32	45	85	87	27	-12
Region V	12	7	7	12	23	47	35	15	73	65	8	-12
Region VI	1	4	2	7	22	43	42	46	101	67	10	-5
Region VII	6	12	14	10	14	20	55	117	84	45	12	-23
Region VIII	14	19	12	19	30	47	44	42	58	33	12	-10
Region IX	11	3	9	8	40	36	25	37	112	92	26	-11
Region X	12	14	8	-12	17	7	50	111	76	25	-3	-40
Region XI	10	20	10	13	18	39	37	37	98	37	9	-11
Region XII	20	13	13	20	31	47	43	55	118	53	10	0
Region XIII	10	11	-13	18	29	48	35	26	68	62	17	-11
BARMM	77	62	42	50	61	70	48	37	93	25	-26	-72
CAR	5	6	17	47	36	15	22	46	130	95	12	-15

BARMM: Bangsamoro Autonomous Region in Muslim Mindanao; CAR: Cordillera Administrative Region; NCR: National Capital Region.

<sup>&</sup>lt;sup>a</sup> P-scores were rounded to the nearest integer.

study in the United States of America, drug overdoses, homicides, suicides and unintentional injuries may have contributed to non-COVID-19 excess deaths in 2020,<sup>25</sup> while a study in Latvia documented varying noncommunicable diseases contributing to excess mortality, such as circulatory diseases, neoplasms, diabetes mellitus and chronic lower respiratory diseases. 33 Data from the Philippines on non-COVID-19 causes of death in 2021 compared to 2020 showed increases in deaths due to ischaemic heart disease (30%), cerebrovascular disease (15%), diabetes mellitus (21%), hypertensive disease (32%) and malnutrition (47%).<sup>22</sup> Cancer-related deaths decreased by 10%, but this was partly attributed to "COVID[-19] cases [crowding] out actual and undiagnosed cancer patients".22

Excess mortality is often calculated using two general models: historical (for example, 5-year) averages and NBR. NBR models can be used for data with low or zero counts, and can account for overdispersion, seasonal fluctuations within a given year, secular trends in data, reporting delays and other time-sensitive covariates, such as internal and external movement of populations or periods with low reporting activities (for example, holidays).7,12,14 Although we used both models to calculate total excess mortality, our analysis focused on the NBR model for two reasons: (1) the accuracy of the NBR model in the ACM Calculator was validated in its documentation; 14 and (2) WHO recently released a document detailing the use of regression models in estimating excess mortality data. 15

The cumulative 2020–2021 excess mortality estimates from our study using the NBR estimate (199 000) was closer to the estimate (184 000) from a 2022 global study<sup>9</sup> from the same time period which used Poisson modelling and a recent WHO-modelled estimate (185 300) as reported in May 2022.<sup>24</sup> Our result using the 5YA model (293 600) was closer to the projected excess deaths (254 897) from a local presentation which also used historical averages and mid-2021 data. 32 Variations in study findings are often influenced by the completeness and reliability of the all-cause mortality data used as well as backward revisions of preliminary data.<sup>7</sup> Although the trend of excess deaths from both methods used in this study were consistent, the total number of excess deaths differed, suggesting that analysis of excess mortality data should take into account the method used to calculate the excess deaths.

There were several limitations to this study. Mortality reporting systems do not cover all deaths, especially in low-resource settings, with civil registration of deaths noted to be as low as 20% in some low- and middleincome countries. Additionally, mortality data are often preliminary which suggests that the earlier data may be more incomplete. The ACM Calculator assumes that reported counts are the actual values and that reports are complete and accurate, but it does not currently account for reporting delays. This may explain the overestimation of our data compared to studies from older datasets. Therefore, the results of the ACM Calculator should be interpreted with caution, particularly when there are timeliness issues and reporting delays. 12,14 Second. our dataset did not contain disaggregated data on age, sex and other factors associated with excess mortality, which limited our analysis to administrative regions. Lastly, we were not able to account for regional variations in testing and reporting accuracy and capacity that may have influenced the dataset.

Analysing excess mortality provided a more comprehensive picture of the direct and indirect impacts of the COVID-19 pandemic in the Philippines. While the pattern of excess mortality was similar to reported COVID-19 deaths, the reported COVID-19 deaths only accounted for a small proportion of excess deaths. We therefore recommend incorporating excess mortality analysis during surveillance of similar events such as outbreaks and pandemics. Our analysis by administrative region highlighted the key regions disproportionately affected by the pandemic, which is information that may not have been fully captured from national COVID-19 surveillance. We recommend that excess mortality be calculated using age- and sex-disaggregated data, as well as other studies on the indirect factors that may contribute to excess mortality. Standardizing the methods of analysing and reporting excess mortality would assist in contextualizing information from different sources. We also recommend the use of open-source tools such as the ACM Calculator to monitor excess mortality especially in low-resource countries, as these tools can provide standardized and timely information that may help decision-makers to optimize the use of health resources and subsequently contribute to the achievement of Sustainable Development Goals in strengthening the capacity of developing countries for early warning, risk reduction and management of national and global health risks.

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# Conflicts of interest

The authors have no conflicts of interest to declare.

#### Ethics statement

The study was reviewed and approved on 1 July 2022 by the Ateneo School of Medicine and Public Health Research Ethics Committee under the study protocol ID: SMPH Mortality 2022.

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# Epidemiology of dengue reported in the World Health Organization's Western Pacific Region, 2013–2019

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The global burden of dengue, an emerging and re-emerging mosquito-borne disease, increased during the 20-year period ending in 2019, with approximately 70% of cases estimated to have been in Asia. This report describes the epidemiology of dengue in the World Health Organization's Western Pacific Region during 2013–2019 using regional surveillance data reported from indicator-based surveillance systems from countries and areas in the Region, supplemented by publicly available dengue outbreak situation reports. The total reported annual number of dengue cases in the Region increased from 430 023 in 2013 to 1 050 285 in 2019, surpassing 1 million cases for the first time in 2019. The reported case-fatality ratio ranged from 0.19% (724/376 972 in 2014 and 2030/1 050 285 in 2019) to 0.30% (1380/458 843 in 2016). The introduction or reintroduction of serotypes to specific areas caused several outbreaks and rare occurrences of local transmission in places where dengue was not previously reported. This report reinforces the increased importance of dengue surveillance systems in monitoring dengue across the Region.

he global burden of dengue, an emerging and reemerging mosquito-borne disease, increased from 2000 to 2019. An estimated 70% of dengue virus infections are thought to occur in Asia.2 It has previously been reported that in the World Health Organization's (WHO's) Western Pacific Region, the number of dengue cases increased from approximately 200 000 in 2008 to more than 450 000 in 2015.3 During this period, several countries and areas in the Region experienced large-scale outbreaks.4-6

Dengue is a public health threat because it is associated with large outbreaks in communities, severe disease and mortality. Host immunity factors, such as serotype interaction, antibody-dependent enhancement and cross-immunity, complicate the clinical course, which leads to challenges in managing severe cases. 1,7 Additionally, socioeconomic and environmental factors,

including climate change, drive disease transmission and complicate prevention and control activities.

In response to these challenges, a revised Western Pacific Regional Action Plan for Dengue Prevention and Control was developed and endorsed at the 67th meeting of the Regional Committee for the Western Pacific in October 2016.<sup>3</sup> The Plan has guided countries and areas in the Region on improving the laboratory diagnosis of dengue, and the clinical management, surveillance and sustainable vector management for the disease to reduce morbidity and mortality, and decrease impacts on health systems.

Sharing information and data about dengue helps countries and areas better understand transmission patterns and supports the implementation of dengue prevention and control measures.<sup>2</sup> As a continuation of

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- World Health Organization Representative Office for Lao People's Democratic Republic, Vientiane, Lao People's Democratic Republic.
- Division of Programmes for Disease Control, World Health Organization Regional Office for the Western Pacific, Manila, the Philippines.
- World Health Organization Representative Office for Viet Nam, Hanoi, Viet Nam.
- World Health Organization Representative Office for China, Beijing, China.
- World Health Organization Representative Office for Cambodia, Phnom Penh, Cambodia.
- World Health Organization Representative Office for the Philippines, Manila, the Philippines.
- Division of Pacific Technical Support, World Health Organization, Suva, Fiji.
- World Health Organization Representative Office for Malaysia, Cyberjaya, Malaysia.

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previous Regional dengue epidemiology updates in 2010, 2011 and 2012,8-10 this analysis reports data collated by the WHO Regional Office for the Western Pacific to describe the epidemiology of dengue in the Region from 2013 to 2019 using regional surveillance data. Data from 2020 to 2021 were excluded due to changes in reporting practices, population movement and people's behaviours as a result of the COVID-19 pandemic.

# **METHODS**

Regional dengue data from 2013 to 2019 were collated from indicator-based surveillance systems from countries and areas in the Region. Information was also collected about laboratory sampling schemes and the confirmation methods used by each country and area. Data were either sent to WHO by ministries of health or collected from official websites where they were publicly available. Additional data - including serotype information, case definitions, and the numbers of clinically confirmed cases, laboratoryconfirmed cases and imported cases and deaths - were provided by Australia, Cambodia, Japan, the Republic of Korea, Malaysia, New Zealand, Pacific Island countries and areas (PICs), the Philippines, Singapore and Viet Nam. Information was reported based on the standard dengue case definitions used in each country or area (Table 1). Missing data were supplemented by using official dengue outbreak situation reports published on ReliefWeb (https:// reliefweb.int/), manuscripts identified through PubMed using keywords ["dengue" AND "outbreak" AND "(country/ area name)"], yearly aggregated data collected from all countries and areas in the Region through International Health Regulations (2005) channels, and WHO Regional biweekly dengue reports.<sup>11</sup>

Table 1 summarizes the dengue surveillance systems, case definitions, laboratory sampling methods and serotype data. It was not possible to compare trends between countries and areas due to the differences in surveillance methods and reporting practices. The crude regional case notification rate per 100 000 population per year was calculated using the number of cases and deaths reported to WHO and standard calculation methods:

Case notification rate per 100 000 population per year  $= (c/p) \times 100\ 000$  and

> 95% confidence interval =  $(100\ 000/p)$  $(c \pm 1.96 \times \sqrt{c}),$

where c is the total dengue notification case count in a given year and p is the population estimate for the Region in a given year. United Nations population estimate data were used for calculations. Population data for the Pitcairn Islands were not included in the United Nations population database.12 Therefore, we used the closest population estimates based on the Pitcairn Islands' government website. In this report, an outbreak is defined as the "occurrence of cases of disease in excess of what would normally be expected in a defined community, geographical area or season". 13

# RESULTS

In the Region, the total number of annual dengue cases reported increased from 430 023 cases from 22 countries and areas in 2013 to 1 050 285 cases from 18 countries and areas in 2019 (data not shown). The lowest annual number of cases during these 7 years was reported in 2014, with 376 972 cases. In 2019, the total number of reported dengue cases surpassed 1 million for the first time. From 2013 to 2019, the case-fatality ratio (CFR) fluctuated between 0.19% (724/376 972 reported in 2014 and 2030/1 050 285 in 2019) and 0.30% (1380/458 843 reported in 2016) (Fig. 1). The number of cases reported from the PICs did not show a clear trend, with more cases reported in 2013 and 2014 compared with 2015 and 2016 (Fig. 2). There were challenges in calculating the CFRs for some countries due to limited reporting on dengue cases or deaths associated with dengue, or both.

From 2013 to 2018, the crude annual case notification rates in the Region ranged from a low of 19.82/100 000 population per year (95% confidence interval [CI]: 19.76–19.89) in 2014 to a high of 26.84/100 000 population per year (95% CI: 26.77-26.92) in 2015. In 2019, the case notification rate increased two-fold to 53.71/100 000 population per year (95% CI: 53.61-53.81) (Table 2).

From 2013 to 2019, large-scale outbreaks with notable increases in the number of cases were reported in multiple countries. Outbreaks were reported from the PICs every year from 2013 to 2019. There were two notable years, 2017 and 2019, when multiple outbreaks were reported across the Region, including in the PICs, with seven countries reporting outbreaks. All dengue serotypes (DENV-1, DENV-2, DENV-3 and DENV-4)

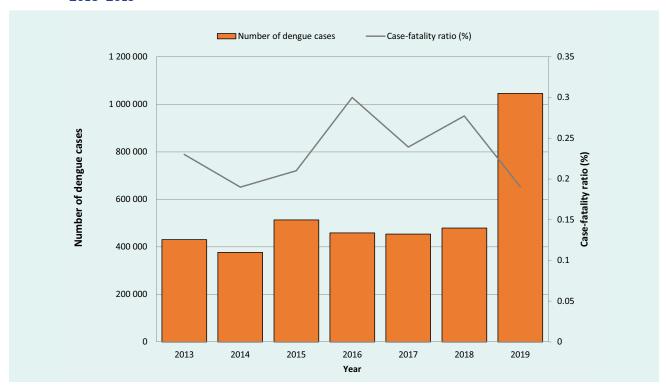
Table 1. Dengue clinical case definitions, and laboratory sampling and testing methods used for surveillance in countries, WHO Western Pacific Region, 2019

	Case definition <sup>a</sup>							
Country	Clinically confirmed case	Laboratory confirmation required	Laboratory sampling and testing method	Surveillance and case reporting				
Australia <sup>46</sup>	Fever, headache, arthralgia, myalgia, rash, nausea or vomiting	Yes	NS1, IgG seroconversion, IgM detection, nucleic acid or virus isolation.  All clinically diagnosed cases have laboratory testing.	All confirmed cases require both laboratory-definitive evidence and clinical evidence.  Both confirmed and probable cases are				
Cambodia <sup>47</sup>	Suspected dengue: high fever (39–40 °C) for 2–7 days (usually 3–4 days), with two or more of the following signs: flushed face, headache, retroorbital pain, myalgia or arthralgia, cutaneous rash, haemorrhagic signs (e.g. petechiae, positive tourniquet test) and leucopoenia  Probable dengue: signs of suspected dengue plus laboratory test results (right column) or a case that occurred in an area where a dengue case has been confirmed	No	Data are collected for the Cambodia Laboratory Information System, composed of 32 hospital laboratories where NS1 detection is conducted.  Laboratory testing: Antibody haemagglutination inhibition ≥1/1280 or IgM- or IgG-positive by ELISA in convalescent serum.	nationally notifiable.  Suspected cases are reported from all national hospitals and all provincial hospitals, but not from private clinics.				
China <sup>b</sup>	More than two of the following symptoms: acute onset fever, severe headache, orbital pain, myalgia, arthralgia, fatigue, a history of travel in a dengue-endemic area during the 15 days before symptom onset or cohabitation with an individual with confirmed dengue, or no travel history but with a rash or positive tourniquet test AND leucopoenia or thrombocytopenia or serum IgM positivity	No	Real-time PCR, NS1 in acute-phase serum or virus isolation from an acutely infected patient's serum.	Both clinically confirmed and laboratory-confirmed cases are notified as an infectious disease.				
Japan <sup>48</sup>	Symptoms including acute onset of fever lasting for 2–7 days (commonly biphasic), headache, retro-orbital pain, arthralgia, myalgia, fatigue, conjunctivitis or rash AND laboratory confirmation (right column)	Yes	All clinically diagnosed cases have laboratory testing. Laboratory confirmation requires at least one of the following: a positive PCR test, NS1 detection, serology (IgM, seroconversion) and/or virus isolation.	All reported cases have laboratory testing.				
Lao People's Democratic Republic <sup>22</sup>	WHO 2009 dengue case classification <sup>c</sup>	No	Laboratory testing is conducted by RDT and PCR on a subset of specimens referred to the laboratories. Serotyping is also conducted on a subset of specimens.	Clinically confirmed cases (dengue with and without warning signs and severe dengue cases) are reported.				
Malaysia <sup>49</sup>	WHO 2009 dengue case classification <sup>c</sup>	Yes	All suspected cases are tested by the rapid combo test for NS1, IgM and IgG; ELISA for the dengue antigen and serology, real-time PCR for detecting viral RNA, or by viral isolation.	All reported cases have laboratory testing.				
New Zealand <sup>31,50</sup>	Acute onset of fever; headache, particularly retro-orbital; myalgia and arthralgia; and a fine rash, which may be itchy and usually begins on the extremities but spares the palms and soles. Other symptoms include weakness, depression, anorexia, abnormal taste, sore throat, coughing, vomiting and abdominal pain.	No	At least one of the following tests is required for laboratory confirmation: viral isolation, dengue virus (DENV) nucleic acid amplification, IgM or IgG seroconversion, a significant increase in antibodies (four-fold or greater) by serological test.	Both clinically confirmed and laboratory-confirmed cases are reported.				

Philippines <sup>51–53</sup>	WHO 2009 dengue case classification <sup>c</sup>	No	A subset of suspected cases have laboratory testing.	Suspected cases are reported.
	In addition, suspected cases are those who were previously well but have acute febrile illness for 2–7 days		Confirmed dengue is defined as a suspected case with positive viral culture isolation and/or PCR.	
	with clinical signs and symptoms of dengue.		Probable dengue cases are NS1- or IgM-positive.	
Republic of Korea <sup>54</sup>	Acute onset of fever, headache, arthralgia, myalgia, leucopoenia, thrombocytopenia or bleeding AND laboratory confirmation (right column)	Yes	All clinically diagnosed cases have laboratory testing by real-time PCR or ELISA (IgM).	All reported cases have laboratory testing.
Singapore <sup>55</sup>	A clinical case meets the criteria of fever, headache, backache, myalgia, rash, abdominal discomfort and thrombocytopenia.	Yes	Samples are tested by the laboratory as ordered by the physician. Laboratory confirmation is done by dengue NS1 antigen testing, IgM or PCR.	All reported cases have laboratory testing.
Viet Nam <sup>56</sup>	Acute onset of fever lasting 2–7 days AND at least two of the following: haemorrhagic manifestation or presentation, headache, loss of appetite, nausea, vomiting, rash, muscle pain, joint pain, orbital pain, lethargy, abdominal pain	No	MAC-ELISA is conducted for at least 7% of clinical cases and virus isolation is conducted for at least 3% of clinical cases. In an outbreak, at least 5–10 suspected cases are tested.	Both clinically confirmed and laboratory-confirmed cases are reported.

ELISA: enzyme-linked immunosorbent assay; IgG: immunoglobulin G; IgM: immunoglobulin M; MAC-ELISA: dengue IgM capture ELISA; NS1: rapid antigen diagnostic test to detect dengue virus non-structural protein; PCR: polymerase chain reaction; RDT: rapid diagnostic test.

Fig. 1. Number of dengue cases and case-fatality ratios reported to WHO from the Western Pacific Region, 2013-2019



a Only the minimum criteria required for fulfilling a clinical definition of dengue are included here; any additional signs and symptoms required for more severe forms are not listed.

<sup>&</sup>lt;sup>b</sup> Data sourced from WHO internal communications.

e In the WHO 2009 dengue classification system, a probable case is any case with fever and two or more of the following: nausea, vomiting, rash, aches and pains, positive tourniquet test, leucopoenia or any warning sign. A case with warning signs is defined as a clinically diagnosed case if they have any of the following: abdominal pain or tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleeding, lethargy, restlessness, liver enlargement >2 cm, or increase in haematocrit concurrent with rapid decrease in platelet count. Severe dengue is defined as severe plasma leakage leading to any of the following: shock, fluid accumulation with respiratory distress OR severe bleeding as evaluated by clinician OR severe organ involvement of the liver (i.e. aspartate amino transferase or alanine amino transferase ≥1000 units/L), central nervous system (i.e. impaired consciousness), heart or other organs.

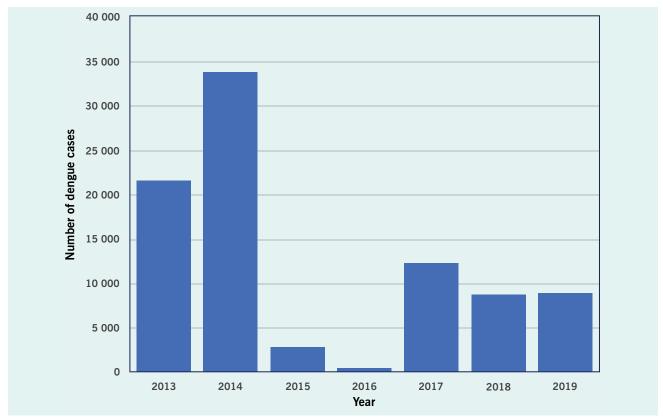


Fig. 2. Number of dengue cases reported to WHO from Pacific Island countries and areas, Western Pacific Region, 2013-2019

The data included in this figure are a subset of the data presented in Fig. 1.

were reported in the Region during the review period. Concurrent infections with two serotypes were reported in some countries. While some countries reported the same predominant serotype from 2016 to 2018, others reported changes in the predominant serotype. Additionally, there were reports of the introduction of a new serotype or switch in the predominant serotype, which was subsequently followed by outbreaks. Rare cases of autochthonous transmission were reported in countries where most previously reported cases had been imported.

Laboratory sampling schemes and confirmation methods varied by country and area. Some countries in this report were using the 2009 WHO dengue case classification system: 14 (i) dengue without warning signs; (ii) dengue with warning signs that include abdominal pain or tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleeding, lethargy or restlessness,

liver enlargement and increase in haematocrit with a rapid decrease in platelet count; and (iii) severe dengue, which is characterized by severe plasma leakage, severe haemorrhage and severe organ impairment. Other countries used other case definitions (Table 1). Some countries and areas in the Region report all identified cases of dengue, whereas others report only dengue cases at sentinel sites. In addition, some countries and areas conduct active surveillance or vector surveillance, or both (Table 1).

# Reporting by country and area

Data for dengue cases were available from 35 countries and areas during this study period, including eight with complete case and death data for all years of this study (Table 3). Data were not available for three countries and areas: the Northern Mariana Islands, the Pitcairn Islands and Tokelau.

Table 2. Crude regional case notification rates for dengue reported to WHO from the Western Pacific Region, 2013-2019

Year	Number of cases reported in the Region	Population in the Region <sup>a</sup>	Case notification / 100 000 population per year <sup>b</sup>	95% confidence interval
2013	430 023	1 889 727 401	22.76	22.69–22.82
2014	376 972	1 901 609 413	19.82	19.76–19.89
2015	513 574	1 913 189 733	26.84	26.77–26.92
2016	458 843	1 924 437 124	23.84	23.77–23.91
2017	454 231	1 935 317 876	23.47	23.40-23.54
2018	479 263	1 945 715 729	24.63	24.56–24.70
2019	1 050 285	1 955 495 216	53.71	53.61-53.81

<sup>&</sup>lt;sup>a</sup> Population data were extracted from United Nations population estimates. <sup>12</sup>

# Asia subregion

# Brunei Darussalam

Brunei Darussalam reported to WHO 2025 cases in 2013 and 436 cases and 2 deaths (CFR: 0.46%) in 2014. Reports for other years were not available.

#### Cambodia

During 2013-2019, Cambodia annually reported from 6372 to 68 597 suspected cases and from 3 to 59 deaths. The highest number of cases was reported during an outbreak in 2019 that peaked between June and August, with more than 5000 cases reported in epidemiological week 26.15,16 The highest number of deaths (59) was reported in 2013 (CFR: 0.34%).

In Cambodia, serotyping was conducted from sentinel laboratory surveillance at five sentinel sites. The predominant serotype reported from 2013 to 2015 was DENV-1, and in 2016, it switched to DENV-2. From the end of 2017 to the end of 2019, the predominant serotype switched back to DENV-1. This latter serotype switch preceded the large-scale outbreak in 2019, during which 73% (details on numerators and denominators are not available) of all serotyped samples between January and July 2019 were DENV-1, and the next most common serotype was DENV-2 (25%), followed by DENV-4 (2.2%) and DENV-3 (0.3%).

# China

During 2013-2019, China annually reported from 2050 to 46 864 cases (including both clinically and laboratoryconfirmed cases) and from 0 to 6 deaths. The highest number of cases and deaths were reported in 2014, with 46 864 cases and 6 deaths (CFR: 0.01%).

Several outbreaks were reported from the southern and central regions of China. Yunnan Province in 2013 reported 1245 cases with 136 that were laboratoryconfirmed, no deaths, and a predominant serotype of DENV-3;17 Henan Province in 2013 reported 106 suspected cases, 73 confirmed cases and no deaths, with the predominant serotype being DENV-3;18 Guangdong Province in 2014 accounted for more than 40 000 cases, including 1942 cases that were laboratory-confirmed and hospitalized and 2 deaths, where the predominant serotype among cases was DENV-1.6

The introduction of a new serotype in China in 2017 caused an outbreak of 1138 autochthonous cases after multiple clades of DENV-2 were introduced to Hangzhou, Zhejiang Province, in a short period. 19 During 2013-2019, Hong Kong Special Administrative Region, China, annually reported between 102 and 163 cases. During 2013-2019, Taiwan, China, annually reported between 10 and 43 467 cases, with the highest number of cases reported in 2015. During 2013-2018,

<sup>&</sup>lt;sup>b</sup> Crude notification rates in the Region should be interpreted with caution, considering that the risks of disease and population sizes vary substantially across the Region, as well as the surveillance systems used to determine cases of dengue.

Table 3. Number of dengue cases (including imported cases), number of dengue-attributed deaths and case-fatality ratios reported to WHO from the Western Pacific Region, 2013–2019<sup>a</sup>

Country or area											Year										
		2013			2014			2015			2016			2017			2018			2019	
	No. of cases	No. of deaths	CFR (%)	No. of cases	No. of deaths	CFR (%)	No. of cases	No. of deaths	CFR (%)	No. of cases	No. of deaths	CFR (%)	No. of cases	No. of deaths	CFR (%)	No. of cases	No. of deaths	CFR (%)	No. of cases	No. of deaths	CFR (%)
Asia subregion																					
Brunei Darussalam	2025	=	=	436	2	0.46	=	=	=	=	=	=	=	=	=	=	=	=	=	=	=
Cambodia	17 533	59	0.34	3684	21	0.57	15 412	-	-	12 843		-	6372	3	0.05	24 684	23	0.09	68 597	48	0.07
China	4663	0	0.00	46 864	6	0.01	3858	0	0.00	2050	0	0.00	5893	2	0.03	5136	1	0.02	22 188	3	0.01
China, Hong Kong Special Administrative Region	103	0	0.00	112	0	0.00	114	0	0.00	124	-	-	102	-	-	163	-	-	198	=	-
China, Macao Special Administrative Region	9	_	-	17	0	0.00	3	0	0.00	11	_	-	17	_	_	18	-	_	_		-
China, Taiwan	596	-	-	15 509	0	0.00	43 467	0	0.00	381	-	-	10	-	-	183	-	-	100	-	-
Japan	249	0	0.00	341	0	0.00	293	0	0.00	338	1	0.30	245	0	0.00	201	0	0.00	463	0	0.00
Lao People's Democratic Republic	44 250	95	0.21	1716	0	0.00	1959	0	0.00	5618	10	0.18	11 067	14	0.13	6446	19	0.29	39 091	76	0.19
Malaysia	43 346	92	0.21	108 698	215	0.20	120 836	336	0.28	109 037	237	0.22	89 487	177	0.20	81 360	147	0.18	130 101	147	0.11
Mongolia	0	0	NA	0	0	NA	0	0	NA	-	-	=	=	-	=	=	=	-	-	=	=
Philippines	204 906	660	0.32	113 485	425	0.37	213 930	647	0.30	220 518	1092	0.50	152 224	811	0.53	216 190	1083	0.50	437 563	1689	0.39
Republic of Korea	251	0	0.00	164	0	0.00	259	0	0.00	313	0	0.00	171	0	0.00	159	0	0.00	273	0	0.00
Singapore	22 170	8	0.04	18 326	6	0.03	11 294	6	0.05	13 085	12	0.09	2767	2	0.07	3283	6	0.18	15 999	3	0.02
Viet Nam	66 322	42	0.06	31 848	30	0.09	97 484	62	0.06	91 609	28	0.03	172 232	40	0.02	131 447	27	0.02	320 702	54	0.02
Total for subregion	406 423	956	0.24	341 200	705	0.21	508 909	1051	0.21	455 927	1380	0.30	440 587	1049	0.24	469 270	1306	0.28	1 035 275	2020	0.20
Pacific subregion																					
American Samoa	_	_	_	_	_	_	479	4	0.84	0	0	0.00	_	_	_	_	-	_	_	-	_
Australia	1841	0	0.00	1721	0	0.00	1716	0	0.00	2237	0	0.00	1132	1	0.09	917	0	0.00	1463	1	0.07
Cook Islands	_	_	_	946	0	0.00	765	0	0.00	0	_	_	0	_	_	0	_	_	126	0	0.00
Fiji	352	0	0.00	26 595	16	0.06	-	-	-	398	0	0.00	2699	9	0.33	4000	9	0.23	2500	0	0.00
French Polynesia	1523	0	0.00	2155	0	0.00	_	_	_	_	_	_	_	_	-	_	_	_	2400	0	0.00
Guam	=	-	=	-	_	_	=	-	-	=	=	=	-	-	-	_	-	_	23	-	_
Kiribati	=	_	_	_	_	_	_	_	_	0	_	_	0	_	_	1899	2	0.11	_	_	_
Marshall Islands	_	-	_	-	_	_	-	_	-	-	_	_	_	_	_	_	_	_	1635	1	0.06
Micronesia (Federated States of)	217	0	0.00	14	0	0.00	1	0	0.00	90	0	0.00	0	_	_	0	_	_	1464	1	0.07
Nauru	_	_	_	251	_	_	_	_	_	0	_	_	964	3	0.31	114	0	0.00	_	_	_
New Caledonia	9958	4	0.04	_	_	_	_	_	_	_	_	_	4200	11	0.26	1997	0	0.00	3916	2	0.05
New Zealand	106	0	0.00	179	0	0.00	125	0	0.00	191	0	0.00	161	0	0.00	294	0	0.00	224	0	0.00
Niue	_	_	_	_	_	_	_	_	_	0	_	_	2	_	_	_	_	_	_	_	_
Northern Mariana Islands	=	=	=	=	-	_	=	_	=	=	=	=	_	-	=	_	=	_	-	=	=
Palau	9	0	0.00	13	2	15.38	20	0	0.00	_	_	_	440	5	1.14	570	2	0.35	737	3	0.41
Papua New Guinea	=	_	=	6	_	_	=	_	-	-	-	-	_	_	_	_	=	_	_	=	_
Pitcairn Islands	-	_	_	_	_	_	-	_	_	_	_	-	_	_	_	_	_	_	_	_	_
Samoa	_	_	_	_	_	_	_	_	_	-	-	-	2724	5	0.18	_	_	_	_	_	_
Solomon Islands	9500	8	0.08	1872	1	0.05	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_
Tokelau	_	_	_			_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_
Tonga	_	_	_	51	0	0.00	1559	0	0.00	_	_	_	100	0	0.00	_	_	_	_	_	_
Tuvalu	=	=	=	408	=	=	=	_	=	=	=	=	=	=	=	=	=	_	522	2	0.38
Vanuatu	_	_	_	1561	_	_	_	_	_	_	_	_	>1000	_	_	_	_	_	_	_	-
Wallis and Futuna	94		_	-	_	_		_		_	_	_	222	0	0.00	202	_	_	_	_	_
Total for subregion	23 600	12	0.05	35 772	19	0.05	4665	4	0.09	2916	0	0.00	13 644	34	0.23	9993	13	0.13	15 010	10	0.05
	_5 555		0.00	55 , , <u>L</u>		0.00	,000		0.03			0.00	20 0 17	-	0.20	2333		0.10	10 010		0.03

CFR: case-fatality ratio; NA: cannot be calculated

<sup>&</sup>lt;sup>a</sup> The – symbol indicates that no data were available.

Macao Special Administrative Region, China, annually reported between 3 and 18 cases.

#### Japan

During 2013-2019, Japan annually reported between 201 and 463 laboratory-confirmed cases, with 1 death reported in 2016. In 2014, an outbreak of 162 autochthonous dengue cases was reported for the first time in nearly 70 years, of which more than 90% (148/160, from available data) had visited or worked near parks in central Tokyo, and the dominant serotype was DENV-1 5,20,21

All cases reported from 2016 to 2018 were imported. The predominant serotype was DENV-2 (36% [61/172] of cases in 2016, 35% [39/113] in 2017, 42% [34/81] in 2018), followed by DENV-3 (23% [39/172] of cases in 2016, 27% [31/113] in 2017, 31% [25/81] in 2018), DENV-1 (31% [54/172] of cases in 2016, 27% [31/113] in 2017, 24% [19/81] in 2018) and DENV-4 (11% [18/172] of cases in 2016, 11% [12/113] in 2017, 4% [3/81] in 2018). In 2019, 17% (78/463) of serotyped cases were DENV-1, 16% (74/463) were DENV-2, 9% (40/463) were DENV-3 and 3% (16/463) were DENV-4.

# Lao People's Democratic Republic

During 2013–2019, the Lao People's Democratic Republic annually reported between 1716 and 44 250 clinically confirmed cases and 0 to 95 deaths. In 2013, the country reported the largest dengue outbreak in its history,<sup>22</sup> with 44 250 cases and 95 deaths reported nationwide. In the southern part of the country alone, 4638 cases and 32 deaths were reported, among which DENV-2, DENV-3 and chikungunya virus were detected, as were concurrent infections with more than one serotype of DENV, or DENV and chikungunya virus.<sup>23</sup> More than 90% (numerator not available) of 537 samples serotyped in 2013 were DENV-3.24 In 2015, an outbreak was reported as predominantly due to DENV-1.24 In 2019, there was a dengue outbreak with 39 091 cases reported and 76 deaths (CFR: 0.19%), and 65% (numerator not available) of 1178 specimens collected and serotyped were found to be DENV-2.24 The predominant serotypes during outbreaks in 2013, 2015 and 2019 were attributed to three different serotypes, indicating two serotype switches.<sup>24</sup>

#### Malaysia

During 2013-2019, Malaysia annually reported between 43 346 and 130 101 laboratory-confirmed cases and 92 to 336 deaths. No imported cases were reported from 2016 to 2018. Malaysia launched the web-based e-Notification system and e-Dengue system in 2014, and all registered dengue cases since January 2014 have been laboratory-confirmed. More than 100 000 cases were reported in 2014, 2015, 2016 and 2019.

All four serotypes were reported in Malaysia, with the predominant serotype differing each year from 2016 to 2018, with significant cocirculation. In 2016, the predominant serotype was DENV-1 (40%, 2211/5482), followed by DENV-3 (32%, 1745/5482), DENV-2 (25%, 1381/5482) and DENV-4 (3%, 145/5482). In 2017, the predominant serotype was DENV-3 (41%, 2200/5420), followed by DENV-2 (35%, 1887/5420), DENV-1 (23%, 1245/5420) and DENV-4 (2%, 88/5420). In 2018, the predominant serotype was DENV-2 (47%, 2608/5544), followed by DENV-3 (33%, 1833/5544), DENV-1 (19%, 1055/5544) and DENV-4 (1%, 48/5544).

# Mongolia

During 2013–2015, Mongolia reported no dengue cases and no deaths. Data for 2016-2019 were not available.

# The Philippines

During 2013-2019, the Philippines annually reported between 113 485 and 437 563 suspected dengue cases and 425 to 1689 deaths. Among these suspected cases, 1488 cases in 2016, 1333 cases in 2017 and 998 cases in 2018 were laboratory-confirmed. The highest number of cases and deaths were reported during a large-scale outbreak in 2019, with 437 563 cases and 1689 deaths (CFR: 0.39%).

All four serotypes were reported from the Philippines. In 2016, the predominant serotype among 1488 cases tested was DENV-1 (44%, 659/1488), followed by DENV-3 (26%, 384/1488), DENV-2 (24%, 349/1488) and DENV-4 (6%, 95/1488); 1 case tested positive for both DENV-1 and DENV-2 (0.1%, 1/1488). In 2017, the predominant serotype among 1333 cases tested was DENV-3 (60%, 795/1333), followed by DENV-1 (24%, 318/1333), DENV-2 (12%, 164/1333) and DENV-4 (4%, 47/1333); 2 cases tested positive for DENV-1 and DENV-2 (0.2%, 2/1333), 5 cases tested positive for DENV-1 and DENV-3 (0.4%, 5/1333) and 2 cases tested positive for DENV-2 and DENV-3 (0.2%, 2/1333). In 2018, the predominant serotype among 998 cases tested was DENV-3 (60%, 598/998), followed by DENV-1 (22%, 223/998), DENV-2 (15%, 149/998) and DENV-4 (3%, 25/988); 2 cases tested positive for DENV-1 and DENV-3 (0.2%, 2/988) and 1 case tested positive for DENV-2 and DENV-3 (0.1%, 1/988). In 2019, the predominant serotype among the 100 cases with serotype data available was DENV-3 (64%), followed by DENV-2 (18%), DENV-1 (15%) and DENV-4 (3%).25

# Republic of Korea

During 2013–2019, the Republic of Korea annually reported between 164 and 313 laboratory-confirmed cases and no deaths. The highest number of cases was reported in 2016. All cases reported from 2016 to 2018 were imported, comprising all four serotypes. In 2016, the predominant serotype was DENV-1 (38%, 57/149), followed by DENV-2 (35%, 52/149), DENV-3 (20%, 30/149) and DENV-4 (7%, 10/149). In 2017, the predominant serotype among imported cases was DENV-1 (44%, 38/86), followed by DENV-3 (23%, 20/86), DENV-2 (19%, 16/86) and DENV-4 (14%, 12/86). In 2018, the predominant serotype among imported cases was DENV-2 (37%, 35/96), followed by DENV-1 (33%, 32/96), DENV-3 (28%, 27/96) and DENV-4 (2%, 2/96).

#### Singapore

During 2013–2019, Singapore annually reported between 2767 and 22 170 laboratory-confirmed cases and 2 to 12 deaths. Large numbers of cases were reported during outbreaks in 2013, 2014, 2015 and 2019. The numbers of reported cases were low in 2017 and 2018. Among the 20 deaths reported during 2016-2018, 14 were autochthonous cases and the rest were imported cases. All four serotypes were reported from Singapore; however, denominators were not available, so the percentage for each serotype is reported along with the number of positive cases. The predominant serotypes from 2016 to 2018 were DENV-2 (51% [2257 positive cases] in 2016, 45% [361] in 2017 and 52% [637] in 2018), followed by in 2016 DENV-1 (29%, 278 positive cases) then DENV-3 (18%, 806), and in 2017 DENV-3 (24%, 192) then DENV-1 (21%, 171), and in 2018 DENV-3 (25%, 305)

and DENV-1 (20%, 240). DENV-4 was reported from 2% (n = 67) of cases in 2016, 10% (77) in 2017 and 4% (47) in 2018.

#### Viet Nam

During 2013–2019, Viet Nam annually reported between 66 322 and 320 702 cases (including both clinically and laboratory-confirmed cases) and 27 to 62 deaths. More than 100 000 cases were reported in 2017, 2018 and 2019; notably, 320 702 cases were reported in 2019. During the outbreak in 2017, more than 59 000 cases were reported in northern Viet Nam, eight times higher than the number of cases in 2016.26

All four serotypes were reported from Viet Nam during 2016-2018. In 2016, the predominant serotype was DENV-1 (61%, 1104/1803), followed by DENV-4 (25%, 453/1803), DENV-2 (13%, 240/1803) and DENV-3 (0.3%, 6/1803). In 2017, the predominant serotype was DENV-1 (72%, 2057/2870), followed by DENV-2 (21%, 607/2870), DENV-4 (7%, 204/2870) and DENV-3 (0.1%, 2/2870). In 2018, the predominant serotype changed to DENV-2 (50%, 988/1980), followed by DENV-1 (33%, 661/1980), DENV-4 (17%, 328/1980) and DENV-3 (0.2%, 3/1980).

# **Pacific subregion**

#### Australia

During 2013–2019, Australia annually reported between 917 and 2237 laboratory-confirmed cases and 0 to 1 death. More than 1700 cases were reported annually in 2013, 2014, 2015 and 2016; in 2016, 2237 cases were reported. During 2016–2018, more than 98% of reported cases were imported (2204/2237 in 2016, 1113/1132 in 2017 and 907/917 in 2018). In Australia, dengue cases occur each year in North Queensland, generally originating from an imported case, although in 2019 an outbreak associated with 13 locally acquired cases was reported for the first time in decades in the Rockhampton region, Queensland.27,28

All four serotypes were reported from Australia, with the predominant serotype being DENV-2 (44% [468/1052 of known and serotyped cases] in 2016, 56% [246/436] in 2017, 43% [120/282] in 2018), followed in 2016 by DENV-3 (24%, 257/1052), DENV-1 (19%,

202/1052) and DENV-4 (12%, 125/1052); in 2017 by DENV-1 (20%, 88/436), DENV-3 (13%, 57/436) and DENV-4 (10%, 45/436); and in 2018 by DENV-1 (30%, 86/282), DENV-3 (20%, 55/282) and DENV-4 (7%, 21/282). In addition to these serotyped cases, concurrent infection with two serotypes was reported in 2016 and 2017. In 2016, concurrent infections were reported with DENV-1 and DENV-2 (1 case), DENV-2 and DENV-3 (1 case), and DENV-3 and DENV-4 (4 cases); in 2017, concurrent infection with DENV-1 and DENV-4 was reported in 1 case; in 2019, concurrent infection with DENV-3 and DENV-4 was reported in 1 case.

# New Zealand

During 2013-2019, New Zealand annually reported between 106 and 294 cases (including both clinically confirmed and laboratory-confirmed cases, although most are laboratory-confirmed); during 2016-2019, no deaths were reported. Among reported cases, 98% (158/161) were laboratory-confirmed in 2017, 95% (280/294) in 2018 and 98% (219/224) in 2019.<sup>29-31</sup> The largest number of cases was reported in 2018, at 294 cases. In 2016, two dengue fever outbreaks were reported that involved 12 cases. During 2013-2019, all cases reported in New Zealand were imported (information on travel history was not available for 1 case in 2015 and 2 cases in 2019).

All four serotypes were reported from New Zealand. In 2016, the predominant serotype was DENV-3 (63%, 59/93), followed by DENV-2 (20%, 19/93), DENV-1 (11%, 10/93) and DENV-4 (5%, 5/93). In 2017 and 2018, the predominant serotype was DENV-2 (83% [82/99] and 84% [167/200], respectively), followed by DENV-1 (10% [10/99] and 9% [18/200], respectively), DENV-3 (6% [6/99] and 5% [9/200], respectively) and DENV-4 (1% [1/99] and 3% [6/200], respectively).

#### American Samoa

American Samoa reported clinically confirmed cases to WHO using the 2009 WHO dengue case classification system. Laboratory confirmation is conducted to confirm outbreaks using reverse transcription polymerase chain reaction (RT-PCR) or an antigen rapid diagnostic test (NS1). In 2015, American Samoa reported 479 cases and 4 deaths (CFR: 0.84%). Outbreaks were also reported in 2017 and 2018, but the total numbers of cases are not available.

#### Cook Islands

The Cook Islands reported clinically confirmed cases to WHO using the 2009 WHO dengue case classification system. In 2014, the Cook Islands reported 946 cases and no deaths, and in 2015 the Islands reported 765 cases and no deaths (CFR: 0%). No cases were reported to WHO during 2016–2018. In 2019, a dengue outbreak was declared in February, with 41 confirmed cases and 85 probable, 48 hospitalizations and no deaths. 32 The predominant serotype in 2019 was DENV-1, accounting for 93% (35/38) of cases with available serotype information. Additionally, 3 cases who were tourists with a history of travelling to French Polynesia were confirmed with DENV-2 in October 2019.33

# Fiji

During 2013–2018, Fiji annually reported between 352 and 26 595 cases and 0 to 16 deaths. Fiji reported clinically confirmed cases to WHO using the 2009 WHO dengue case classification system. Samples from different health divisions were tested using RT-PCR, an antigen rapid diagnostic test (NS1) and an enzymelinked immunosorbent assay (ELISA). An outbreak was reported in 2014 of at least 26 595 cases (more than 27 000 reported according to some sources) and 16 deaths (CFR: 0.06%). From 2017 to 2018, an outbreak was reported, for which the predominant serotype was DENV-2.34

#### French Polynesia

French Polynesia used the 2009 WHO dengue case classification system, and the laboratory method for confirmation was RT-PCR. In 2013, French Polynesia reported 1523 dengue cases associated with an outbreak, with 258 being laboratory-confirmed; during the outbreak, 70% (170/244) of cases with the serotype identified had DENV-1 infections, 30% (73/244) had DENV-3 infections (genotype III) and 0.4% (1/244) had coinfection with both serotypes.35 DENV-3 was reported to have been introduced from South America.<sup>35</sup> In 2014, 2155 confirmed and 34 000 suspected cases were reported in French Polynesia, and outbreaks were also reported in 2016 and 2017. In 2016 and 2017, DENV-1 was reported, and in 2018, DENV-2 was reported. In April 2019, an outbreak of DENV-2 was declared, with 2400 autochthonous cases reported.36

#### Guam

Guam reported clinically confirmed cases to WHO: 23 cases were reported in 2019, with no further information available.

#### Kiribati

Kiribati reported clinically confirmed cases to WHO using the 2009 WHO dengue case classification system. Laboratory testing to confirm outbreaks is conducted using RT-PCR or an antigen rapid diagnostic test (NS1). In Kiribati, outbreaks were reported in 2013 and 2014, and no cases were reported in 2016 and 2017. In 2018, 1899 cases and 2 deaths were reported, with DENV-2 detected.

# Republic of the Marshall Islands

In the Republic of the Marshall Islands, outbreaks were reported in 2013 and 2014. In 2019, a DENV-3 outbreak was reported with at least 1395 cases of dengue-like illness, including 431 laboratory-confirmed cases and 1 death.<sup>37</sup> A health emergency was declared in relation to this event; internal movement restrictions were imposed between the affected and unaffected islands; and emergency medical teams were deployed to support the dengue response.

# Federated States of Micronesia

The Federated States of Micronesia reported clinically confirmed cases to WHO using the 2009 WHO dengue case classification system. Laboratory methods used to confirm outbreaks include RT-PCR and an antigen rapid diagnostic test (NS1). There were 217 cases reported to WHO in 2013, associated with an outbreak of 729 suspected dengue cases and no deaths in Kosrae from September 2012 to March 2013. DENV-4 was detected from 3 specimens collected during this period; 11% (728/6600) of Kosrae residents met the case definition for suspected dengue, and almost 4% (242/6600) were hospitalized.<sup>38</sup> In 2018, DENV-4 was reported. In 2019, 1464 dengue cases including 1 death were reported from Yap state, and the predominant serotype was DENV-3. The dengue outbreak in 2019 coincided with a concurrent leptospirosis outbreak in Yap state, and an executive order determining a public health crisis was issued.

#### Nauru

Nauru reported clinically confirmed cases to WHO using the 2009 WHO dengue case classification system. Laboratory testing to confirm outbreaks uses RT-PCR or an antigen rapid diagnostic test (NS1). Nauru reported 251 cases in 2014, no cases in 2016, 964 cases and 3 deaths in 2017 and 114 cases and no deaths in 2018. In 2017, DENV-2 was reported and in 2018, DENV-1 was reported.

#### New Caledonia

New Caledonia reported cases to WHO using the 2009 WHO dengue case classification system and RT-PCR for laboratory confirmation. In 2013, New Caledonia reported 9958 cases including 4 deaths during an outbreak in which the predominant serotype was DENV-1.39 Based on available information, an outbreak was also reported in 2014. In 2017, 4200 cases and 11 deaths were reported, with DENV-1, DENV-2 and DENV-3 detected. From November 2018 to September 2019, a dengue outbreak was declared. From 1 January to 31 December 2019, 3916 cases, 368 hospitalizations and 2 deaths were reported. Among the 316 cases with serotype information available, the predominant serotype was DENV-2. Two cases of DENV-1 and 1 case of DENV-4 were imported from French Polynesia and Indonesia, respectively.40

#### Niue

Niue reported clinically confirmed cases to WHO. In Niue, 2 cases were reported in 2017. In 2018, DENV-2 was reported, but information on the number of cases was not available.

# Palau

Palau reported cases to WHO using the 2009 WHO dengue case classification system and RT-PCR or an antigen rapid diagnostic test (NS1) for laboratory testing to confirm outbreaks. During 2013-2017, Palau annually reported between 9 and 737 cases and 0 to 5 deaths. Outbreaks were reported in 2016 and again in 2017, the latter comprising 440 cases and 5 deaths, with a predominant serotype of DENV-2. In 2018, 570 cases and 2 deaths were reported, and in 2019, there were 737 cases including 3 deaths. From December 2018 to September 2019, 160 cases were confirmed as DENV-3. Two serotypes were reported from Palau; DENV-2 was reported in 2016 and 2017, and DENV-3 was reported in 2018.

# Papua New Guinea

In 2014, Papua New Guinea reported 6 cases. Further information was not available.

# Samoa

Samoa reported cases to WHO using the 2009 WHO dengue case classification system and RT-PCR or an antigen rapid diagnostic test (NS1) to confirm outbreaks. In Samoa, outbreaks were reported in 2015 and 2016. In 2017, 2724 cases and 5 deaths were reported, with the predominant serotype being DENV-3. In 2018, DENV-2 was reported.

#### Solomon Islands

The Solomon Islands reported cases to WHO using the 2009 WHO dengue case classification system. In the Solomon Islands in 2013, 9500 cases and 8 deaths (CFR: 0.10%) were associated with an outbreak in Honiara. DENV-3 genotype I was isolated from specimens collected during this outbreak, suggesting introduction from south-east Asia after 18 years of dengue absence in the PICs.35 In 2014, 1872 cases and 1 death (CFR: 0.05%) were reported. The introduction of DENV-2 to the Solomon Islands resulted in outbreaks in 2016 and 2017.41,42 From September 2016 to April 2017, an outbreak of DENV-2 was reported in 9 of 10 provinces in the Solomon Islands, with 12 329 suspected cases, including 1510 cases positive by dengue rapid diagnostic test, and 16 deaths. 42 An outbreak was also reported in 2019.

# Tonga

Tonga reported cases to WHO using the 2009 WHO dengue case classification system. In Tonga, 51 cases and no deaths were reported in 2014; 1559 cases and no deaths were reported in 2015; and more than 100 cases were reported in 2017.

#### Tuvalu

Tuvalu reported cases to WHO using the 2009 WHO dengue case classification system. In Tuvalu, 408 cases were reported in 2014. In March 2019, a dengue outbreak was declared. In 2019, 522 cases were reported, including at least 21 hospitalizations and 2 deaths in children. The predominant serotype in the 2019 outbreak was DENV-1.

#### Vanuatu

Vanuatu reported clinically confirmed cases to WHO. In Vanuatu, 1561 cases were reported in 2014 and more than 1000 cases were reported in 2017; DENV-2 was reported in 2018.

#### Wallis and Futuna

Wallis and Futuna reported cases to WHO using the 2009 WHO dengue case classification system. In Wallis and Futuna, 94 cases were reported in 2013. In 2017, an outbreak was declared in November, with 222 cases and no deaths, and DENV-1 was identified from 2 samples. In 2018, 202 cases and DENV-1 were reported. In November 2019, an outbreak was declared in Wallis and Futuna, and 30 confirmed cases were reported from February to December 2019, with the predominant serotype being DENV-2.43

# DISCUSSION

Dengue continued to pose a health burden in the Region during 2013–2019, with the number of annually reported cases ranging from a little more than 430 000 to more than 1 million and with the annual number of reported deaths ranging from 724 to 2025. Outbreaks were reported from the Region every year during the study period. The introduction or reintroduction of serotypes to specific areas caused several outbreaks and rare occurrences of local transmission in places where dengue had not been previously reported. With support from countries and areas, WHO continued to share timely information during the study period through its biweekly dengue epidemiological reports for the Region<sup>11</sup> and conducted regional and country-specific risk assessments to inform dengue prevention and control efforts.

The increases in reported cases and regional case incidence may be attributed to several factors. First, a true increase in dengue incidence may have occurred due to expanding urbanization and increasing population size and density, particularly in settings with increased exposure to competent dengue vectors and mosquito breeding grounds.44 Shifts in ecological factors due to climate change, such as intensified rainy seasons and higher ambient temperatures, have expanded the geographical range of Aedes mosquitos globally during the past 50 years and led to intensified dengue transmission.45 Second, increased international travel and trade have led to the importation of cases with different serotypes and the introduction of mosquito eggs through the importation of goods to areas where the population is susceptible and competent mosquitos exist. 44,45 Third, reports to national health authorities likely increased due to strengthened surveillance systems and diagnostic capacities, including laboratory networks that supported confirmatory diagnosis in the PICs, as well as an emphasis on risk communication activities to improve the awareness of dengue among the public.3 The range of CFRs may be associated with differences in case reporting, the timing of the case presentation to health-care facilities and clinical management.

The number of cases reported in 2019 was higher than in the years from 2013 to 2018, and the CFR was relatively low. This increase in 2019 included at least 14 countries and areas that reported dengue outbreaks in the Region, including large-scale outbreaks; during 2019, four countries and areas in the Asia subregion and three in the Pacific subregion reported their highest number of cases of the 7-year study. It is possible that case detection and reporting increased due to improved awareness of dengue among health-care professionals and the public because of the large outbreaks. These outbreaks may have also increased health-care-seeking behaviour, leading to fewer deaths, thereby decreasing the CFR.

Our findings show that there is a substantial burden of dengue in the Region and that it continues to increase over time. However, dengue surveillance practices throughout the Region are inconsistent and require strengthening. To inform national and regional risk assessments and actions, information is required not only on the time, place and demographics of a case, such as age and sex, but also on the DENV serotype and

whether the infection was locally acquired or imported. These details will also support risk assessments for and responses to events with new epidemiological patterns, such as outbreaks associated with the introduction or reintroduction of serotypes to specific areas, as well as rare occurrences of local transmission in places where it was not previously reported. Furthermore, in some settings, the capacities for surveillance, outbreak response, clinical management and diagnosis may be limited. Several approaches could fill these gaps, including strengthening laboratory capacity and laboratory networks, institutionalizing active surveillance to detect dengue cases who are self-managed and inapparent, and implementing integrated vector surveillance.

Although several countries and areas have adopted the 2009 WHO dengue case classification system, 14 there are differences in countries and areas across the Region in surveillance methodology, including whether universal or sentinel reporting is used; laboratory sampling schemes and confirmation methods; and reporting practices. These differences are a limitation of this report, indicating why comparison across countries should be avoided and comparisons within one country should be informed by the local reporting practices, which may change over time. As a result of differences in case definitions and other factors, there is likely to be underreporting and, thus, an underestimation of the true regional burden in terms of the number of cases, CFRs and incidence. 1,2 Despite these limitations, continued reporting of dengue in line with the Regional Action Plan is important to guide public health authorities in their national and subnational response efforts.

The burden of dengue, including the increased risks of dengue outbreaks, will continue amid other public health emergencies. Disaggregating data by age and sex at all levels will enable public health authorities to implement improved and targeted response measures. Additional information about cases, including their travel history and serotype, should also be routinely collected and reported. The Region's capacity to mitigate the impact of dengue can be strengthened by making a shift in its management, from a reactive, acute outbreak response to one that reduces fatalities through undertaking activities, including sustainable implementation of mosquito control measures, engaging communities to raise their awareness about the risk of dengue and to communicate relevant behavioural changes, and strengthening diagnostics and case management. Enhancing collaboration and coordination within and beyond the health sector is key to carrying out these activities successfully.

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# Conflicts of interest

MC, LB, SO, CKL, RRA, SC and TM are associate editors and BO is executive editor of the Western Pacific Surveillance and Response journal. They were not involved in the editorial decision to publish the manuscript. All other authors have no conflicts of interest to declare.

#### Ethics statement

Ethical clearance was not required because this report used routinely available data and no personal identifying information was collected.

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# Epidemiology of tuberculosis in the Pacific island countries and areas, 2000-2020

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Objective: Tuberculosis (TB) is one of the most important infectious diseases with an estimated 9.9 million people falling ill globally in 2020. We describe the epidemiology of TB in the Pacific island countries and areas (PICs) to inform potential priority actions to implement the Western Pacific Regional Framework to End TB 2021-2030.

Methods: A descriptive analysis was conducted using annual TB surveillance data submitted by national TB programmes to the World Health Organization (WHO) and TB burden estimates (incidence rates and number of deaths) generated by WHO for the PICs, for the period 2000–2020. We also analysed TB case numbers, multidrug-resistant/rifampicin-resistant TB (MDR/RR-TB), recent risk factor indicators and treatment outcomes.

Results: The estimated TB incidence rate in the PICs increased between 2000 and 2020 from 62 to 69 per 100 000 population, with an 8% reduction observed since 2015. TB cases increased by 29% during 2000-2020, with 1746 cases in 2020 and a high proportion in children (19%). Bacteriological diagnosis was used for 58% of total TB cases, although some countries reported clinical diagnoses in over 60% of cases. From 2015 to 2019, 52 MDR/RR-TB cases were reported and there were 94 TB/HIV coinfected cases in 2015-2020. Treatment success was 74% in 2019 due to 18% of cases being unevaluated. In 2020, the estimated proportion of TB cases attributable to smoking, malnutrition, alcohol abuse and diabetes was 17%, 16%, 11% and 9%, respectively.

Discussion: There was an increasing trend in TB cases, estimated incidence and deaths between 2000 and 2020. Laboratory services were scaled up in some PICs and case-finding activities greatly contributed to the detection of cases. In order to end the incidence of TB, continued efforts on case finding, contact investigation and scaling up TB preventive treatment should be prioritized. At the same time, collaboration with other sectors for risk factor management and decentralized management need to be considered.

uberculosis (TB) remains a disease with a major global impact. In 2020, an estimated 9.9 million people developed TB; there were an estimated 1.3 million deaths among human immunodeficiency virus (HIV)-negative TB cases and an estimated 214 000 deaths among HIV-positive TB cases reported worldwide. The World Health Organization (WHO) Western Pacific Region, which consists of 37 countries and areas, accounted for 18% of these estimated cases. From 2015 to 2020, the estimated global TB incidence and number of deaths declined by 6% and 13%, respectively, with annual reductions of 1.2% and 2.6%, respectively.

The population of the 20 Pacific island countries and areas (PICs) of the Western Pacific Region included in this paper is approximately 3.4 million. The PICs are

made up of around 1300 islands with limited transport services between them.<sup>2,3</sup> Economic status varies by country and area, with gross national income data available for six of the 16 PICs which are classified as highincome countries, while the remainder are classified as middle-income countries. 4 Twelve PICs are supported by the Global Fund to fight AIDS, Tuberculosis and Malaria, three of which are classified as high-income countries.<sup>5</sup>

The estimated TB incidence in the PICs is lower than other countries in the Western Pacific.<sup>6</sup> However, the epidemiology of TB is diverse, ranging from countries with high TB burdens to those in the pre-elimination stage (defined as <10 TB cases per million). Among the PICs, Kiribati, the Marshall Islands and the Federated States of Micronesia had a high estimated TB incidence per capita in 2020.8 Some countries reported a low

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treatment success rate despite the relatively young age group affected.6

In 2015, the Regional Framework for Action on Implementation of the End TB Strategy in the Western Pacific 2016-2020 was endorsed by the WHO Regional Committee for the Western Pacific. 9 following the release of the End TB Strategy. 10 Since then, recommended interventions from the Framework have been implemented in countries and areas to achieve the 2020 milestones and targets. The new Western Pacific Regional Framework to End TB 2021-2030 was endorsed by the Regional Committee in October 2021.8 The Framework is intended to support Member States in making further progress towards ending TB. In this paper, we describe the epidemiology of TB in the PICs by analysing existing TB surveillance and burden estimate data available in the WHO Global TB Programme for the period 2000-2020, focusing particularly on 2015 and 2020. The results may inform potential priority actions required to implement the Western Pacific Regional Framework to End TB 2021-2030 in the PICs.

# **METHODS**

This descriptive analysis used annual TB surveillance data submitted by national TB programmes to WHO and TB burden estimates (incidence and mortality) generated by WHO for the PICs for the period 2000-2020. This timeframe was selected as burden estimates were available for that period. A baseline of 2015 was used to monitor progress against the milestones and targets set by the End TB Strategy and the Regional Framework for 2016-2020.

Routine TB surveillance data were submitted annually by 20 national TB programmes in the PICs – American Samoa, the Cook Islands, Fiji, French Polynesia, Guam, Kiribati, the Marshall Islands, the Federated States of Micronesia, Nauru, New Caledonia, Niue, the Northern Mariana Islands, Palau, Samoa, the Solomon Islands, Tokelau, Tonga, Tuvalu, Vanuatu and Wallis and Futuna - referred to as a subregion in this paper. The Pitcairn Islands are excluded from annual TB data collection and are not included in the analysis. The verified data are published on the WHO website in the annual Global Tuberculosis Report 2022, together with estimates of the TB disease burden, which are measured by incidence

rates and deaths. 11 Methods used to estimate the TB disease burden are described in the technical annexes of the Report. 12

The descriptive analysis included estimated incidence and deaths, case numbers (totals, by type of TB and diagnosis category), numbers of multidrug-resistant/ rifampicin-resistant TB (MDR/RR-TB) cases detected and enrolled in multidrug-resistant tuberculosis (MDR-TB) treatment and key indicators of collaborative TB/HIV activities. The proportion of bacteriologically confirmed, clinically diagnosed pulmonary TB (PTB) and extrapulmonary TB (EPTB) cases, as well as age and sex distributions and treatment outcomes, were compared across countries and areas. The proportion of TB cases attributable to alcohol abuse, diabetes mellitus, smoking and undernutrition were also analysed. The estimated numbers of cases attributable to these risk factors generated by WHO data were used to make an overall comparison of the cases in the PICs and the Western Pacific Region. The number of PICs with these estimations is limited and, therefore, the risk factors vary.

The definitions of cases and treatment outcomes were in accordance with the WHO reporting framework for TB.<sup>13</sup> The diagnosis category was changed in 2013 when new case definitions of bacteriologically confirmed TB and clinically diagnosed TB were introduced to replace smear-positive and smear-negative TB, respectively, to align with the increased availability of Xpert testing. Most of the analyses, such as age and sex distribution, HIV testing data and treatment outcomes, are of incident cases which were redefined as "new and relapse (or previous history unknown)" cases, regardless of bacteriological confirmation.

Estimated incidence and deaths, 95% confidence intervals (CI) and total case numbers for the subregion were calculated by aggregating existing burden estimates and data from each country and area. We used population estimates from the United Nations Population Division to calculate rates per capita where required. Data analyses and visualization were conducted with the statistical software package R 4.1.2 (Comprehensive R Archive Network: https://cran.r-project.org/). Only those countries and areas that had data for each variable, with more than five cases between 2015 and 2020, were included in the analyses.

# **RESULTS**

#### **Estimates of TB burden**

The estimated incidence rate of TB in the subregion increased from 62 (95% CI: 46-80) per 100 000 population in 2000 to 75 (95% CI: 57-96) per 100 000 population in 2015, before decreasing to 69 (95% CI: 54-86) per 100 000 population in 2020 (Fig. 1A). This equates to an estimated 1680 cases (95% CI: 1266-2185) in 2000, 2390 cases (95% CI: 1825-3061) in 2015 and 2356 cases (95% CI: 1827-2936) in 2020. The estimated number of TB deaths increased from 176 (95% CI: 126-234) in 2000 to 212 (95% CI: 158-281) in 2015 and further increased to 268 (95% CI: 188-366) in 2020 (Fig. 1B).

The estimated TB incidence rate and the number of deaths among people living with HIV (PLHIV) per 100 000 population in 2020 have remained low in the PICs at 0.9 (95% CI: 0.5-2.0) and 10 (95% CI: 9-13), respectively.

By country and area, the Marshall Islands and Kiribati had the highest estimated TB incidence rates of 483 (95% CI: 370-611) and 425 (95% CI: 323-540) per 100 000 population, respectively (Fig. 2). Fiji had the highest estimated number of TB cases (n = 590), followed by Kiribati (n = 510), the Solomon Islands (n = 450) and the Marshall Islands (n = 290). These four PICs accounted for 78% of the total cases in the subregion. American Samoa, Samoa and Wallis and Futuna had an estimated TB incidence rate of <10 cases per 100 000 population in 2020.

#### TB cases

The number of reported TB cases (new and relapse) in the subregion has increased over the last two decades, ranging from 1229 in 2002 to 1991 in 2018 (Fig. 3). Between 2000 and 2020, the number of TB cases increased by 29% to 1746 in 2020. The number of bacteriologically confirmed or smear-positive TB cases increased by 66%, from 485 in 2000 to 804 in 2020. The number of clinically diagnosed or smear-negative cases ranged from 474 in 2000 to 429 in 2020, with some fluctuations. The number of EPTB cases increased by 55%, from 331 in 2000 to 513 in 2020. Among new and relapse PTB cases, 65% (n = 804/1233)

were bacteriologically confirmed in 2020, with clinically diagnosed cases accounting for the rest. The proportion of EPTB among all TB cases was 29% (n = 513/1746) in 2020.

By country and area, between 2000 and 2020, TB cases increased in Fiji (from 144 to 431), Kiribati (from 252 to 385) and the Marshall Islands (from 34 to 147) (Fig. 4). TB cases decreased between 2000 and 2020 in New Caledonia, the Northern Mariana Islands, Samoa, Tonga, Vanuatu and Wallis and Futuna, with some fluctuations observed over the period. In Samoa, TB cases decreased by 70% (from 43 to 13) over the same period.

# Age and sex distribution

TB cases with data on age and sex were reported from 16 PICs in 2020. Among these 1695 cases, 56% (n = 945) were male, 19% (n = 328) were children aged <15 years and 8% (n = 141) were older adults aged ≥65 years. In the subregion, the notification rate was higher for older age groups, with the highest rate for both males and females aged 55-65 years (117 cases and 79 cases per 100 000 population, respectively) (Fig. 5). Notification rates were higher in males aged ≥25 years, while they were higher for females among children and younger adults.

High TB notification rates were reported for children aged <15 years for both sexes in the Marshall Islands, at over 250 per 100 000 population. Also, the Marshall Islands had the highest proportion of TB cases in children at 37% (n = 54/147). In Kiribati and Tuvalu, rates of over 800 per 100 000 population were reported for males aged 55-64 years (Fig. 5).

# Diagnosis category and type of TB

Diagnosis category and type of TB were reported from 20 PICs, four of which were excluded from the analysis as they reported less than five cases cumulatively between 2015 and 2020. Bacteriological diagnosis was more common compared to clinical diagnosis in 2020 in 13 of the 16 PICs that reported diagnosis category (Fig. 6) with 58% of PTB cases in 2020 being bacteriologically confirmed (n = 4809/8302). There were higher proportions of clinical diagnosis for PTB cases in the Federated States of Micronesia (69% from 2015 to 2020), Fiji (53% from 2019 to 2020) and the Marshall Islands (80% from 2018

(A) (B) 100 Incidence and notification rate per 100 000 population 300 Total TB deaths 100 0 2000 2000 2005 2010 2015 2020 2005 2010 2015 2020 · · · 2020 milestone Estimated incidence rate Notification rate Estimated number of deaths Estimated incidence rate (HIV positive) · · · 2020 milestone Estimated number of deaths (HIV positive)

Fig. 1. (A) Estimated TB incidence and notification rates of new and relapse TB cases, and (B) estimated number of TB deaths in Pacific island countries and areas (including among people living with HIV), 2000-2020

to 2020). In the Marshall Islands, the number of PTB cases that were clinically diagnosed increased from 83 in 2017 to 321 in 2018. The proportion of PTB among new and relapse cases in the subregion between 2015 and 2020 was 78% (8752/11 189).

# **Drug-resistant TB**

MDR/RR-TB cases were reported from 15 PICs between 2015 and 2019, while five PICs (the Cook Islands, Nauru, Niue, Tonga and Wallis and Futuna) reported no cases. There were 52 MDR/RR-TB cases detected, of which 87% (n = 45) were enrolled in MDR-TB treatment. The number of MDR/RR-TB cases fluctuated between eight and 14 per year with nine cases in 2019 (Fig. 7). The highest number of MDR/RR-TB cases was reported in Kiribati with nine detected and treated.

#### Indicators of collaborative TB/HIV activities

Data on known HIV status and HIV prevalence were available from 18 PICs, and data on cases of TB and HIV

coinfection receiving antiretroviral therapy (ART) were available from eight PICs. The prevalence of HIV among TB cases and the proportion of TB and HIV coinfection receiving ART have been sparsely recorded or reported by the majority of PICs. Data on PLHIV eligible for TB preventive treatment and PLHIV who were started on the treatment were not available in any of the PICs.

The proportion of TB cases with HIV status recorded in the subregion increased from 33% in 2003 to 71% in 2020 (Fig. 8). This proportion varies by PIC, with 100% reported in Fiji, the Northern Mariana Islands, Palau and Samoa in 2020, and less than 50% reported in French Polynesia (43%), Kiribati (42%) and the Solomon Islands (38%).

The number of reported TB cases coinfected with HIV was low in the subregion, with 94 cases reported between 2015 and 2020 (16 cases per year on average, 0.8% [n = 94/11 311] of total notified cases). The prevalence of HIV among TB cases who were tested for HIV has remained below 5%, except for 2004 when

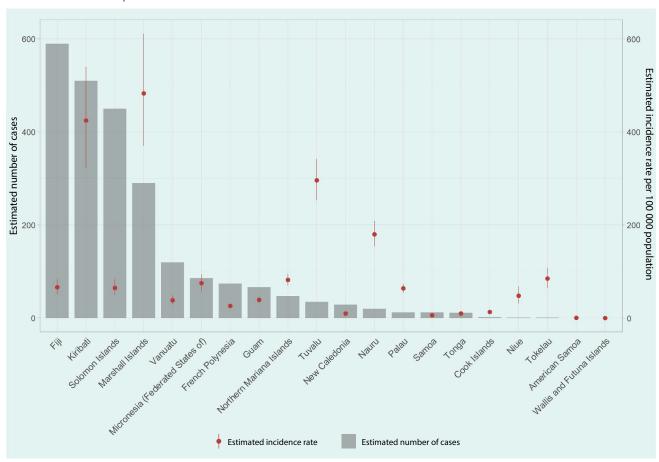


Fig. 2. Estimated number of TB cases and TB incidence rate per 100 000 population in Pacific island countries and areas, 2020

9% (n = 2/22) was observed due to a small number of cases tested and detected. Despite the decrease in HIV prevalence among TB cases in the subregion, there has been an increase in Fiji, from a low of 0.8% in 2005 to 6.2% in 2019 and 5.0% in 2020.

The proportion of TB and HIV coinfected cases receiving ART was 79% in 2020, a decrease from over 88% reported between 2009 and 2019 (Fig. 8). Fiji submitted 81% (n = 109/135) of the data on ART.

# **Treatment outcomes**

Treatment outcomes were reported from 19 PICs for the 2019 patient cohort, of which three PICs reported no cases. The treatment success rate was 74% for new and relapse cases, 44% for retreatment cases (excluding relapse) and 57% for HIV-positive TB cases (Fig. 9). Approximately 18% of the new and relapse cases were not evaluated on their treatment outcomes.

Treatment success rates of 90% or more were reported in eight PICs for the 2019 patient cohort, and 100% in American Samoa, the Cook Islands, Palau and Tonga (Fig. 10). Eight of the 16 PICs had treatment success rates of less than 90%, while four of the PICs reported less than 85%: Tuvalu, the Federated States of Micronesia, French Polynesia and Fiji reported 84%, 81%, 80% and 31%, respectively. In Fiji, 58% of cases (n = 333/572) were either not evaluated or did not have their treatment outcome recorded.

#### Risk factors

Data on the estimated proportion of TB cases attributable to alcohol abuse, diabetes mellitus, smoking and undernutrition are available for 12, 13, 10 and seven PICs, respectively. These proportions were 17% (n = 226/1299) for smoking, 16% (n = 206/1297) for undernutrition, 11% (n = 154/1392) for alcohol abuse and 9% (n = 133/1509) for diabetes mellitus. The

Fig. 3. Number of TB notifications by diagnosis category in Pacific island countries and areas, 2000-2020

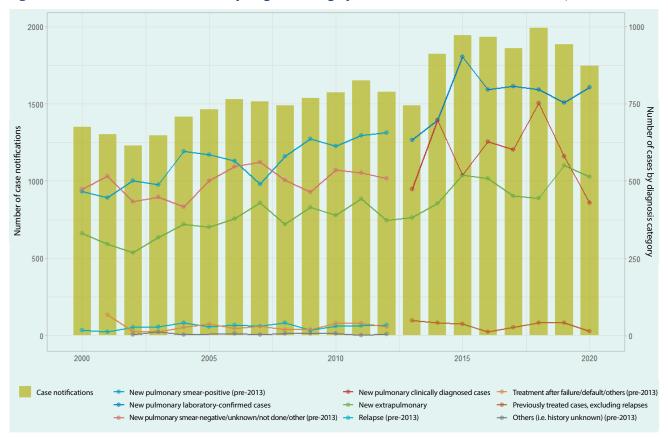


Fig. 4. Number of TB notifications (new and relapse) by year in Pacific island countries and areas that provided data, 2000-2020





Age and sex distribution of TB notifications (new and relapse) per 100 000 population in the subregion Fig. 5. overall and in Pacific island countries and areas that provided data, 2020

proportion of cases attributable to diabetes mellitus was higher in PICs compared to the proportion in the entire Western Pacific Region at 6%. Conversely, the proportion of cases attributable to the other risk factors was almost the same or lower in PICs than in the Region overall, where it was 17% for smoking, 20% for undernutrition and 16% for alcohol abuse.

Among the PICs, the highest proportions of TB cases attributable to smoking and undernutrition were estimated in the Solomon Islands at 19% (n = 61/170) and 31% (n = 100/321), respectively. Of the 13 PICs with data available for diabetes mellitus, the proportion was highest in Nauru at 12% (n = 2/17) and in the Marshall Islands at 12% (n = 17/147), followed by Kiribati at 10% (n = 39/385). Of the 12 PICs with data available for alcohol abuse, Vanuatu reported the highest proportion at 13% (n = 11/83), followed by the Solomon Islands at 12% (n = 38/321).

# TB preventive treatment

In 2020, of the 19 PICs that reported case notification data, 53% reported the number of household contacts of new and relapse PTB cases that were bacteriologically confirmed and started on TB preventive treatment. In these PICs, the number of contacts identified totalled 3049 in 2020. Of those, 38% (n = 1159/3049) started TB preventive treatment, 19% (n = 220/1159) of whom were children aged under 5 years.

# DISCUSSION

This analysis showed increases in the estimated TB incidence rates and the number of TB cases and deaths in the Pacific islands subregion between 2000 and 2020. There was an increased proportion of bacteriological confirmation for TB diagnosis, increased HIV testing coverage in TB patients and sustained high ART coverage in the

Fig. 6. Number of TB notifications by year and type of diagnosis in Pacific island countries and areas that provided data, 2015-2020

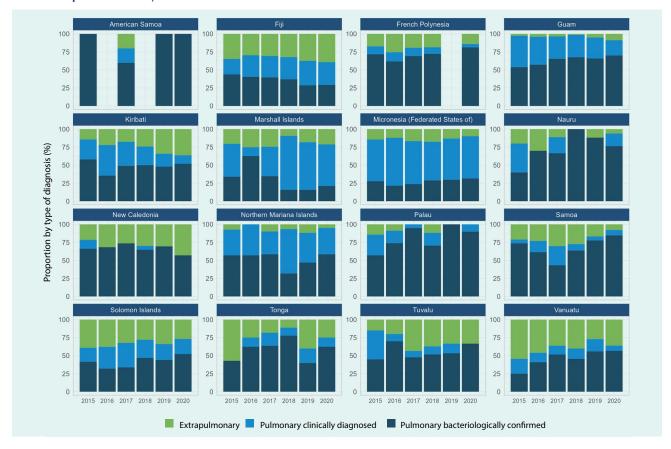
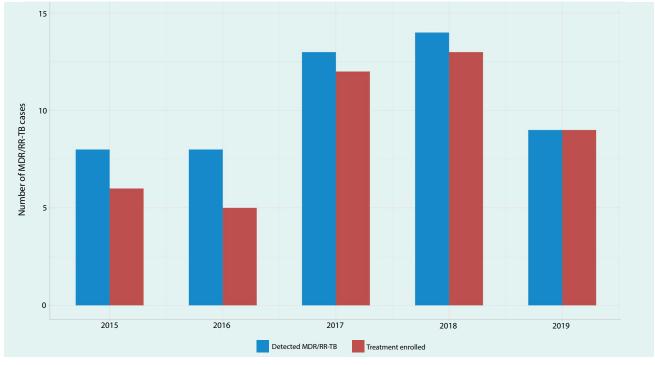


Fig. 7. Number of MDR/RR-TB cases reported and enrolled in MDR-TB treatment in Pacific island countries and areas that provided data, 2015-2019



MDR/RR-TB: multidrug-resistant/rifampicin-resistant tuberculosis; MDR-TB: multidrug-resistant tuberculosis.

Known HIV statu HIV prevalence in TB patients ART coverage in TB/HIV 100 60 7.5 75 Percentage (%) 5.0 50 20 2.5 0 0.0 0 2015 2005 2010 2015 2020 2005 2010 2015 2020 2005 2010 2020

Fig. 8. Known HIV status, HIV prevalence in TB patients and antiretroviral therapy coverage for TB/HIV patients in Pacific island countries and areas that provided data, 2003-2020

ART: antiretroviral therapy.





small number of patients requiring ART. The results also highlighted a high proportion of TB cases in the younger population, poor treatment outcomes in some PICs, and a large number of TB cases with underlying diabetes mellitus and other risk factors. PICs have diverse TB burdens, with Fiji, Kiribati, the Marshall Islands and the Solomon Islands all considered high TB burden countries in the Pacific, which was confirmed by the results of this analysis. In these PICs, increased efforts to strengthen national TB programmes and secure domestic and external support are essential.

The number of TB notifications increased in Fiji, Kiribati and the Marshall Islands over the last two decades. Increases in notifications can be driven by various factors including the improvement of TB screening, implementation of active case finding activities, <sup>14</sup> improved recording and reporting, 15 and increased TB transmission within the community. In Fiji, for example, the TB notification rate in the younger population increased in the early 2010s, which might indicate increased community transmission. 16 At 19%, the proportion of TB cases in children from the subregion in 2020 was higher than the WHO Western Pacific Region at 4% and the global proportion at 12%. This underscores the importance of intensifying household contact investigation to cut the chain of transmission. In the Marshall Islands, case notifications sharply increased in 2018, mostly

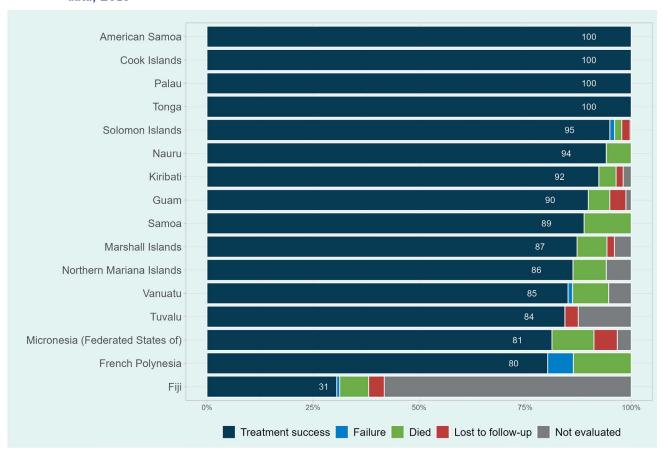


Fig. 10. Treatment outcomes among new and relapse TB cases in Pacific island countries and areas that provided data, 2019

in clinically diagnosed cases. This is probably due to population-based screening programmes for latent and active TB which were conducted on Ebeye and Majuro islands in 2017 and 2018, covering nearly 75% of the national population.<sup>17</sup> Such population-based mass screening and treatment of latent and active TB has the potential to reduce the incidence of TB in a short period<sup>17</sup> and could be a key intervention in advancing efforts to eliminate TB in PICs, given their geographical isolation and limited population size.<sup>18</sup>

The number of reported MDR/RR-TB cases has increased but fluctuated over the last two decades, as observed in the Western Pacific Region where small numbers and irregular MDR-TB caseloads were reported in the selected PICs. 19 Since this report in 2014, Kiribati has detected its first MDR/RR-TB cases with three each year since 2017.7 Other areas, such as French Polynesia and Guam, have consistently reported MDR/RR-TB cases since 2015. These diagnoses may reflect improved surveillance systems and the expanded use of Xpert MTB/ RIF. The number of Xpert testing sites has increased over time in Fiji, Kiribati, the Solomon Islands and Vanuatu, 11 which may have contributed to the early detection of drug-resistant TB cases and improved the proportion of bacteriological confirmation in TB diagnoses. Treatment outcomes among MDR/RR-TB cases were not analysed in this report as the data were not available. This might be due to a lack of follow-up, recording or reporting.

HIV prevalence among TB cases in the subregion was low, although an increased prevalence was reported in Fiji. This is probably due to an increase in new HIV infections among the general population in Fiji, which increased from 0.15 per 1000 population among adults aged 15-49 in 2010 to 0.32 per 1000 population in 2021.20 It is strongly recommended that PLHIV be systematically screened for TB disease at each visit to a health facility.<sup>21</sup> Proper management of HIV, including initiation and continuation of ART, is essential to prevent the development of TB disease among PLHIV.<sup>22</sup> Simultaneously, continuous HIV screening among TB patients and timely initiation of treatment among HIV coinfected cases is imperative.<sup>23</sup>

Management of diabetes mellitus should be highlighted in the subregion, considering its high prevalence among the general population. Of the 16 PICs with these data available, nine reported a prevalence higher than 20% in 2021.<sup>24</sup> Among them, six were ranked in the top 10 countries with the highest prevalence of diabetes mellitus, with French Polynesia exceeding 25%. For optimal management of diabetes mellitus, it is important to ensure accessibility to primary health-care services and community-level health promotion programmes targeting younger age groups.<sup>25</sup> Additionally, close collaboration and coordination between multiple disease programmes and sectors are crucial in addressing TB and its risk factors simultaneously.8

Treatment success for new and relapse TB cases in the PICs that reported the data was 74%. This is low when compared to the whole Western Pacific Region where it has been approximately 90% over the past decade,<sup>5</sup> and to the global data where it was 86% in 2019.1 The treatment success rate was low in Fiji due to the high proportion of unevaluated cases, which may be attributable to the recent transition from the Global Fund-supported vertical programme, resulting in limited human resources responsible for recording and reporting. There are several more PICs with success rates below 90%. These rates might be attributable to delays in diagnosis and treatment due to limited access to health facilities that provide TB services, coupled with the unique geographical challenges of PICs. This may be underpinned by fear of financial burden and stigma. For example, in Vanuatu, the majority of TB cases report having experienced stigma after diagnosis, and more than half of patients first consult a traditional healer due to the cost and distance to health facilities.<sup>26</sup>

This analysis has several limitations. There is great uncertainty in the estimated incidence rates and number of deaths as evidenced by the wide range of confidence intervals. Firstly, estimated TB incidence is calculated based on case notifications with a standard adjustment or adjustments made based on expert opinions, which might not reflect the actual incidence. 12 Most PICs have their mortality estimates indirectly derived from the incidence. In settings with a limited number of notified cases, modelled estimates are less appropriate compared

to other methods of estimation that are based on surveys due to the strong stochasticity of the reported cases. Secondly, the observed increase in the estimated number of deaths in 2020 might not reflect the actual number of deaths in the subregion. While the modelled estimate accounted for the shortfall in TB case detection due to the disruption of health services caused by the coronavirus disease (COVID-19) pandemic, most PICs reported no or limited COVID-19 community transmission in 2020. Therefore, extensive TB service disruption was unlikely. Data submitted by the PICs are often incomplete. Notably, data on age and sex distribution and HIV test results were missing for 71% and 76% of the cohort, respectively. Hence, some data shown in this report might not represent the subregion.

In conclusion, the number of notified TB cases in PICs has increased over the years, with signs of ongoing active community transmission, and the burden is distributed unevenly across countries and areas. The ongoing effort to scale up laboratory services is an achievement, and the implementation of community-based screening appears promising especially in small island settings. Greater effort and investment are needed to reach the unreached population including those who have risk factors and socioeconomic and geographical disadvantages. Furthermore, strengthening routine contact investigation, scaling up TB preventive treatment, and ensuring proper management of TB cases and comorbidities through a patient-centred approach are priority interventions to end TB in the context of PICs.

#### Conflicts of interest

The authors have no conflicts of interest to declare.

#### Ethics statement

Ethics approval was not required as we used publicly available, routinely collected and anonymized surveillance data.

#### Funding

None.

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# Epidemiology of tuberculosis in Mongolia: analysis of surveillance data, 2015–2019

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Mongolia has a high tuberculosis (TB) burden. Data from routine paper-based surveillance were used to describe the epidemiology of TB in Mongolia; the data included testing presumptive TB cases, TB notifications, drug-resistant cases, treatment outcomes and notifications in prisoners. The proportion of the population tested for TB increased between 2015 and 2019. The number and rate per 100 000 population of TB notifications decreased between 2015 and 2018 and then increased in 2019. Most TB notifications in 2019 were in the capital, Ulaanbaatar (59.3%), followed by the central (16.8%), Khangai (10.4%), east (8.5%) and west (5.0%) regions. About half of TB notifications nationally were bacteriologically confirmed (45.4% in 2015, 48.1% in 2019), with the proportion of bacteriologically confirmed TB per province or district varying from 0% to 66%. High TB notification rates were observed in 2019 for males aged 15–54 years (202 per 100 000 population) and females aged 15-34 years (190 per 100 000 population). Treatment success for all forms of TB was 90% in 2019 but was below the 90% target for bacteriologically confirmed cases. Between 2015 and 2019, the number of RR/MDR-TB notifications ranged from 265 to 211. The Mongolian National Tuberculosis Programme needs to continue its efforts in TB control, to further increase the programmatic impact and reduce the TB burden. It is recommended that Mongolia continue to increase TB screening, the use of Xpert testing, contact investigations and preventive treatments, and targeting interventions to the high-burden areas identified in this subnational analysis.

n 2021, there were an estimated 10.6 million cases and 1.4 million deaths from tuberculosis (TB) globally, with 14% of cases in the Western Pacific Region.<sup>1</sup> The first national TB prevalence survey in Mongolia was conducted in 2014-2015; it estimated the pulmonary TB prevalence to be 441 per 100 000 population, and the prevalence of all forms of TB to be 757 per 100 000 population.<sup>2</sup> Based on the newly available data, TB incidence was re-estimated by the World Health Organization (WHO) to be 437 (uncertainty range: 224–719) per 100 000 population,<sup>3</sup> ranking Mongolia among the 30 countries with the highest TB incidence in the world.1

Mongolia's National Tuberculosis Programme (NTP) surveillance system is a combination of a paper-based aggregated system and a digital case-based system that covers TB cases from screening through to completion of treatment. Subnational analysis of key TB indicators and trends over time is useful for programmatic decisionmaking and helps to increase programmatic impact where interventions can be tailored to local dynamics.<sup>4,5</sup> Through analysis of routine surveillance data, we report TB epidemiology and key programmatic indicators at the national and subnational levels for 2015-2019.

# **METHODS**

# Description of the surveillance system

In Mongolia, TB cases can be detected through passive case detection, in which symptomatic individuals attending primary care facilities are screened for TB. Those who present with a persistent cough are referred to a TB dispensary for a diagnostic evaluation by sputum smear microscopy. If smear-positive, the patient is registered as a confirmed TB case and is started on treatment; if smear-negative, a chest X-ray is conducted. Since 2017, the Xpert MTB/RIF test is also conducted where possible.

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Cases can also be detected through screening of close contacts of TB cases or through active case finding in high-risk groups (e.g. people living with HIV, miners and prisoners). Contacts and high-risk groups are tested through symptom screening and chest X-ray, and the tuberculin skin test (TST) is also used for child contacts. Contacts and those from high-risk groups who are positive on screening are referred for diagnostic evaluation to TB dispensaries.

All cases are registered on paper forms at the TB dispensaries; staff then compile aggregate monthly reports of notifications and treatment outcomes and send them to the provincial level, where they are aggregated each quarter and sent to the national level, where they are collated and reviewed for timeliness, completeness and accuracy by an NTP statistician. The system uses standardized TB collection forms updated with the latest WHO reporting framework for TB case detection and treatment outcomes.<sup>6</sup> From 2018, the digital case-based system, TUBIS, has been used to collect individual case data, capturing 90% of the data from the paper-based system.

# Data analysis

National TB surveillance data for 2015–2019 were retrospectively analysed, using data sourced from the aggregated paper-based system. Rates were calculated using population projections from the National Statistical Office of Mongolia, and vital and civil registration from the 2010 census for the denominator. Analysis included testing of presumptive TB cases and number of notifications by age, sex, patient type and location, drug-resistant cases, treatment outcomes and notifications in prisoners.

Patient type was classified into bacteriologically confirmed TB, extra-pulmonary TB, clinically diagnosed TB and other previously treated TB. Subnational analysis was conducted for the east, central, Khangai and west regions, plus the capital Ulaanbaatar. Regions were further analysed by their provinces, and Ulaanbaatar by its districts. Drug resistance categories included cases with mono-drug and poly-drug resistance, and cases with rifampicin resistance or multidrug resistance (RR/MDR). Treatment outcomes for bacteriologically confirmed TB cases included treatment success, treatment failure, death and loss to follow-up (LTFU). Stata software (Stata

Corp, 16.0, College Station, TX, United States of America) was used for analysis. RR/MDR-TB treatment outcomes were analysed for the 2017 cohort only because in most cases treatment duration is 24 months.

### RESULTS

### Testing of presumptive TB cases

The proportion of the population tested for TB increased from 2015 to 2019, as did the proportion of the population tested by X-ray (Fig. 1).

In 2019, 85.7% (n = 4664/5422) of registered TB contacts were tested, with 4.0% (n = 185) diagnosed with TB. These were slight increases compared with 2015 (81% and 3.3%, respectively). The proportion of child contacts (aged 0-14 years) who were TST-positive was 20.2% (n = 424/2102) in 2019, an increase from 16.7% (n = 324/1936) in 2015. The proportion of TST-positive child contacts who started on TB-preventive treatment was 71.2% (n = 302/424) in 2019, an increase from 46.0% (n = 149/324) in 2015.

The smear positivity rate was 8% (n = 2376/28753) in 2019, a decrease from 12% (n = 2812/23703) in 2015. This varied subnationally, from 5% (n = 570/14 301) in 21 provinces to 10% (n = 3565/36714) in Ulaanbaatar. Of the 17 854 Xpert MTB/RIF tests done in 2019, 3070 (17.2%) were MTB-positive, of which 261 (8.5%) were RR-TB.

# Case notifications by patient type

The number and rate of notified TB cases decreased between 2015 and 2018, and then increased in 2019 (Fig. 2A). The increase in 2019 was observed for bacteriologically confirmed TB, extra-pulmonary TB and clinically diagnosed TB (Fig. 2B).

In 2019, there were 133 per 100 000 population new and relapse TB cases notified, representing 31% of the WHO-estimated incident cases (n = 14 000). Of all TB notifications in 2019, 85.4% (n = 3624) were new cases, 11.0% (n = 465) were relapse cases, 3.4%(n = 146) were cases requiring retreatment after treatment failure or LTFU and 0.2% (n = 9) had unknown TB treatment history.



Proportion of the population examined for TB by test, Mongolia, 2015-2019 Fig. 1.

The combined proportion of cases requiring retreatment and relapse cases increased from 13.2% (n = 652/4935) in 2015 to 14.4% (n = 611/4244) in 2019. The proportion of extra-pulmonary TB cases decreased from 41.9% (n = 2068/4935) in 2015 to 35.7%(n = 1513/4244) in 2019. Bacteriologically confirmed TB cases comprised about half of all TB cases (45.5% [n = 2244/4935] in 2015 and 48.1% [n]2041/49244] in 2019). Of the pulmonary cases, 74.8% (n = 2043/2731) were bacteriologically confirmed in 2019.

#### Subnational case notifications

Most notifications in 2019 occurred in Ulaanbaatar, followed by the central (excluding Ulaanbaatar), Khangai, east and west regions (Table 1). The notification rate increased in the east region from 2017, and in the other four regions from 2018 (Fig. 3A). The proportion of cases that were bacteriologically confirmed increased from 2016 in Ulaanbaatar and Khangai, from 2017 in central and from 2018 in the west region (Fig. 3B). Notification rates per 100 000 varied substantially across provinces in 2019, ranging from 37 to 172 (Fig. 4). In 2019, the proportion of bacteriologically confirmed TB per province or district within each region varied substantially (Ulaanbaatar: 0-51%, east: 34-60%, central: 43–66%, Khangai: 38–57% and west: 39–58%) (Fig. 5).

### Case notifications by sex and age in 2019

The highest numbers of case notifications in 2019 were seen in males aged 15-54 years and females aged 15-34 years (Fig. 6). This distribution varied by TB type: 57.2% of new cases were male, with a mean (± standard deviation [SD]) age of 33 (± 17.3) years, whereas 66.9% of relapse cases were male, with a mean age of 40 ( $\pm$  13.9) years. In 2019, 9.1% (n = 415) of TB notifications were aged under 15 years and 2.7% (n = 121) were aged under 5 years. Subnational analysis showed large variations in the proportion of cases by age group and among children, with some provinces having no paediatric TB notifications or only small numbers of such notifications (Fig. 7).

#### **Drug-resistant TB**

Between 2015 and 2019, the number of RR/MDR-TB notifications ranged from 265 to 211 (Fig. 8). In 2019, 211 RR/MDR-TB cases were diagnosed; of these, 92% (n = 193) were enrolled in second-line TB treatment, an increase from 85% of the 265 cases in 2015. Seven extensively drug-resistant TB (XDR-TB) cases were diagnosed in 2019.

Of the 211 RR/MDR-TB cases, 46.9% (n = 99) were new cases and 41.7% (n = 88) were relapse and

5000 180 Α Notifications Rates 160 160 149 4800 100 000 population 138 140 128 125 Number of TB notifications 4600 120 100 4400 rate per 80 4200 60 TB notification 40 4000 20 3800 0 2015 2016 2017 2018 2019 В 80 TB notification rate per 100 000 population 70 60 58.4 50 45.8 40 30 20 20.9 10 0 2015 2016 2017 2018 2019 Bacteriologially confirmed, new and relapse
 EPTB, new and relapse Clinically diagnosed, new and relapse Other previously treated

Fig. 2. (A) Number and rate per 100 000 population of TB notifications, and (B) TB notification rates per 100 000 population by type of TB, Mongolia, 2015-2019

EPTB: extra-pulmonary tuberculosis.

other previously treated cases. Of new RR/MDR-TB cases, 40.4% were female, similar to the proportion seen in all TB notifications. The mean age for new RR/ MDR-TB cases was 34.9 (± 18.4) years, similar to the proportion seen in all TB notifications (33  $\pm$  17.3). The mean age for relapse and other previously treated RR/ MDR cases was 41 (± 14.3).

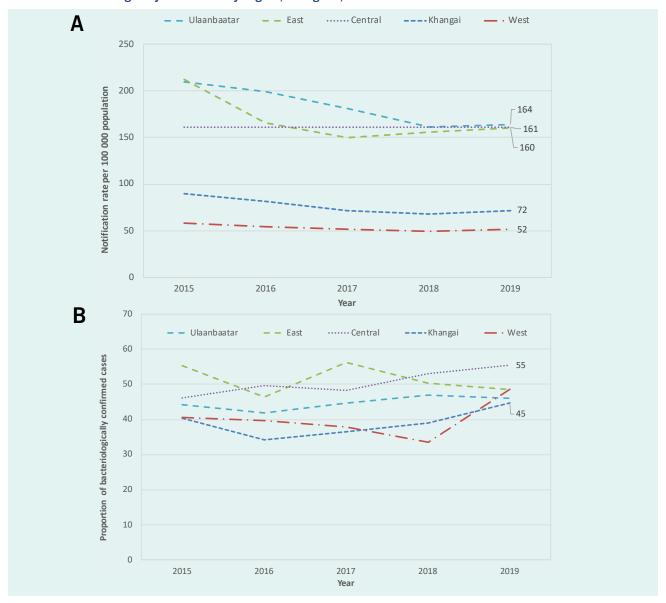
#### **Treatment outcomes**

The proportion of TB notifications with treatment success increased from 88.8% in 2015 to 90.0% in 2019. The proportion of deaths decreased from 4.6% in 2015 to 2.5% in 2019. The proportion of cases that were LTFU was stable (4.6% in 2018), as was the proportion

Table 1. Number and rate per 100 000 population of TB notifications by treatment history and proportion of retreatment and extra-pulmonary TB by province or district, Mongolia, 2019

		Natifica	tions (NI)	Rates pe	r 100 000	Ромоси	.togo (9/)	
Region and	Population	Notifica	Notifications (N)		population		Percentage (%)	
provinces or districts	. opalation	New and relapse	Previously treated	New and relapse	Previously treated	Retreatment	Extra- pulmonary TB	
Ulaanbaatar	1 515 593	2359	127	156	8	5.1	37.1	
Baganuur	28 570	25	0	88	0	0	28.0	
Bayangol	225 840	318	7	141	3	2.2	48.0	
Bayanzurkh	361 689	638	52	176	14	7.5	48.0	
Nalaih	37 659	40	5	106	13	11.1	37.8	
Songinokhairkhan	327 580	581	30	177	9	4.9	38.3	
Sukhbaatar	144 409	154	0	107	0	0	35.7	
Khan-Uul	187 278	246	10	131	5	3.9	25.8	
Chingeltei	148 977	304	16	204	11	5.0	38.4	
Bagakhangai	4123	0	0	0	0	0	0	
East	221 764	348	7	157	3	2	30.7	
Khentii	77 493	139	1	179	1	0.7	40.0	
Dornod	81 519	112	5	137	6	4.3	20.5	
Sukhbaatar	62 752	97	1	155	2	1.0	29.6	
Central	515 025	696	7	135	1	1	31.0	
Selenge	110 757	174	2	157	2	1.1	25.0	
Umnugovi	67 955	36	0	53	0	0	44.4	
Tuv	94 956	173	2	182	2	1.1	36.6	
Darkhan-Uul	106 470	172	2	162	2	1.1	29.3	
Govisumber	17 862	18	0	101	0	0	27.8	
Dundgov	46 866	31	0	66	0	0	51.6	
Dornogovi	70 159	92	1	131	1	1.1	23.7	
Khangai	604 784	427	7	71	1	2	50.5	
Orkhon	106 810	90	4	84	4	4.3	52.2	
Uvurkhangai	116 922	61	0	52	0	0	58.8	
Bayankhongor	88 514	59	0	67	0	0	51.3	
Arkhangai	95 857	58	0	61	0	0	58.0	
Khuvsgul	134 530	111	3	83	2	2.6	44.7	
Bulgan	62 151	48	0	77	0	0	40.0	
West	410 507	209	3	51	1	1	39.2	
Uvs	83 766	46	1	55	1	2.1	23.4	
Bayan-Ulgii	106 810	44	0	41	0	0	52.3	
Zavkhan	72 801	36	2	49	3	5.3	52.6	
Khovd	89 021	50	0	56	0	0	36.0	
Gobi-Altai	58 109	33	0	57	0	0	33.3	

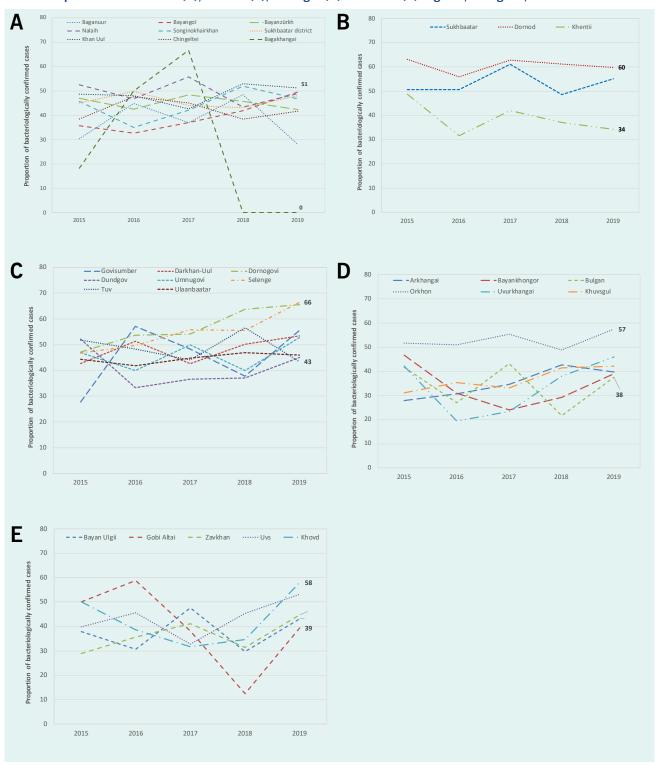
Fig. 3. (A) TB notification rates per 100 000 population by region, and (B) proportion of TB cases that were bacteriologically confirmed by region, Mongolia, 2015-2019



Map of TB notification rates per 100 000 population by province, Mongolia, 2019 Fig. 4.



Fig. 5. Proportion of TB cases that were bacteriologically confirmed by district in Ulaanbaatar (A) and by province in the east (B), central (C), Khangai (D) and west (E) regions, Mongolia, 2015-2019



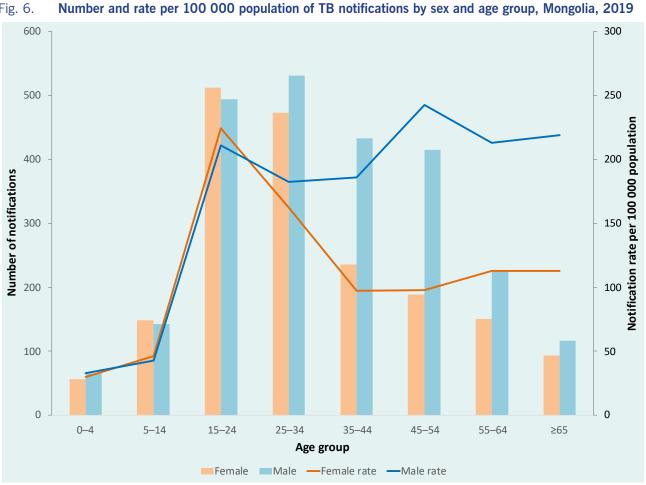


Fig. 6.

of those not evaluated (0.4% in 2019). Since 2016, the treatment success rate has been above 90% for all types of TB except for bacteriologically confirmed TB cases (85.4%). The death rate was highest among relapse cases (4.8%).

In 2019, the treatment success rate for bacteriologically confirmed cases was less than 90% in three provinces (Dornogovi, Khovd and Orkhon) and Ulaanbaatar (Fig. 9). Ulaanbaatar reported relatively poor treatment outcomes compared with other provinces; 8% of bacteriologically confirmed cases were LTFU, 5% failed and 4% died.

In 2017, 56% (n = 122/216) of RR/MDR-TB patients enrolled in treatment were successfully treated, a slight decrease from 60% in 2015-2016. The LTFU rate among RR/MDR-TB cases increased from 16% in 2016 to 26% in 2017. Of seven XDR-TB cases in the 2017 patient cohort, two (28.6%) were successfully treated, one (14.3%) failed, three (42.9%) died and one (14.3%) was LTFU.

#### TB in prisoners

TB notifications in prisoners decreased from 92 (1.9%) in 2015 to 54 (1.3%) in 2019. A higher proportion of bacteriologically confirmed cases (64.3%) and relapse cases (25.9%) were notified than from the national data (58.5% and 11%, respectively).

# **DISCUSSION**

The results of this TB surveillance analysis demonstrate the progress of the NTP in Mongolia, with increases in the proportion of the population screened for TB, bacteriological confirmation, treatment success and TB-preventive treatment in children. Intensification of case-finding activities through the expansion of Xpert

Khuvsgul Zavkhan Bayan-Ulgii Gobi-Altai Uvs Khovd

0

10

20

30

Ulaanbaatar Khentii East Dornod Sükhbaatar Umnugovi Darkhan-Uul Dornogovi Govisumber Selenge Dundgovi Tuv Bayankhongor Orkhon Khangai Bulgan Uvurkhangai Arkhangai

Fig. 7. Proportion of TB notifications by age group and province, Mongolia, 2019



40

■ 0-14 ■ 15-24 ■ 25-34 ■ 35-44 ■ 45-54 ■ 55-64

50

Percentage

60

70

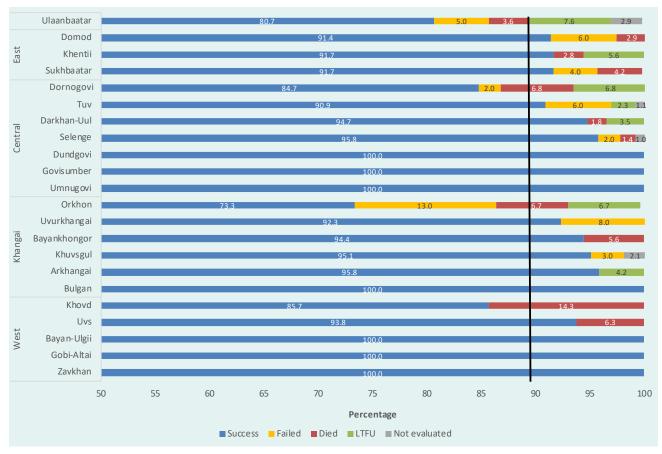
80

90

100



DR: drug resistance; RR/MDR: rifampicin resistance or multidrug resistance.



Proportion of bacteriologically confirmed TB notifications by treatment outcomes and province, Fig. 9. Mongolia, 2019

The black line indicates the WHO 90% target for TB treatment success. LTFU: loss to follow-up.

testing and sustaining treatment success, particularly in Ulaanbaatar, will probably increase the impact of the NTP and reduce the national TB burden.

The number and rate of TB notifications decreased in 2015-2018 and increased in 2019, despite increases in screening. Similar trends have also been observed in other high-burden countries such as Cambodia, where estimated TB incidence is declining. 4,5 The expansion of X-ray and Xpert testing and the strengthening of the specimen transportation system may have resulted in an increase in notifications and an increased proportion of bacteriological confirmation in 2019. However, WHO estimates that the TB notification system is detecting only 31% of TB cases in the country. To fill this gap, the NTP needs to intensify its efforts in screening high-risk populations.7

The WHO-estimated incidence of RR/MDR-TB for Mongolia was one of the highest among countries in the Western Pacific Region. However, the number of RR/ MDR-TB notifications did not increase during the study period, highlighting a case-detection gap that is also found in other countries.4 To respond to the burden of DR-TB, there is an urgent need to increase the coverage of Xpert as an initial diagnostic test and reduce diagnostic delays.

The high caseload in younger age groups suggests recent transmission, emphasizing the need to expand and accelerate case detection. Exposure to tobacco and solid fuels for heating has been significantly associated with bacteriological TB,8 which may contribute to the higher rates in these age groups. The proportion of TB in children varied widely across provinces. As in many settings

globally, there is a need to strengthen the capacities of physicians in diagnosing paediatric TB and expand Xpert testing in children to increase correct and timely diagnoses.<sup>1,9</sup> TB among prisoners decreased during the study period, as it did in the previous decade. 10 Furthermore, the proportion of relapse cases among prisoners was more than double that of the general population.

A decrease in the proportion of deaths of TB cases has improved overall treatment outcomes, but because of persistently high rates of LTFU, bacteriologically confirmed TB treatment success rates remain below 90%. Addressing physical barriers to TB services for mobile populations (including nomads) and reducing financial barriers may improve health access for vulnerable patients. The low treatment success rate among DR-TB cases needs attention, especially considering the increase in the notification rate of MDR-TB found in the national drug resistance survey in 2017, compared with that in 2007.<sup>11</sup> The use of Xpert as a front-line test and the implementation of a shorter all-oral regimen for MDR-TB treatment should be prioritized. 12

Our analysis is limited to TB cases diagnosed and reported to the NTP; thus, it does not represent all estimated cases of TB in Mongolia. The 70% casedetection gap estimated at the national level is likely to vary between provinces and this was not detected by our analysis. A full transition to the digital case-based system and discontinuing the paper-based system would bolster routine data analysis because individual case data provide more detail than the aggregate data.

The Mongolian NTP needs to continue its efforts in TB control to achieve further progress. Expanding and accelerating case detection with Xpert and ensuring the treatment success of bacteriologically confirmed TB would probably reduce the TB burden. Other priorities are addressing transmission in men and young adults, and strengthening paediatric TB diagnosis. The focus should be on Ulaanbaatar because it has higher notification rates and suboptimal treatment outcomes, and overcrowding and pollution that increase the risk of transmission. Advancing a multisectoral response is critical to addressing social determinants of TB such as indoor air pollution.

TB surveillance data provide an opportunity to conduct subnational analyses, to inform districts of their comparative epidemiological trends and programmatic performance. National and subnational TB programmes can tailor and target interventions addressing local-level issues identified in routine analysis, contributing to ending TB by 2030.

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# Conflicts of interest

The authors have no conflicts of interest to declare.

#### Ethics statement

Ethical clearance was not required because the analysis was based on routine data with no identifiable information.

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# After-action reviews for emergency preparedness and response to infectious disease outbreaks

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ince early 2020, health systems around the world have faced challenges in adequately responding to the coronavirus disease (COVID-19) pandemic. Systems have adapted to the evolving epidemic, and different measures have been implemented at different times in different contexts. Evaluating responses to significant public health events such as outbreaks of infectious diseases is often not prioritized or undertaken due to a lack of resources or time, despite its established importance in improving future preparedness and response measures. 1-3 Notable examples of evaluations of responses to major infectious disease outbreaks include those for the 2014–2015<sup>4</sup> Ebola virus disease epidemic in the European Union and the 2013<sup>5</sup> H1N1 influenza epidemics in Canada and the United States of America. Evaluations have also been conducted for responses to natural disasters, such as the 2017 wildfires in Portugal<sup>6</sup> and Hurricane Katrina in the United States in 2005.7

In 2015, the World Health Organization (WHO) developed the after-action review (AAR) toolkit as a component of the International Health Regulations (2005; IHR).8-11 AARs aim to assess the what, how and why of a response to a significant public health event, to identify the best practices and challenges encountered during the response, and to propose mid- and long-term actions for improvement. The WHO AAR methods were developed to evaluate responses generally to any type of public health event. 11 AARs consist of nine pillars for which best practices, challenges and lessons learned are to be identified: (i) country-level coordination and monitoring, (ii) risk communication, (iii) surveillance, (iv) points of entry, (v) the national laboratory system,

(vi) infection prevention and control, (vii) case management, (viii) operations and logistics and (ix) maintaining health services. 11

Conducting and reporting on an AAR requires three steps: (i) objective observation (i.e. a structured review of response activities); (ii) an analysis of gaps, best practices and contributing factors to the results of the response; and (iii) identification of areas for improvement and proposed follow-up actions. WHO suggests four methods that can be used to conduct an AAR: (i) debriefings, (ii) working groups, (iii) interviews with key informants and (iv) mixed-methods studies. Depending on the context, AARs can be conducted in different formats and cover different areas of the response. WHO also suggests that the findings of evaluations are compared against the IHR (2005) core capacities. 11 Final results should be summarized in a qualitative format, and evaluations by participants contributing to it are encouraged.

It is unclear to what extent WHO's AAR methods are being used to assess public health responses to events involving emerging infectious diseases and, in particular, how closely such evaluations follow WHO guidance. We undertook a rapid review of the global literature with the objective of understanding how the WHO AAR methods are being used to assess public health responses to infectious disease events.

We searched PubMed using different combinations of keywords such as "after action review", "infectious disease", "World Health Organization", "epidemic", "outbreak" and "emergency" (Table 1). We also searched the

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Search terms used and number of records retrieved from PubMed for study of after-action reviews that Table 1. use WHO criteria, 2015-2021

Search	Fields searched	Query (filter: English)	No. of records
1	AII	after action review	49
2	AII	infectious disease	677 493
3	AII	epidemic OR outbreak OR emergency	549 053
4	AII	World Health Organization	98 489
5	All	infectious disease OR epidemic OR outbreak OR emergency (searches 2 and 3 combined)	1 176 137
6	All	after action review AND infectious disease OR epidemic OR outbreak OR emergency (searches 1 and 5 combined)	20
7	All	after action review AND World Health Organization (searches 1 and 4 combined)	4
8	AII	after action review AND infectious disease OR epidemic OR outbreak OR emergency OR after action review AND World Health Organization (searches 6 and 7 combined)	22
9	Date of publication	(2015[Date - Publication]: 2021[Date - Publication])	8 222 679
10	AII	after action review AND infectious disease OR epidemic OR outbreak OR emergency OR after action review AND World Health Organization AND (2015[Date - Publication]: 2021[Date - Publication]) (searches 8 and 9 combined)	16

WHO Strategic Partnership for Health Security and Emergency Preparedness' After Action Review database, 12 WHO's main public repository for AARs. We included all articles and reports in English published or uploaded from January 2015 to December 2021 that described using WHO AAR methods to evaluate responses to infectious disease outbreaks. Reports or publications were excluded if they were incomplete, did not use the WHO AAR toolkit, were not published in English or did not evaluate infectious disease events. Results were merged, duplicates removed and the remaining reports screened against the inclusion and exclusion criteria, and reasons for exclusion were documented.

For the included reports, we extracted the key characteristics of the AAR method for use in a descriptive analysis. We also assessed how closely the included AARs followed the WHO AAR methods and how effective the methods were in assessing the response. The following data were extracted from each record: general information, including authors and year of publication; setting; scope of evaluation (national, regional or agency level); the event being evaluated; and the year of the event. The reports were then compared against WHO's AAR guideline (Table 2). After screening 86 records, 8 were included in the analysis, 4 from the WHO AAR database and 4 peer-reviewed articles retrieved from PubMed (Fig. 1, Table 3).

Three AARs<sup>13–15</sup> used WHO-recommended methods in combination with other evaluation tools, such as document reviews or surveys in addition to quantitative assessments. The remaining five 16-20 strictly followed WHO's nine evaluation pillars and three steps, and were conducted as conferences that brought together all stakeholders. Four of the eight reports used working groups, 16-19 three used debriefings 13-15 and one used key-informant interviews, 20 following WHO's AAR readyto-use toolkits.

Public health systems were a common focus of evaluations, appearing in seven AARs, 13-19 while another AAR focused on a hospital setting.<sup>20</sup> Five AARs were conducted at the local level in response to outbreaks<sup>13–15,19,20</sup> and three at the national level. 16–18

Three AARs included participants' evaluations of and feedback on the AAR method. 17-19 Although the overall assessment of the suitability of AARs to connect stakeholders, provide a platform for ideas and to pool experiences was positive, as evidenced by responses from more than 80% of participants in each of these three studies, only half of the participants agreed that AARs actually achieved their objectives. 17-19 In terms of strengthening interdisciplinary collaboration and coordination, less than 20% of participants in these studies rated this as being accomplished by the AAR. 17-19 Ad-

Data extracted from reports of after-action reviews that use WHO criteria, 2015-2021 Table 2.

Data extracted	Variable
Format	WHO guideline: debriefing, working group, key-informant interviews or mixed-methods study Other
Pillar of evaluation	WHO guideline: (i) country-level coordination and monitoring; (ii) risk communication; (iii) surveillance; (iv) points of entry; (v) the national laboratory system; (vi) infection prevention and control; (vii) case management; (viii) operations and logistics; and (ix) maintaining health services Other
Phases of evaluation	WHO guideline: design, preparation and implementation Other
Comparison with International Health Regulations (2005) core capacities	WHO guideline: Yes No
Final evaluation by participants	WHO guideline: Yes No
Reporting format	WHO guideline: qualitative format with three-part structure: (i) objective observation (i.e. a structured review of response activities); (ii) analysis of gaps, best practices and contributing factors to the results of the response; (iii) identification of areas for improvement and proposals for follow-up actions Other
Follow-up plan for improvement	WHO guideline: Yes No

ditionally, the importance of allowing AAR methods to be adjusted to best fit their purposes (e.g. for smaller-level analyses, such as within a unit, region or single institution) is highlighted by the fact that three of the eight reports did not strictly follow WHO's AAR structure. 13-15 The importance of making modifications to conduct a more focused system evaluation was also flagged by Sorbello et al.<sup>20</sup> as a way to improve follow-up actions within local contexts and to enhance multidisciplinary cooperation. Despite being recommended by WHO, none of the AARs used the IHR (2005) core capacities as a comparator.

Only a limited number of AARs have been published in the scientific and grey literature. As of August 2022, the global public repository for AARs at WHO<sup>12</sup> listed 81 entries since 2016. However, 66 (88%) of the 75 entries categorized as having been conducted were incomplete, of which 41 were older than 2 years and hence are unlikely to ever be finalized. Furthermore, many entries had only minimal information about the setting and category of emergency, and were without much content about the AAR itself. It was also often difficult to establish whether an AAR had actually been conducted and completed successfully. The problem of identifying and accessing information about AARs has also been recognized in a recent review from Australia.21

From the completed reports, it is evident that WHO's methods were not always strictly followed, but they were often used in combination with other methods for qualitative and quantitative assessment. While the qualitative element of WHO's AAR toolkit seems to have been easier to follow in conference settings with all relevant stakeholders present, several AARs required methodological modifications, using, for example, surveys or document reviews, and also incorporated quantitative methods, depending on the local context. One of WHO's main recommendations for conducting AARs is to compare the outcomes of the response with the IHR (2005) core capacities - a country-level assessment - yet this comparison was not done in any of the studies included in our analysis.

WHO's AAR methodology is relatively broad and geared towards whole-of-system evaluations. The nine AAR evaluation pillars and the accompanying toolkit are also rather general. As a result, AARs were more frequently used for evaluations of district- and national-level systems rather than for specific systems (e.g. surveillance systems, national laboratories or point-of-entry screening). However, assessments should be conducted for all levels and aspects of health systems to ensure a comprehensive response; therefore, AAR toolkits should

Table 3. Summary of articles and reports included in the study of after-action reviews that use WHO criteria, 2015-2021

Author (year)	Publication type	Setting	Scope of evaluation	Event under evaluation (year)	Evaluation approaches	Areas being evaluated	Application of WHO AAR methodology
Mase et al. (2017) <sup>13</sup>	Peer- reviewed journal article	Ohio, USA	Public health departments	H1N1 influenza mass vaccination campaign (2017)	Document review Debriefings	(1) Mass vaccination (2) Volunteer management	<ul><li>☐ Followed AAR structure</li><li>☑ Followed AAR pillars for evaluation</li></ul>
					Questionaire survey	<ul> <li>(3) Community mitigation</li> <li>(4) Interoperable communications</li> <li>(5) Risk communication</li> <li>(6) Epidemiological surveillance and investigation</li> </ul>	(focus on vaccination)  I Followed AAR approaches (in combination)  Comparison with IHR (2005)  Followed AAR qualitative reporting format  Final evaluation from participants
Tapo et al. (2021) <sup>14</sup>	Peer- reviewed journal article	Vanuatu	International health centre	COVID-19 epidemic (2020)	Document review  Debriefing	<ol> <li>Coordination and staffing</li> <li>Pre-arrival preparations</li> <li>Pre-departure preparations (point of origin)</li> <li>Upon arrival at the airport in Vanuatu</li> <li>Check in to quarantine facilities</li> <li>During quarantine</li> <li>Quarantine discharge</li> </ol>	<ul> <li>□ Followed AAR structure</li> <li>☑ Followed AAR pillars for evaluation (focus on point of entry)</li> <li>☑ Followed AAR approaches (in combination)</li> <li>□ Comparison with IHR (2005)</li> <li>☑ Followed AAR qualitative reporting format</li> <li>□ Final evaluation from participants</li> </ul>
Boland et al. (2017) <sup>15</sup>	Peer- reviewed journal article	Sierra Leone	District health sys- tem, Port Loko district and Kambia district	Ebola virus disease outbreak (2014–2017)	Document review  Debriefing  Question- naire survey	<ul><li>(1) Environment and infrastructure</li><li>(2) Sociocultural aspects</li><li>(3) Political and organizational aspects</li></ul>	<ul> <li>□ Followed AAR structure</li> <li>□ Followed AAR pillars for evaluation</li> <li>☑ Followed AAR approaches (in combination)</li> <li>□ Comparison with IHR (2005)</li> <li>☑ Followed AAR qualitative reporting format (in combination with quantitative report)</li> <li>□ Final evaluation from participants</li> </ul>

Author (year)	Publication type	Setting	Scope of evaluation	Event under evaluation (year)	Evaluation approaches	Areas being evaluated	Application of WHO AAR methodology
Nigeria Centre for Disease Control and WHO (2017) <sup>16</sup>	Non-peer- reviewed report	Nigeria	National public health system	Lassa fever outbreak (2016–2017)	Working groups	<ol> <li>(1) Coordination</li> <li>(2) Epidemiological surveillance</li> <li>(3) Case management and infection prevention and control</li> <li>(4) National laboratory system</li> <li>(5) Logistics</li> <li>(6) Risk communication</li> </ol>	<ul> <li>➢ Followed AAR structure</li> <li>➢ Followed AAR pillars for evaluation</li> <li>➢ Followed AAR approaches</li> <li>☐ Comparison with IHR (2005)</li> <li>➢ Followed AAR qualitative reporting format</li> <li>☐ Final evaluation from participants</li> </ul>
Nigeria Centre for Disease Control and WHO (2018) <sup>17</sup>	Non-peer- reviewed report	Nigeria	National public health system	Lassa fever outbreak (2018)	Working groups	<ol> <li>Coordination and logistics</li> <li>Case management, safe burial, and infection prevention and control</li> <li>Risk communication and social mobilization</li> <li>National laboratory system</li> <li>Epidemiological surveillance</li> </ol>	<ul> <li>☒ Followed AAR structure</li> <li>☒ Followed AAR pillars for evaluation</li> <li>☒ Followed AAR approaches</li> <li>☒ Comparison with IHR (2005)</li> <li>☒ Followed AAR qualitative reporting format</li> <li>☒ Final evaluation from participants</li> </ul>
Nigeria Centre for Disease Control and WHO (2018) <sup>18</sup>	Non-peer- reviewed report	Nigeria	National public health system	National cerebrospinal meningitis outbreak (2017–2018)	Working groups	<ol> <li>Coordination</li> <li>Epidemiological surveillance</li> <li>Case management</li> <li>Risk communication and social mobilization</li> <li>National laboratory system</li> <li>Logistics for vaccination</li> </ol>	<ul> <li>☑ Followed AAR structure</li> <li>☑ Followed AAR pillars for evaluation</li> <li>☑ Followed AAR approaches</li> <li>☐ Comparison with IHR (2005)</li> <li>☑ Followed AAR qualitative reporting format</li> <li>☑ Final evaluation from participants</li> </ul>

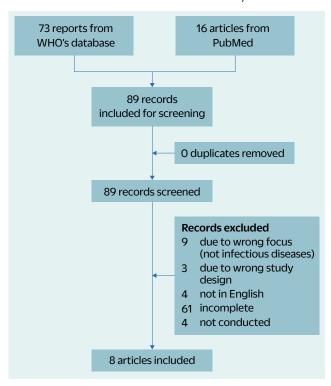
Author (year)	Publication type	Setting	Scope of evaluation	Event under evaluation (year)	Evaluation approaches	Areas being evaluated	Application of WHO AAR methodology
Nigeria Centre for Disease Control and WHO (2018) <sup>19</sup>	Non-peer- reviewed report	Nigeria	Public health system, Maiduguri Borno state	Cholera outbreak in camp for displaced people (2017)	Working groups	<ol> <li>Coordination and logistics</li> <li>Epidemiological surveillance and the national laboratory system</li> <li>Case management, and infection prevention and control</li> <li>Risk communication and community engagement</li> <li>Water, sanitation and hygiene</li> <li>Oral cholera vaccination</li> </ol>	<ul> <li>☒ Followed AAR structure</li> <li>☒ Followed AAR pillars for evaluation</li> <li>☒ Followed AAR approaches</li> <li>☐ Comparison with IHR (2005)</li> <li>☒ Followed AAR qualitative reporting format</li> <li>☒ Final evaluation from participants</li> </ul>
Sorbello et al. (2021) <sup>20</sup>	Peer-reviewed journal article	Italy	Hospital of San Raffaele Scientific Institute, Milan	COVID-19 epidemic (2020)	Key- informant interviews	<ul> <li>(1) Staff management</li> <li>(2) Logistics and supplies</li> <li>(3) COVID-19 diagnosis and clinical management</li> <li>(4) Risk communication</li> </ul>	Followed AAR structure  Followed AAR pillars for evaluation (modified to quantitative ranking of effectiveness)  Followed AAR approaches  Comparison with IHR (2005) Followed AAR qualitative reporting format  Final evaluation from participants

AAR: after-action review; IHR: International Health Regulations; WHO: World Health Organization.

be flexible enough to be adapted to different jurisdictions and scopes of assessment to accommodate diverse evaluation needs. Thus, modifications to WHO's AAR guidance are important to ensure that relevant information can be gathered from a wider range of sources and a more diverse group of stakeholders to fully consider local contexts and different scopes of evaluation. Furthermore, understanding IHR (2005) core capacities could offer important lessons for conducting AARs. However, comparison against IHR (2005) core capacities is rarely done as part of AARs despite being encouraged by WHO. We also found that several AARs in the WHO repository were implemented without assessments from participants and stakeholders.

WHO issued a modified version of its methods for AARs at the beginning of the COVID-19 pandemic, known as intra-action reviews (IARs), to meet the need to rapidly assess health systems' performance during the ongoing pandemic. As of August 2022, there were 144 IARs listed in the WHO database; 22 129 of them (89.6%) were categorized as conducted, but only 19 of these (14.7%) were accompanied by a completed report, suggesting there are issues in finalization and publication similar to those for AARs. IARs include four additional pillars that are relevant to the ongoing COVID-19 pandemic: (i) COVID-19 vaccination, (ii) vulnerable and marginalized populations, (iii) national legislation and financing, and (iv) public health and social measures.<sup>23</sup> However, only two

Flow chart of studies and reports retrieved Fig. 1. from PubMed for assessment of after-action reviews that use WHO criteria, 2015-2021



IARs categorized as conducted in the database included information about COVID-19 vaccination, and none of the IARs provided information about the other three pillars. Therefore, it is unclear whether IARs have contributed to improving evaluations of health system responses. The IAR adaptation of the AAR remains relatively broad and geared towards national-level responses. Similar to AARs, we believe that IARs would greatly benefit from regular evaluation of the methodology itself to better guide and prepare countries and health-care systems for future, protracted health emergencies beyond the COVID-19 pandemic.<sup>23</sup>

We acknowledge several limitations to our work. First, the small number of included records did not allow for strong conclusions. Second, there were many AARs listed in the WHO repository that did not have a completed report, which again led to only a small number of records being included in our study and possible publication bias in our assessment. Third, the range of countries with completed AARs was limited and quite focused on WHO's African Region, which restricts the generalizability of our findings. Fourth, less than half of the included studies reported on participants' evaluations

of AARs, which hindered our ability to obtain sufficient information about their reflections on the suitability of the AAR method to achieve its objectives. All of these constraints could be resolved through more stringent reporting requirements for AARs. Unfortunately, there is no formal requirement to report on and publish AARs upon completion or to finalize reports in a timely manner. Especially during the COVID-19 pandemic, as more and more health systems need up-to-date data on effective and ineffective measures for addressing the pandemic, it is important to disseminate these evaluations widely and rapidly to ensure that incremental and strategic improvements are made to health-care systems worldwide. However, it seems that COVD-19-specific IARs suffer from the same issues as AARs in terms of insufficient conclusions and lack of publication of reviews.

It is crucial to evaluate public health systems regularly during a prolonged and evolving event such as the COVID-19 pandemic. Selecting appropriate methods for these evaluations is important to their successful implementation and to ultimately improve and adapt responses to the pandemic. Considering the variability of the COVID-19 pandemic and countries' public health capacities, a global methodology such as WHO's AAR toolkit needs to be sufficiently adaptable to local contexts and priorities, and also able to gain the most value from stakeholders' practical experiences during the response. The COVID-19-specific IAR adaptation of the AAR is a laudable example of this type of approach, and future pandemics might require similar adaptations. Furthermore, more subnational reviews, which have been proposed in the latest version of the IAR, are needed to enable better operational analysis of public health responses in specific high-priority areas. Importantly, the reporting and publication of completed AARs should be strengthened to allow public health responders and researchers from other countries and settings to benefit from the knowledge generated and lessons learned to strengthen the capacities of health-care systems to respond to future health emergencies.<sup>23</sup>

#### Conflicts of interest

The authors have no conflicts of interest to declare.

#### Ethics statement

Not applicable.

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None.

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# A descriptive assessment of the National Institute of Public Health's contribution to the COVID-19 response in Cambodia, 2020-2021

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Objective: This paper examines the contributions made by the National Institute of Public Health to Cambodia's response to the coronavirus disease (COVID-19) pandemic during 2020-2021.

Methods: The activities conducted by the Institute were compared with adaptations of the nine pillars of the World Health Organization's 2020 COVID-19 strategic preparedness and response plan. To gather relevant evidence, we reviewed national COVID-19 testing data, information about COVID-19-related events documented by Institute staff, and financial and technical reports of the Institute's activities.

Results: The main contributions the Institute made were to the laboratory pillar and the incident management and planning pillar. The Institute tested more than 50% of the 2 575 391 samples for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) testing and provided technical advice about establishing 18 new laboratories for SARS-CoV-2 testing in the capital city of Phnom Penh and 11 provinces. The Institute had representatives on many national committees and coauthored national guidelines for implementing rapid COVID-19 testing, preventing transmission in health-care facilities and providing treatment. The Institute contributed to six other pillars, but had no active role in risk communication and community engagement.

Discussion: The Institute's support was essential to the COVID-19 response in Cambodia, especially for laboratory services and incident management and planning. Based on the contributions made by the Institute during the COVID-19 pandemic, continued investment in it will be critical to allow it to support responses to future health emergencies in Cambodia.

he coronavirus disease (COVID-19) pandemic has impacted people's well-being globally; Cambodia was no exception. The first case of COVID-19 in Cambodia was detected on 27 January 2020. By 31 December 2021, the country had recorded 120 487 cases and 3012 deaths, with a case-fatality rate of 2.5%.<sup>2</sup> During the 305 days after the first case of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was detected, there were only 308 cases, the majority of which were imported, and there were no deaths.<sup>2</sup> This suggests that SARS-CoV-2 was contained early on during the pandemic in Cambodia. Experts believed that this low number of cases was due to the early implementation of stringent public health and social measures, such as border and school closures, the cancellation of public events and gatherings, extensive mass testing and intensive contact tracing.<sup>3</sup> With the arrival of the SARS-CoV-2 vaccine in February 2021, Cambodia was among the few countries to achieve more than 90% vaccination coverage (i.e. two doses or a complete series of doses) of its population aged 12 years and older by September 2021.2

The mission of Cambodia's National Institute of Public Health (NIPH) is to be the leading public health institute in the country. During the past 10 years, prior to the COVID-19 pandemic, NIPH committed to building its workforce to fulfil this mission by providing opportunities

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for staff to lead research projects and facilitating staff attendance at short- and long-term capacity-building training activities abroad. More recently, NIPH provided opportunities for staff to be directly involved in responding to the COVID-19 pandemic. NIPH has three specialized technical units: the School of Public Health, the Health Systems Research and Policy Support Center and the National Reference Laboratory. The School of Public Health was founded in 2007 and offers master's degrees in public health, epidemiology, human nutrition, hospital administration, and health and community development. The Health Systems Research and Policy Support Center promotes evidence-based health systems policies and governance by conducting research and translating findings into policies or actions. The National Reference Laboratory promotes and strengthens the quality of laboratory services for public health, as well as housing a biosafety level 2-plus facility that is capable of conducting molecular surveillance, using methods such as polymerase chain reaction (PCR)-based amplification and next-generation sequencing, to detect pathogenic or infectious organisms posing moderate health hazards.

NIPH was involved in many aspects of the COVID-19 response in Cambodia, and this descriptive assessment documents its contributions.

#### **METHODS**

This descriptive assessment examines the contributions made by NIPH to the COVID-19 response in Cambodia between 1 January 2020 and 31 December 2021 by comparing it with the country's adaptations of the nine pillars of the World Health Organization's (WHO's) 2020 COVID-19 strategic preparedness and response plan.4 The nine pillars were adapted and used in Cambodia's master plan for its COVID-19 response as (i) incident management and planning, (ii) laboratory services, (iii) surveillance, (iv) points of entry, (v) rapid response teams, (vi) infection prevention and control, (vii) case management and continuity of essential services, (viii) logistics, procurement and supply management and (ix) risk communication and community engagement (Table 1).4

We conducted secondary analyses of national COVID-19 testing data owned by the Inter-ministerial Committee to Combat COVID-19 that was managed by the Communicable Disease Control Department (CDCD).

We conducted a desk review of COVID-19 policies and guidelines developed during the pandemic to identify those authored by NIPH and reviewed training reports related to COVID-19 that were obtained from NIPH's accounting team to assess the number of people trained and the topics of the trainings. Therefore, the findings reflect an internal audit of the roles of and activities conducted by NIPH staff and should be interpreted with this in mind.

#### **RESULTS**

This descriptive assessment of the roles of and activities conducted by NIPH staff as part of the COVID-19 response showed that NIPH was involved in actions that supported all but one of the pillars – that is, NIPH was not involved in risk communication and community engagement (Table 1).

### Pillar i: incident management and planning

During Cambodia's COVID-19 response, the Prime Minister was the lead incident manager, with high-level committees providing advice. The high-level committees included the Provincial COVID-19 Committee, chaired by the Provincial Governors, which monitored responses in each province; the High-level Ministry of Health Task Force, which mobilized resources; and the Technical Working Group, led by Cambodia's CDCD with technical support from governmental and nongovernmental stakeholders, which provided technical advice about all aspects of the COVID-19 emergency response.

The COVID-19 response in Cambodia was flexible and continually evolving. To manage the increase in COVID-19 cases in 2021, the Prime Minister issued six strategies:

- Strategy 1 prevent imported cases of Delta variant SARS-CoV-2;
- Strategy 2 decrease the number of areas considered to be at high risk (as defined by the Cambodian government) and prevent new infections:
- Strategy 3 improve recovery rates and reduce the case-fatality rate;
- Strategy 4 strengthen the identification of cases and contacts;

Table 1. The nine pillars of the World Health Organization's 2020 COVID-19 strategic preparedness and response plan as adapted by the Cambodia National Institute of Public Health and how the Institute supported each pillar

	Pilar	Description	Roles of NIPH
i.	Incident management and planning	Ability of the government to provide guidance and planning assumptions, and make appropriate modifications to laws or regulations at all levels and sectors to enable an effective response	NIPH had representation on six national subcommittees, as well as on Ministry of Health committees; provided technical advice and coauthored four national guidelines and policies addressing rapid testing for COVID-19, conducting vaccination campaigns, preventing transmission in health-care facilities and providing treatment.
ii.	Laboratory services	Ability to perform SARS-CoV-2 testing rapidly without the need to ship specimens overseas	NIPH's laboratory tested 50% of all samples for SARS-CoV-2 and provided technical advice to help establish 18 new laboratories for this testing.
iii.	Surveillance	Ability to detect cases and report to global surveillance databases	NIPH tested 4636 samples for the national severe acute respiratory infection and influenza-like illness surveillance systems, collaborated to establish COVID-19 testing sites throughout Phnom Penh and produced 31 reports that used epidemiological and laboratory data and that were distributed to stakeholders.
iv.	Points of entry	Ability to detect cases, isolate them and quarantine contacts properly at the points of entry (international borders)	NIPH collected specimens at the Phnom Penh International Airport and trained 238 trainers in specimen collection, COVID-19 case management and the fundamentals of isolation and quarantine.
V.	Rapid response teams	Teams were created to investigate suspected COVID-19 cases and initiate treatment, if appropriate	NIPH trained 504 rapid response team trainers in COVID-19 responses and contact tracing.
vi.	Infection prevention and control	Ensure health-care workers are protected from infection with SARS-CoV-2 during amplification events in health-care facilities, such as while providing testing and care	NIPH coauthored the standard operating procedures for COVID-19 vaccination and also information about prevention and control of COVID-19 transmission at health facilities and clinics in Cambodia.
vii.	Case management and continuity of essential services	Designate referral facilities to care for patients with SARS-CoV-2 and ensure that essential services for other patients are continued	NIPH in collaboration with its partners, trained 1497 trainers, including health-care staff and volunteers, to build capacity to care for COVID-19 patients.
viii.	Logistics, procurement and supply management	Ability to communicate rapidly, regularly and transparently with the population	In 2021, NIPH prepared testing packages for mobile testing teams that were used to collect 735 396 specimens in Phnom Penh.
ix.	Risk communication and community engagement	NIPH did not play a role in supporting activities associated with this pillar.	NIPH did not play a role in supporting activities associated with this pillar.

COVID-19: coronavirus disease; NIPH: National Institute of Public Health; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

- Strategy 5 improve the handling of the bodies of those who died from COVID-19 while transferring them for cremation; and
- Strategy 6 boost the vaccination rate.

The government created 10 subcommittees to implement these strategies, which were chaired by the Inter-ministerial Committee.

To aid in incident management and planning, NIPH provided technical advice and developed guidelines and policies. NIPH experts took part in several subcommittees, including the Subcommittees for:

- Evaluation, Planning and Strategy;
- Management at Points of Entry and Quarantine;
- Rapid Response and Investigation;

- Technical Advice and Treatment;
- Laboratory Services; and
- Education, Training and Public Affairs.

NIPH was also an active member of the High-level Ministry of Health Task Force, the Technical Working Group and the Committee for Vaccination. As a member of these committees, NIPH contributed to shaping the national COVID-19 response. NIPH experts coauthored four national guidelines. The policies and guidelines coauthored by NIPH included the:

- guideline for the prevention and control of COVID-19 transmission in health facilities and clinics in Cambodia (July 2020);
- guidelines for the use of rapid tests for COVID-19 in private health services (May 2021);
- standard operating procedures for COVID-19 vaccination (June 2021); and
- fourth version of the clinical treatment protocol for COVID-19 (Jan 2022).

### Pillar ii: laboratory services

At the beginning of the pandemic, Cambodia heavily relied on the nongovernmental testing capacity available at the Institut Pasteur du Cambodge. NIPH's laboratory had to be set up and scaled up rapidly. Of the 2 575 391 COVID-19 tests conducted in Cambodia during 2020 and 2021, NIPH conducted 1 294 016 (50.2%; Fig. 1), while the Institut Pasteur conducted 827 613 (32.1%) and the other 18 laboratories conducted 453 762 (17.6%).

NIPH also provided technical advice during the establishment of 18 additional laboratories in Phnom Penh and 11 other provinces about nucleic acid amplification tests (e.g. PCR, Cepheid's GeneXpert platform and the Roche cobas test).<sup>5</sup> NIPH supported five essential elements under Pillar ii: assessing provincial laboratories' quality management systems to ensure that all target laboratories could maintain good-quality testing services; providing training for provincial laboratory staff in PCR testing (i.e. training between 3 and 10 staff in PCR techniques and approximately 5 more staff to conduct related work, such as data entry and basic data management); providing guidance to provincial laboratory

staff to ensure that appropriate infrastructure, equipment and supplies for performing PCR testing were available; establishing each provincial laboratory's information management system to ensure that results could be appropriately recorded and reported to the Ministry of Health; and providing guidance to provincial laboratory staff to ensure that the PCR testing process was verified correctly.

#### Pillar iii: surveillance

The CDCD managed the COVID-19 surveillance system with support from NIPH and other institutions. To support this pillar, NIPH undertook three activities.

First, NIPH tested the specimens collected through the national severe acute respiratory infection (SARI) and influenza-like illness (ILI) surveillance systems.<sup>6</sup> These specimens were tested for SARS-CoV-2 and influenza. Between 1 January 2020 and 31 December 2021, NIPH tested a total of 6706 of these specimens: 4636 (69.1%) were SARI and SARS-CoV-2 specimens and 2070 (30.9%) were ILI and SARS-CoV-2 specimens.

Second, NIPH collaborated with the Samdech Techo Voluntary Youth Doctor Association (TYDA) to establish COVID-19 testing sites throughout Phnom Penh. In 2020 and 2021, these sites collected 852 137 specimens, accounting for 33.1% of all specimens collected in the country.

Last, NIPH formed a COVID-19 data team that produced weekly reports for timely dissemination to several key stakeholders involved in the response. These reports included epidemiological data (i.e. the numbers of cases and deaths, specifying person, place and time); laboratory data (i.e. the number of samples tested and positivity rates, by district and commune); and other dynamic content (i.e. vaccine effectiveness rates, case forecasts, case reproduction numbers [the estimated number of secondary cases caused by a primary case] and proportions of different COVID-19 strains among positive samples). NIPH had produced 31 reports by 30 April 2022.

#### Pillar iv: points of entry

Up until 31 December 2021, NIPH in collaboration with TYDA collected specimens from travellers at Phnom Penh International Airport and trained 238 trainers in border

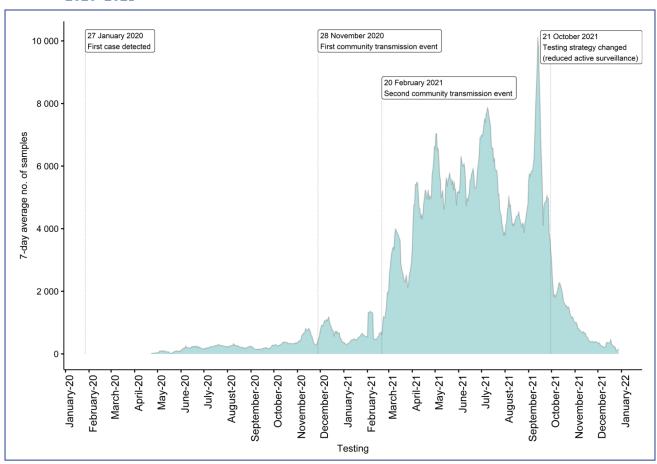


Fig. 1. Number of samples tested daily for COVID-19 at the National Institute of Public Health, Cambodia, 2020-2021a

a On 21 October 2021, the government reduced active surveillance, advising that testing teams should no longer be sent into communities to collect specimens and only passive surveillance would be maintained (e.g. at hospitals or sentinel sites).

management for COVID-19. The training covered specimen collection, infection prevention, and fundamentals of isolation and quarantine.

#### Pillar v: rapid response teams

By the time Cambodia detected its first COVID-19 case on 27 January 2020, the CDCD had enlisted more than 2000 rapid response team members. Between April and July 2020, NIPH in collaboration with the CDCD trained 504 trainers in COVID-19 responses and contact tracing (additional staff were also trained, but NIPH was not involved).

#### Pillar vi: infection prevention and control

NIPH experts were coauthors of two guidelines about infection prevention and control: the standard operating procedures for COVID-19 vaccination and the guidelines for prevention and control of COVID-19 transmission at health facilities and clinics.

# Pillar vii: case management and continuity of essential services

In 2020, NIPH in collaboration with other partners provided 26 trainings to 1497 trainers, both health centre staff and volunteers, about caring for and treating patients with COVID-19. Training partners included the Ministry of Health's Department of Hospital Service, the CDCD, the University of Health Sciences, Calmette Hospital, Khmer-Soviet Friendship Hospital and the Cambodia-China Friendship Preah Kossamak Hospital.

# Pillar viii: logistics, procurement and supply management

In Cambodia, this pillar focused on (a) strengthening supply chains and the distribution of COVID-19 commodities, test kits and other material for testing; and (b) mobilizing resources from both domestic and development partners.

In 2020, NIPH estimated the need for materials and developed distribution strategies using a COVID-19 emergency loan and grants from the World Bank, the Global Fund and other agencies. In July 2020, NIPH successfully applied for a World Bank grant of more than US\$ 1 million to purchase equipment and materials to set up the new laboratories for PCR testing in Phnom Penh and 11 provinces. After the laboratories were set up, NIPH received reports on the usage of the test kits and materials, as well as requests for additional kits and materials. For the Ministry of Health, the NIPH also estimated the need for test kits and materials among all public laboratories.

In 2021, NIPH also prepared testing packages for mobile testing teams that were used to collect 735 396 specimens in Phnom Penh.

# Pillar ix: risk communication and community engagement

NIPH did not contribute to any risk communication and community engagement activities. These were coordinated through the Subcommittee for Education, Training and Public Affairs, with strong organizational and financial support from partners.8

# **DISCUSSION**

During the first 2 years of the COVID-19 response in Cambodia, NIPH contributed to eight of the nine pillars adapted from WHO's 2020 strategic preparedness and response plan. NIPH's main contributions were to support laboratory services and incident management and planning.

The NIPH laboratory tested half of the total 2 575 391 COVID-19 samples collected in Cambodia during 2020 and 2021 and provided technical advice for the establishment of 18 additional laboratories for SARS-CoV-2 testing across the country. NIPH's laboratories did not expect to do so much of the testing. Before the pandemic, NIPH tested only a few hundred SARI and ILI specimens per week. By July 2021, NIPH had increased its capacity from 100 PCR tests per day in April 2020 to 6000 PCR tests per day. In September 2021, during a few extreme days, NIPH performed 10 000 PCR tests per day. Investing in a network of high-quality governmental laboratories was vital to address the current COVID-19 crisis, and these will be important assets for future emergency responses.

NIPH participated in policy development and provided advice by having representation on six national COVID-19 response subcommittees, as well as on the High-level Ministry of Health Task Force, the Technical Working Group and the Committee for Vaccination. NIPH's Health Systems Research and Policy Support Center and the School of Public Health had increased the Institute's capabilities in research and policy development prior to the pandemic, which enabled it to make contributions to the subcommittees. Investments in NIPH should be sustained to consolidate and further strengthen public health capacities and readiness in the country.

This is the only report that describes NIPH's contribution to the COVID-19 response in Cambodia from the perspective of those from the Institute who implemented the response. However, the report has limitations. First, as most authors are NIPH staff, the report may be biased toward the Institute. Second, the contributions made by other institutions to the COVID-19 response, such as those of the Institut Pasteur du Cambodge and the CDCD, have not been included. Finally, the overall governance and collaboration of all relevant institutions during the COVID-19 response was also not assessed.

The role of NIPH was essential to the COVID-19 response in Cambodia, particularly in providing laboratory services and technical advice and in contributing to policy development through membership of its staff on national committees. Based on the contributions made by NIPH during the COVID-19 pandemic, continued investment in the Institute is critical to enable it to provide support during future health emergencies in Cambodia.

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#### Conflicts of interest

SC, IVW, PK, C Chhorn, PI and C Chhea work at NIPH. These authors may have positive bias toward NIPH. AP is an associate editor of Western Pacific Surveillance and Response. She was not involved in the editorial decision to publish this manuscript.

#### Ethics statement

Not applicable.

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# Post-COVID-19 health-care utilization: one year after the 2020 first wave in Brunei Darussalam

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Objective: Patients who recover from coronavirus disease (COVID-19) infection are at risk of long-term health disorders and may require prolonged health care. This retrospective observational study assesses the number of health-care visits before and after COVID-19 infection in Brunei Darussalam.

Methods: COVID-19 cases from the first wave with 12 months of follow-up were included. Health-care utilization was defined as health-care visits for consultations or investigations. Post-COVID condition was defined using the World Health Organization definition.

Results: There were 132 cases; 59.1% were male and the mean age was 37.1 years. The mean number of health-care visits 12 months after recovery from COVID-19 (123 cases, 93.2%; mean 5.0 ±5.2) was significantly higher than the prior 12 months (87 cases, 65.9%, P<0.001; mean 3.2 ±5.7, P<0.001). There was no significant difference when scheduled COVID-19 visits were excluded (3.6  $\pm 4.9$ , P = 0.149). All 22 cases with moderate to critical disease recovered without additional health-care visits apart from planned post-COVID-19 visits. Six patients had symptoms of post-COVID condition, but none met the criteria for diagnosis or had alternative diagnoses.

Discussion: There were significantly more health-care visits following recovery from COVID-19. However, this was due to scheduled post-COVID-19 visits as per the national management protocol. This protocol was amended prior to the second wave to omit post-COVID-19 follow-up, except for complicated cases or cases with no documented radiological resolution of COVID-19 pneumonia. This will reduce unnecessary health-care visits and conserve precious resources that were stretched to the limit during the pandemic.

he coronavirus disease (COVID-19) pandemic continues to have significant negative impacts on health-care services worldwide as a result of the diversion of resources to mitigate the impact of the disease, 1,2 which will have immediate and long-term consequences. Patients affected by COVID-19 are at risk of both medical and psychological long-term health issues. As COVID-19 is predominantly a respiratory illness, long-term respiratory problems are expected.<sup>3,4</sup> However, a range of adverse outcomes of COVID-19 have also been observed involving the immune system (e.g. Guillain-Barré syndrome and paediatric inflammatory multisystem syndrome), cardiovascular system (e.g. cardiomyopathy and coagulopathy), neurological system (e.g. sensory dysfunction and stroke), cutaneous and digestive manifestations as well as mental health issues.4

Patients with mild disease from COVID-19 infection who then experienced long-term symptoms<sup>5,6</sup> are also of concern. This constellation of non-specific symptoms has been referred to as long COVID, chronic COVID syndrome or post-COVID condition, 5,7 with varying definitions between countries and organizations. The World Health Organization (WHO) defines post-COVID condition as a condition occurring usually 3 months from the onset of COVID-19 with symptoms that last for at least 2 months that cannot be explained by an alternative diagnosis. The United States Centers for Disease Control and Prevention (CDC) defines it as a wide range of new, returning or ongoing health problems for 4 or more weeks after COV-ID-19.8 Common symptoms include fatigue, shortness of breath and cognitive dysfunction that generally impact everyday functioning.<sup>7</sup> Symptoms may begin after initial

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recovery from COVID-19, or may persist from the initial COVID-19 illness, and can fluctuate or relapse over time. The CDC characterized post-COVID conditions into three subtypes: new or ongoing symptoms; multiorgan effects of COVID-19 (i.e. multisystem inflammatory syndrome); and effects of COVID-19 or hospitalization.8 Reported risk factors for chronic sequelae of COVID-19 include disease severity, older age, sex, ethnicity, comorbidities especially pre-existing respiratory disease, and higher body mass index.5,9 Female patients have been associated with a higher likelihood of developing mental and psychological long-term sequelae.9,10

To date, few studies have looked at health-care utilization after recovery from COVID-19.11-15 One study reported that 10.3% of COVID-19 patients would require re-admission to hospital and an all-cause mortality of 7.9% after recovery from COVID-19, with the majority of deaths occurring within the first 30 days after the index admission. 12 The assessment of the burden on the healthcare system post-COVID-19 infection from earlier waves can assist with health-care utilization planning. This study of COVID-19 patients from the first wave in Brunei Darussalam aims to: (1) compare health-care utilization of COVID-19 patients 12 months before and 12 months after their infection; (2) assess if severity of disease, underlying psychiatric disorders and need for counselling during hospitalization affected health-care utilization; and (3) assess the prevalence and characteristics of patients diagnosed with post-COVID condition.

### **METHODS**

#### Study design

This was a retrospective observational study of cases who recovered from COVID-19 during the first wave (from 9 March 2020 to 6 August 2021) in Brunei Darussalam. All COVID-19 cases in Brunei Darussalam diagnosed during the first wave were admitted to the National Isolation Centre (NIC) for isolation and treatment. All COVID-19 cases from the first wave who were alive 12 months after their COVID-19 recovery and had resided in Brunei Darussalam 12 months before and 12 months after their recovery from COVID-19 were eligible for the study.

In order to document recovery, scheduled post-COVID-19 health-care visits, as defined in the national post-discharge management protocol, included a reverse transcription polymerase chain reaction (RT-PCR) test on

day 11 post-discharge to document viral clearance, and follow-up appointments with cases who had COVID-19 pneumonia as documented on chest radiographs or other unresolved issues directly related to COVID-19 (e.g. thrombocytopenia or unresolved symptoms) at discharge.

#### Data collection

Data were retrieved from the database maintained by the NIC management team that had been established at the start of the COVID-19 outbreak. Data collected included age, sex, ethnicity, comorbidities, date of positive RT-PCR test, symptoms at presentation, severity of illness at presentation and daily progress, outcomes and discharge date. Data on health-care utilization during the 12 months before and 12 months after COVID-19 diagnosis were retrieved from the Brunei Darussalam Health and Management System, a national electronic healthcare system that links all government health institutions (hospitals and peripheral clinics). Established in 2011, this system captures all patients' health-care encounters.

Five categories of disease were defined: (i) asymptomatic; (ii) mild (symptomatic without evidence of pneumonia on chest imaging); (iii) moderate (clinical or imaging evidence of pneumonia); (iv) severe (required oxygen supplementation); and (v) critical (respiratory failure requiring mechanical ventilation with or without other organ failure). These were grouped into two categories: asymptomatic/mild and moderate to critical.

#### Data analysis

Analyses were conducted using IBM® SPSS version 26.0. Mean, standard deviation and range were calculated for continuous variables and frequency and percentage for categorical variables. The number of health-care visits 12 months before and 12 months after COVID-19 infection were compared. The Mann-Whitney U test was used to test the difference between the mean number of healthcare visits for non-parametric continuous variables and the chi-square test was used for categorical variables. A P value of <0.05 was taken as significant.

## RESULTS

#### Study population

Of the 340 COVID-19 cases from the first wave, 205 had not resided in Brunei Darussalam 12 months before and 12 months after their recovery from COVID-19 and three had died, leaving 132 cases eligible for the study.

The mean age of the study population was 37.1  $\pm 17.2$  years with more males (59.1%) than females. The ethnic breakdown was consistent with the national distribution. A total of 39 patients (29.5%) had underlying comorbidities, the most common being hypertension and dyslipidaemia (Table 1). Nearly half (46.3%) were overweight or obese. Symptoms were reported by 69.7% of cases at admission with the most common being cough (39.0%), fever (26.5%) and rhinorrhoea (23.5%). The majority of cases (83.3%; n = 110) had asymptomatic/mild disease and 16.7% (n = 22) had moderate to critical disease (Table 1). Four cases were admitted to the intensive care unit with two needing mechanical ventilation. The mean length of hospitalization was 20.2 ±8.7 days.

#### Health-care utilization

Most cases (64.4%) visited health-care facilities 12 months before and 12 months after recovering from COVID-19 (Table 2). Figure 1 shows the breakdown in the number of health-care visits before and after COVID-19 (unrelated and related to COVID-19). This shows scheduled COVID-19-related visits ranging from one to six visits, most with one visit, mainly for postdischarge testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to document viral clearance following our management protocol at the time.

Overall, there were significantly more health-care visits (n = 660, mean 5.0  $\pm 5.2$  visits) in the 12 months after COVID-19 compared to the 12 months before  $(n = 431, \text{ mean } 3.2 \pm 5.7; P < 0.001)$ . There was a significant increase in the mean number of visits observed between each characteristic assessed except for Chinese ethnicity (Table 1). Cases with comorbidities (diabetes mellitus, hypertension, dyslipidaemia, ischaemic heart disease and respiratory disorders) had more health-care visits compared to those without comorbidities. However, there was no significant increase in health-care visits post-COVID-19.

There were 190 scheduled post-COVID-19 visits, with a mean of  $1.4 \pm 1.3$  per case (range 1-6). When scheduled post-COVID-19 visits were excluded, there was no significant difference between the mean number

of health-care visits pre- and post-COVID-19 (n = 470, mean 3.6  $\pm$ 4.9; P = 0.149). Similarly, when scheduled COVID-19 visits were excluded, there was no significant difference between the mean number of health-care visits for each characteristic assessed pre- and post-COVID-19, except for patients with abnormal chest radiography (P = 0.019).

Among non-COVID-19 health-care visits, there were 11 for COVID-19 vaccinations: five partial (one dose) and three complete (two doses).

# Patients with moderate to severe COVID-19 disease

There were 22 (16.7%) cases with COVID-19 pneumonia (moderate to critical disease) including two who required mechanical ventilation. Eleven had radiological resolutions documented at discharge and 11 had complete resolutions documented at follow-up. All were cleared of any residual respiratory issues. None had any further health-care visits for respiratory or other problems related to COVID-19 other than their scheduled post-COVID-19 visits.

#### Psychiatric encounters

During hospitalizations for COVID-19, six patients required counselling or psychiatric treatment (Table 3), four of whom were diagnosed with underlying mild psychiatric disorders during admission but did not have prior encounters with public or mental health-care services. One case was referred due to concern about prolonged hospitalization and because their family members had recovered much earlier. Four patients were given treatment. Post-discharge, four had follow-up appointments, of whom two were already known to the service and two were new. Both cases 5 and 6 had improved when they were reviewed. One was seen once before missing her scheduled follow-up appointment, and the other patient continued routine follow-up (Table 3).

# Post-COVID condition

Six patients had some symptoms of post-COVID condition but none met the criteria for diagnosis. Four of these patients had hospital encounters within 60 days and two after 8 months following their initial COVID-19 infection (Table 4). Three patients had pre-existing psychiatric

Characteristics of COVID-19 cases by mean number of health-care visits 12 months before and Table 1. 12 months after COVID-19 illness during the first wave,  $^{\rm a}$  Brunei Darussalam (N=132)

Male         78 (59.1)         3.2 ± 5.2         4.7 ± 4.7         <0.001							
Female	Characteristic	N (%)	12 months before COVID-19	visits 12 months after COVID-19	<b>P</b> ⁵	care visits 12 months after COVID-19	<b>P</b> c
Male         78 (59.1)         3.2 ± 5.2         4.7 ± 4.7         <0.001         3.3 ± 4.5         0.400           Nationality           Malay         107 (81.1)         3.7 ± 6.1         5.3 ± 5.6         <0.001	Sex						
Nationality  Malay 107 (81.1) 3.7 ±6.1 5.3 ±5.6 <0.001 3.8 ±5.2 0.340   Chinese 5 (3.8) 1.0 ±0.7 2.2 ±1.9 0.310 1.0 ±1.7 0.546   Other 20 (15.2) 1.7 ±2.9 4.1 ±3.1 0.003 2.9 ±3.0 0.081   Age group (years) <p> <a href="#">48 group (years)</a> <a href="#">48 0.039</a> <a href="#">2.6 ±5.8</a> <a href="#">0.58 6</a> <a href="#">0.58 6</a> <a href="#">30.039</a> <a href="#">2.6 ±5.8</a> <a href="#">0.58 6</a> <a href="#">0.58 6</a> <a href="#">0.039</a> <a href="#">2.6 ±5.8</a> <a href="#">0.58 6</a> <a href="#">0.58 6</a> <a href="#">0.039</a> <a href="#">2.6 ±5.8</a> <a href="#">0.58 6</a> <a href="#">0.58 6</a> <a href="#">0.001</a> <a href="#">3.4 ±4.8</a> <a href="#">0.016</a> <a href="#">5.5 ±5.8</a> <a href="#">0.058 6</a> <a href="#">0.58 5</a> <a href="#">0.001</a> <a href="#">3.4 ±4.8</a> <a href="#">0.166</a> <a href="#">0.5 ±5.3</a> <a href="#">0.001</a> <a href="#">2.7 ±4.4</a> <a href="#">0.292</a> <a href="#">0.292</a> <a href="#">0.001</a> <a href="#">2.7 ±4.4</a> <a href="#">0.292</a> <a href="#">0.292</a> <a href="#">0.001</a> <a href="#">2.7 ±4.4</a> <a href="#">0.292</a> <a href="#">0.292</a> <a href="#">0.183</a> <a href="#">0.902</a> <a href="#">0.91 ±8.8</a> <a href="#">0.6666</a> <a href="#">8.1 ±8.6</a> <a href="#">0.931</a> <a href="#">0.931</a> <a href="#">0.91 ±8.8</a> <a href="#">0.6666</a> <a href="#">8.1 ±8.6</a> <a href="#">0.931</a> <a href="#">0.931</a> <a href="#">0.942</a> <a< td=""><td>Female</td><td>54 (40.9)</td><td><math>3.7 \pm 6.1</math></td><td><math>5.3 \pm 5.9</math></td><td>&lt; 0.001</td><td>3.9 ±5.5</td><td>0.204</td></a<></p>	Female	54 (40.9)	$3.7 \pm 6.1$	$5.3 \pm 5.9$	< 0.001	3.9 ±5.5	0.204
Malay         107 (81.1)         3.7 ±6.1         5.3 ±5.6         <0.001         3.8 ±5.2         0.340           Chinese         5 (3.8)         1.0 ±0.7         2.2 ±1.9         0.310         1.0 ±1.7         0.548           Other         20 (15.2)         1.7 ±2.9         4.1 ±3.1         0.003         2.9 ±3.0         0.081           Age group (years) </td <td>Male</td> <td>78 (59.1)</td> <td><math>3.2 \pm 5.2</math></td> <td><math>4.7 \pm 4.7</math></td> <td>&lt; 0.001</td> <td><math>3.3 \pm 4.5</math></td> <td>0.400</td>	Male	78 (59.1)	$3.2 \pm 5.2$	$4.7 \pm 4.7$	< 0.001	$3.3 \pm 4.5$	0.400
Chinese 5 (3.8) 1.0 ±0.7 2.2 ±1.9 0.310 1.0 ±1.7 0.548   Other 20 (15.2) 1.7 ±2.9 4.1 ±3.1 0.003 2.9 ±3.0 0.081   Age group (years) <a href="#page-14"></a> <a href="#page-14"><a href="#page-14"><a< td=""><td>Nationality</td><td></td><td></td><td></td><td></td><td></td><td></td></a<></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a>	Nationality						
Other         20 (15.2)         1.7 ± 2.9         4.1 ± 3.1         0.003         2.9 ± 3.0         0.081           Age group (years)         30         48 (36.4)         3.1 ± 6.4         3.7 ± 5.8         0.039         2.6 ± 5.8         0.582           30-50         47 (35.6)         2.8 ± 5.7         5.0 ± 5.3         <0.001	Malay	107 (81.1)	$3.7 \pm 6.1$	$5.3 \pm 5.6$	< 0.001	$3.8 \pm 5.2$	0.340
Age group (years)	Chinese	5 (3.8)	$1.0 \pm 0.7$	$2.2 \pm 1.9$	0.310	$1.0 \pm 1.7$	0.548
Comparison   Co	Other	20 (15.2)	1.7 ±2.9	4.1 ±3.1	0.003	2.9 ±3.0	0.081
30–50 47 (35.6) 2.8 ±5.7 5.0 ±5.3 <0.001 3.4 ±4.8 0.160	Age group (years)						
Comorbidities Yes 39 (29.5) 5.2 ±6.8 7.1 ±5.7 0.014 5.5 ±5.4 0.294 No 93 (70.5) 2.5 ±4.9 4.1 ±4.7 <0.001 2.7 ±4.4 0.202 No 93 (70.5) 2.5 ±4.9 4.1 ±4.7 <0.001 2.7 ±4.4 0.202 No 93 (70.5) 2.8 ±4.9 4.7 ±4.8 0.666 8.1 ±8.6 0.931 No 123 (93.2) 2.8 ±4.9 4.7 ±4.8 0.001 3.2 ±4.4 0.137 No 110 (83.3) 2.6 ±5.1 4.4 ±4.8 <0.001 3.2 ±4.4 0.147 No 110 (83.3) 2.6 ±5.1 4.4 ±4.8 <0.001 2.9 ±4.4 0.147 No 112 (84.5) 2.8 ±5.1 4.7 ±5.4 <0.001 2.9 ±4.4 0.147 No 112 (84.5) 2.8 ±5.1 4.7 ±5.4 <0.001 3.2 ±5.0 0.29 No 125 (94.7) 3.2 ±5.7 5.0 ±5.3 <0.001 3.2 ±5.0 0.29 No 127 (96.2) 3.2 ±5.7 5.0 ±5.3 <0.001 3.6 ±4.9 0.128 No 127 (96.2) 3.2 ±5.7 5.0 ±5.3 <0.001 3.6 ±4.9 0.128 No 125 (94.7) 3.3 ±5.8 4.9 ±5.2 <0.001 3.5 ±4.9 0.19 No 125 (94.7) 3.3 ±5.8 4.9 ±5.2 <0.001 3.5 ±4.9 0.19 No 125 (94.7) 3.3 ±5.8 4.9 ±5.2 <0.001 3.7 ±4.9 0.13 No 40 (30.3) 2.7 ±3.4 4.4 ±5.1 0.020 3.2 ±4.9 0.74 No No 125 (94.7) 3.5 ±6.4 5.3 ±5.3 <0.001 3.7 ±4.9 0.13 No 40 (30.3) 2.7 ±3.4 4.4 ±5.1 0.020 3.2 ±4.9 0.74 No No 101 (82.1) 3.1 ±5.9 4.2 ±4.6 <0.001 3.1 ±4.6 0.387 No No 101 (82.1) 3.1 ±5.9 4.2 ±4.6 <0.001 3.1 ±4.6 0.387 No No 101 (82.1) 3.1 ±5.9 4.2 ±4.6 <0.001 3.1 ±4.6 0.387 No No 101 (82.1) 3.1 ±5.9 4.2 ±4.6 <0.001 3.1 ±4.6 0.387 No No 101 (82.1) 3.1 ±5.9 4.2 ±4.6 <0.001 3.1 ±4.6 0.387 No	<30	48 (36.4)	$3.1 \pm 6.4$	$3.7 \pm 5.8$	0.039	2.6 ±5.8	0.589
Comorbidities           Yes         39 (29.5)         5.2 ±6.8         7.1 ±5.7         0.014         5.5 ±5.4         0.294           No         93 (70.5)         2.5 ±4.9         4.1 ±4.7         <0.001	30–50	47 (35.6)	$2.8 \pm 5.7$	$5.0 \pm 5.3$	< 0.001	$3.4 \pm 4.8$	0.160
Yes         39 (29.5)         5.2 ±6.8         7.1 ±5.7         0.014         5.5 ±5.4         0.294           No         93 (70.5)         2.5 ±4.9         4.1 ±4.7         <0.001         2.7 ±4.4         0.202           Diabetes         Yes         9 (6.8)         9.0 ±10.5         9.1 ±8.8         0.666         8.1 ±8.6         0.931           No         123 (93.2)         2.8 ±4.9         4.7 ±4.8         <0.001         3.2 ±4.4         0.137           Hypertension         Yes         22 (16.7)         6.4 ±7.3         8.0 ±6.4         0.134         6.6 ±6.1         0.502           No         110 (83.3)         2.6 ±5.1         4.4 ±4.8         <0.001         2.9 ±4.4         0.147           Dyslipidaemia           Yes         20 (15.2)         5.9 ±7.8         6.7 ±3.9         0.063         5.5 ±3.7         0.285           No         112 (84.5)         2.8 ±5.1         4.7 ±5.4         <0.001         3.2 ±5.0         0.225           Ischaemic heart disease         Yes         5 (3.8)         4.2 ±3.8         4.4 ±4.4         1.000         3.8 ±4.3         0.841           No         127 (96.2)         3.2 ±5.7         5.0 ±5.3         <0.001         <	>50	37 (28.0)	4.1 ±4.5	6.7 ±3.8	0.001	5.0 ±3.3	0.089
No         93 (70.5)         2.5 ±4.9         4.1 ±4.7         <0.001         2.7 ±4.4         0.202           Diabetes           Yes         9 (6.8)         9.0 ±10.5         9.1 ±8.8         0.666         8.1 ±8.6         0.931           No         123 (93.2)         2.8 ±4.9         4.7 ±4.8         <0.001	Comorbidities						
Diabetes  Yes 9 (6.8) 9.0 ±10.5 9.1 ±8.8 0.666 8.1 ±8.6 0.931 No 123 (93.2) 2.8 ±4.9 4.7 ±4.8 <0.001 3.2 ±4.4 0.137 Hypertension  Yes 22 (16.7) 6.4 ±7.3 8.0 ±6.4 0.134 6.6 ±6.1 0.502 No 110 (83.3) 2.6 ±5.1 4.4 ±4.8 <0.001 2.9 ±4.4 0.147 Dyslipidaemia  Yes 20 (15.2) 5.9 ±7.8 6.7 ±3.9 0.063 5.5 ±3.7 0.289 No 112 (84.5) 2.8 ±5.1 4.7 ±5.4 <0.001 3.2 ±5.0 0.229 Ischaemic heart disease  Yes 5 (3.8) 4.2 ±3.8 4.4 ±4.4 1.000 3.8 ±4.3 0.841 No 127 (96.2) 3.2 ±5.7 5.0 ±5.3 <0.001 3.6 ±4.9 0.128 Respiratory disease  Yes 7 (5.3) 2.0 ±2.8 6.4 ±5.2 0.073 4.6 ±4.5 0.535 No 125 (94.7) 3.3 ±5.8 4.9 ±5.2 <0.001 3.5 ±4.9 0.192 Reported symptoms at admission  Yes 92 (69.7) 3.5 ±6.4 5.3 ±5.3 <0.001 3.7 ±4.9 0.131 No 40 (30.3) 2.7 ±3.4 4.4 ±5.1 0.020 3.2 ±4.9 0.741 Abnormal chest radiographyd  Yes 22 (17.9) 3.8 ±4.9 9.6 ±6.1 0.001 6.5 ±6.1 0.015 No 101 (82.1) 3.1 ±5.9 4.2 ±4.6 <0.001 3.1 ±4.6 0.387 Disease severity  Asymptomatic/mild 110 (83.3) 3.0 ±5.7 4.0 ±4.5 <0.001 2.9 ±4.6 0.471 disease contributed in the several contribut	Yes	39 (29.5)	5.2 ±6.8	7.1 ±5.7	0.014	5.5 ±5.4	0.294
Yes         9 (6.8)         9.0 ±10.5         9.1 ±8.8         0.666         8.1 ±8.6         0.931           No         123 (93.2)         2.8 ±4.9         4.7 ±4.8         <0.001	No	93 (70.5)	$2.5 \pm 4.9$	$4.1 \pm 4.7$	< 0.001	$2.7 \pm 4.4$	0.202
No       123 (93.2)       2.8 ±4.9       4.7 ±4.8       <0.001       3.2 ±4.4       0.137         Hypertension         Yes       22 (16.7)       6.4 ±7.3       8.0 ±6.4       0.134       6.6 ±6.1       0.502         No       110 (83.3)       2.6 ±5.1       4.4 ±4.8       <0.001       2.9 ±4.4       0.147         Dyslipidaemia         Yes       20 (15.2)       5.9 ±7.8       6.7 ±3.9       0.063       5.5 ±3.7       0.285         No       112 (84.5)       2.8 ±5.1       4.7 ±5.4       <0.001       3.2 ±5.0       0.225         Isolatemic heart disease         Yes       5 (3.8)       4.2 ±3.8       4.4 ±4.4       1.000       3.8 ±4.3       0.841         No       127 (96.2)       3.2 ±5.7       5.0 ±5.3       <0.001       3.6 ±4.9       0.126         Respiratory disease         Yes       7 (5.3)       2.0 ±2.8       6.4 ±5.2       0.073       4.6 ±4.5       0.535         No       125 (94.7)       3.3 ±5.8       4.9 ±5.2       <0.001       3.7 ±4.9       0.131         No       40 (30.3)       2.7 ±3.4       4.4 ±5.1       0.020       3.2 ±4.9       0.741	Diabetes						
Hypertension         Yes       22 (16.7)       6.4 ± 7.3       8.0 ± 6.4       0.134       6.6 ± 6.1       0.502         No       110 (83.3)       2.6 ± 5.1       4.4 ± 4.8       < 0.001	Yes	9 (6.8)	$9.0 \pm 10.5$	9.1 ±8.8	0.666	8.1 ±8.6	0.931
Yes         22 (16.7)         6.4 ±7.3         8.0 ±6.4         0.134         6.6 ±6.1         0.502           No         110 (83.3)         2.6 ±5.1         4.4 ±4.8         <0.001         2.9 ±4.4         0.147           Dyslipidaemia           Yes         20 (15.2)         5.9 ±7.8         6.7 ±3.9         0.063         5.5 ±3.7         0.289           No         112 (84.5)         2.8 ±5.1         4.7 ±5.4         <0.001         3.2 ±5.0         0.289           Ischaemic heart disease         Yes         5 (3.8)         4.2 ±3.8         4.4 ±4.4         1.000         3.8 ±4.3         0.841           No         127 (96.2)         3.2 ±5.7         5.0 ±5.3         <0.001         3.6 ±4.9         0.128           Respiratory disease           Yes         7 (5.3)         2.0 ±2.8         6.4 ±5.2         0.073         4.6 ±4.5         0.535           No         125 (94.7)         3.3 ±5.8         4.9 ±5.2         <0.001         3.5 ±4.9         0.192           Reported symptoms at admission         Yes         92 (69.7)         3.5 ±6.4         5.3 ±5.3         <0.001         3.7 ±4.9         0.131           No         40 (30.3)         2.7 ±3.4         4.4 ±5.1 <td>No</td> <td>123 (93.2)</td> <td><math>2.8 \pm 4.9</math></td> <td>4.7 ±4.8</td> <td>&lt; 0.001</td> <td><math>3.2 \pm 4.4</math></td> <td>0.137</td>	No	123 (93.2)	$2.8 \pm 4.9$	4.7 ±4.8	< 0.001	$3.2 \pm 4.4$	0.137
No       110 (83.3)       2.6 ±5.1       4.4 ±4.8       <0.001       2.9 ±4.4       0.147         Dyslipidaemia         Yes       20 (15.2)       5.9 ±7.8       6.7 ±3.9       0.063       5.5 ±3.7       0.285         No       112 (84.5)       2.8 ±5.1       4.7 ±5.4       <0.001	Hypertension						
Dyslipidaemia           Yes         20 (15.2)         5.9 ± 7.8         6.7 ± 3.9         0.063         5.5 ± 3.7         0.28 ± 5.0           No         112 (84.5)         2.8 ± 5.1         4.7 ± 5.4         < 0.001         3.2 ± 5.0         0.22 ± 5.2           Ischaemic heart disease         Yes         5 (3.8)         4.2 ± 3.8         4.4 ± 4.4         1.000         3.8 ± 4.3         0.84 ± 1.2           No         127 (96.2)         3.2 ± 5.7         5.0 ± 5.3         < 0.001         3.6 ± 4.9         0.128 ± 1.2           Respiratory disease         7         5.3         2.0 ± 2.8         6.4 ± 5.2         0.073         4.6 ± 4.5         0.53 ± 5.8           No         125 (94.7)         3.3 ± 5.8         4.9 ± 5.2         < 0.001         3.5 ± 4.9         0.192           Reported symptoms at admission         Yes         92 (69.7)         3.5 ± 6.4         5.3 ± 5.3         < 0.001         3.7 ± 4.9         0.131           No         40 (30.3)         2.7 ± 3.4         4.4 ± 5.1         0.020         3.2 ± 4.9         0.741           Abnormal chest radiography <sup>d</sup> Yes         22 (17.9)         3.8 ± 4.9         9.6 ± 6.1         0.001         6.5 ± 6.1         0.019           No	Yes	22 (16.7)	$6.4 \pm 7.3$	$8.0 \pm 6.4$	0.134	$6.6 \pm 6.1$	0.502
Yes         20 (15.2)         5.9 ± 7.8         6.7 ± 3.9         0.063         5.5 ± 3.7         0.289           No         112 (84.5)         2.8 ± 5.1         4.7 ± 5.4         < 0.001	No	110 (83.3)	$2.6 \pm 5.1$	$4.4 \pm 4.8$	< 0.001	$2.9 \pm 4.4$	0.147
No       112 (84.5)       2.8 ±5.1       4.7 ±5.4       <0.001       3.2 ±5.0       0.22 strong transparence of the strong transparence of transparence of the strong transparence of transparence of the strong transparence of the stro	Dyslipidaemia						
Ischaemic heart disease         Yes       5 (3.8)       4.2 ±3.8       4.4 ±4.4       1.000       3.8 ±4.3       0.841         No       127 (96.2)       3.2 ±5.7       5.0 ±5.3       <0.001       3.6 ±4.9       0.128         Respiratory disease       Yes       7 (5.3)       2.0 ±2.8       6.4 ±5.2       0.073       4.6 ±4.5       0.538         No       125 (94.7)       3.3 ±5.8       4.9 ±5.2       <0.001       3.5 ±4.9       0.192         Reported symptoms at admission       Yes       92 (69.7)       3.5 ±6.4       5.3 ±5.3       <0.001       3.7 ±4.9       0.131         No       40 (30.3)       2.7 ±3.4       4.4 ±5.1       0.020       3.2 ±4.9       0.741         Abnormal chest radiographyd       Yes       22 (17.9)       3.8 ±4.9       9.6 ±6.1       0.001       6.5 ±6.1       0.019         No       101 (82.1)       3.1 ±5.9       4.2 ±4.6       <0.001       3.1 ±4.6       0.387         Disease severity       Asymptomatic/mild       110 (83.3)       3.0 ±5.7       4.0 ±4.5       <0.001       2.9 ±4.6       0.471	Yes	20 (15.2)	$5.9 \pm 7.8$	6.7 ±3.9	0.063	5.5 ±3.7	0.289
Yes         5 (3.8)         4.2 ±3.8         4.4 ±4.4         1.000         3.8 ±4.3         0.841           No         127 (96.2)         3.2 ±5.7         5.0 ±5.3         <0.001	No	112 (84.5)	$2.8 \pm 5.1$	4.7 ±5.4	< 0.001	$3.2 \pm 5.0$	0.229
No $127 (96.2)$ $3.2 \pm 5.7$ $5.0 \pm 5.3$ $<0.001$ $3.6 \pm 4.9$ $0.128$ Respiratory disease         Yes $7 (5.3)$ $2.0 \pm 2.8$ $6.4 \pm 5.2$ $0.073$ $4.6 \pm 4.5$ $0.535$ No $125 (94.7)$ $3.3 \pm 5.8$ $4.9 \pm 5.2$ $<0.001$ $3.5 \pm 4.9$ $0.192$ Reported symptoms at admission       Yes $92 (69.7)$ $3.5 \pm 6.4$ $5.3 \pm 5.3$ $<0.001$ $3.7 \pm 4.9$ $0.131$ No $40 (30.3)$ $2.7 \pm 3.4$ $4.4 \pm 5.1$ $0.020$ $3.2 \pm 4.9$ $0.741$ Abnormal chest radiographyd       Yes $22 (17.9)$ $3.8 \pm 4.9$ $9.6 \pm 6.1$ $0.001$ $6.5 \pm 6.1$ $0.019$ No $101 (82.1)$ $3.1 \pm 5.9$ $4.2 \pm 4.6$ $<0.001$ $3.1 \pm 4.6$ $0.387$ Disease severity         Asymptomatic/mild $110 (83.3)$ $3.0 \pm 5.7$ $4.0 \pm 4.5$ $<0.001$ $2.9 \pm 4.6$ $<0.471$	Ischaemic heart diseas	se					
Respiratory disease  Yes 7 (5.3) 2.0 $\pm 2.8$ 6.4 $\pm 5.2$ 0.073 4.6 $\pm 4.5$ 0.535 No 125 (94.7) 3.3 $\pm 5.8$ 4.9 $\pm 5.2$ <0.001 3.5 $\pm 4.9$ 0.192 Reported symptoms at admission  Yes 92 (69.7) 3.5 $\pm 6.4$ 5.3 $\pm 5.3$ <0.001 3.7 $\pm 4.9$ 0.131 No 40 (30.3) 2.7 $\pm 3.4$ 4.4 $\pm 5.1$ 0.020 3.2 $\pm 4.9$ 0.741 Abnormal chest radiographyd  Yes 22 (17.9) 3.8 $\pm 4.9$ 9.6 $\pm 6.1$ 0.001 6.5 $\pm 6.1$ 0.019 No 101 (82.1) 3.1 $\pm 5.9$ 4.2 $\pm 4.6$ <0.001 3.1 $\pm 4.6$ 0.387 Disease severity  Asymptomatic/mild 110 (83.3) 3.0 $\pm 5.7$ 4.0 $\pm 4.5$ <0.001 2.9 $\pm 4.6$ 0.471	Yes	5 (3.8)	4.2 ±3.8	$4.4 \pm 4.4$	1.000	$3.8 \pm 4.3$	0.841
Yes $7 (5.3)$ $2.0 \pm 2.8$ $6.4 \pm 5.2$ $0.073$ $4.6 \pm 4.5$ $0.535$ $0.$	No	127 (96.2)	$3.2 \pm 5.7$	$5.0 \pm 5.3$	< 0.001	$3.6 \pm 4.9$	0.128
No $125  (94.7)$ $3.3 \pm 5.8$ $4.9 \pm 5.2$ $< 0.001$ $3.5 \pm 4.9$ $0.192$ Reported symptoms at admission  Yes $92  (69.7)$ $3.5 \pm 6.4$ $5.3 \pm 5.3$ $< 0.001$ $3.7 \pm 4.9$ $0.131$ No $40  (30.3)$ $2.7 \pm 3.4$ $4.4 \pm 5.1$ $0.020$ $3.2 \pm 4.9$ $0.741$ Abnormal chest radiographyd  Yes $22  (17.9)$ $3.8 \pm 4.9$ $9.6 \pm 6.1$ $0.001$ $6.5 \pm 6.1$ $0.019$ No $101  (82.1)$ $3.1 \pm 5.9$ $4.2 \pm 4.6$ $< 0.001$ $3.1 \pm 4.6$ $0.387$ Disease severity  Asymptomatic/mild $110  (83.3)$ $3.0 \pm 5.7$ $4.0 \pm 4.5$ $< 0.001$ $2.9 \pm 4.6$ $0.471$	Respiratory disease						
Reported symptoms at admission  Yes 92 (69.7) 3.5 $\pm$ 6.4 5.3 $\pm$ 5.3 <0.001 3.7 $\pm$ 4.9 0.131  No 40 (30.3) 2.7 $\pm$ 3.4 4.4 $\pm$ 5.1 0.020 3.2 $\pm$ 4.9 0.741  Abnormal chest radiography <sup>d</sup> Yes 22 (17.9) 3.8 $\pm$ 4.9 9.6 $\pm$ 6.1 0.001 6.5 $\pm$ 6.1 0.019  No 101 (82.1) 3.1 $\pm$ 5.9 4.2 $\pm$ 4.6 <0.001 3.1 $\pm$ 4.6 0.387  Disease severity  Asymptomatic/mild 110 (83.3) 3.0 $\pm$ 5.7 4.0 $\pm$ 4.5 <0.001 2.9 $\pm$ 4.6 0.471	Yes	7 (5.3)	$2.0 \pm 2.8$	$6.4 \pm 5.2$	0.073	$4.6 \pm 4.5$	0.535
Yes 92 (69.7) $3.5 \pm 6.4$ $5.3 \pm 5.3$ <0.001 $3.7 \pm 4.9$ 0.131 No 40 (30.3) $2.7 \pm 3.4$ 4.4 $\pm 5.1$ 0.020 $3.2 \pm 4.9$ 0.741 Abnormal chest radiography <sup>d</sup> Yes 22 (17.9) $3.8 \pm 4.9$ 9.6 $\pm 6.1$ 0.001 6.5 $\pm 6.1$ 0.019 No 101 (82.1) $3.1 \pm 5.9$ 4.2 $\pm 4.6$ <0.001 $3.1 \pm 4.6$ 0.387 Disease severity  Asymptomatic/mild 110 (83.3) $3.0 \pm 5.7$ 4.0 $\pm 4.5$ <0.001 2.9 $\pm 4.6$ 0.471	No	125 (94.7)	$3.3 \pm 5.8$	4.9 ±5.2	< 0.001	$3.5 \pm 4.9$	0.192
No 40 (30.3) 2.7 $\pm$ 3.4 4.4 $\pm$ 5.1 0.020 3.2 $\pm$ 4.9 0.741 Abnormal chest radiography <sup>d</sup> Yes 22 (17.9) 3.8 $\pm$ 4.9 9.6 $\pm$ 6.1 0.001 6.5 $\pm$ 6.1 0.019 No 101 (82.1) 3.1 $\pm$ 5.9 4.2 $\pm$ 4.6 <0.001 3.1 $\pm$ 4.6 0.387 Disease severity  Asymptomatic/mild 110 (83.3) 3.0 $\pm$ 5.7 4.0 $\pm$ 4.5 <0.001 2.9 $\pm$ 4.6 0.471	Reported symptoms at	t admission					
Abnormal chest radiographyd Yes 22 (17.9) $3.8 \pm 4.9$ $9.6 \pm 6.1$ $0.001$ $6.5 \pm 6.1$ $0.019$ No $101 (82.1) 3.1 \pm 5.9$ $4.2 \pm 4.6$ $<0.001$ $3.1 \pm 4.6$ $0.387$ Disease severity Asymptomatic/mild $110 (83.3)$ $3.0 \pm 5.7$ $4.0 \pm 4.5$ $<0.001$ $2.9 \pm 4.6$ $0.471$	Yes	92 (69.7)	$3.5 \pm 6.4$	$5.3 \pm 5.3$	< 0.001	3.7 ±4.9	0.131
Yes $22 (17.9)$ $3.8 \pm 4.9$ $9.6 \pm 6.1$ $0.001$ $6.5 \pm 6.1$ $0.019$ No $101 (82.1)$ $3.1 \pm 5.9$ $4.2 \pm 4.6$ < 0.001 $3.1 \pm 4.6$ 0.387 Disease severity  Asymptomatic/mild $110 (83.3)$ $3.0 \pm 5.7$ $4.0 \pm 4.5$ < 0.001 $2.9 \pm 4.6$ 0.471	No	40 (30.3)	$2.7 \pm 3.4$	4.4 ±5.1	0.020	$3.2 \pm 4.9$	0.741
No 101 (82.1) 3.1 $\pm$ 5.9 4.2 $\pm$ 4.6 <0.001 3.1 $\pm$ 4.6 0.387 Disease severity Asymptomatic/mild 110 (83.3) 3.0 $\pm$ 5.7 4.0 $\pm$ 4.5 <0.001 2.9 $\pm$ 4.6 0.471	Abnormal chest radiog	graphyd					
Disease severity Asymptomatic/mild 110 (83.3) $3.0 \pm 5.7$ $4.0 \pm 4.5$ < 0.001 $2.9 \pm 4.6$ 0.471	Yes	22 (17.9)	$3.8 \pm 4.9$	$9.6 \pm 6.1$	0.001	$6.5 \pm 6.1$	0.019
Asymptomatic/mild 110 (83.3) $3.0 \pm 5.7$ $4.0 \pm 4.5$ < 0.001 $2.9 \pm 4.6$ 0.471	No	101 (82.1)	3.1 ±5.9	4.2 ±4.6	< 0.001	3.1 ±4.6	0.387
• •	Disease severity						
Moderate to critical 22 (16.7) $4.7 \pm 5.5$ $10.0 \pm 5.8$ $0.001$ $7.0 \pm 6.0$ $0.062$	Asymptomatic/mild	110 (83.3)	$3.0 \pm 5.7$	4.0 ±4.5	< 0.001	2.9 ±4.6	0.471
(-1, 1	Moderate to critical	22 (16.7)	$4.7 \pm 5.5$	$10.0 \pm 5.8$	0.001	$7.0 \pm 6.0$	0.062

<sup>&</sup>lt;sup>a</sup> The first wave lasted from 9 March 2020 to 6 August 2021.

<sup>&</sup>lt;sup>b</sup> Comparison between health-care visits 12 months before COVID-19 and overall health-care visits 12 months after COVID-19.

comparison between health-care visits 12 months before COVID-19 and non-COVID-19 health-care visits 12 months after COVID-19.

<sup>&</sup>lt;sup>d</sup> Nine cases (children) did not undergo chest radiography.

Table 2. Proportion of cases during the first wave<sup>a</sup> with health-care visits 12 months before and 12 months after COVID-19 illness, Brunei Darussalam (N = 132)

Health-care visits before / after COVID-19 illness	n (%)		
No / No	7 (5.3)		
No / Yes	38 (28.8)		
Yes / No	2 (1.5)		
Yes / Yes	85 (64.4)		

<sup>&</sup>lt;sup>a</sup> The first wave lasted from 9 March 2020 to 6 August 2021.

disorders, which were exacerbated by COVID-19 illness in two of these patients. The third patient had transient forgetfulness which the patient described as brain fog. Psychometric evaluations for this patient were normal.

One case developed palpitations 54 days after discharge and investigations revealed idiopathic supraventricular tachycardia. Coronary angiography assessment prior to diagnosis of COVID-19 was normal. Another case developed non-specific symptoms which resolved, although they were later diagnosed with bulimia, and the

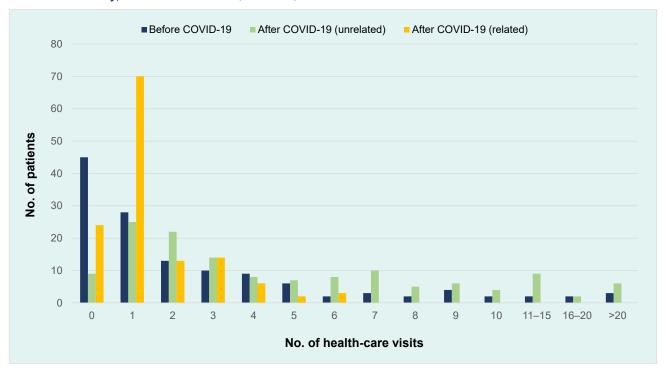
final case had transient localized musculoskeletal chest pain (Tietze syndrome) (Table 4).

# DISCUSSION

Our study showed a significantly higher mean number of health-care visits among recovered COVID-19 cases from the first wave in Brunei Darussalam 12 months after recovery compared with the 12 months prior to infection. However, this increase in health-care visits was mainly due to scheduled post-COVID-19 healthcare visits as per the national management protocol at the time. Although some cases had symptoms of post-COVID condition, none fulfilled the WHO criteria for diagnosis<sup>7</sup> or they had alternate diagnoses, and their symptoms were self-limiting. None of the cases with COVID-19 pneumonia had long-term respiratory effects during the 12 months after recovering from COVID-19.

Post-COVID condition is a well-recognized disorder, 7,8 with varying definitions regarding symptoms and duration. Although there were cases with some symptoms of post-COVID condition, all had alternative diagnoses to account for their symptoms, either due to

Distribution of COVID-19 cases during the first wave by number of health-care visits 12 months before Fig. 1. illness, and number of health-care visits unrelated and related to COVID-19 in the 12 months after recovery, Brunei Darussalam (N = 132)



<sup>&</sup>lt;sup>a</sup> The first wave lasted from 9 March 2020 to 6 August 2021.

Encounters with psychiatric counselling services 12 months before COVID-19 infection, during Table 3. hospitalization and 12 months after recovery during the first wave,  $^{a}$  Brunei Darussalam (N = 132)

	12 months before COVID-19	During hospitalization for COVID-19	12 months after COVID-19
Encounters, n (%)	4 (2.9)	6 (4.4)	4 (2.9)
Case no.: Disorder	1: Psychotic depression 2: Learning disability 3: Autism spectrum disorder (paediatric) 4: Autism spectrum disorder (paediatric)	2: Learning disability (risk of impulsivity/aggression)  5: Anxiety and panic attacks  6: Anxiety and panic attacks  7: Anxiety disorder (reactive anxiety and insomnia)  8: Attention deficit hyperactivity disorder  9: Concern of staff	1: Psychotic depression 2: Learning disability (lost to follow-up) 5: Anxiety and panic attacks 6: Anxiety and panic attacks

<sup>&</sup>lt;sup>a</sup> The first wave lasted from 9 March 2020 to 6 August 2021.

Table 4. Cases with symptoms of post-COVID condition during the first wave,  $^{a}$  Brunei Darussalam (N=6)

Case no.	Sex/age (years)	Disease severity	Length of hospitalization (days)	Pre-existing condition	Symptoms	Outcomes	Last consult	Days between discharge and first health-care visit
5	Female/23	Mild	14	Yes: Anxiety	Anxiety, palpitation, insomnia, nightmares	Resolved	Discharged	20
6	Female/23	Mild	17	Yes: Anxiety and panic	Anxiety attacks	Resolved	Discharged	18
8	Male/39	Mild	23	Yes: Attention deficit hyperactivity disorder	Forgetfulness/ unable to find words, unable to concentrate	Resolved	Discharged	255
10	Male/43	Moderate	20	No	Localized chest pain and itchy rash	Resolved	Discharged	36
11	Male/62	Moderate	33	No	Palpitation	Diagnosed with supraventricular tachycardia	Cardiology follow-up	54
12	Female/19	Mild	35	No	Atypical chest pain, cramps, choking sensation	Bulimia	Still on follow-up	284

<sup>&</sup>lt;sup>a</sup> The first wave lasted from 9 March 2020 to 6 August 2021.

exacerbations of pre-existing conditions, chest musculoskeletal pain similar to Tietze syndrome or cardiac arrhythmias that were unrelated to COVID-19. Some of our cases did meet the definition of other diagnostic criteria, including the CDC criteria.<sup>5,8</sup> Fortunately, most cases recovered without further consultations or treatment, indicating that post-COVID-19 symptoms were mild and self-limiting. However, it remains to be seen if post-COVID condition will be a significant problem in our setting with a larger number of patients affected by COVID-19 in subsequent waves.

Our findings differ from other studies reported in the literature. A meta-analysis of 91 studies showed a prevalence of hospital readmissions during the first 30 days, 90 days and 1 year post-discharge of 8.97%, 9.79% and 10.34%, respectively. 12 Most cases of hospital readmissions occurred within 30 days after discharge. 12 A study from Switzerland of 385 patients with COVID-19, 81 of whom required hospitalization during initial illness, reported that at 6-8 months after illness, 26% (n = 111) had not fully recovered, 40% (n = 111) = 170) reported at least one visit to the general practitioner and 10% (n = 81) of those hospitalized were rehospitalized. 11 Individuals who had not fully recovered or suffered from fatigue, dyspnoea or depression were more likely to have further health-care contacts. However, a third of individuals (37/111) who had not fully recovered did not seek further care. 11 This indicated that despite residual symptoms persisting, they may not have been significant enough to require health-care visits. The difference between our findings and those of other studies may be due to the small total number of patients affected by COVID-19 in Brunei Darussalam during the first wave, including those categorized as severe. However, it is possible that the difference is due to factors such as vulnerability or susceptibility to post-COVID-19 illness, and is influenced by social, cultural and religious factors. 16,17 Other factors may also be at play and will require further study.

There are many reasons why patients may have physiological or psychological issues after recovery from COVID-19.4-9 Apart from patients with COVID-19 pneumonia and a case of transient thrombocytopenia, none of the cases from this study had any other symptoms. As previously reported, cases in this cohort with moderate to critical COVID-19 all had abnormal chest radiography. 18 All cases were reviewed by the

respiratory department, cleared of any long-term pulmonary issues and eventually discharged to their primary care doctors. None had further health-care visits for pulmonary issues. In the first wave, only chest radiography was used for imaging as computed tomography, which is superior in detecting respiratory changes due to COVID-19, was not available. 19 If it had been available and used, this would have likely resulted in more unnecessary scheduled post-COVID-19 visits. One study has reported persistent air exchange dysfunction after recovering from COVID-19.20 It is uncertain if symptoms will become apparent after a much longer period and, therefore, longer follow-up studies are required.

The mental wellbeing of COVID-19 patients is likely to be impacted either directly due to their COVID-19 infection or as a psychological impact of implemented restrictive measures. 4,10 Six of our patients needed counselling during their hospitalizations. Common indications for counselling were anxiety-related issues that were exacerbated by COVID-19 illness. This was not surprising, given that at the time COVID-19 was a novel viral illness without effective treatment. Furthermore, our management protocol required all COVID-19 cases to be admitted for isolation in single isolation rooms or warded with strangers for a minimum duration of 14 days.<sup>21</sup> Movement was also restricted to the wards or rooms. This was further compounded by frequent medical investigations (blood draws, radiological imaging and nasopharyngeal swabbing). All these can incur anxiety and fear in addition to stressors brought on by the COVID-19 illness itself. However, this did not translate to additional health-care visits.

This study of the first wave of COVID-19 in Brunei Darussalam showed that most patients recovered without further issues and significant post-COVID conditions were uncommon. COVID-19 remains a novel infectious disease, especially with new SARS-CoV-2 variants of concern appearing. However, the knowledge gained has resulted in a better understanding of COVID-19, as reflected in changes to our national management protocols. After the peak of the first wave in 2020, postdischarge testing was omitted as it was shown that the number of cases re-testing positive after discharge was not insignificant. 22-24 Longer follow-up for non-resolving symptoms or laboratory monitoring also stopped and instead cases were directed to their primary care clinics.

The current management protocols require follow-up for patients with unresolved chest radiography findings with moderate to severe COVID-19 or for those who had a complicated illness.

There are several limitations that need to be considered when interpreting our findings. Using encounters from government health-care institutions based on the electronic record system excluded encounters with private clinics. However, the demographics of our study patients are consistent with patients whose health-care needs are usually met by the public sector. Furthermore, encounters with the private sector are likely to be minor and considered non-significant, as in Brunei Darussalam specialty services are only available from public healthcare institutions. The sample size was small, and further studies with larger cohorts would be useful and should be considered. Prior to the second wave, there were only 340 patients with COVID-19 in Brunei Darussalam and, of these, the majority were excluded as they were expatriates who had just entered Brunei Darussalam or did not have 12 months of follow-up. Despite these limitations, the study population was representative of the situation in Brunei Darussalam. The small number of cases may account for differences between our study and other literature with higher re-admission rates. Studies on post-COVID condition would likely capture more cases by survey rather than electronic records, as patients with milder conditions may self-manage and not present at a health-care facility. However, our study is unique in that our findings are representative of the whole country as all COVID-19 cases were admitted to a single designated centre.

In conclusion, our study showed that there were significantly more health-care visits 12 months after recovery from COVID-19 compared with the 12 months prior to infection. However, most post-COVID-19 health-care utilization was due to scheduled COVID-19 health-care visits. Post-COVID condition was not officially diagnosed, and related symptoms were mild and self-limiting. However, our sample size was small and this is a limitation that needs to be taken into account. Further studies are required with a larger sample size. The larger cohort of patients affected by the second wave in Brunei Darussalam would be ideal for further study.

## Conflict of Interest

The authors have no conflicts of interest to declare.

#### Ethics statement

This study was conducted in accordance with the ethical standards set out in the Declaration of Helsinki (October 2013). Permission was obtained from the Ministry of Health, Brunei Darussalam, to conduct this study using aggregated, anonymized data.

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# How the Commonwealth of the Northern Mariana Islands stalled COVID-19 for 22 months and managed its first significant community transmission

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**Objective:** The Commonwealth of the Northern Mariana Islands (CNMI) is a remote Pacific island territory with a population of 47 329 that successfully prevented the significant introduction of coronavirus disease (COVID-19) until late 2021. This study documents how the response to the introduction of COVID-19 in CNMI in 2021 was conducted with limited resources without overwhelming local clinical capacity or compromising health service delivery for the population.

Methods: Data from COVID-19 case investigations, contact tracing, the Commonwealth's immunization registry and whole genome sequencing were collated and analysed as part of this study.

Results: Between 26 March 2020 and 31 December 2021, 3281 cases and 14 deaths due to COVID-19 were reported in CNMI (case fatality rate, 0.4%). While notification rates were highest among younger age groups, hospitalization and mortality rates were disproportionately greater among those aged >50 years and among the unvaccinated. The first widespread community transmission in CNMI was detected in October 2021, with genomic epidemiology and contact tracing data indicating a single introduction event involving the AY.25 lineage and subsequent rapid community spread. Vaccination coverage was high before widespread transmission occurred in October 2021 and increased further over the study period.

Discussion: Robust preparedness and strong leadership generated resilience within the public health sector such that COVID-19 did not overwhelm CNMI's health system as it did in other jurisdictions and countries around the world. At no point was hospital capacity exceeded, and all patients received adequate care without the need for health-care rationing.

n terms of vulnerabilities to infectious disease epidemics, the Pacific island countries and areas (PICs) have some unique advantages and disadvantages. Their remote location facilitates application of border control measures, and their low populations are often below the required threshold for the establishment of many epidemic-prone diseases. On the other hand, once an infectious disease is introduced, the populace is prone to explosive outbreaks and responses are often hampered by limited availability of healthcare personnel and facilities, as well as supply chain constraints. Moreover, the islands – especially those with a high level of dependency on tourism income like the Commonwealth of the Northern Mariana Islands (CNMI) - can only remain closed off for so long without incurring a negative economic impact. Given that a number of PICs were able to effectively protect their population from the 1918–1919 influenza outbreak by introducing strict quarantine measures, 1 it is not surprising that this strategy was adopted by many at the start of the novel coronavirus disease (COVID-19) pandemic. Success among the PICs, however, has been variable.<sup>2,3</sup>

CNMI is a commonwealth in political union with the United States of America (USA) in the western Pacific Ocean, consisting of 14 tropical islands stretching over

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400 nautical miles (740 km). More than 90% of the Commonwealth's population lives on the island capital of Saipan (area, 46.5 square miles or 115 km<sup>2</sup>). Of the 13 other islands, only Rota and Tinian have a significant population. In Saipan, there is a single 86-bed hospital with four intensive care beds, five private clinics, and approximately 200 licensed physicians and advanced practice providers. CNMI has a shortage of health-care professionals, with the nurse-to-patient ratio in the hospital sometimes reaching levels of 1:7.4 The semiautonomous Commonwealth Healthcare Corporation (CHCC), an integrated health-care and public health system, serves as the Department of Health.

In response to reports of a novel coronavirus disease spreading in China, CNMI adopted a strict border policy in February 2020, which facilitated the identification and isolation of travel-associated cases.<sup>5</sup> The first community cases were identified on 26 March 2020 with limited further transmission. After eliminating local transmission in 2020, CNMI experienced its next community outbreak, again comprising only a small cluster of cases, in March 2021. A larger, more prolonged outbreak occurred at the end of 2021, extending into 2022. Before this large outbreak, CNMI's leadership had time to obtain adequate resources, train personnel and deliver a community-based vaccination campaign. Thus, by the time of the first significant community spread, CNMI was uniquely protected; the case fatality rate was low and there was sufficient capacity within the health-care system to cope with increased case numbers as a result of the importation of both the Delta and Omicron variants of concern (VOCs).

The objective of this study is to describe CNMI's adaptive public health response, which included strong border measures, contact tracing and a successful vaccination campaign, and its impact on COVID-19 transmission, morbidity and mortality. We also describe the characteristics and genomic epidemiology of COVID-19 cases in CNMI.

## **METHODS**

# Data sources and case definitions

Laboratory-confirmed cases were reported to the COVID-19 Communicable Disease Investigation team who then conducted detailed case investigations, contact tracing and additional monitoring activities. Persons under investigation (PUI) were individuals with suspected COVID-19 based on clinical presentation. COVID-19 vaccination data were recorded by the Commonwealth's immunization tracking system, WebIZ.6 Age-group population estimates (denominators for vaccine coverage calculations) were extrapolated from the US Census Bureau's International Database (IDB) 2020 age pyramid using the 2020 total census population of 47 329.7,8 Racial and ethnic proportions of the population were sourced from the 2010 US Census.9

## Public health response

The CHCC led the public health response. In accordance with Public Law 13-63, the Territorial Health Official coordinated territorial leadership, with the support of the Governor and his COVID-19 Task Force, chaired by the Director of Hospital and Public Health Preparedness. 10

## Community and hospital-based testing

Community-based testing evolved during the pandemic, especially after the start of the larger COVID-19 outbreak in October 2021. By late 2021, daily nucleic acid amplification tests (NAATs) were conducted by appointment, while antigen-based surveillance testing was performed on an as-needed basis at fire stations and quarterly in schools. Diagnostic testing was conducted for PUIs or symptomatic persons in quarantine at a community COVID-19 site using US Food and Drug Administration (FDA)-approved rapid antigen tests. All patients presenting to hospital with symptoms (or close contacts of positive cases) were tested using NAATs. Also, all health-care workers at CHCC were offered NAATs weekly.

# Contact tracing, isolation and quarantine

For the first 3 months of the October 2021 outbreak, all laboratory-confirmed cases were questioned about their recent contacts (during the 3 days before their symptom onset or positive test result). Isolation and quarantine periods followed contemporaneous US Centers for Disease Control and Prevention (CDC) guidelines. All cases and contacts were housed in government facilities - three contracted hotels - until this became logistically and financially untenable in November 2021 due to the high volume of cases. From then onwards, only symptomatic cases, those at higher risk of severe COVID-19 outcomes or those whose household was not completely vaccinated were required to complete isolation in government-managed facilities, while other cases completed isolation at home. All guarantined contacts were tested twice: once when identified as a contact and then again after completion of quarantine.

## Point-of-entry screening

Point-of-entry (POE) screening evolved during the pandemic as the science behind adequate guarantine and testing strategies progressed, additional testing became available and vaccination rates increased. Revisions to POE protocols were aligned with external recommendations and US CDC guidelines.

Beginning in March 2020, all arriving travellers were quarantined in a government-contracted quarantine hotel for 14 days and then tested before their release. From May 2020 onwards, all travellers were additionally tested on arrival. By July 2020, all visitors were required to complete an online travel registration form 72 hours before their entry into CNMI, quarantine at a government facility for 5 days (or at home for residents) and test negative for COVID-19 before release. For visitors who refused to be tested, the quarantine period was extended to 14 days. In August 2020, in a reaction to rising COVID-19 case numbers in the USA and nearby Guam, all travellers had to quarantine in a government facility for 5-7 days, depending on their vaccination status. By June 2021, rapid antigen testing was made available at POEs for arrival testing. After the identification of community cases in late October 2021, the quarantine period for all travellers was changed to 5-10 days, depending on vaccination status. Protocols were again adjusted in November 2021, allowing fully vaccinated travellers to complete quarantine under active surveillance outside of a government facility. However, travellers were required to take a NAAT on day 5 for clearance from self-quarantine. Throughout the acute period of the pandemic, qualified essential workers were granted modifications to entry requirements but only after submitting to a rigorous CHCC approval process.

### Health facility preparedness

Seventeen hospital rooms were upgraded to COVID-19 isolation rooms and fitted with air scrubbers and ultraviolet lights (one for labour and delivery, two for obstetrics, two for paediatrics and 12 for medical cases). In early 2021, a 25-bed Alternative Care Site (ACS) was established at a local hotel to expand bed capacity for less severely ill COVID-19 patients and as a step-down unit for those hospitalized in the main hospital. The ACS also supplied specialized services (e.g. haemodialysis) for patients in isolation. All COVID-19 patients were assessed for risk factors for severe disease and offered monoclonal antibody treatment at the ACS.

During the October 2021 outbreak, in order to overcome difficulties in sharing information with patients without access to phones and Wi-Fi, the COVID-19 Task Force established a physical community centre where patients could be tested, treated, and receive their test results and health advice.

# Community-based vaccination

From December 2020, all adults in CNMI were offered COVID-19 vaccines in line with the contemporaneous US CDC guidelines; as vaccines were authorized for use in children, vaccination was extended to those aged >5 years. A community-based approach was used to maximize vaccine uptake, supplemented by a government mandate for all health-care workers and government employees. A directed "house-to-house" outreach campaign for vaccination and boosters targeting high-risk and low-turnout communities proved highly effective. Other initiatives included the "Road to 80" campaign, the aim of which was to fully vaccinate 80% of the population against COVID-19. The campaign ran from July to September 2021 and offered raffle prizes to any CNMI resident who had received the first dose of any available vaccine. Vaccine supply, technical assistance and logistics were provided by the US CDC.

#### **Diagnostics**

Samples for laboratory diagnostics comprised either nasopharyngeal swabs placed in universal transport media for NAATs (except for ID NOW [Abbott Laboratories, Abbott Park, IL, USA] which uses a disposable dry swab) or nasal swabs for antigen detection assays. Initially, testing was performed at Guam Public Health Laboratory. From mid-April 2020 onwards, once FDA authorization had been obtained, NAAT was conducted locally in CNMI using the DiaPlexQ novel coronavirus detection kit (SolGent Co., Ltd., Daejeon, Republic of Korea). Travellers, PUIs presenting to the hospital and individuals testing positive with the DiaPlexQ assay were tested by NAAT with either ID NOW or GeneXpert; all positives were considered laboratory-confirmed cases. PUIs and symptomatic persons from the community in quarantine were tested using BinaxNOW (Abbott Laboratories) rapid antigen test and considered laboratory-confirmed cases if their test was positive. The COVICHEK antigen kit (WiZChem Co., Ltd., Kangwon, Republic of Korea) was used for communitybased surveillance, but all positive test results were confirmed by NAAT or BinaxNOW assay.

# Genomic and phylogenetic analysis

Specimens positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were sent to the US CDC Division of Viral Diseases for whole genome sequencing. Samples were sequenced using Illumina (San Diego, CA, USA) platforms and consensus sequence genomes were uploaded to GISAID. Nextstrain<sup>11</sup> was used to conduct all phylogenetic analyses. Between December 2019 and July 2022, 13 090 phylogenetic analyses were conducted: 2945 genomes from CNMI and 10 145 contextual genomes, with preference given to specimens from countries with geographical proximity to CNMI, including Guam, Indonesia, Japan, Malaysia, Papua New Guinea, the Philippines, the Republic of Korea and the USA. Following the standard Nextstrain Augur<sup>12</sup> pipeline, nucleotide alignment was conducted with MAFFT,13 maximum-likelihood phylogenetic trees were created with IQ-TREE2, 14 time-resolved phylogenetic trees were created with TreeTime<sup>15</sup> and results were visualized using Auspice. Nodes on the phylogenetic tree were annotated to indicate how the cases were identified (i.e. through travel screening, hospitalization, community testing or contact tracing) and inferred dates estimated. The inferred date is the date when a specific SARS-CoV-2 genotype arose, which may not necessarily be the date it was introduced. This date, by definition, must be earlier than when the first case attributable to a given genotype was detected.

# Statistical analysis

Frequencies for categorical variables were tabulated. Crude event rates were calculated by dividing the number of infections, hospitalizations or deaths by the total population (or vaccination status subgroup). Risk ratios were calculated for the risk of hospitalization by vaccination status and were adjusted for age and sex. All analyses were performed using R version 4.1.1.

# **RESULTS**

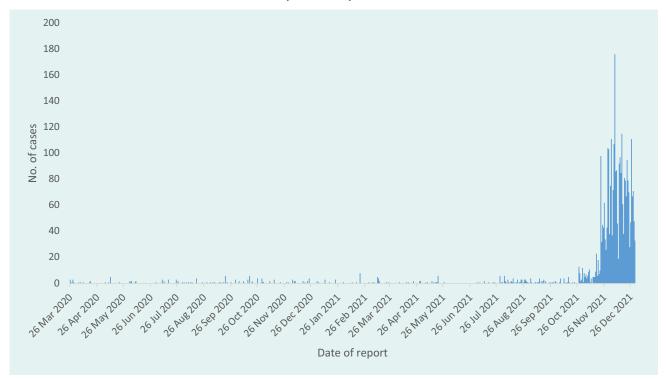
# Descriptive epidemiology

From 26 March 2020 to 31 December 2021, 3281 cases of COVID-19 were recorded in CNMI (Fig. 1). There were 87 hospitalized cases (2.6%) and 14 deaths listing COVID-19 as either a cause of death or a contributing condition (case fatality rate, 0.4%; 30 deaths per 100 000 population). Nearly one third of cases (30.8%; n = 1009) reported symptoms characteristic of COVID-19 (e.g. fever, cough, shortness of breath, anosmia, ageusia). By December 2021, approximately 7% of CNMI's population had been infected with COVID-19. Virtually all cases were identified on Saipan; just nine cases (0.3%) were identified among residents of Tinian.

Between March 2020 and October 2021, the period between the first case notification and the start of the larger community outbreak, CNMI recorded just 291 cases (Fig. 1): 250 were identified from travel quarantine, 26 from contact tracing (primarily in recent travellers), 8 from hospital testing and 7 from communitybased testing.

After the introduction of COVID-19 in March 2020 and subsequent elimination of community transmission by April 2020, the next community outbreak of COVID-19 comprised 11 cases, the first of which was identified on 12 March 2021 through outbound travel testing and the last on 17 March 2021. The much larger community outbreak started on 28 October 2021, with the first cases identified through school-based testing. At the time of writing (early 2022), this outbreak was still ongoing, albeit at lower levels.

The mean age of all COVID-19 cases was 31 years (range: 0-95 years) and 53.9% were in men. Notification rates during the study period were highest in those aged 20-49 years (963.4 cases per 10 000 persons; n = 1621), followed by those aged 0-4 years (680.9) cases per 10 000 persons; n = 233) and those aged 5–19 years (622.8 cases per 10 000 persons; n = 790). The lowest rates were seen in the oldest age group, those aged ≥65 years (399.8 cases per 10 000 persons; n = 137), and the next oldest group, those aged 50–64 years (455.7 cases per 10 000 persons; n = 400). Weekly notification rates increased especially rapidly in people aged <50 years from the week of 20 November



Daily number of laboratory-confirmed COVID-19 cases, Commonwealth of the Northern Mariana Islands, Fig. 1. 26 March 2020–31 December 2021 (N = 3281)

to the week of 11 December 2021; rates in those aged >50 years increased more gradually over the same time frame (Fig. 2).

The mean age of hospitalized cases was 49 years (range: 0-95 years). Hospitalization rates were highest among those aged ≥65 years (61.3 hospitalizations per 10 000 persons; n = 21), followed by those aged 50–64 years (24.6 per 10 000 persons; n = 27) and those aged 20–49 years (19.6 per 10 000 persons; n = 33). Hospitalization rates were low in children, with 8.8 per 10 000 persons (n = 8) among those <5 years and 2.4 per 10 000 persons (n = 3) in those aged 5–19 years. Over two fifths of hospitalized cases (43.7%) were admitted through the emergency department (n = 38). After a medical assessment, 378 (11.5%) patients received monoclonal antibodies.

All but one of the 14 COVID-19-related deaths occurred in people aged >50 years; there was one death in a 44-year-old. Relative to the 2010 US Census population estimates, Carolinian, Chamorro and other Pacific Islanders were overrepresented in the deaths (Fig. 3). Of the 14 deaths, nine (64.3%) were in unvaccinated individuals.

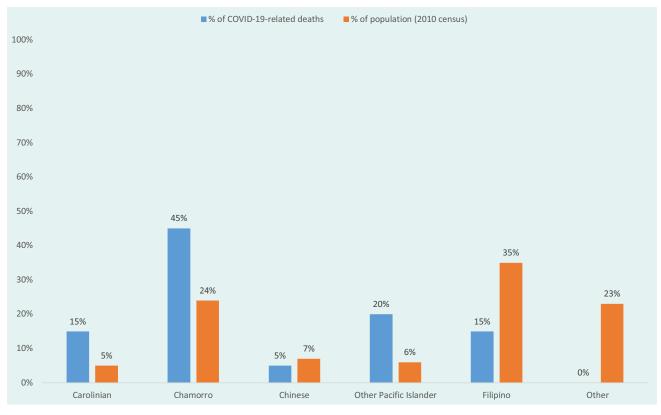
Two thirds of cases had received at least one dose of a COVID-19 vaccine; 60.2% (n = 1975) were fully vaccinated and 5.7% (n = 188) were partially vaccinated. Of the remainder, 25.7% (n = 845) were unvaccinated and 8.3% (n = 273) were ineligible for COVID-19 vaccination. Cases who were unvaccinated had a risk of hospitalization 2.64 times (95% confidence interval [CI]: 1.71–4.07) higher and a risk of death 3.63 times (95% CI: 1.14–11.55) higher than those who were fully vaccinated.

Almost half of all reported cases (46.4%; n = 1524) were identified through contact tracing. Nearly another third were identified from community-based testing (27.8%; n = 912), with the remainder of cases coming from hospital testing (16.3%; n = 535) and incoming travellers (9.6%; n = 314). A total of 14 672 contacts were actively monitored by public health staff, with an average of 4.5 contacts monitored per case (range: 0-48).

Fig. 2. Weekly notification rates of COVID-19 by age group, Commonwealth of the Northern Mariana Islands, 29 October-31 December 2021



Fig. 3. COVID-19-related deaths by race/ethnicity compared to 2010 Census population, Commonwealth of the Northern Mariana Islands, March 2020–December 2021 (N = 14)



# Genomic epidemiology

Of the 3281 COVID-19 cases, genomes were sequenced from 2945 (89.8%). Ten of the 11 cases from the March 2021 community outbreak were sequenced, revealing that this cluster not only comprised viruses in the B.1.2 Pango lineage<sup>16</sup> but was also a monophyletic cluster of largely identical genomes. Genomes from this cluster were direct descendants of two cases identified through travel screening on 2 February 2021.

Genome sequencing of cases from the larger October 2021 community outbreak also revealed a large monophyletic cluster of a virus from the AY.25 (Delta variant) Pango lineage (Fig. 4), suggestive of a single introduction event. Many of the samples from the early cases fell into a large polytomy of identical genomes with subsequent branches coming from the polytomy, consistent with rapid spread following the introduction. Three mutations separate the internal CNMI cluster, and this branch has an estimated inferred date of 27 July 2021 (CI: 4 June-5 August 2021).

Phylogenetic analysis further showed that the monophyletic cluster of CNMI genomes were direct descendants of genomes sequenced from Guam earlier in 2021 (Fig. 4). Genomes collected from Guam in late July-early August 2021 were the most recent common ancestor of the CNMI cluster. This suggests that the large outbreak in CNMI was caused by an introduction of a single genotype in the AY.25 lineage, most likely from Guam. Supporting evidence comes from contact tracing data, which dated the earliest symptom onset in a community case to early October 2021. This individual reported recent contact with a traveller with "essential worker" status from Guam prior to their symptom onset.

### Vaccination coverage

By 31 December 2021, 96 745 vaccine doses had been administered in CNMI - 82 145 doses of Pfizer-BioNTech, 13 348 doses of Moderna, 1245 doses of Johnson & Johnson/Janssen and seven unknowns. Before the October 2021 outbreak, vaccine coverage was 73.4% (n = 34745) in the overall population and 90.4% of the vaccine-eligible population (i.e. those aged >12 years). By 31 December 2021, vaccine coverage reached 84.8% in the overall population (n = 40 121) and 91.4% among the vaccine-eligible population (i.e. those aged >5 years); 32.2% of those eligible (n = 14 140) were up to date with boosters (Fig. 5). Of note, the vaccine coverage rate among adults aged ≥65 years was >99%.

# DISCUSSION

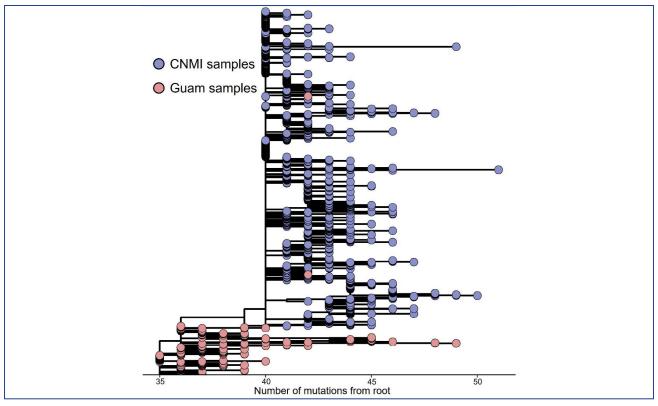
CNMI demonstrated a well-coordinated public health response to the COVID-19 pandemic. Initial efforts stalled major community transmission of COVID-19 for 22 months and provided a window of opportunity to prepare for the eventual community introduction of COVID-19 by implementing a vaccination campaign as well as measures to ensure preparedness and efficient use of federal and partner emergency health system resources.

In common with other PICs, CNMI's initial response to COVID-19 relied on strict border controls; however, these were inadequate to identify and isolate all cases with POE screening. Nevertheless, the rapid containment of the small community outbreak of COVID-19 in March 2021, which was limited to just 11 cases, showed the ability of CNMI to successfully implement an elimination model of disease transmission for breakthrough cases.

As the pandemic progressed, and given the reality of increased border crossings, lapses in quarantine processes or testing, and shorter quarantine times as PICs titrated efforts to maintain tourism and protect their economies, most PICs had to face the inevitability of community transmission of COVID-19. Indeed, in CNMI, the large community outbreak in October 2021 was traced to close contact with an essential worker and the bypassing of the rigid quarantine system that had helped to prevent widespread disease introduction for almost 22 months.

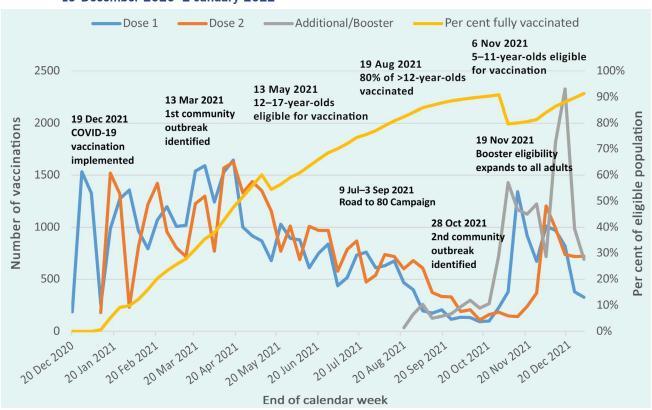
The epidemiology of COVID-19 in CNMI mirrors that observed in other jurisdictions around the world, with case rates highest among younger age groups and rates of severe disease, hospitalizations and deaths highest in those aged >50 years. 17 Given the high transmissibility of the Delta VOC18 and the CHCC's limited capacity to monitor a large number of cases, CNMI's leadership when formulating its response to the October 2021 outbreak made the decision to scale back its resourceintensive contact tracing, quarantine and isolation measures. By this time, the vaccination programme had fully

Fig. 4. Phylogenetic tree of the large COVID-19 outbreak of Delta lineage AY.25, Commonwealth of the Northern Mariana Islands, July 2021-January 2022



Branch lengths are representative of single nucleotide polymorphisms. Nodes are coloured by the location of sampling.

Timeline of the COVID-19 vaccination programme, Commonwealth of the Northern Mariana Islands, Fig. 5. 19 December 2020-2 January 2022



vaccinated 73.5% of the eligible population in CNMI, helping to keep hospitalization and mortality rates low and preventing the health-care system from being overwhelmed. Lessons learned from the success of the Delta response have since been used to inform the response to the Omicron variant which - unlike the situation in other countries where there was a gap between the Delta and Omicron waves - was also circulating in the community by December 2021.

In CNMI, unique challenges such as limited health-care facility capacity and delayed access to surge personnel and supplies served as drivers for aggressive preparedness and response actions. Strict POE protocols prevented widespread community transmission initially and delayed the worst of the impacts of COVID-19 while local efforts focused on learning, assembling and vaccinating. However, as POE restrictions were relaxed and more transmissible variants (Delta and later Omicron) overwhelmed contact tracing efforts, widespread community transmission ultimately occurred, and resources were redirected to other critical response efforts. Nonetheless, the alignment of political and health leadership with a community-based approach tempered many of the challenges faced on the US mainland, including overstretched hospitals and high mortality rates. The high vaccination rate, achieved in a multi-ethnic, multi-racial community despite the spread of misinformation, was also a major contributor to the success of the response. CNMI has had relatively mild morbidity and mortality from this pandemic thanks to its model health response.

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#### Conflicts of interest

The authors have no conflicts of interest to declare.

#### Ethics statement

The collection and analysis of the surveillance data in this study was part of an emergency response. The public reporting activity was determined to be routine public health practice by the Territorial Health Officer. No animals or small children were harmed in the writing of this paper.

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# Early pandemic use of face masks in Papua New Guinea under a mask mandate

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Objective: During the coronavirus disease (COVID-19) pandemic, face mask wearing was mandated in Port Moresby, Papua New Guinea in July 2020, but compliance was observed to be low. We aimed to determine the frequency of face mask wearing by the general public in Papua New Guinea under the mask mandate.

Methods: To estimate compliance with the mandate, we analysed photographs of people gathering in Port Moresby published between 29 September and 29 October 2020. Photo-epidemiology was performed on the 40 photographs that met predefined selection criteria for inclusion in our study.

Results: Among the total of 445 fully visible photographed faces, 53 (11.9%) were observed wearing a face mask over mouth and nose. Complete non-compliance (no faces wearing masks) was observed in 19 (4.3%) photographs. Physical distancing was observed in 10% of the 40 photographs. Mask compliance in indoor settings (16.4%) was higher than that observed in outdoor settings (9.8%), and this difference was statistically significant (P < 0.05). Mask compliance was observed in 8.9% of large-sized gatherings (>30 people), 12.7% of medium-sized gatherings (11-30 people) and 25.0% of small-sized gatherings (4–10 people; photographs with <4 people were excluded from analysis).

Discussion: We found very low population compliance with face mask mandates in Papua New Guinea during the prevaccine pandemic period. Individuals without face coverings and non-compliant with physical distancing guidelines are considered to be in a high-risk category for COVID-19 transmission particularly in medium- and large-sized gatherings. A new strategy to enforce public health mandates is required and should be clearly promoted to the public.

The coronavirus disease (COVID-19) pandemic has affected all countries but has had a disproportionate impact on low- and middle-income countries such as Papua New Guinea. Papua New Guinea is one of the world's most diverse countries - geographically, ethnically, linguistically, environmentally and culturally. The majority of the population (>85%) lives in rural villages, which are often difficult to access due to the country's challenging terrain.<sup>2</sup> As of 3 February 2023, there were 46 750 confirmed cases of COVID-19 and 670 confirmed deaths in Papua New Guinea.<sup>3</sup> However, these case numbers are likely underestimates due to low testing rates.4

Several factors have increased the vulnerability of the population of Papua New Guinea to COVID-19. Cultural practices and events unique to Papua New Guinea, including funeral practices (haus krai), religious and sporting gatherings, as well as cultural events such as singings, have the potential to cause widespread transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) within communities. Traditional greeting practices, which include shaking hands or embracing,<sup>5</sup> and crowded community living also pose a high risk for transmission of SARS-CoV-2 and other diseases, such as tuberculosis.<sup>6</sup> In Papua New Guinea, the average household size is 6.24 people in rural areas and 8.01 in urban areas. The highest density is in the National Capital District (NCD), with 9.19 people per household.<sup>7</sup> These factors, combined with poor sanitation and hygiene practices, greatly increase the risk of SARS-CoV-2 transmission in many communities.<sup>8</sup> As the transmission of SARS-CoV-2 is predominantly via an airborne route,

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crowded gatherings have been identified as an important contributor to the spread of COVID-19. Although large mass gatherings have been frequently cited as a major source of case transmission, the so-called super-spreader events, gatherings of less than 100 people in private or enclosed public places, have been shown to cause the highest incidence of new cases, suggesting that density and ventilation may have more effect on transmission risk than crowd size.9

In 2020, as COVID-19 case numbers increased globally, Papua New Guinea adopted several public health and social measures to prevent community transmission, including travel restrictions, quarantine and isolation measures, physical distancing and face mask wearing. 10 However, despite the government-imposed restrictions, daily routine mobility persisted, especially in rural areas or communities where enforcement of restrictions was limited. 11 On 3 October 2020, following a plateau in case numbers across the nation, most of the measures were relaxed, including restrictions on domestic and international flights, and business premises and recreational centres reopened.<sup>3</sup> In contrast, the face mask mandate, implemented on 23 July 2020, remained in place in areas with continued levels of community transmission such as Port Moresby, NCD, which had accounted for 70 of the 91 cases nationwide from the month of September 2020.3,12 As of 4 October 2020, NCD accounted for 60% (n = 322) of the country's cumulative reported cases.3

Evidence suggests that mask wearing by healthy people in community settings provides protection against SARS-CoV-2 infection, 13 and face mask wearing is also a well established method of source control.<sup>14</sup> In addition, a study conducted in Australia, the United Kingdom of Great Britain and Northern Ireland and the United States of America showed that mandating the use of face masks results in higher usage of masks. 15 In Papua New Guinea, however, anecdotal evidence was suggestive of widespread non-compliance with mandatory face mask wearing. 16 This study therefore aimed to estimate the frequency of face mask wearing by the general public in Port Moresby during the early stages of the COVID-19 pandemic prior to vaccines being available, when community transmission was established and mask wearing was mandated.

### **METHODS**

A search was conducted in the online archives of The National newspaper for photographs of gatherings in Port Moresby between 29 September and 29 October 2020. This month-long time period was chosen because at that time the mask mandate remained in place in NCD due to ongoing community transmission (rather than a COVID-19 surge), while across the country all other restrictions had been lifted, including those on schools, sporting matches and international travel. 12 A list of sources for each photograph is given in Supplementary Table 1. Only one newspaper was searched to avoid duplication of photographs capturing the same event.

Each photograph was assessed against a set of inclusion and exclusion criteria (Table 1). In order to be included in the study, photographs had to be of gatherings held in Port Moresby between 29 September and 29 October 2020, spontaneous and of sufficient quality with clear visibility for easy counting purposes. In addition, there had to be a minimum of four people in the photograph.

# Data analysis

Photo-epidemiology was performed by two reviewers independently (DH and MK); any discrepancies were resolved by a third reviewer (AQ).17,18 A manual head count was done to determine the gathering size, and a count of all faces with the mouth and nose visible was performed. Finally, a mask count was performed; to be included in the mask count, masks had to cover both the mouth and nose (masks covering only the mouth were not included in the count). Masks could be of the surgical, N95, disposable or cloth types; any other form of face covering was excluded from the count. Mask wearing was calculated as the number of people wearing a mask as a percentage of the number of visible faces. Each photograph was counted twice by each reviewer, with the average of the four counts used for analysis. Inter-rater reliability score was calculated to ascertain the level of agreement between the two reviewers (DH and MK) who performed the counting of the photographs. The statistical package R (version 3.6.3) was used for this analysis, with the Kappa coefficient obtained using the "psych" and "irr" packages. 19 Inter-rater reliability

Table 1. Inclusion and exclusion criteria for photograph selection

Inclusion criteria	Exclusion criteria
Photograph captured in Port Moresby between 29 September and 29 October 2020	Photograph taken outside of the reporting period
Photograph clearly visible for purpose of counting	Photograph is blurred or unclear
Photograph used only once	Duplicate photograph
A minimum of four people in the photograph	Less than four people in the photograph
Photograph is taken spontaneously/unplanned	Photograph is arranged, planned or orchestrated (e.g. group portrait)

was high: Cicchetti-Allison weighted Kappa = 0.995 (confidence interval: 0.991–0.997), <sup>20</sup> implying an almost perfect level of agreement between the two reviewers.

The United States Centers for Disease Control and Prevention defines small gatherings as informal and usually occurring with family and friends within a regular social gathering, and large gatherings as consisting of many people from multiple households in a public space, such as conferences, sporting events, festivals and large parties.<sup>21</sup> As risk of COVID-19 transmission is considered to vary according to the size of gatherings, <sup>22</sup> photographs were further categorized according to small (4-10), medium (11–30) and large (>30) in-person gatherings, which was extrapolated from the head count (as a minimum number of people at the gathering).<sup>22</sup>

The photographs were also examined for evidence of physical distancing; photographs were rated as "yes" if people were more than 1.5 m apart in the photographs, and "no" if the distance between people was less than this. Photographed gatherings were also categorized as either "indoor" or "outdoor". We calculated the proportions of mask compliance by setting (indoor vs outdoor), presence of physical distancing (yes vs no) and gathering size (small vs medium vs large). To ascertain whether there were significant differences in mask wearing compliance by setting and presence of physical distancing, a two-sample z-test was used. To assess the effect of gathering size on compliance, we used a chi-squared test (3x2 contingency table). A 95% level of significance was used for all statistical tests.

# **RESULTS**

A total of 72 photographs published from 29 September to 29 October 2020 were identified by the search and

screened for eligibility; 31 photographs were subsequently excluded because they had the appearance of being "non-spontaneous" (i.e. staged), and one was excluded because it was of fewer than four people. Analysis was performed on the 40 remaining photographs that met all study inclusion criteria. A total of 944 people were captured in the photographs; 445 faces were sufficiently visible to assess mask wearing. Averaged across all 40 photographs, the proportion of people observed wearing a mask was 11.9% (n = 53) (**Table 2**).

In nearly half of the photographs (n = 19; 47.5%), no one was wearing a mask. Of these 19 photographs where zero mask compliance was observed, 4 were of indoor settings and 15 were of outdoor settings; 18 of the 19 exhibited no evidence of physical distancing. Nearly two thirds of the 19 photographs showing no mask compliance (n = 12; 63.1%) were of small-sized gatherings; 5 (26.4%) were of medium-sized gatherings and 2 (10.5%) were of large-sized gatherings (P < 0.05).

Table 2 shows the levels of mask compliance by setting (indoor vs outdoor), presence of physical distancing (yes vs no) and gathering size (small vs medium vs large) across all 40 photographs. There were statistically significant differences between the proportion of people wearing masks by setting, presence of physical distancing and gathering size. The proportion of faces with masks was higher in indoor settings than in outdoor settings (16.4% vs 9.8%; P < 0.05). The prevalence of mask wearing was higher among those who were observed practising physical distancing relative to those who were not (37.8% vs 9.6%; P < 0.0001). Finally, mask compliance was highest among those attending small gatherings (25.0%), followed by those participating in medium-sized gatherings (12.7%). At 8.9%, the lowest level of compliance was observed among those attending large gatherings.

Table 2. Mask compliance according to setting, presence of physical distancing and gathering size

	Number of photo		Mask compliance		
Variable	Number of photo- graphs (% of column total)	Total number of faces (% of column total)	Number of faces with masks (% of faces)	P	
Setting					
Indoor	11 (27.5%)	140 (31.5%)	23 (16.4%)	< 0.05	
Outdoor	29 (72.5%)	305 (68.5%)	30 (9.8%)		
Total	40 (100.0%)	445 (100.0%)	53 (11.9%)		
Physical distancing present					
Yes	4 (10.0%)	37 (8.3%)	14 (37.8%)	< 0.0001	
No	36 (90.0%)	408 (91.7%)	39 (9.6%)		
Total	40 (100.0%)	445 (100.0%)	53 (11.9%)		
Gathering size					
Small (1–10 people)	8 (20.0%)	32 (7.2%)	8 (25.0%)	< 0.0001	
Medium (11–30 people)	23 (57.5%)	221 (49.7%)	28 (12.7%)		
Large (>30 people)	9 (22.5%)	192 (43.1%)	17 (8.9%)		
Total	40 (100.0%)	445 (100.0%)	53 (11.9%)		

Note: Final count numbers are expressed as an average of three reviewers and represented as whole persons.

# **DISCUSSION**

Using photo-epidemiology, we found low levels of compliance with government-mandated regulations relating to face mask wearing in Port Moresby during October 2020. An overall compliance of just 11.9% was observed; compliance was especially low among people attending outdoor events and medium- and large-sized gatherings, highlighting the potential for higher COVID-19 transmission in these settings.

In Papua New Guinea, sociocultural norms, as well as personal, social and environmental barriers, are likely to impact population attitudes and compliance with public health measures.<sup>23</sup> In July 2020, Papua New Guinea formally adopted Niupela Pasin - guidelines for the "new normal" in the time of the COVID-19 pandemic. These guidelines included physical distancing, hand hygiene, respiratory etiquette and the use of face masks when physical distancing is not possible.24 However, widespread adoption of Niupela Pasin, including hand washing and face mask wearing, failed to materialize and there was little evidence of compliance.<sup>25</sup> Cultural factors and social barriers, such as a fear of being considered sick with COVID-19 when wearing a mask, being stigmatized when wearing a mask or fear of judgement when wearing a mask, have been suggested as possible reasons for low compliance.

Mask wearing has a strong cultural significance in Papua New Guinean societies and features prominently in many traditional ceremonies and festivals. Mask types differ by region and serve a variety of purposes, including representation of totems, entertainment, intimidation and concealment of the wearers' identity. In the majority of circumstances, traditional masks are worn by men.<sup>26</sup> Wearing of face masks for protection from an airborne virus was an unfamiliar context, with high potential for cultural resistance and low uptake.

In a study of risk perceptions and responses to COVID-19 conducted early in the pandemic on a university campus, both students and lecturers reported physical distancing as being contrary to Papua New Guinean culture. Hugging, shaking hands and standing closely in groups are seen as cultural practices and "a way of life" that is very difficult to stop.<sup>27</sup> This study also noted that although there were directions by university management to wear a mask on campus, compliance diminished quickly, and there was a lack of compliance with mask use on campus by both students and lecturers.<sup>27</sup>

Other possible reasons for low compliance include difficulties in obtaining face masks because of a lack of supply, a lack of accessibility and/or high cost. Supplies of personal protective equipment (PPE) were indeed limited in Papua New Guinea during the height of the COVID-19 pandemic, with most PPE donated by foreign organizations for use within the health service.<sup>28</sup> Many people could not afford disposable masks for daily use or had difficulty cleaning reusable masks due to lack of water supply. Strategies aimed at removing those barriers would be needed to improve face mask use.

Understanding the reasons behind the lack of enforcement of the mask mandate would also help to strengthen COVID-19 prevention efforts. Although the Papua New Guinea National Pandemic Act 2020 specifies which geographical areas and settings require mandatory face mask wearing, when people should be exempted and who is responsible for enforcing the orders, it does not describe how the mandate should be enforced.<sup>29</sup> Similar regulatory gaps were evident in other countries, such as the United States of America, where the state governments relied on businesses to enforce the mandate, but businesses expected the government to enforce the mandate.<sup>30</sup> This implies that any attempts to improve face mask wearing through mandatory regulations would need to be accompanied by a greater level of community engagement and better health promotion messaging.

This study is subject to some limitations. Photoepidemiology is not a well established science. However, in the absence of more rigorous methods for monitoring mask wearing, it serves as an appropriate surrogate measure and has been used effectively in other fields of research. 17,18 The sample we captured may not be representative of the whole community. Physical distancing calculations were estimated and may have introduced measurement error. Counting issues may arise as the visibility of faces in photographs is subjective and could differ between viewers. We addressed this by calculating an inter-rater reliability score to assess variability between reviewers. We acknowledge that some people may have taken their mask off for a photo but took this into account by excluding posed photographs. A qualitative study to assess behaviour around taking photographs while wearing a face mask would have addressed this issue but was beyond the scope of this study. The photographs taken during the study period may not be representative of normal daily life. Finally, the level of community transmission declined during the study period, with cases decreasing in NCD from 70 in the previous month (September 2020) to 22 confirmed cases during the study period (October 2020), 3,4,12 which may have impacted attitudes towards mask wearing.

In conclusion, we found very low face mask compliance in Port Moresby, Papua New Guinea during a mask mandate in the period prior to vaccines being available. Health authorities in Papua New Guinea will require better strategies to address the individual, social and cultural barriers to improve population attitudes towards face mask use and prevent SARS-CoV-2 transmission, especially in high-risk gatherings.

## Conflicts of interest

RM currently consults for mask manufacturers Detmold and Ascend, and receives funding for investigator-driven research on influenza from Sanofi. She currently receives funding from Australian grant bodies, the National Health and Medical Research Council (NHMRC) and the Medical Research Future Fund. She is on the World Health Organization (WHO) Technical Advisory Group on COVID-19 Vaccine Composition and the WHO Strategic Advisory Group of Experts on Immunization (SAGE) on smallpox and mpox vaccines. The other authors have no conflicts of interest to declare.

#### Ethics statement

Not applicable.

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