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Western Pacific Surveillance and Response

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Looking back, looking forward: lessons from COVID-19 communication measurement, evaluation and learning (MEL)

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Problem: Communication is an integral component of an emergency response, including to the coronavirus disease (COVID-19) pandemic. Designing effective communication requires systematic measurement, evaluation and learning.

Context: In the Western Pacific Region, the World Health Organization (WHO) responded to the COVID-19 pandemic by using the Communication for Health (C4H) approach. This included the development and application of a robust measurement, evaluation and learning (MEL) framework to assess the effectiveness of COVID-19 communication, and to share and apply lessons in real time to continuously strengthen the pandemic response.

Action: MEL was applied during the planning, implementation and summative evaluation phases of COVID-19 communication, with evidence-based insights and recommendations continuously integrated in succeeding phases of the COVID-19 response.

Lessons learned: This article captures good practices that helped WHO to implement MEL during the COVID-19 pandemic. It focuses on lessons from the evaluation process, including the importance of planning, data integration, collaboration, partnerships, piggybacking, using existing data and leveraging digital media.

Discussion: Despite some limitations, the systematic application of MEL to COVID-19 communication shows its value in the planning and implementation of effective, evidence-based communication to address public health challenges. It enables the evaluation of outcomes and reflection on lessons identified to strengthen the response to the current pandemic and future emergencies.

PROBLEM

Communication is an integral component of an infectious disease outbreak response, such as the response to the coronavirus disease (COVID-19) pandemic.[1,2] Successful communication requires cutting through the informational overload, uncertainty and misinformation to reach a diverse public with information that is accessible, understandable, relevant, credible, trusted, timely and actionable.[3,4] Communication is essential to support adherence to the public health and social measures (PHSMs) necessary for pandemic management.[2,4]

Responses to past public health crises have provided robust evidence to support the design and implementation of effective communication interventions; nevertheless, the COVID-19 pandemic presented many new challenges. It was therefore valuable to establish a systematic measurement and evaluation process to ensure that the World Health Organization's (WHO's) approach to communication during the COVID-19 response was grounded in the best information and evidence, and was able to evaluate the relevance, effectiveness and efficiency of the communication response. It was also valuable to understand the extent to which communication shaped risk perceptions and contributed to promoting risk-reduction behaviours so that future communication can improve on the successes and address any limitations.

This article describes the measurement, evaluation and learning (MEL) plan used and the lessons identified from the evaluation of WHO's COVID-19 communication

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in the Western Pacific Region from 2020 to early 2023. The presentation of MEL findings is beyond the scope of this article.

CONTEXT

Since 2019, the WHO Regional Office for the Western Pacific has been using the Communication for Health (C4H) approach (**Fig. 1**), a key component of which is robust and systematic MEL. C4H is a priority for the implementation of *For the Future* – the shared vision for WHO's work with Member States and partners to make the Western Pacific the safest and healthiest region.[5,6] The vision recognizes the potential of strategic communication as a public health intervention and a tool for contributing to better health outcomes. The C4H approach brings together a set of principles and practices to help ensure that communication interventions are designed to inform and change attitudes and behaviours in ways that support the achievement of defined public health outcomes.[7] MEL is the organizational approach to evaluating C4H.[8,9] It enables the identification of lessons that are used to fine-tune and adapt strategies, understand what is or is not working, and improve or scale up the effectiveness of communication to help achieve target public health outcomes.

A MEL framework was used during the COVID-19 response to assess the effectiveness of WHO communication in meeting the objectives of informing and changing COVID-19-related knowledge, attitudes and behaviours (KABs) of people across the Region and contributing to the broader goal of reducing transmission and protecting populations from the health impacts of COVID-19.

ACTION

Measurement, evaluation and learning

MEL served as a tool to plan and monitor COVID-19 communication interventions progressively from inputs and activities to outputs, outcomes and impact. The MEL plan included metrics and indicators to measure success at formative (before), process (during) and summative (after) evaluation stages,[9,10] as well as the methods used to generate those indicators (**Fig. 2**).

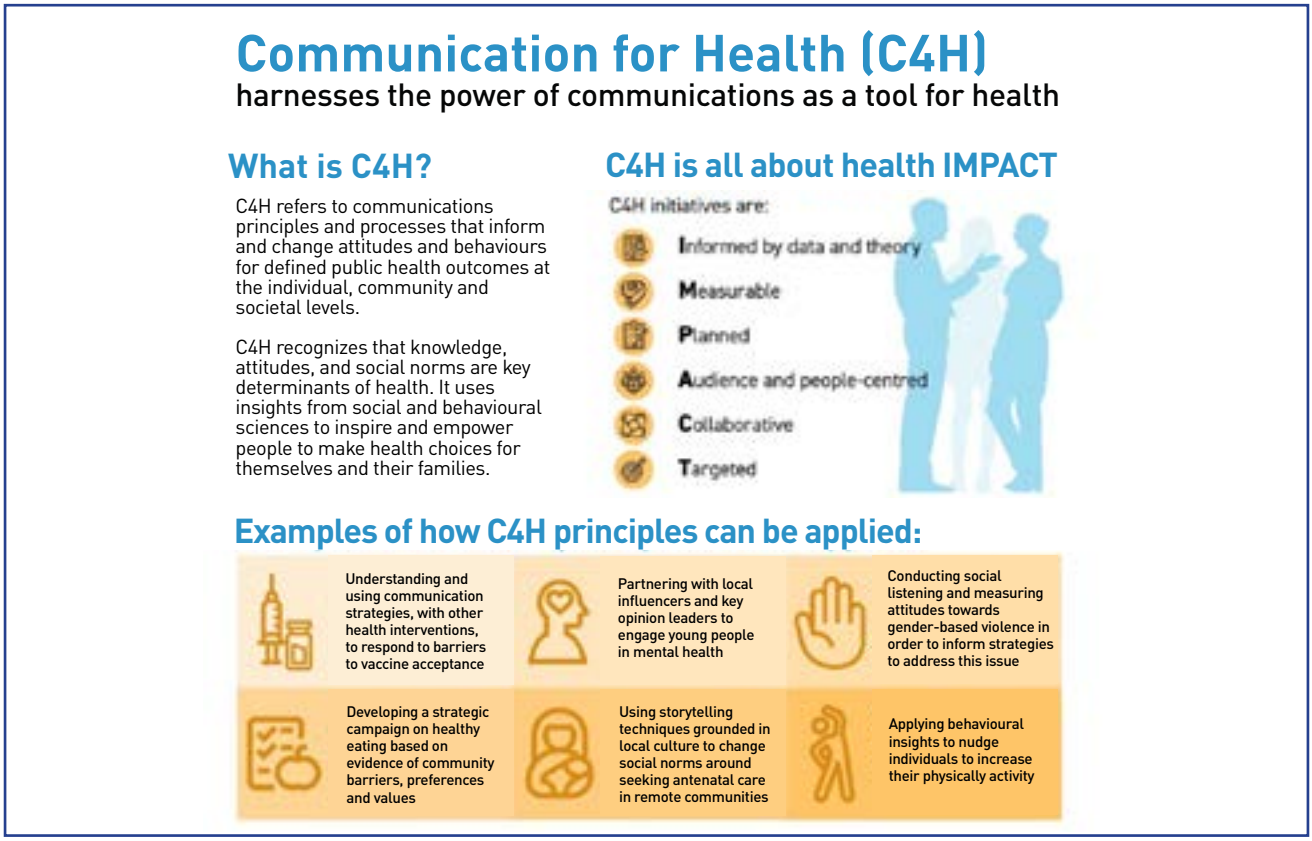
Formative MEL

MEL was implemented from the outset, starting with the planning stage of COVID-19 communication. Data from a variety of sources – offline and online, quantitative and qualitative, primary and secondary – were used. Findings collected through these mechanisms were used to plan evidence-informed strategic communication activities as part of the COVID-19 response by Member States, WHO country and regional offices. These data also served as a baseline for KABs to benchmark outcomes related to COVID-19 communication.

In collaboration with partners and global research companies, the communication team at the WHO Regional Office for the Western Pacific conducted two large-scale surveys. The first survey collected evidence on COVID-19 perceptions and behaviours; it was implemented in seven countries in six rounds throughout 2021, 2022 and 2023. The second survey on vaccine confidence was conducted in two rounds across 13 countries in 2021–2022. Focus group discussions in seven countries provided more in-depth responses for some aspects of the quantitative findings (e.g. vaccine hesitancy by age, sex and among people with underlying health conditions). Secondary research data shared by partner agencies were also used to triangulate findings; such agencies included, among others, the United Nations Office for the Coordination of Humanitarian Affairs and the International Federation of Red Cross and Red Crescent Societies, which together with WHO chaired the Asia Pacific Risk Communication and Community Engagement Working Group.

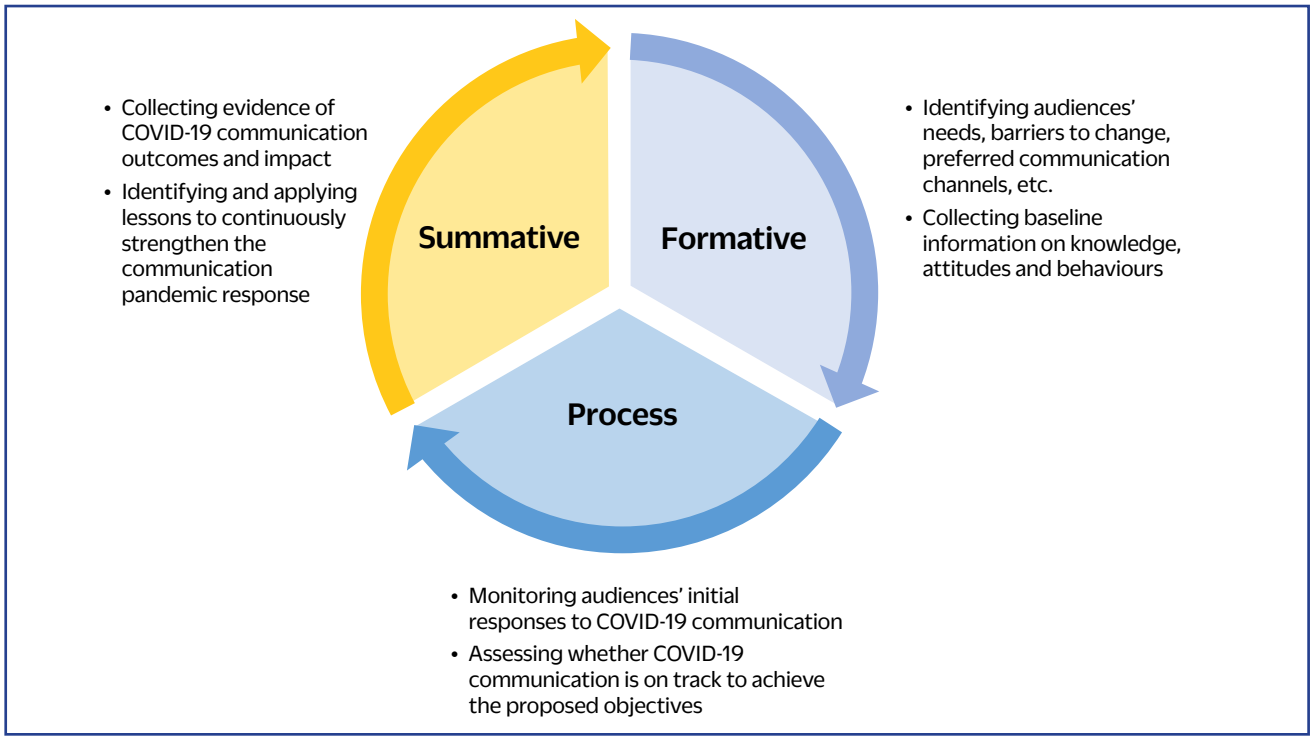
In addition, multisource social listening was routinely employed to track and monitor public opinions expressed online about COVID-19, including emerging concerns, questions and informational needs. This listening involved collecting and analysing native social media and website analytics, and using existing partnerships and collaborations with media monitoring and social networking platforms to monitor various channels, such as social media, online news, print, broadcasts and podcasts. Although most of the tools used supported analysis of content in multiple languages, media intelligence was interpreted with caution because it skewed towards content produced in English. To respond

Fig. 1. **The Communication for Health approach**



Source: Communication for Health in the WHO Western Pacific Region.[5]

Fig. 2. **Measurement, evaluation and learning stages**



COVID-19: coronavirus disease.

to this and other data limitations, the team relied on multiple sources to cross-check evidence.

A group of communication professionals at the Regional Office used these data to plan, develop, test and implement COVID-19 communication inputs and activities, hence operationalizing the C4H approach of planned and evidence-based communication.

Process MEL

Process evaluation was conducted during communication implementation, after the distribution of targeted communication activities, such as social media posts, website articles, press conferences, media interviews, and online and offline campaigns. This involved monitoring outputs and short-term outcomes to capture message relevance and determine whether progress was being made towards the achievement of objectives.

Lockdown and quarantine measures resulted in dynamic changes to the informational landscape as more people were using digital media for information. WHO's communication mirrored this shift, with products being disseminated also through social media and the website. The evaluation at this stage involved analysis of social media and website analytics, to assess the comments and reactions to social media posts and track the number of visits to WHO's regional COVID-19 webpage. Analysis of social media comments, for instance, allowed the team to capture and rapidly address misperceptions or misinformation and assess ongoing interest in certain topics.

Summative MEL

Finally, the team gathered evidence of long-term outcomes and impact after implementation. This included collecting data on knowledge of COVID-19 transmission and protective measures, support for and adherence to PHSMs, and vaccine acceptance among those exposed to WHO advice and those not exposed. Data were also collected on trust in WHO and the role it played in the pandemic.

To capture outcomes and impact, the team relied on the repeat survey data collected through the two large-scale surveys on COVID-19 perceptions and behaviours and on vaccine confidence. The results of each survey round were used to assess the outcomes of WHO communication activities for the preceding months, with results of past rounds used as the baseline. Also, findings were triangulated with secondary research data, where available.

LESSONS LEARNED

As with the implementation of any activity in the context of COVID-19, evaluating COVID-19 communication has been complex and challenging. Implementing MEL during the pandemic included challenges such as competing priorities for staff time and resources, the vast amount of communication materials distributed through different channels, and the limitations that lockdowns and other PHSMs imposed on traditional data collection (i.e. face-to-face and fieldwork). Reflecting on 3 years of evaluating COVID-19 communication in WHO, this section captures good practices and lessons identified that helped the team to navigate these challenges, assess communication effectiveness and improve through MEL. This list is not exhaustive but is intended to facilitate reflection on how MEL can be adapted to the communication response during crisis situations.

Integrate data sets

The WHO communication team in the Region used data integration to consolidate disparate but overlapping datasets collected from different sources (**Fig. 3**) into a single dataset. This enabled the evaluation of communication as a whole and the measurement of the combined success of different teams. It also ensured a methodical MEL process that provided clear and comprehensive data about what people in the Western Pacific thought, said and did in relation to WHO's diverse COVID-19 communication.

Piggyback on other processes

The main purpose of the intelligence gathered through the regional surveys and focus group discussions on COVID-19 perceptions and behaviours and on vaccine confidence was to inform evidence-based and targeted communication for the pandemic response (formative MEL). However, the team was able to include several MEL-related outcomes and impact questions in these research tools to gain insights on the use of, usefulness of and trust in WHO as a source of COVID-19 information,

Fig. 3. **COVID-19 communication MEL indicators and methods**

Inputs *Communication planning and preparation*	**Activities** *Communication production and implementation*	**Outputs** *Reaching and engaging target audiences*	**Short-term outcomes** Target audiences' reactions and responses	**Long-term outcomes** Sustainable effects of communication	**Impact** Results caused, in full or in part, by communication
• Baselines established *(e.g. existing knowledge, attitudes and behaviours)* • Audiences' needs, preferences, etc. identified • Channel preferences identified	• Web articles published • Social media materials posted • Press conferences, media releases, interviews and op-eds issued • Materials developed for offline distribution • Campaigns conducted	• Reach • Website visits • Clickthrough rates • Media mentions • Sentiment	• Engagement • Exposure to WHO advice • Usefulness of WHO advice • Knowledge of COVID-19 transmission • Knowledge of COVID-19 protective measures	• Vaccine confidence • Support for public health and social measures • WHO advice influential in changing behaviours • Belief that WHO played a critical role in COVID-19 response • Trust in WHO	• Adherence to public health and social measures • COVID-19 infection prevention and control
• Desktop research • Regional surveys (CPBI, VCS) • Secondary survey data • Social media and web analytics	• Activity reports	• Social media analytics • Website analytics • Media monitoring	• Social media analytics • Regional surveys (CPBI, VCS) • Focus group discussions • Secondary survey data	• Regional surveys (CPBI, VCS) • Focus group discussions • Secondary survey data	• Regional surveys (CPBI, VCS) • Secondary survey data • Public health data

COVID-19: coronavirus disease; CPBI: COVID-19 perceptions and behaviours; MEL: measurement, evaluation and learning; VCS: vaccine confidence survey; WHO: World Health Organization.

and the role WHO played in the COVID-19 response. The other data collected through these surveys provided the communication team with an understanding of the differences in KABs among those who had seen, read or heard about WHO advice and those who had not.

It was cost effective to add summative MEL questions to these data collection tools that were not necessarily planned to collect evidence of WHO's communication outcomes and impact. Of particular use was the compilation of a list of possible data mechanisms to which outcome and impact MEL questions could be added during the planning phase.

Plan MEL early

The success of including MEL questions in the surveys reinforces the importance of planning MEL data sources as early as possible and before implementing communication. Such planning involved clearly defining indicators and selecting the appropriate methods to generate them, as well as mechanisms and roles for data collection and analysis, its uses, reporting schedules and formats. This allowed the team to measure as close to real time as possible, collect realistic and high-quality data, and ensure consistency if changes in reporting responsibilities occurred.

Use existing data

In addition to primary research, the team used data from the extraordinary amount of research conducted worldwide on COVID-19. Some of the publicly available data collected by other entities met the team's evaluation needs. Much of the external public health data included information on WHO as a source of COVID-19 information, acknowledging the Organization's role in disseminating up-to-date information and recommendations.

Secondary data were an effective resource; they were particularly useful owing to the limitations on traditional methods of data collection from PHSMs and because busy communication practitioners did not always have the time and resources to collect data themselves.

Collaborate across teams

MEL was not the sole responsibility of one evaluator; rather, it was undertaken collaboratively with those planning and implementing different communication activities. There was collaboration between practitioners working on multisource social listening; risk communication and community engagement; content creation and dissemination; outcomes and impact data collection; and the integration, analysis and synthesis of diverse data sources for strategic and actionable insights. This collaboration broke down silos by providing insights into the work of different communication practitioners, contributed to a stronger MEL design and implementation, enhanced data collection and analysis, and produced results that communication practitioners understood and were therefore more likely to use.

Measure selectively

Prioritizing evaluation increased confidence that resources were being used efficiently and sustainably. When developing the MEL plan, consideration was given to the evaluation mechanisms that could be managed alongside other responsibilities, and to the data collection and analysis that would be available. It is critical to be strategic about what to evaluate, given the limitations in time and resources – it is not necessary or possible to evaluate every single activity. The broader the scope of the evaluation, the more resource-intensive and time-consuming it can be.

Leverage digital media

The "infodemic" (i.e. too much information, including false or misleading information in digital and physical environments during a disease outbreak)[11] presented particular challenges and necessitated activities to combat disinformation, misinformation and rumours in real time.[12] The team leveraged the huge increase in visitors to the WHO website and social media pages, and used available analytics to regularly identify concerns that needed addressing, implement activities designed to debunk specific types of misinformation and disinformation with accurate information, and evaluate audience responses to WHO messages.

Team up for better design and more MEL

An innovative step in using MEL to understand particular concerns and improve the reach and effectiveness of communication involved teaming up with the social media company Meta (Menlo Park, CA, USA). Through the collaboration, the advice of a specialized digital agency and credits for targeting populations across the Region with advertising campaigns were provided to WHO free of charge. These resources contributed to stronger messaging and more shareable formats that could reach broader and more targeted audiences. For instance, through the analytics of the ad campaigns, the team could identify patterns (i.e. in imagery, format, colours and typography) and the age and sex groups with the highest reach. In turn, this made it possible to tailor future campaigns to the needs and preferences of audiences with whom the previous ad did not resonate.

The collaboration also provided another tool for evaluation: Brand Lift studies.[13] These studies measure the effect of a campaign on the target audience's recall, awareness, motivation and intention, in line with campaign objectives, by comparing two groups – people who have seen the campaign and people who have not. Results of Brand Lift studies were also used to identify areas for improvement and replication.

Test messages

To improve communication effectiveness, the team determined messaging priorities through social listening and findings from the regional surveys during the MEL planning stage. These were further filtered and drafted into messages that were tested through different methods such as surveys, focus group discussions and viewing panel sessions.

A collaboration with Stickybeak (Auckland, New Zealand), a research and message-testing platform provider, resulted in an innovative approach that used public quantitative chat-based surveys with online target audiences who evaluated various iterations of text, messaging angles and visuals. The findings were used to tweak and refine messages and visuals, and create content that resonated with target audiences, to address their informational needs in the continuously evolving context of the pandemic.

Build internal MEL capacity

Since the adoption of C4H, WHO in the Western Pacific has trained communication professionals from its regional and country offices in MEL concepts, methods

and frameworks. The resulting capacity, in which MEL is recognized as an integral part of the communication cycle, enabled much of the evaluation to be undertaken in-house and helped to ensure that results were delivered in the required time frames and within budget and amid competing priorities.

DISCUSSION

The COVID-19 pandemic has highlighted the importance of strategic communication as a public health intervention, and the value of applying C4H principles and practices in communication responses to emergencies. Using MEL as part of the C4H approach during the COVID-19 response in the Region has been vital. The Regional Office applied robust MEL at various levels of the planning, implementation and post-implementation phases of COVID-19 communication, and continuously integrated evidence-based insights and recommendations into succeeding phases of the COVID-19 response.

MEL has allowed for the assessment of the effectiveness of WHO communication and a real-time sharing of lessons necessary to adjust plans and strategies for the ongoing crisis response. It encouraged continuous learning and improvement, and thus "supported informed decision-making, encouraged appropriate behaviour change and maintenance among populations, and helped to mitigate adverse health outcomes".[14]

The pandemic provided an intensely dynamic environment in which to implement MEL. Evaluation approaches had to be adjusted to account for the pandemic context. Good practices that helped the communication team of the WHO Regional Office for the Western Pacific to carry out its MEL plan included thinking about and planning evaluations from the outset, using secondary research, applying data integration for comprehensive analysis, piggybacking summative MEL questions onto other data collection tools, leveraging the use of digital media as a real-time source of communication and teaming up with social media platforms. Having internal MEL capacity also allowed for a stronger framework and smoother implementation of MEL.

The team acknowledges that the evaluations undertaken had several limitations. The results are not representative of communities with limited or no access to the internet and mobile networks, and are unlikely to represent the views of vulnerable populations. To respond to this limitation, at least partially, rounds of the regional surveys undertaken in 2023 included face-to-face in-depth interviews with hard-to-reach populations.

It is especially challenging to draw a causal relationship between communication interventions and impact; hence, the team does not make claims of direct results. Impact is multicausal and "communication is just one factor leading to impact".[3] MEL should have evidence that C4H at least contributed to impact.[15] The COVID-19 communication MEL evidence showed clear outcomes (e.g. exposure to and trust in WHO advice, knowledge and attitude change, and support for and adherence to protective measures), indicating a direct line from contribution to impact.

Continuing to learn and apply MEL lessons from the pandemic is critical in fully realizing the potential of communication as a public health intervention, including in emergencies, and bringing the Western Pacific closer to achieving the vision, as set out in For the Future,[6] of being the safest and healthiest region.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

Ethical approval was not required for this report.

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Impact of vaccination on COVID-19 severity during the second wave in Brunei Darussalam, 2021

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Objective: Coronavirus disease (COVID-19) vaccinations have been shown to prevent infection with efficacies ranging from 50% to 95%. This study assesses the impact of vaccination on the clinical severity of COVID-19 during the second wave in Brunei Darussalam in 2021, which was due to the Delta variant.

Methods: Patients included in this study were randomly selected from those who were admitted with COVID-19 to the National Isolation Centre between 7 August and 6 October 2021. Cases were categorized as asymptomatic, mild (symptomatic without pneumonia), moderate (pneumonia), severe (needing supplemental oxygen therapy) or critical (needing mechanical ventilation) but for statistical analysis purposes were dichotomized into asymptomatic/mild or moderate/severe/critical cases. Univariate and multivariable analyses were conducted to identify risk factors associated with moderate/severe/critical disease. Propensity score-matched analysis was also performed to evaluate the impact of vaccination on disease severity.

Results: The study cohort of 788 cases (mean age: 42.1 ± 14.6 years; 400 males) comprised 471 (59.8%) asymptomatic/mild and 317 (40.2%) moderate/severe/critical cases. Multivariable logistic regression analysis showed older age group (≥45 years), diabetes mellitus, overweight/obesity and vaccination status to be associated with increased severity of disease. In propensity score-matched analysis, the relative risk of developing moderate/severe/critical COVID-19 for fully vaccinated (two doses) and partially vaccinated (one dose) cases was 0.33 (95% confidence interval [CI]: 0.16–0.69) and 0.62 (95% CI: 0.46–0.82), respectively, compared with a control group of non-vaccinated cases. The corresponding relative risk reduction (RRR) values were 66.5% and 38.4%, respectively. Vaccination was also protective against moderate/severe/critical disease in a subgroup of overweight/obese patients (RRR: 37.2%, $P = 0.007$).

Discussion: Among those who contracted COVID-19, older age, having diabetes, being overweight/obese and being unvaccinated were significant risk factors for moderate/severe/critical disease. Vaccination, even partial, was protective against moderate/severe/critical disease.

By February 2023, the total number of reported cases of coronavirus disease (COVID-19) exceeded 757 million and over 6.8 million lives had been lost globally.[1] The rapid development and approval for emergency use of multiple novel COVID-19 vaccines within a year of detection of the first cases represented a pivotal moment in the global effort to reduce the impact of the pandemic.[2–6] The first emergency use authorization of a COVID-19 vaccine was made by the United States Food and Drug Administration on 11 December 2020, after the completion of phase 3 trials that demonstrated efficacy in preventing symptomatic infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) of up to 95%.[2,7] Vaccination programmes commenced shortly afterwards, and several COVID-19 vaccines were prequalified for emergency use by the World Health Organization (WHO).

During 2021, several studies confirmed that vaccination was highly effective in reducing symptomatic SARS-CoV-2 infection, as well as the risk of hospitalization, serious illness and death.[8] However, cases of breakthrough infection after vaccination were reported, especially after the emergence of the Delta strain of SARS-CoV-2 (B.1.617.2). For all three prequalified mRNA vaccines, efficacy against infection with the Delta variant dropped to below 80%.[9] Neutralization with post-vaccination sera assay studies also showed a 19- to 42-fold reduction in neutralizing

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activity against the Beta variant (B.1.351).[10] However, vaccination remained important for reducing the risk of infection and severe disease and mitigating the impact of COVID-19.

In Brunei Darussalam, the first wave of COVID-19 started on 9 March 2020 and was rapidly controlled, with the last community spread documented on 6 May 2020. Control measures included public health and social measures such as mask wearing and restrictions on movements and social gatherings, coupled with testing, close monitoring and surveillance of cases, and regular review and updating of infection control and outbreak management protocols in response to the evolving nature of the pandemic.[11] An important part of the national response, and one that was instrumental in the containment of the first wave, was the establishment of a designated centre, the National Isolation Centre (NIC), to isolate and treat all positive cases.[11] Brunei Darussalam started rolling out vaccination with four WHO-prequalified vaccines (Vaxzevria [AstraZeneca], BBIBP-CorV [Sinopharm], Comirnaty [Pfizer-BioNTech] and Spikevax [Moderna]) on 3 April 2021, 4 months before the start of the second wave on 7 August 2021. The second wave was due to the Delta variant of SARS-CoV-2,[11] a more contagious variant than the original and Alpha strains.

This study assesses the effectiveness of vaccination in preventing severe disease among patients with COVID-19 in Brunei Darussalam during the second wave and investigates the role of vaccination in modifying selected known risk factors for severe to critical COVID-19.

METHODS

Study design

This study used a retrospective cohort study design to assess the impact of vaccination on the risk of developing severe COVID-19 among patients who were admitted to the NIC during the second wave of the COVID-19 outbreak in Brunei Darussalam between 7 August and 6 October 2021.

Setting

The management of the COVID-19 outbreak in Brunei Darussalam has been previously described.[11] In brief, at the start of the second wave, all patients with COVID-19 were admitted to the NIC. However, over the course of the second wave, increasing numbers of mild cases of COVID-19 were admitted to the newly established community isolation centres for isolation and treatment. Symptomatic patients with moderate or severe disease, as well as those with mild disease plus significant comorbidities (i.e. diabetes, obesity, older age and end-stage renal failure) and persistent fever, dyspnoea or diarrhoea continued to be admitted to the NIC for management and treatment.

Study population

Patients included in the study were those admitted to the NIC between 7 August and 6 October 2021, who tested positive for COVID-19 through laboratory-confirmed reverse transcription-polymerase chain reaction (RT-PCR) testing. To counter the effect of changing NIC admission criteria and ensure equal representation across the spectrum of COVID-19 disease severity in the study population, patients were randomly selected (using Microsoft Excel's random number generator) at three time points (early August, mid-September and early October). Patients aged ≤18 years, pregnant women and patients with end-stage renal disease were excluded, as these patient subgroups were not eligible for vaccination at the time of the start of the second wave.

Data collection

Patient data were prospectively collected using a specially designed database that was set up to monitor and aid the management of patients admitted to the NIC. Information on patients' demographic characteristics (age, sex) was collected, as well as data on relevant clinical risk factors such as body mass index (BMI), diabetes mellitus, hypertension and dyslipidaemia. Patients' vaccination status was retrieved from patients' Bru-HIMS health records and coded as either "complete" (if patients had received their second dose at least 14

days prior to contracting COVID-19), "partial" (if patients had received their first dose at least 14 days prior to contracting COVID-19 or less than 14 days had elapsed since their second dose) or "unvaccinated" (if patients were unvaccinated prior to contracting COVID-19 or less than 14 days had elapsed since their first dose).[4]

Clinical severity categories

Patients were assigned to one of five categories according to clinical severity: asymptomatic, mild (symptomatic without pneumonia), moderate (clinical or radiological evidence of pneumonia), severe (moderate respiratory decompensation requiring non-invasive supplementary oxygen) and critical (respiratory decompensation requiring intubation and mechanical ventilation or extracorporeal membrane oxygenation support).[11] Patients' clinical severity was recorded daily for management decision-making.

Primary outcome

The primary outcome was defined as the highest clinical severity category attained by the patient during their hospitalization. For the purposes of subsequent statistical analyses, the outcome variable was dichotomized into two categories: asymptomatic/mild disease and moderate/severe/critical disease. Patients who died were included in the moderate/severe/critical category, irrespective of cause of death. Deaths were recorded as a COVID-19 death if supported by evidence of COVID-19 pneumonia.

Statistical analysis

All statistical analyses were performed using IBM SPSS software (version 26). Patient characteristics, stratified by disease severity, were summarized in a descriptive analysis. Continuous data were presented as a mean ± standard deviation and compared using the independent Student's *t*-test. Categorical data were presented as frequency and percentages and compared using Pearson's chi-squared test. Univariate analyses, with disease severity as the outcome, were used to explore which potential risk factors (demographic characteristics, clinical risk factors and vaccination status) were associated with more severe disease. Significant risk factors ($P < 0.05$) derived from univariate analysis were then input into a multivariable logistic regression model to calculate the odds ratio (OR) for each significant variable.

To investigate the effectiveness of vaccination in reducing the clinical severity of COVID-19 cases, patients were matched 1:1 according to their vaccination status (vaccinated or unvaccinated) using propensity scores derived from summing the probabilities of being vaccinated given patients' demographic characteristics (age and sex) and the presence of selected clinical risk factors (diabetes, hypertension, hyperlipidaemia and overweight/obesity). These probabilities were derived using binary logistic regression. The relative risk (RR) of more severe COVID-19 disease comparing the two propensity score-matched groups (vaccinated and unvaccinated) was estimated using a 2x2 contingency table chi-squared test. This comparison was repeated in a subgroup analysis designed to determine the effect of complete and partial vaccination status on disease severity. Additional analyses were conducted in selected COVID-19 patient subgroups: patients aged ≥45 years, overweight/obese patients and patients with diabetes mellitus. Estimates of the relative risk reduction (RRR), the absolute risk reduction (ARR) and the number needed to treat (NNT) were also derived from the analyses of the matched groups. $P < 0.05$ was considered statistically significant.

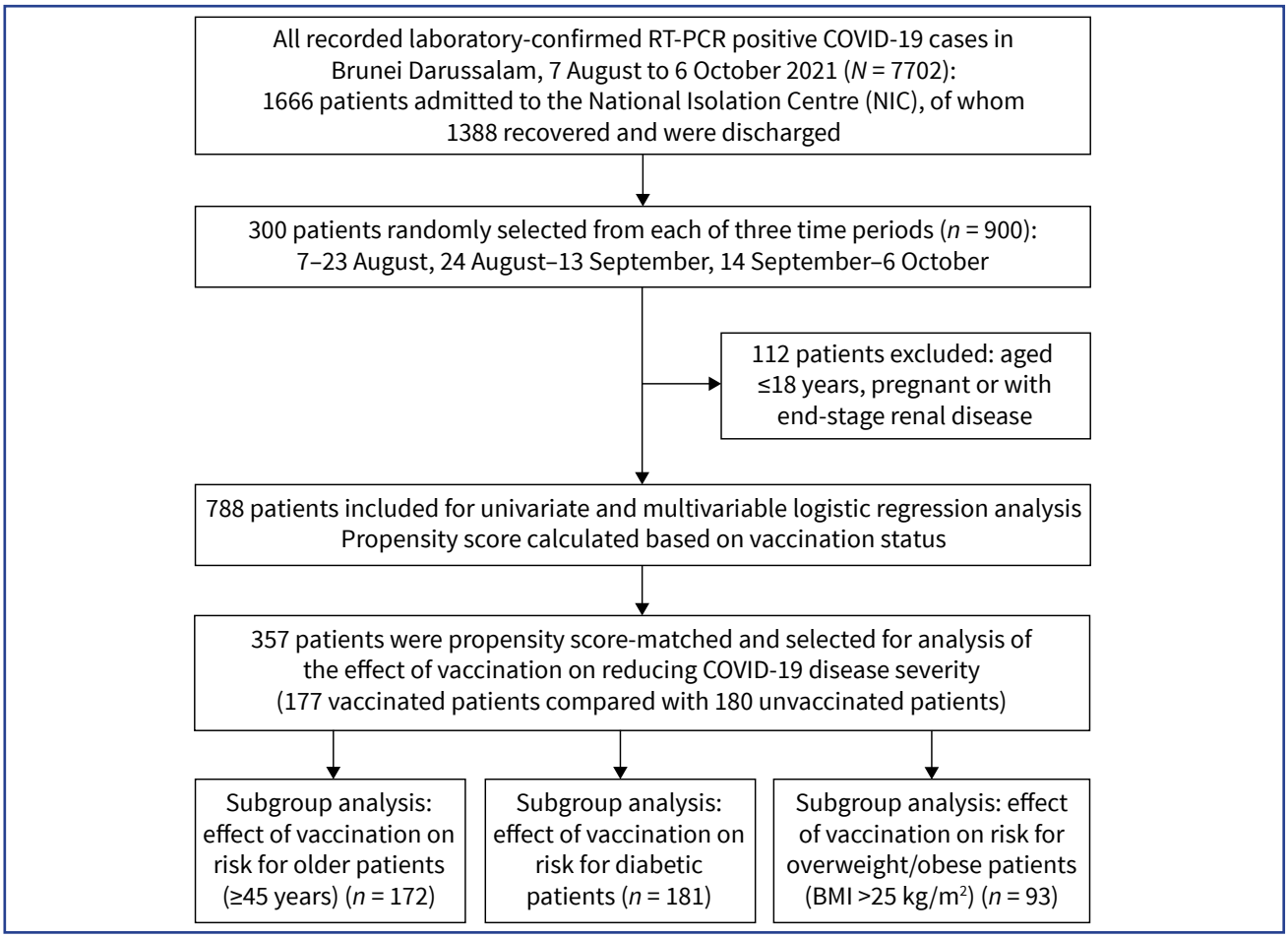
RESULTS

Study population

Between 7 August and 6 October 2021, there were 7702 recorded cases of COVID-19 in Brunei Darussalam, of which 1666 were admitted to the NIC. Nine hundred patients were randomly selected (300 from each of three time periods), 112 of whom were subsequently excluded based on the above-mentioned exclusion criteria. The study population thus comprised a total of 788 patients (**Fig. 1**).

The mean age of patients was 42.1 ± 14.6 years; 400 were male and 388 were female (**Table 1**). Over half ($n = 471$) had either asymptomatic or mild COVID-19 (14.7% and 45.1%, respectively); of the remaining 317 patients, 169 (21.4%) were categorized as moderate cases, 127 (16.1%) as severe and 21 (2.7%) as critical. Most asymptomatic/mild patients were aged <40 years;

Fig. 1. **Flowchart showing recruitment of COVID-19 cases into the study, Brunei Darussalam, 7 August to 6 October 2021**



BMI: body mass index; COVID-19: coronavirus disease; RT-PCR: reverse transcription-polymerase chain reaction.

severe and critical patients were older, with a mean age of at least 50 years (**Table 1**).

Around one third (n = 237, 30.1%) of patients had received at least one dose of a COVID-19 vaccine (75 completed two doses, 162 completed one dose); 551 (69.9%) were unvaccinated. Within the critical severity category (n = 21), there were 18 unvaccinated patients (85.7%) and three (14.3%) partially vaccinated patients. None of the critical patients had been fully vaccinated. There were 28 deaths in the study sample; in this group of patients, 22 (78.6%) were unvaccinated, 6 (21.4%) were partially vaccinated and none were fully vaccinated.

Univariate and multivariable logistic regression analyses

Univariate analysis showed that age, diabetes mellitus, hypertension, dyslipidaemia, overweight/obesity and vaccination status were significantly associated with COVID-19 disease severity (**Table 1**).

After adjustment in a multivariable logistic regression analysis, age, diabetes mellitus, overweight/obesity and vaccination status remained significantly associated with COVID-19 disease severity. The odds of developing moderate/severe/critical disease were significantly lower in those who had been vaccinated, even partially (OR: 0.45, 95% confidence interval [CI]: 0.30–0.67, $P < 0.001$) (**Table 2**).

Propensity score-matched analyses

A total of 357 patients were matched on their propensity score for vaccination: 177 vaccinated (65 complete and 112 partial) and 180 unvaccinated. There were no significant differences in the demographic and clinical characteristics between the vaccinated and

Table 1. **Demographic characteristics and clinical risk factors of 788 COVID-19 cases, by disease category, admitted to the National Isolation Centre between 7 August and 6 October 2021, Brunei Darussalam**

Characteristic/ risk factor	*N*	Disease severity					*P*[a]
		Asymptomatic *n* (% of total)	Mild *n* (% of total)	Moderate *n* (% of total)	Severe *n* (% of total)	Critical *n* (% of total)	
Demographic characteristics							
Age (mean ± SD)		39.13 ± 14.53	37.57 ± 13.10	44.90 ± 13.57	52.16 ± 13.94	50.05 ± 14.80	**<0.001**[b]
Age group							
<30 years	109	33 (28.5)	117 (33.0)	25 (14.8)	6 (4.7)	2 (9.5)	
30–39 years	130	31 (26.7)	101 (28.4)	40 (23.7)	19 (15.0)	2 (9.5)	
40–49 years	173	23 (19.8)	78 (22.0)	41 (24.2)	25 (19.7)	6 (28.6)	**<0.001**[c]
50–59 years	193	14 (12.1)	31 (8.7)	40 (23.7)	40 (31.5)	5 (23.8)	
≥60 years	183	15 (12.9)	28 (7.9)	23 (13.6)	37 (29.1)	6 (28.6)	
Sex							
Male	400	61 (52.6)	175 (49.3)	87 (51.5)	64 (50.4)	13 (62.0)	0.822[c]
Female	388	55 (47.4)	180 (50.7)	82 (48.5)	63 (49.6)	8 (38.0)	
Clinical risk factors							
Diabetes mellitus							
Yes	146	12 (10.3)	37 (10.4)	43 (25.4)	48 (37.8)	6 (28.6)	**<0.001**[c]
No	642	104 (89.7)	318 (89.6)	126 (74.6)	79 (62.2)	15 (71.4)	
Hypertension							
Yes	237	32 (27.6)	76 (21.4)	55 (32.5)	66 (52.0)	8 (38.1)	**<0.001**[c]
No	551	84 (72.4)	279 (78.6)	114 (67.5)	61 (48.0)	13 (61.9)	
Dyslipidaemia							
Yes	158	15 (12.9)	46 (13.0)	40 (23.7)	49 (38.6)	8 (38.1)	**<0.001**[c]
No	630	101 (87.1)	309 (87.0)	129 (76.3)	78 (61.4)	13 (61.9)	
Overweight/obesity							
Yes	409	49 (42.2)	165 (46.5)	105 (62.1)	75 (59.1)	15 (71.4)	**<0.001**[c]
No	379	67 (57.8)	190 (53.5)	64 (37.9)	52 (40.9)	6 (28.6)	
Vaccination status							
Complete	75	19 (16.4)	38 (10.7)	11 (6.5)	7 (5.5)	0 (0)	
Partial	162	34 (29.3)	71 (20.0)	38 (22.5)	16 (12.6)	3 (14.3)	**<0.001**[c]
Unvaccinated	551	63 (54.3)	246 (69.3)	120 (71.0)	104 (81.9)	18 (85.7)	
Total sample	**788**	**116**	**355**	**169**	**127**	**21**	

SD: standard deviation.

[a] Bold *P* values are statistically significant (<0.05).

[b] Analysis of variance (ANOVA) comparison of mean age.

[c] Pearson's chi-squared test.

unvaccinated groups, indicating that the propensity score matching produced similar comparison groups (**Table 3**). Being vaccinated (either fully or partially compared with no vaccination) decreased the risk of severe disease, with a RR of 0.62 (95% CI: 0.46–0.82), a RRR of 38.5% (95% CI: 18.9–53.8%), an ARR of 0.17 (95% CI: 0.17–0.54) and a NNT of 6 (95% CI: 2–6) (**Table 4**). Similar values were obtained when the analysis was restricted to the partially vaccinated subgroup (n = 111) (RR: 0.62, 95% CI: 0.46–0.82; RRR: 38.4%, 95% CI: 18.0–53.8%, respectively). However, for those who were fully vaccinated (two doses), the reduction in risk (compared with no vaccination) was higher still (RR: 0.33, 95% CI: 0.16–0.69; RRR: 66.5%, 95% CI: 31.2–83.7%, respectively) (**Table 5**).

Table 2. **Adjusted odds ratios for the association between selected risk factors and the risk of severe COVID-19 disease in a cohort of 788 cases admitted to the National Isolation Centre between 7 August and 6 October 2021, Brunei Darussalam**

Risk factor[a]	Asymptomatic/mild *n* (%)	Moderate/severe/critical *n* (%)	*P*[b]	Odds ratio	Lower CI	Upper CI
Age group (1)	133 (28.2)	176 (55.5)	**<0.001**	2.96	2.05	4.26
Diabetes mellitus (1)	49 (10.4)	97 (31.0)	**<0.001**	2.70	1.65	4.41
Overweight/obesity (1)	214 (45.4)	195 (61.5)	**0.001**	1.75	1.28	2.42
Hypertension (1)	108 (22.9)	129 (40.7)	0.213	1.36	0.84	2.18
Dyslipidaemia (1)	61 (13.0)	97 (30.6)	0.228	0.73	0.44	1.22
Vaccination status						
Complete (1)	57 (12.1)	18 (5.7)	**0.007**	0.44	0.24	0.80
Partial (2)	105 (22.3)	57 (18.0)	**<0.001**	0.45	0.30	0.67

CI: confidence interval.

[a] Risk factors included here are those that were statistically significant in univariate analysis: Age group (≥45 years = 1, <45 years = 2), Diabetes mellitus (Yes = 1, No = 2), Overweight/obesity (Yes = 1, No = 2), Hypertension (Yes = 1, No = 2), Dyslipidaemia (Yes = 1, No = 2) and Vaccination status (Complete = 1, Partial = 2, Unvaccinated = 3).

[b] Bold *P* values are statistically significant (<0.05).

Table 3. **Demographic characteristics and clinical risk factors of 357 COVID-19 cases that were propensity score matched by vaccination status**

Variables	Vaccinated[a] *n* (% of total)	Unvaccinated *n* (% of total)	*P*[b]
Total	177	180	
Age (mean ± SD)	45.85 ± 14.54	45.72 ± 14.61	0.93
Age group			
<30 years	23 (48.9)	24 (51.1)	1.00
30–39 years	43 (49.4)	44 (50.6)	
40–49 years	41 (50.0)	41 (50.0)	
50–59 years	35 (50.0)	35 (50.0)	
≥60 years	35 (49.3)	36 (50.7)	
Sex			
Male	95 (49.0)	99 (51.0)	0.83
Female	82 (50.3)	81 (49.7)	
Clinical risk factors			
Diabetes mellitus			
Yes	49 (52.7)	44 (47.3)	0.55
No	128 (48.5)	136 (51.5)	
Hypertension			
Yes	80 (53.3)	70 (46.7)	0.24
No	97 (46.9)	110 (53.1)	
Dyslipidaemia			
Yes	51 (52.0)	47 (48.0)	0.64
No	126 (48.6)	133 (51.4)	
Overweight/obesity			
Yes	86 (47.5)	95 (52.5)	0.46
No	91 (51.7)	85 (48.3)	

SD: standard deviation.

[a] Vaccinated patients included those who had received at least one dose of a COVID-19 vaccine at least 14 days prior to their COVID-19 infection. Unvaccinated patients included those who had not received a COVID-19 vaccine or had received their first dose within 14 of their COVID-19 infection.

[b] Pearson's chi-squared test used with $P < 0.05$ considered significant.

Table 4. **Effect of vaccination status on risk of developing more severe COVID-19 in a cohort of 357 propensity score-matched cases admitted to the National Isolation Centre between 7 August and 6 October 2021, Brunei Darussalam**

Vaccination status	*N*	COVID-19 severity		*P*[b]	RR (95% CI)	RRR (95% CI)	ARR (95% CI)	NNT (95% CI)
		Asymptomatic/ mild *n* (%)	Moderate/ severe/ critical *n* (%)					
Vaccinated[a]	177	128 (72.3)	49 (27.7)	0.001	0.62 (0.46–0.82)	38.5 (18.0–53.8)	0.17 (0.17–0.54)	6 (2–6)
Unvaccinated	180	99 (55.0)	81 (45.0)					

ARR: absolute risk reduction; CI: confidence interval; NNT: number needed to treat; RR: relative risk; RRR: relative risk reduction.

[a] Vaccinated patients included those who had received at least one dose of a COVID-19 vaccine at least 14 days prior to their COVID-19 infection. Unvaccinated patients included those who had not received a COVID-19 vaccine or had received their first dose within 14 of their COVID-19 infection.

[b] Pearson's chi-squared test used with $P < 0.05$ considered significant.

Table 5. **Subgroup analysis to explore the effect of vaccination status (fully, partial, none) on the risk of developing more severe COVID-19 disease in a cohort of 354 propensity score-matched cases admitted to the National Isolation Centre between 7 August and 6 October 2021, Brunei Darussalam**[a]

Vaccination status[a]	*N*	COVID-19 severity		*P*[b]	RR (95% CI)	RRR (95% CI)
		Asymptomatic / mild *n* (%)	Moderate / severe / critical *n* (%)			
Complete	65	57 (87.7)	8 (12.3)	**0.001**	0.33 (0.16–0.69)	66.5 (31.2–83.7)
Unvaccinated	68	43 (63.2)	25 (36.8)			
Partial	111	70 (63.1)	41 (36.9)	**0.001**	0.62 (0.46–0.82)	38.4 (18.0–53.8)
Unvaccinated	110	44 (40.0)	66 (60.0)			

CI: confidence interval; RR: relative risk; RRR: relative risk reduction.

[a] For subgroup analysis by vaccination status, propensity score matching resulted in the exclusion of three patients, one in the partially vaccinated and two in the unvaccinated group. Hence, the total number of patients included in this analysis was 354.

[b] Fully vaccinated patients included those who had received two doses of COVID-19 vaccine, with the second dose administered at least 14 days before COVID-19 infection. Partially vaccinated patients were those who had received one dose of a COVID-19 at least 14 days before their COVID-19 infection; patients who had received their second dose within 14 days of their COVID-19 infection were also included in this category. Unvaccinated patients included those who had not received a COVID-19 vaccine or had received their first dose within 14 days of their COVID-19 infection.

[c] Pearson's chi-squared test used with $P < 0.05$ considered significant.

Separate subgroup analyses were conducted for older patients (aged ≥45 years), those with diabetes mellitus and those being overweight/obese. Vaccination was significantly protective against developing more severe disease in the overweight/obese group with a RR of 0.63 (95% CI: 0.44–0.89) and a RRR of 37.2% (95% CI: 10.8–55.7%). In contrast, among the older population (aged ≥45 years) and those with diabetes mellitus, there was no difference in the risk of more severe disease between those who had received at least one dose of a COVID-19 vaccine and those who were unvaccinated (**Table 6**).

DISCUSSION

Among a cohort of 788 patients who tested positive for COVID-19 and were admitted to the NIC during the second wave in Brunei Darussalam, older age, having diabetes mellitus, being overweight/obese and being unvaccinated were found to be independent risk factors for greater severity of COVID-19 disease. Our propensity score-matched analysis showed that patients who had received at least one dose of a COVID-19 vaccine were at reduced risk of developing more severe disease compared with people who were unvaccinated. In our cohort of patients, none of the fully vaccinated patients developed critical disease or died of COVID-19.

Other studies have also found that patients with these three clinical risk factors – older age, diabetes mellitus and overweight/obesity – are at increased risk for severe COVID-19 disease and death and are thus considered to be high-risk groups.[12–17] The higher risk associated with older age groups can be attributed to a waning immunity

Table 6. **Subgroup analysis to explore the effect of older age, overweight/obesity and diabetes on the association between vaccination status and the risk of developing more severe COVID-19 disease in a cohort of 357 propensity score-matched cases admitted to the National Isolation Centre between 7 August and 6 October 2021, Brunei Darussalam**

Risk factor	COVID-19 severity		*P*[b]	RR (95% CI)	RRR (95% CI)	ARR (95% CI)	NNT
	Asymptomatic/mild *n* (%)	Moderate/severe/critical *n* (%)					
Older age group (≥45 years)							
Vaccinated	44 (51.2)	42 (48.8)	0.17	0.81 (0.61–1.06)	19.2	0.12	9
Unvaccinated	34 (39.5)	52 (60.5)					
Overweight/obesity							
Vaccinated	57 (66.3)	29 (33.7)	0.007	0.63 (0.44–0.89)	37.2 (10.8–55.7)	0.20 (0.11–0.56)	5 (2–9)
Unvaccinated	44 (46.3)	51 (53.7)					
Diabetes mellitus							
Vaccinated	17 (34.7)	32 (65.3)	0.66	0.93 (0.70–1.23)	7.3	0.05	20
Unvaccinated	13 (29.5)	31 (70.5)					

ARR: absolute risk reduction; CI: confidence interval; NNT: number needed to treat; RR: relative risk; RRR: relative risk reduction.

[a] Vaccinated patients included those who had received at least one dose of a COVID-19 vaccine at least 14 days prior to their COVID-19 infection. Unvaccinated patients included those who had not received a COVID-19 vaccine or had received their first dose within 14 of their COVID-19 infection.

[b] Pearson's chi-squared test used with $P < 0.05$ considered significant.

in both adaptive and innate immune responses, which has been shown to predispose older individuals to greater risk of infections and some cancers.[18,19] In a longitudinal study looking at antibody response to SARS-CoV-2 infection, 100% of patients aged 10–17 years retained their antibody titre 3 months after seropositive conversion; in those aged ≥40 years, this fell to 84%.[20] Both diabetes and obesity are on the spectrum of metabolic diseases that are associated with immune dysfunction and chronic inflammation, which increase susceptibility to COVID-19 infection.[21–23] Pulmonary function tests in obese patients, in particular those with abdominal obesity, have revealed a tendency towards restrictive respiratory patterns and reduced lung volumes compared with people with a lower BMI.[24] This reduction in pulmonary reserves may explain why a higher proportion of obese patients with COVID-19 decompensated rapidly and required oxygen supplementation and intubation.[14] Cardiovascular risk factors such as hypertension and dyslipidaemia, previously reported to be significant risk factors for severe COVID-19 infection,[25] were not significantly more common in the moderate/severe/critical COVID-19 group in this study. This is consistent with the findings of a study from Guangzhou, China,[15] and may be specific to this variant of the virus.

Our propensity score-matched analysis showed that vaccination, independently of several clinical risk factors or the type of vaccine (mRNA or inactivated), was protective against developing moderate/severe/critical COVID-19. Fully vaccinated patients, i.e. those who had received two doses of vaccine, were 67% less likely to be in the moderate/severe/critical group compared with those who were unvaccinated. Conversely, an unvaccinated patient had three times the risk of moderate/severe/critical disease than a fully vaccinated patient. Even being partially vaccinated, i.e. having received one dose of vaccine at least 14 days prior to infection, was associated with a RR of 0.62 and RRR of 38% (relative to unvaccinated patients).

While directly comparable studies are limited in number, our results are broadly consistent with those from other studies. For example, in a case-control study involving 119 partially vaccinated patients who were age- and sex-matched to 476 unvaccinated patients, vaccination was associated with a 69.3% RRR in death (and an ARR of 22.3%).[26] Likewise, a recent community-wide serosurvey conducted in 5310 subjects in Hong Kong Special Administrative Region, China, demonstrated that three or four doses of BNT162b2 or CoronaVac were effective against Omicron infection 7 days after vaccination (vaccine effectiveness ranged from 30% to 69%).[27] However, 100 days after vaccination, this effectiveness had waned to 6–26%. Another study involving 969 PCR-confirmed SARS-CoV-2 cases showed that 46%

of the 54 fully vaccinated patients admitted to hospital developed moderate/severe/critical disease, almost twice as many as our cohort of patients with complete vaccination status.[28] Nevertheless, both this study and ours identified older age (≥80 years), overweight (BMI >25 kg/m^2), cardiovascular disease and diabetes as risk factors for more severe COVID-19 disease.

Our real-world findings further support and strengthen the evidence from clinical trials for the efficacy of vaccination in preventing severe COVID-19. In a study using the Comirnaty vaccine, the protective effect of the vaccine in preventing symptomatic COVID-19 infection was evident as early as 12 days after the first dose with an efficacy of 52%, which increased to 95% at 7 days after the second dose.[3] Similarly, a trial of Spikevax reported an efficacy of 95.2% in preventing symptomatic COVID-19 infection 14 days after the first dose.[4]

Based on our analysis, we estimated that the NNT to prevent one case of moderate/severe/critical disease in this cohort was six. That is to say, for every six people vaccinated with at least one dose of a COVID-19 vaccine who subsequently contracted COVID-19, one was prevented from developing moderate/severe/critical disease. This suggests that the impact of vaccination was large for the Delta variant outbreak in Brunei Darussalam. Our findings also provide strong evidence in favour of vaccination, especially in settings with limited specialist health-care resources, such as bed capacity in intensive care units, and thus limited capacity to care for severely ill COVID-19 patients. More broadly, and as repeatedly demonstrated by the COVID-19 pandemic, vaccination will undoubtedly continue to play an important role in managing disease outbreaks, even those caused by less virulent strains such as Omicron.[29] Preliminary analysis of more recent data collected during subsequent outbreaks of COVID-19 in Brunei Darussalam dominated by the Omicron variant, which are not reported here, suggests that the effectiveness of vaccination in protecting against moderate to critical disease remains significant despite the reduced virulence of the Omicron variant.

Our study has highlighted the fact that older patients or those with diabetes mellitus are at significantly higher risk of developing moderate/severe/critical infections, despite vaccination.[12,13] For elderly patients, breakthrough infection despite vaccination is due to immunosenescence and a reduced effectiveness of immune response to vaccination.[19] A recent study showed that one third of patients aged ≥80 years had no detectable neutralizing antibodies despite receiving two doses of a COVID-19 vaccine, whereas among those aged <60 years, only 2.2% had no detectable neutralizing antibodies.[30] Data from the United States Centers for Disease Control and Prevention have confirmed that adults aged ≥50 years were 2–8 times more likely to be hospitalized with breakthrough COVID-19 infection despite being fully vaccinated.[31] It has been suggested that the same immune dysregulation and dysfunction combined with chronic inflammation may account for the increased risk seen in patients with diabetes mellitus, especially if their diabetes is suboptimally controlled.[32]

There are several limitations that need to be considered when interpreting our study results. First, the study group comprised a hospital-based cohort and hence the results can only be applied to other hospital settings. Second, this study did not consider the effect of treatments (e.g. steroids and remdesivir) on the outcome. However, since our primary outcome was the highest severity category obtained during hospitalization, any impact of such treatments is unlikely to have affected the allocation of the primary outcome. Third, the clinical severity categories used in our study were based on a severity scale used in South-East Asia to triage patients for admission to hospital and may differ from severity categories used elsewhere. However, our definition for the moderate/severe/critical group was equivalent to the definition of severe COVID-19 used in published randomized controlled trials evaluating the efficacy of COVID-19 vaccine candidates.[4] Importantly, the categories used were simple and effective for daily monitoring of patients and reporting to the Ministry of Health. Fourth, this study did not evaluate the effectiveness of the different types of COVID-19 vaccines but rather combined all vaccines (mRNA or inactivated) into a single group. In addition, this study only assessed the impact of vaccination on the Delta strain, and therefore the results will not be applicable to subsequent newer strains, such as Omicron. Lastly, we used propensity score matching to generate similar comparison groups for our analysis, thus eliminating the effect of known important confounding variables on our effect estimates for the impact of vaccination on disease severity. We

consider that propensity score matching is a suitable alternative in pandemic settings where conducting a randomized control study may not be feasible, ethical or cost-effective.

In conclusion, in a cohort of patients hospitalized with COVID-19 during the second wave in Brunei Darussalam, which was dominated by the Delta variant (B.1.617.2), vaccination was effective in reducing the risk for moderate/severe/critical disease by up to 67%. For every six fully or partially vaccinated cases infected with the Delta variant, one moderate/severe/critical case can be prevented, thereby reducing health-care utilization. The protective effect of vaccination was also observed in the group of overweight or obese patients, although to a lesser degree (37%). As the pandemic progresses or transitions to an endemic phase, the severity of COVID-19 infections will continue to impact high-risk populations, and thus the case for vaccination remains.

Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics approval

Ethical approval for the study was obtained from the Medical and Health Research Ethics Committee, Ministry of Health, Brunei Darussalam (MHREC/MOH/2021/13(1)). All work was conducted in accordance with the guidelines of the Declaration of Helsinki.

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Tuberculosis in elderly Australians: a 10-year retrospective review

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Objective: This report describes the epidemiology of active tuberculosis (TB) in elderly Australians (≥65 years) with analysis of the factors associated with TB disease and successful treatment outcomes.

Methods: A retrospective study of TB cases reported to the National Notifiable Diseases Surveillance System over a 10-year period from 2011 to 2020 was conducted. Cases were stratified by sex, age, risk factors, drug resistance, treatment type and outcome. Notification rates and incidence rate ratios with 95% confidence intervals were calculated and factors associated with treatment success analysed using multivariable logistic regression.

Results: A total of 2231 TB cases among elderly people were reported over the study period, with a 10-year mean incidence rate of 6.2 per 100 000 population. The median age of cases was 75 years (range 65–100 years); most were male (65%) and born overseas (85%). Multivariable analysis found that successful treatment outcome was strongly associated with younger age, while unsuccessful treatment outcome was associated with being diagnosed within the first 2 years of arrival in Australia, ever having resided in an aged-care facility and resistance to fluoroquinolones.

Discussion: Compared to other low-incidence settings in the Western Pacific Region, TB incidence in elderly people is low and stable in Australia, with most cases occurring among recent migrants from TB-endemic settings. Continued efforts to reduce TB importation and address migrant health, especially among elderly people, are important.

The Western Pacific Region, including Australia, is home to over 1.9 billion people across 27 countries and 10 areas.[1,2] The Region has undergone rapid demographic change in recent years, with declining fertility and increasing life expectancy,[1] and is now home to the largest and fastest-growing ageing population in the world. There are currently more than 240 million elderly people (aged ≥65 years) living within the Region, with population numbers expected to increase twofold by 2050.[2,3] The World Health Organization (WHO) Regional Office for the Western Pacific is prioritizing a large Healthy Ageing initiative through multisectoral action, which includes reducing tuberculosis (TB) among elderly people.[2]

TB is caused by the bacterium *Mycobacterium tuberculosis* complex and is a leading cause of morbidity and mortality worldwide.[4,5] It is estimated that a quarter of the world's population is infected with TB bacteria,[5] also referred to as latent TB infection (LTBI),[6] but disease occurs when a person develops clinical manifestations such as coughing, fever, weight loss and night sweats.[6,7] LTBI is an asymptomatic condition that cannot be transmitted to others,[8] although 5–15% of people living with LTBI are at risk of future progression to TB disease due to host, environmental and social risk factors.[8] Recognized TB risk factors include age, immunosuppression, alcohol and illicit drug use, smoking tobacco, malnutrition, diabetes mellitus, health-care work and incarceration.[9]

The Western Pacific Region has one of the highest TB disease burdens globally.[5] In TB-endemic settings with high rates of ongoing transmission, disease incidence rates are highest in younger adults (<50 years).[5] However, in lower-incidence settings with declining rates of TB transmission, disease incidence rates among elderly people (aged ≥65 years) are often highest.[5] This is mainly due to increased comorbidity and immune dysfunction

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associated with increasing life expectancy and high rates of LTBI in older people who are at risk of reactivation of disease, together with reduced transmission and disease rates in the general population.[10]

Australia has sustained low incidence rates of TB over the last four decades.[11] However, due to the vast majority of cases occurring among recent migrants from high-incidence countries, elimination of TB continues to pose clinical and epidemiological challenges. Between 2011 and 2020, the absolute number of TB cases in Australia increased by 16%, in line with population growth[11] that includes a high proportion of people who were born in countries with high TB incidence, including China, India, Indonesia, Nepal and the Philippines.[12] Although Australia employs stringent pre-migration screening measures, this only includes screening for active pulmonary TB disease.[13] Most cases are identified in the first 5 years after arrival in Australia, representing likely disease reactivation.[11,14]

To date, there are few published reports outlining the epidemiology, risk factors and outcomes associated with TB in elderly people, despite accounting for close to 20% of all cases in Australia.[11] This study will address the current knowledge gap by describing the epidemiology of TB in elderly Australians and examining factors associated with it and successful treatment outcomes.

METHODS

Confirmed TB notifications[15] received between 1 January 2011 and 31 December 2020 were extracted in July 2022 from the National Notifiable Diseases Surveillance System (NNDSS). Data were stratified into two age group categories, elderly (≥65 years) and non-elderly (≤64 years), and were analysed using Stata/SE 17.0 (StataCorp, College Station, United States of America) and Excel (Microsoft Corporation, Redmond, United States of America). Australian Bureau of Statistics (ABS) mid-year resident population estimates were used to calculate annual notification rates per 100 000 population by age group, sex and country of birth. Incidence rate ratios (IRRs) were calculated with associated 95% confidence intervals (CIs) and *P* values for 5-year age groups and sex. The methodology outlined in a previous national TB analysis[16] was followed, in which categorical data on "TB treatment outcome" were aggregated into four outcomes for descriptive analysis and binary outcomes for inferential analysis (**Box 1**). Crude odds ratios (ORs) and *P* values were calculated to determine if demographic details, clinical symptoms, treatment regimens and drug resistance profiles were associated with treatment success using univariate logistic regression. Variables that were statistically significant ($P < 0.05$) in the univariate analysis were included in multivariable logistic regression. This model controlled for the effects of age, resistance to fluoroquinolones, ever having resided in an aged-care facility, and time from arrival to TB diagnosis (0–2 years), using backwards stepwise elimination at a 0.05 significance level to create a final reduced model. Migrants were defined as those born overseas.

RESULTS

During the study period, 13 917 cases were notified, of which 11 686 (83.9%) were aged ≤64 years and 2231

Box 1. **TB treatment outcomes extracted from the Australian NNDSS, 1 January 2011 to 31 December 2020**

NNDSS TB treatment outcomes

Cured; completed treatment; still under treatment; interrupted treatment; transferred out; defaulted on treatment; treatment failure; died of TB; died of another cause; or not followed up – outcome unknown ($N = 2231$)

Aggregated TB outcomes used

Treatment success: cured, completed treatment ($n = 1599$)

No treatment success: died of TB, defaulted on treatment, treatment failure ($n = 156$)

Treatment outcome unknown: interrupted treatment, died of another cause, transferred out, not followed up – outcome unknown ($n = 465$)
Still under treatment ($n = 52$)

Binary TB outcomes used

Treatment success: cured, completed treatment ($n = 1599$)

No treatment success: died of TB, defaulted on treatment, treatment failure ($n = 156$)

All other treatment outcomes were excluded ($n = 517$)

NNDSS: National Notifiable Diseases Surveillance System; TB: tuberculosis.

(16.1%) were aged ≥65 years, with average notification rates of 5.6 per 100 000 population and 6.2 per 100 000 population, respectively. The mean number of notifications in elderly people remained low, with a non-significant increase when comparing the reporting periods 2011–2015 (n = 197) and 2016–2020 (n = 249).

Australian-born TB cases represented 10.5% of non-elderly and 15.1% of elderly cases. Elderly cases reported their country of birth in the following order of frequency: Australia, China, Viet Nam, India and the Philippines (**Table 1**). Compared with non-elderly, elderly cases experienced more treatment failure (2.2% vs 6.9%, respectively) and unknown treatment outcome (8.1% vs 19.0%, respectively).

Over the 10-year period, there were consistent sex-specific differences in TB epidemiology, with significantly more men than women developing TB (IRR: 2.17 [95% CI: 1.64–2.90]; $P < 0.05$) (**Fig. 1**). Among elderly cases, the median age was 75 years (range: 65–100 years), with the highest notification rates observed in the 65–69-year age group. The majority (84.6%, n = 1887) of elderly cases were born overseas, and a small proportion (1.5%, n = 33) identified as Aboriginal and Torres Strait Islander people. Most elderly cases (91.7%) were classified as new, with 7.4% classified as relapse/recurrent cases (**Table 2**). Of those classified as relapse/recurrence, 65.2% had received full or partial treatment overseas, compared to 34.7% who had received full or partial treatment in Australia. Pulmonary TB was reported in 75.4% of cases, and only extra-pulmonary TB was reported in 24.4% of cases (**Table 2**). The most frequently reported risk factors documented among elderly TB cases included past travel to or residence (for at least 3 months cumulatively anytime in their life) in a country with high TB incidence (74.1%), having a household or other close contact with active TB (10.9%), and currently receiving immunosuppressive therapy (8.5%) (**Table 2**). Elderly overseas-born cases had a median time of 25 years (interquartile range [IQR]: 9–38 years) between arrival in Australia and their TB diagnosis. Among Australian-born cases, the median time from their initial health presentation to diagnosis was longer (44 days; IQR: 16–102 days), compared with overseas-born cases (31 days; IQR: 13–70 days).

The majority of TB cases were bacteriologically confirmed (90.6%), of which 88.5% (n = 1789) were confirmed by culture, and 98.2% (n = 1756) of isolates underwent drug susceptibility testing (**Table 2**). Drug susceptibility testing results were available for 86.6% (1815/2095) of all elderly TB cases, with isoniazid mono-resistance found in 4.2% (n = 77), rifampicin mono-resistance in 0.3% (n = 6), multidrug resistance (MDR) in 0.7% (n = 13) and pre-extensive drug resistance (pre-XDR) in 0.2% (n = 4) (**Table 2**).

Table 1. **Notifications of TB in Australians aged ≥65 years by selected demographic characteristics and treatment outcomes, Australia, 2011–2020**

Characteristics	*n* (%) *N* = 2231
Age group	
65–69 years	556 (24.9)
70–74 years	481 (21.6)
75–79 years	433 (19.4)
80–84 years	350 (15.7)
≥85 years	411 (18.4)
Country of birth	
Australia	336 (15.1)
China (excludes Hong Kong SAR, Macao SAR and Taiwan)	312 (14.0)
Viet Nam	275 (12.3)
India	175 (7.9)
Philippines	148 (6.6)
Cambodia	72 (3.2)
Other	911 (40.9)
Unknown	2 (0.09)
On a TB health undertaking[a] at time of diagnosis (yes)	78 (3.5)
Treatment outcomes	
Treatment success[b]	1599 (71.7)
Treatment outcome unknown[c]	424 (19.0)
No treatment success[d]	156 (6.9)
Still under treatment	52 (2.3)
Died of TB[e]	109 (4.9)

SAR: Special Administrative Region; TB: tuberculosis.

[a] A TB health undertaking refers to an individual who completed an agreement with the Australian Government to meet the health requirement in relation to TB at the time of diagnosis. This applies to individuals who have a significant health condition and had their health examinations outside Australia or applied for a protection visa.

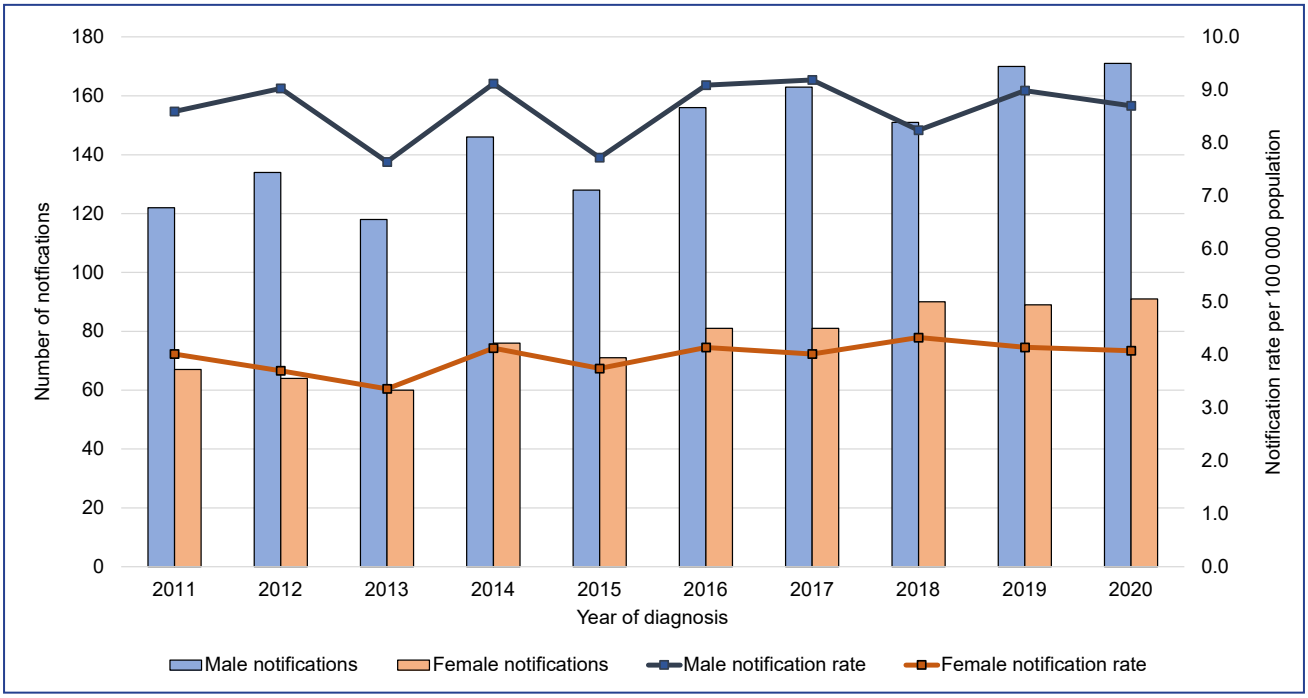
[b] Treatment success refers to a case who is cured of TB and completed treatment for TB.

[c] Treatment outcome unknown refers to interrupted treatment, cases who died of another cause, transferred out, or were not followed up – outcome unknown.

[d] No treatment success refers to cases who died of TB, defaulted on treatment, or treatment failure.

[e] In Australia, the cause of death in relation to TB varies among experienced TB clinicians and public health officers, using representative TB death scenarios.[17]

Fig. 1. **Sex-specific tuberculosis notification rates in elderly Australians, 2011–2020**[a]



[a] Excludes two cases whose sex was not reported.

Unsuccessful treatment, which included those with treatment failure, default on treatment, and death while on treatment, was reported in 6.9% of cases (n = 156) (**Table 1**). Among these, 8.7% (n = 10) were relapse/recurrence cases and one (0.9%) had MDR-TB. A relatively high percentage of elderly cases, 4.9% (n = 109), died of TB during treatment, of whom 81.7% (89/109) were born overseas, 88.9% (97/109) were newly diagnosed, 88.9% (97/109) had pulmonary TB, 39.4% (43/109) were ≥85 years of age and 0.9% were pre-XDR (1/109).

In both univariate and multivariable analyses, the most important risk factor influencing treatment success was age, with more favourable outcomes in younger age groups (**Table 3**). The odds of treatment success in cases who had a history of travel or residence in a country with high TB incidence were nearly twice that of cases who did not. The odds of treatment success with those diagnosed ≥10 years after their arrival in Australia were 1.5 times greater than those who were diagnosed <10 years after arrival (**Table 3**).

The multivariable analysis found treatment success was significantly associated with the 65–69-year, 70–74-year and 75–79-year age groups compared with all other age groups among elderly cases. Risk factors associated with poor TB treatment outcome included being ≥80 years of age with resistance to fluoroquinolones, having resided at any time in an aged-care facility, and being diagnosed within 2 years of arrival in Australia (**Table 3**).

DISCUSSION

Cases of TB in elderly people are not a major contributor to the Australian TB burden, and elderly patients are not at significantly higher odds of developing TB compared to younger age groups. The epidemiological features of TB cases are broadly similar across elderly and non-elderly age groups. Our findings contrast with most other low-burden countries in the Western Pacific Region, where the highest burden of TB occurs among elderly people (≥65 years) with disease rates linked to increased longevity.[5,18] Although the notification rate is slightly higher among older age groups in Australia, it is not increasing over time and the highest disease burden is occurring among those aged 15–44 years. Most elderly cases in Australia were born overseas and/or had a history of past travel to or residence in a high-incidence country, and ageing likely contributed to reactivation of LTBI.

Migrants from countries with high TB incidence in South and Central Asia[14,19] accounted for 85% of elderly cases in Australia. Increases in the notification rate of

Table 2. **Characteristics of TB notifications in Australians aged ≥65 years, Australia, 2011–2020**

Characteristics	*n* (%) *N* = 2231
Case classification	
New[a]	2047 (91.7)
Relapse[b]	164 (7.4)
Unknown	20 (0.9)
Case detection method	
Clinical	1827 (81.9)
Screening	100 (4.5)
Contact tracing / epidemiological investigation	15 (0.7)
Unknown	289 (12.9)
Diagnostic site (anatomical site)	
Pulmonary TB[c]	1681 (75.4)
Extra-pulmonary TB only[d]	544 (24.4)
Unknown site of disease	6 (0.3)
HIV testing	
Positive	9 (0.4)
Negative	1398 (62.7)
Unknown	824 (36.9)
Confirmed TB	
Bacteriologically confirmed[e]	2021 (90.6)
Culture-confirmed	1789 (88.5)
Drug susceptibility testing[f]	1756 (98.2)
Clinically confirmed only	210 (9.4)
Risk factors for TB[g]	
Past travel to or residence in a country with high TB incidence[h]	1550 (74.1)
Household or other close contact with TB	228 (10.9)
Currently receiving immunosuppressive therapy	177 (8.5)
Chest X-ray suggestive of old untreated TB	125 (6.0)
Employed in the health industry in Australia or overseas, currently or in the last 5 years	73 (3.5)
Resided in an aged-care facility within the last 5 years	48 (2.3)
Resided in a correctional facility within the last 5 years	13 (0.6)
Homeless within the last 5 years	13 (0.6)
Employed at an aged-care facility, correctional facility or homeless shelter within the last 5 years	7 (0.3)
Total cases assessed for risk factors	**2092 (93.8)**

Characteristics	*n* (%) *N* = 2231
Drug susceptibility profile[i]	
Fully susceptible	1553 (85.6)
Resistance to at least one first-line anti-TB agent[j]	168 (9.3)
Mono-resistance to isoniazid	77 (4.2)
Mono-resistance to rifampicin	6 (0.3)
Resistance to at least one second-line injectable anti-TB agent[k]	3 (0.2)
Resistance to fluoroquinolones[l]	4 (0.2)
MDR-TB[m]	13 (0.7)
Pre-XDR-TB[n]	4 (0.2)
XDR-TB[o]	0 (–)
Total cases with drug susceptibility testing results	1815 (86.6)[p]

MDR: multidrug-resistant; TB: tuberculosis; XDR: extensively drug-resistant.

[a] A new case refers to a patient who has never been treated for TB or has been treated previously for <1 month.

[b] A relapse case refers to a patient who is diagnosed with TB and has been previously treated (fully or partially) for TB in Australia or overseas.

[c] Pulmonary TB including other sites refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree.

[d] Extra-pulmonary TB refers to any bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lungs, for example, pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, and meninges. More than one extra-pulmonary site may be reported for each notified case of TB.

[e] Bacteriologically confirmed TB is confirmed through laboratory diagnosis.[15] A bacteriologically confirmed TB case is one in which a biological specimen is positive by smear microscopy, culture or WHO-approved rapid diagnostics (such as Xpert® MTB/RIF assay).

[f] Drug susceptibility testing here refers to cases that are culture-confirmed.

[g] Excludes cases with no reported risk factors. More than one risk factor may be reported for each notified case of TB. Risk factor information for acquiring TB is collected at the time of diagnosis by the relevant health departments or medical practitioners.

[h] A high-risk TB country is defined by the Australian Government Department of Home Affairs and National TB Advisory Committee as a country with an annual TB incidence >60 cases per 100 000 population.[20]

[i] Totals do not add up to 100% as cases may be counted across multiple resistance categories.

[j] First-line anti-TB agents are rifampicin, isoniazid, ethambutol and pyrazinamide.

[k] Second-line injectable anti-TB agents are kanamycin, capreomycin and amikacin.

[l] Fluoroquinolones are ciprofloxacin, ofloxacin, moxifloxacin and levofloxacin.

[m] Multidrug-resistant TB is resistant to at least isoniazid and rifampicin but not XDR-TB.

[n] Pre-XDR-TB is resistant to isoniazid, rifampicin and a fluroquinolone OR isoniazid, rifampicin and a second-line injectable (amikacin, capreomycin, kanamycin).

[o] XDR-TB is resistant to isoniazid and rifampicin, and any of the fluoroquinolones, and to at least one of the three injectable second-line drugs.

[p] From a total of *n* = 2095.

Table 3. **Univariate and multivariable analyses of factors associated with TB treatment success, Australia, 2011–2020**

Variable	Univariate analysis treatment outcome (n = 1755)[a]	Multivariable analysis treatment outcome (n = 1752)[a,b,c]
	Crude OR (95% CI)	Adjusted OR (95% CI)
Demographics		
Male sex	0.77 (0.54–1.11)	–
Female sex	1.28 (0.89–1.82)	–
Age groups (years)		
65–69	**3.72 (2.15–6.39)**	**5.5 (3.14–9.81)**
70–74	**2.16 (1.32–3.54)**	**3.61 (2.14–6.08)**
75–79	0.94 (0.62–1.41)	**1.79 (1.16–2.77)**
80–84	**0.52 (0.35–0.76)**	–
≥85	**0.35 (0.24–0.49)**	–
Aboriginal and/or Torres Strait Islander	0.61 (0.18–2.10)	–
Born in Australia	0.67 (0.44–1.01)	–
Born overseas	1.48 (0.98–2.25)	–
Diagnosis		
Pulmonary TB (including other sites)	1.01 (0.69–1.47)	–
HIV-positive (coinfection)	0.48 (0.06–4.19)	–
Treatment history		
Any previous TB treatment	1.16 (0.61–2.19)	–
Drug susceptibility		
Fully susceptible	1.03 (0.72–1.47)	–
Resistance to first-line anti-tuberculosis agents	0.95 (0.53–1.69)	–
Resistance to second-line injectables	0.19 (0.02–2.15)	–
Resistance to fluoroquinolones	**0.10 (0.01–0.69)**	**0.11 (0.01–0.78)**
Multidrug-resistant TB	0.87 (0.11–6.97)	–
Pre-extensively drug-resistant TB	0.29 (0.30–2.82)	–
Risk factors for TB		
Past travel to or residence in a country with high TB incidence	**1.80 (1.26–2.58)**	–
Household or other close contact with TB	1.01 (0.63–1.85)	–
Currently receiving immunosuppressive therapy	0.96 (0.51–1.84)	–
Chest X-ray suggestive of old untreated TB	1.74 (0.69–4.36)	–
Employed in the health industry in Australia or overseas, currently or in the last 5 years	0.86 (0.31–2.45)	–
Resided in an aged-care facility within the last 5 years	**0.14 (0.07–0.30)**	**0.24 (0.11–0.52)**
Resided in a correctional facility within the last 5 years	0.97 (0.12–7.68)	–
Homeless within the last 5 years	0.68 (0.08–5.58)	–
Time from arrival to diagnosis		
<2 years	**0.50 (0.35–0.71)**	**0.48 (0.34–0.69)**
2–4 years	5.91 (0.81–42.93)	–
5–9 years	1.49 (0.72–3.11)	–
≥10 years	**1.45 (1.04–2.02)**	–

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

CI: confidence interval; OR: odds ratio; TB: tuberculosis.

[a] Univariate and multivariable analysis binary outcome comparison groups: "variable (ref: reference group variable)"; for males (ref: non-males); females (ref: non-females); each 5-year age group (ref: all other elderly age groups combined); Aboriginal and/or Torres Strait Islander (ref: non-Aboriginal or Torres Strait Islander); born in Australia (ref: not born in Australia); born overseas (ref: not born overseas); pulmonary TB (ref: non-pulmonary TB); HIV-positive (ref: non-HIV-positive); previous treatment (ref: no previous treatment); resistance to first-line TB agents (ref: no resistance to first-line TB agents); resistance to second-line injectables (ref: no resistance to second-line injectables); resistance to fluoroquinolones (ref: no resistance to fluoroquinolones); multidrug-resistant TB (ref: non-multidrug-resistant TB); each risk factor category (ref: all other risk factors combined); and time (years) since arrival to diagnosis (ref: all other time since arrival of groups combined).

[b] Total observations were 1752 for the multivariable model due to three unknowns from time of arrival to diagnosis.

[c] Odds were adjusted for three 5-year age groups, resistance to fluoroquinolones, ever residing in an aged-care facility, and from time of arrival to diagnosis (0–2 years).

TB in Australia and in other low-incidence countries are strongly influenced by migration flows and population growth.[19,21–25] Elderly migrants from Cambodia, China, India, the Philippines and Viet Nam contributed a high proportion of TB notifications in Australia, despite the stringent pre-migration screening. Interestingly, the frequency of the top five countries of birth differed between the elderly and non-elderly age groups. China was among the top five countries where migrants in the elderly age group were born, while Nepal was one of the most common countries of birth for migrants in the non-elderly age group. The differences in the top countries of birth across these broad age groups may reflect a relationship with migration patterns, purpose of migration (for example, students or elderly people migrating with family members on permanent visas), offshore pre-migration testing, and the historical TB burden in their country of birth.[19,26] Even though Australia has a sustained low annual TB incidence rate,[27] it is important to note that Australian-born cases represented 15% of all elderly notifications. We hypothesized that individuals were likely to have been exposed to the bacteria during travel to an endemic country or may have acquired LTBI prior to the 1950s in Australia when the incidence of TB was higher, with over 45 cases per 100 000 population.[28] Our findings showed that being born in Australia led to poorer treatment outcomes compared with cases who were born overseas, although these results were borderline significant. Potential reasons for this could include delayed diagnosis, which is suggested by the longer median time from first health presentation to diagnosis compared with people born overseas.

Migrants to Australia and long-term visa holders from TB-endemic countries may be at increased risk of disease during their lifetime, due to a greater likelihood of travel to and extended stays in their country of origin. A study in the United States of America found that children were at increased risk of TB from travel to high-incidence countries or exposure to household visitors from these settings.[29] Similar to previous findings, common risk factors associated with TB in elderly people included past travel to or residence in a high-incidence country or close contact with an active TB case.[11,27] Outbreaks may occur among migrant communities due to different living conditions upon arrival that increase their vulnerability, extensive social networks, and co-residence with multiple generations.[14,30–32] The higher frequency of TB in patients born overseas may also reflect the barriers migrants face, including discrimination, fear of deportation, as well as language, social support, health literacy challenges, and access to free and timely health care.[24] The median time from migration to diagnosis with TB in Australia was 25 years. Research from the United Kingdom of Great Britain and Northern Ireland suggested that early case detection is improved with the implementation of catch-up screening 4 years after migration from a country with high TB incidence.[21] However, significant evidence gaps still remain around effective approaches to LTBI screening and management in migrants.[13] As outlined in a TB elimination framework for low-incidence settings, to overcome migrant health-care and treatment barriers, migrant countries must incorporate culturally and socially appropriate strategies into their health services.[24] The Netherlands has documented treatment success in over 90% of migrants through TB policies that enable access to health care through social support.[33] Given the disproportionate number of TB cases among migrants, TB services in Australia may need to consider prioritizing earlier or systematic health-services support for elderly migrants from high-incidence countries.

Ageing is a major contributor to TB reactivation risk due to a large burden of undiagnosed LTBI in elderly people,[34–36] which represents an important reservoir of TB infection.[14,37] In Hong Kong SAR (China), Japan and Singapore, the TB epidemic is largely driven by reactivation of disease due to age-related immune senescence and the prevalence of comorbidities.[38] An Australian study found a low (5.1% in 2016) but increasing prevalence of LTBI, with the largest proportion among overseas-born residents aged ≥65 years.[34] In our study, most cases of TB also represented likely LTBI reactivation given that most have been in Australia for an extended period of time or did not have recent known TB contact. In China, identified TB risk factors among elderly people included age, being male, low socioeconomic status, smoking, previous treatment for TB, and low body mass index (<18.5).[39] Many of these social and lifestyle risk factors are not routinely reported and could not be assessed in our study.

The multivariable analysis showed that greater odds for successful treatment were associated with the ages 65–79 years. The analysis also showed that the odds of unsuccessful treatment were associated with resistance to fluoroquinolones, residing in an aged-care facility, and being diagnosed within 0–2 years of arrival in Australia.

Residing in an aged-care facility is an important risk factor for people from high-income countries to be exposed to TB,[36,38] but there is limited evidence regarding treatment outcomes and residing in these settings. Contrary to expectations, being diagnosed earlier (0–<2 years) was associated with poorer treatment outcomes. This may be due to a number of reasons, for example, a more clinically advanced or severe infection, a lack of culturally appropriate health services or a specialist migrant health workforce. There may also be individual barriers including different health-seeking behaviours, health literacy, physical access to health-care facilities, and linguistic skills, which may impact treatment compliance and continued health-care engagement.[40]

The literature suggests that most TB disease in elderly people is due to the reactivation of LTBI,[10,34–36] the treatment for which may be a principal preventive factor for the control of TB among those of advanced age. Historically, elderly people have not been prioritized for LTBI treatment due to a higher risk of adverse events.[41] However, in recent years, shorter rifamycin-containing regimens have also been recommended, with a lower risk of toxicity.[41] Further research to support the efficacy of this approach including informing elderly people of the risk–benefit ratio of TB preventive therapy is warranted.[42]

A strength of our study is that it used a comprehensive national TB dataset. The backward stepwise approach to the multivariable model enabled us to exclude variables with collinearity and to consider the effects of all variables simultaneously. Australia is a country with low TB incidence, with a universal health-care system providing treatment and care for people with TB for free or with no out-of-pocket expenses, regardless of eligibility for free public health care. Therefore, the results of our analysis will be most relevant to other low-incidence settings with universal health-care systems.

The analyses had several limitations. There were completeness and quality issues for several variables due to changes in reporting over time for risk factor information and HIV status. The NNDSS dataset also lacked a treatment completion date, a TB death date, relevant comorbidities, and known lifestyle risk factors, which may have been unknown confounders when assessing treatment success. Our multivariable analysis had high standard errors for the 65–69-year and 70–75-year age groups, representing greater variability and uncertainty in these results. Additionally, the group size of some variables in our multivariable analysis was small (<10 cases), which may have potentially led to a reduced association with the outcome of successful treatment.

Our findings showed that elderly people represent only a small proportion of all TB cases reported in Australia. Similar to non-elderly age groups, most elderly cases are migrants from countries with high TB incidence. Australia has committed to working towards the elimination of TB by 2035. A critical component to achieving this goal will be the prioritization of the needs of our migrant population and identifying optimal ways to reduce LTBI reactivation. TB elimination in low-incidence settings is contingent upon the diagnosis and treatment of LTBI, as per the WHO End TB Strategy. In line with the National TB Advisory Committee strategic plan (2021–2025), migrants are a critical group for the prevention of TB and the reduction of its incidence in Australia. Our findings have demonstrated that the majority of elderly TB cases in Australia are migrants and an unknown number of these could have reactivated LTBI. Additional research into the LTBI reactivation risk and LTBI treatment among this group would be valuable to explore this possibility. The risk-benefit ratio of these interventions in Australia has not been fully established.

Australia has well-functioning jurisdictional TB control programmes that limit secondary cases and local transmission of TB, which is essential in maintaining and continuing to reduce Australia's low incidence of TB. Further exploration of the elderly population could be undertaken to investigate the differences between non-elderly and elderly TB cases, the relationship between risk factor information and treatment outcomes, risk factors for LTBI in migrants, and predictors for unsuccessful treatment in elderly cases.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

The study protocol was approved by the Australian National University Human Research Ethics Committee (protocol number: 2021/812).

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Hepatitis B virus infection on Kwajalein Atoll, Marshall Islands: a seroprevalence, knowledge and attitudes study

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Objective: A study was conducted to determine the seroprevalence of chronic hepatitis B virus (HBV) infection among children and their mothers on Kwajalein Atoll in the Marshall Islands two decades after routine vaccination was introduced in the 1990s. Mothers' knowledge and attitudes towards HBV disease and vaccination were also assessed.

Methods: Results of a national seroprevalence survey conducted in 2016–2017 and antenatal records were used to determine the prevalence of HBV seropositivity in children aged 6–8 years and their biological mothers. The associations between demographic, social and vaccination-related factors and seropositivity were explored using Fisher's exact tests.

Results: HBV seroprevalence was 0.3% in children and 6.8% in their mothers (during pregnancy). Coverage of timely HBV vaccination was 90.3% for the birth dose and was significantly associated with factors related to place of residence ($P < 0.001$), place of birth ($P < 0.001$) and number of antenatal visits ($P < 0.001$). Maternal attitudes towards infant vaccination and antenatal screening were largely positive (95.8% and 96.7%, respectively) despite low vaccination rates (20.9%) among mothers. Knowledge levels were low for disease complications, treatment and transmission.

Discussion: Prevalence of HBV in children and mothers residing on Kwajalein Atoll in 2016–2017 was lower than the national average for the Marshall Islands. Timely birth dose administration appears to have been effective in preventing mother-to-child transmission of HBV in this setting and should be promoted in remote settings where antiviral therapy is not available. Provision of out-of-cold-chain HBV vaccines should be considered to improve access in remote settings.

Prior to the introduction of the hepatitis B virus (HBV) vaccine in the 1980s, chronic HBV infection was highly endemic among countries in the World Health Organization (WHO) Western Pacific Region, with prevalence typically in excess of 8%.[1–3] The Region's goals for HBV disease control are <0.1% prevalence in 5-year-olds by 2030 and >95% vaccination coverage for birth and third doses.[4,5]

Many Pacific island countries and areas (PICs) have reported significant reductions in HBV prevalence following the introduction of routine HBV vaccination.[6–8] However, timely, reliable and disaggregated estimates of disease prevalence are lacking for many Member States in the Region.[9,10] Reported estimates for HBV infection rates tend to be based on infrequent seroprevalence surveys[10,11] and are often expressed in terms of national averages that mask the within-country variations that likely exist across island groups in many PICs.

Existing strategies for HBV disease control in the Region emphasize the need for more granular, contextual epidemiological estimates of disease burdens in Member States and the need to expand disease control efforts beyond immunization once coverage targets have been achieved. Significant challenges exist in the delivery of both vaccines and treatment for HBV in PICs, including lack of resources, geographical dispersion, limited infrastructure and sociocultural barriers to immunization.[1,9,12,13]

The self-governing Marshall Islands comprise 34 low-lying atolls and islands,[14] with a population of 42 418.[15]

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The majority of the population resides in two urban centres on large atolls, 430 kilometres apart: Majuro on Majuro Atoll (55%) and Ebeye on Kwajalein Atoll (23%).[15] A United States military base is present on Kwajalein Atoll but remains largely segregated from the Marshallese population.

Data on the seroprevalence of chronic HBV infection in the Marshall Islands are limited. The most recent available data are from a national seroprevalence survey conducted during the 2016–2017 school year.[1] According to this survey, the prevalence of HBV among first graders (children aged 6–8 years) was 1.2%.[1] Comparisons with earlier seroprevalence surveys, and thus analyses of temporal trends in hepatitis B disease burden, are problematic as these were conducted in different study populations. Available data from the 1980s showed a HBV prevalence in excess of 8% among adult blood donors, indicating previously high endemicity.[2,16] According to data from 2007, seropositivity among children in first grade and unrelated prenatal women from the two main urban centres (i.e. Majuro and Ebeye combined) averaged 1.8% and 9.5%, respectively.[17] While the 2016–2017 national seroprevalence survey included children from Kwajalein Atoll, reported results were not disaggregated by geographic areas. Currently, there is no systematic screening for HBV in adults in the Marshall Islands and no current estimates of seroprevalence in prenatal women[17] or HBV vaccine coverage among adults.[2,16]

Timely HBV birth dose vaccine coverage for the whole of the Marshall Islands in 2016 was 87%; third dose vaccine coverage was 76%.[18] However, immunization rates are known to differ between atolls, with the outer remote islands typically having lower coverage rates.[9,17] This may be due to a higher number of non-hospital births in the more remote islands, which often means the birth dose is delayed.[9,17] While information about HBV disease awareness and attitudes toward vaccination is generally lacking among the adult population in the Marshall Islands,[19] one study conducted in another PIC suggests a baseline knowledge of HBV in up to 60% of adults.[12]

Nearly a quarter (23%) of the national population resides on Kwajalein Atoll, the largest and most densely populated atoll in the Marshall Islands. However, the atoll is relatively remote from the nation's capital, Majuro, and has limited infrastructure and resources.[15] The risk of HBV disease transmission is high on Kwajalein Atoll due to its high population density,[15] low HBV vaccine coverage among adults,[13] and high prevalence of high-risk behaviours for transmission in resident adolescents and young adults.[13,20] Evaluation of disease prevalence among children and mothers on the atoll is needed to improve understanding of the hepatitis B disease burden and to inform strategies for expanding disease control measures. Assessment of knowledge and attitudes is also needed to support implementation of appropriate measures for improving vaccine uptake and screening.[19,21]

The objective of this study was therefore to determine the seroprevalence of chronic HBV infection among young children and their mothers on Kwajalein Atoll in the Marshall Islands two decades post vaccine introduction and to assess the knowledge and attitudes of mothers towards HBV disease and vaccination.

METHODS

Study setting

Kwajalein Atoll comprises 90 islets and has a population of 9739, half of which resides in Ebeye, the one major urban centre located on the main islet.[15] The population is predominantly native Marshallese.[15] The atoll has a 55-bed hospital, three primary care facilities (dispensaries) and 11 primary schools. Across the Marshall Islands, prenatal care is accessed by 81% of pregnant women.[22] At 95%, primary school enrolment on Kwajalein Atoll is higher than the national average of 85% (2016 data).[23]

On average, Kwajalein Atoll has 255 live births per year, the majority of which (95%) are delivered in Ebeye Hospital. HBV vaccination services are provided by immunization programme staff of the Ebeye Public Health Department. Routine childhood vaccination for HBV was introduced in Kwajalein Atoll in 1992 and administration of a timely birth dose (i.e. within 24 hours of birth) began in 1998.[17] Reported HBV vaccination coverage for the 2010 birth cohort was 99% for a timely birth dose and 97% for a complete course of three doses.[10] At the time of this study, immunoglobulin therapy for treatment of neonates delivered from seropositive mothers was not available in the Marshall Islands.

Study participants

First grade students aged between 6 and 8 years and their biological mothers were selected for this study. All first grade students enrolled in all 11 primary schools on Kwajalein Atoll in November 2016 were recruited to this study, apart from one who migrated and was therefore excluded. The choice to conduct the study in first grade students, who are older than the target age group recommended by the WHO for seroprevalence surveys (5 years), was a pragmatic one, given that school-aged children are easier to reach through school-based immunization activities.

The mothers of the first grade students were identified through school records. As there were two sets of twins in the study cohort of first grade students, the number of biological mothers was slightly lower (n = 296). An additional 64 mothers were randomly selected from mothers of second grade students attending the two largest elementary schools on Kwajalein Atoll in order to increase the number of knowledge and attitude survey participants to meet the required sample size (n = 357, assuming 80% power and an expected prevalence of baseline knowledge of 60%).[21]

Data collection

For all first graders, seroprevalence data were obtained from the results of the national survey conducted in 2016–2017. Demographic data (age, sex, ethnicity, place of birth, parents' names) were also extracted from the survey data and cross-checked against their birth and vaccination records for verification purposes.

Demographic data and perinatal HBsAg screening results for biological mothers were extracted from available antenatal, medical and immunization records. Structured face-to-face interviews were conducted from July to August 2018 with the mothers to assess their knowledge and attitudes towards HBV infection and vaccination. The interviews were conducted by public health nurses using a standardized data collection tool at participants' residences. Demographic information on mothers was also collected during the interviews to verify data in their antenatal records.

Data analysis

Children were considered seropositive for HBV infection if according to the results of the national seroprevalence survey they had tested positive for HBsAg. The national survey used a rapid test kit (Abbott Determine; Chiba, Japan) to test for HBsAg from whole blood from finger pricks; all positive results were verified at a medical laboratory in Hawaii. A timely HBV birth dose vaccination was defined as receipt of HBV vaccine within 24 hours of birth as documented in birth records. Mothers who had a positive HBsAg test result recorded during their pregnancy were defined as having a chronic HBV infection. For mothers with no antenatal record (n = 60) for the pregnancy of interest, HBV status was assessed in subsequent pregnancies and other sociodemographic data were extracted from their medical records. Maternal chronic HBV infection was assessed in two age groups, above and below 25 years, to distinguish those born before and after HBV vaccine introduction to the Marshall Islands.

Characteristics of the study population were summarized in a descriptive analysis using counts, means, standard deviations and proportions, as appropriate. Associations between dependent (HBV infection and vaccination status) and independent variables (sociodemographic and clinical factors) were explored and Fisher's exact tests used to determine the significance of these relationships. Statistical significance was set at $P < 0.05$.

The knowledge and attitude survey was structured around 10 knowledge questions and six attitude questions, which required "yes" or "no" answers for both sets of questions. The survey was designed to be as simple as possible to account for low education levels and the need to conduct interviews in the Marshallese language. Overall knowledge and attitude scores for each participant were calculated as the proportion of "yes" answers. A knowledge score of <6 and attitude score of <4 was considered poor. The proportion of mothers showing a positive response for specific knowledge and attitude items was calculated with 95% confidence intervals (CIs). All analyses were conducted using Stata version 17.

Informed consent

The seroprevalence survey of the children was conducted as part of a national campaign, and informed consent was obtained from parents and guardians prior to their inclusion. Prior written informed consent was obtained from women who participated in the survey of knowledge and attitudes.

RESULTS

Seroprevalence survey

Seroprevalence survey data for 2016–2017 were available for a total of 298 first grade students from Kwajalein Atoll. Of these, 57.0% (170/298) were males, the mean age was 6 years (range, 6–8 years; SD = 0.6) and most (87.6%) were residents of Ebeye. Nearly all first graders (90.6%) were born in hospital. A similar proportion (90.3%) received a timely HBV vaccine birth dose; 58.1% completed the third dose by 6 months of age (**Table 1**). Only one child was seropositive for HBsAg (0.3%, 95% CI: 0.32–0.99%) and had a seropositive mother. Further analysis for factors associated with seropositivity in children was not attempted.

As two of the mothers had twin deliveries, a total of 296 biological mothers were included in the seroprevalence analysis; the majority (97.6%) were aged 25 years or over. The prevalence of chronic HBV infection among mothers during pregnancy was 6.8% (95% CI: 3.90–9.62%). Around one fifth (n = 62; 20.9%) had completed a three-dose course of HBV vaccination (**Table 2**). All 20 mothers with chronic HBV infection were aged 25 years or over, and 90.0% (18/20) had not been vaccinated against HBV, not even partially. Among this group of mothers, only education level was associated with chronic HBV infection (**Table 2**). The outer island of Santo had the highest proportion of missing antenatal records (16/21, 76.2%).

Timely completion of HBV vaccination at birth and at 6 months of age were both significantly associated with place of residence ($P < 0.001$), place of birth ($P < 0.001$) and number of return antenatal visits ($P < 0.001$). The proportion of children receiving a timely birth dose of HBV vaccine was much lower in Santo (3/21; 14.3%) compared with the other areas (>95.0%). The proportion of children who had their third dose of HBV vaccine by 6 months of age was greatest in Ebeye (166/259 births; 64.1%); in the other regions this proportion dropped to 25.0% or below. Completion of the third dose by 6 months of age was also significantly associated with maternal employment (**Table 3**).

Knowledge and attitudes

The 360 mothers who were interviewed had a mean age of 35 years (range, 20–51 years; SD = 7). The majority (89.2%) were from Ebeye. Although most mothers (84.2%) were aware of HBV, knowledge about modes of transmission, vaccination and treatment was generally much lower (**Table 4**). Although around half of mothers (53.1%) scored ≥6 in the knowledge survey, the mean knowledge score was low (mean, 5.5; SD = 3.3). Questions relating to awareness of the potential complications of HBV infection and the availability of treatment received the fewest "yes" answers (**Table 4**). In contrast, responses to the six attitude questions were almost all positive, with 96.9% of mothers scoring ≥4; the mean attitude score was 5.9 (SD = 0.94). Questions relating to vaccination of children and antenatal screening received the highest proportion of positive responses (**Table 4**).

DISCUSSION

This study found the seroprevalence of HBV infection among first grade children on Kwajalein Atoll to be very low (0.3%) and confirms that good progress towards the 2030 target of <0.1% is being made.[5] While the prevalence of chronic HBV infection among the children's mothers was higher, at 6.8%, this figure is lower than that reported in a previous study conducted in perinatal women,[17] emphasizing the importance of subnational data for fully understanding the epidemiology of the HBV burden in the Marshall Islands. Our results also suggest that timely birth dose vaccination on Kwajalein Atoll may have reduced mother-to-child transmission of HBV despite the absence of hepatitis B immunoglobulin treatment and lower-than-optimal HBV vaccination coverage levels (i.e. below the 95% target for the Western Pacific Region).[17]

Timely HBV birth dose vaccine coverage for the first grade children included in this study was 90%; the three-dose coverage at 6 months was 58%. Both timely birth dose and three-dose completion at 6 months were significantly associated with factors related to place of birth and residence, with children living in areas outside the main urban centre of Ebeye more likely to miss out on their HBV vaccinations. This suggests that increasing the coverage of timely birth doses in these more remote areas, where there was less than 100% coverage and ensuring completion of three doses before 6 months of age in all areas will promote further reduction in childhood infection rates.

Interventions that have the potential to increase HBV vaccine coverage in remote settings such as

Table 1. **Characteristics of first grade children from Kwajalein Atoll included in the 2016–2017 national seroprevalence study of HBV infection, by infection status**

Characteristic	All children (*N* = 298) n (%)	Seropositive (*N* = 1) n (%)	Seronegative (*N* = 297) n (%)
Age (years)			
6	177 (59.4)	1 (100)	176 (59.3)
7	101 (33.9)	0 (0)	101 (34.0)
8	20 (6.7)	0 (0)	20 (6.7)
Sex			
Male	170 (57.0)	0 (0)	170 (57.2)
Female	128 (43.0)	1 (100)	127 (42.6)
Residence			
Ebeye	261 (87.6)	1 (100)	260 (87.5)
Carlos	4 (1.3)	0 (0)	4 (1.3)
Ebadon	4 (1.3)	0 (0)	4 (1.3)
Mejatto	8 (2.7)	0 (0)	8 (2.7)
Santo	21 (7.0)	0 (0)	21 (7.0)
Place of birth			
Hospital[a]	270 (90.6)	1 (100)	269 (90.6)
Primary care facility[b]	26 (8.7)	0 (0)	26 (8.8)
Home	2 (0.7)	0 (0)	2 (0.7)
HBV vaccination			
Timely birth dose <24 hrs	269 (90.3)	1 (100)	268 (90.2)
Birth dose given at >24 hrs	29 (9.7)	0 (0)	29 (9.8)
Third dose at <6 months	173 (58.1)	1 (100)	172 (57.9)
Third dose at >6 months	125 (41.9)	0 (0)	125 (42.1)

HBV: hepatitis B virus.

Analysis of statistical significance was not done due to insufficient numbers of seropositive children.

[a] Includes those born in hospitals outside Kwajalein Atoll such as Majuro Hospital.

[b] Includes all dispensaries outside Ebeye.

Kwajalein Atoll include provision of out-of-cold-chain vaccines. Studies have shown that HBV vaccines are heat stable,[24] and that out-of-cold-chain vaccines can improve uptake in low-resource settings where refrigeration may be limited.[25,26] This strategy has been shown to be a potentially cost-effective approach for PICs and should be considered for the Marshall Islands as a whole.[27] Introduction of HBV immunoglobulin use in neonates may also further reduce mother-to-child transmission and should also be considered for the Marshall Islands.

In this study, all the mothers who had chronic HBV infection were born prior to the introduction of routine childhood immunization on Kwajalein Atoll. Based on the assumption that rates of maternal HBV infection are a useful proxy for disease prevalence in the adult population, the relatively high prevalence of HBV infection in mothers observed in this study suggests that ongoing transmission on the atoll is likely, possibly through unprotected sexual contact. Treatment for chronic HBV infections is not widely available in the Marshall Islands,[13] and, as demonstrated by this study, knowledge levels surrounding both the disease and its treatment among adults are low. Without greater awareness and treatment, a large number of adults in the Marshall Islands remain at risk of complications associated with chronic HBV infection, such as hepatocellular carcinoma.[19,28]

The findings of poor knowledge of HBV infection among women on the atoll indicate an important need for culturally appropriate public education and awareness-raising interventions to improve vaccination

Table 2. **Characteristics of the biological mothers of first grade children from Kwajalein Atoll included in the 2016–2017 national seroprevalence study of HBV infection, by infection status**

Characteristic	All mothers (*N* = 296) n (%)	Seropositive (*N* = 20) n (%)	Seronegative (*N* = 276) n (%)	*P*
Age (years)				
<25	7 (2.4)	0 (0)	7 (2.5)	1.00
≥25	289 (97.6)	20 (100)	269 (97.5)	
Education				
Primary	28 (9.5)	3 (15.0)	25 (9.1)	0.03
Some high school	140 (47.3)	4 (20.0)	136 (49.3)	
Completed high school/college	128 (43.2)	13 (65.0)	115 (41.7)	
Employment				
Employed	79 (26.7)	7 (35.0)	72 (26.1)	0.43
Not employed	217 (73.3)	13 (65.0)	204 (73.1)	
HBV vaccination status				
Vaccinated	62 (20.9)	2 (10.0)	60 (21.7)	0.27
Not vaccinated	234 (79.1)	18 (90.0)	216 (78.3)	
No. of return antenatal visits				
<3	27 (9.1)	0 (0)	27 (9.8)	0.16
≥3	209 (70.6)	18 (90.0)	191 (69.2)	
Unknown[a]	60 (20.3)	2 (10.0)	58 (21.0)	

HBV: hepatitis B virus.

P values compare the proportions of mothers who are seropositive and seronegative using Fisher's exact test.

[a] Antenatal records were missing for the pregnancy of interest and HBV status was assessed from a subsequent pregnancy.

rates. Antenatal visits appear to be important settings for educating women. Prenatal HBV screening programmes provide a valuable opportunity to identify chronic HBV infections and to immunize unvaccinated pregnant women. Strategies for expanding screening of partners during and following pregnancy to encourage vaccine uptake should be considered by the national immunization programme. Integrated strategies for increasing access to prenatal care and screening for co-infections should also be explored. Standardized reporting of vaccination coverage and seroprevalence survey data is needed to ensure that subnational data are available for monitoring purposes.

In common with the situation reported in other high-burden settings, this study found that despite relatively poor disease knowledge, attitudes toward vaccination of infants were predominantly positive.[29] This finding, coupled with the observation that high levels of knowledge are not always positively correlated with favourable attitudes toward vaccination,[30] suggests that the barriers to screening and vaccination in this setting are complex and require further investigation.

While our study findings on the prevalence of HBV infection are not generalizable outside this setting, when viewed in the context of the data on vaccination coverage, they do provide some information that may be applicable to other PICs. Moreover, similarities between our knowledge and attitudes survey results and those derived from work conducted in other Pacific settings also indicate some commonality.[19,21] Our finding that seropositivity was more common in mothers with higher measures of socioeconomic status (higher education) requires further investigation.

This study has several limitations. The seroprevalence survey results for the children in this study date from 2016–2017 and for their mothers from 6–8 years prior to this when they were pregnant with these children. As such, the seroprevalence data may not represent the current HBV disease status on Kwajalein Atoll. As new

Table 3. **Sociodemographic factors associated with timely birth dose of HBV vaccine and completion of three-dose vaccination schedule by 6 months of age in schoolchildren aged 6–8 years in Kwajalein Atoll**

Characteristic	Total[a] *N* = 296	Timely birth dose given (*N* = 296)[a] n (%)	Birth dose given at >24 hours (*N* = 29) n (%)	*P*	Timely third dose (*N* = 173) n (%)	Third dose given at >6 months (*N* = 123) n (%)	*P*
Child's age (years)							
6	175 (59.1)	156 (58.4)	19 (65.5)		108 (62.4)	67 (54.5)	
7	101 (34.1)	92 (34.5)	9 (31.0)	0.774	58 (33.5)	43 (35.0)	0.070
8	20 (6.8)	19 (7.1)	1 (3.5)		7 (4.1)	13 (10.6)	
Residence							
Ebeye	259 (87.5)	248 (92.9)	11 (37.9)		166 (96.0)	93 (75.6)	
Carlos	4 (1.4)	4 (1.5)	0	<0.001	1 (0.6)	3 (2.4)	<0.001
Ebadon	4 (1.4)	4 (1.5)	0		1 (0.6)	3 (2.4)	
Mejatto	8 (2.7)	8 (3.0)	0		2 (1.2)	6 (4.9)	
Santo	21 (7.1)	3 (1.1)	18 (62.1)		3 (1.7)	18 (14.6)	
Place of birth							
Hospital[b]	268 (90.5)	264 (98.9)	4 (13.8)		170 (98.3)	98 (79.7)	
Primary care facility[c]	26 (8.8)	1 (0.4)	25 (86.2)	<0.001	2 (1.2)	24 (19.5)	<0.001
Home	2 (0.7)	2 (0.8)	0		1 (0.6)	1 (0.8)	
Maternal age (years)							
<25	7 (2.5)	7 (2.6)	0	1.00	5 (2.9)	2 (1.6)	0.703
≥25	289 (97.6)	260 (97.4)	29 (100)		168 (97.1)	121 (98.4)	
Education							
Primary	28 (9.5)	27 (10.1)	1 (3.5)	0.381	16 (9.3)	12 (9.8)	
Some high school	140 (47.3)	123 (46.1)	17 (58.6)		79 (45.1)	61 (49.6)	0.741
Completed high school/college	128 (43.2)	117 (43.8)	11 (37.9)		78 (45.7)	50 (40.7)	
Employment							
Employed	79 (26.7)	69 (25.8)	10 (34.5)	0.376	54 (31.2)	25 (20.3)	0.045
Not employed	217 (73.3)	198 (74.2)	19 (65.5)		119 (68.8)	98 (79.7)	
Maternal HBV vaccination status							
Vaccinated	62 (21.0)	58 (21.7)	4 (13.8)	0.471	36 (20.8)	26 (21.1)	1.00
Not vaccinated	234 (79.1)	209 (78.3)	25 (86.2)		137 (79.2)	97 (78.9)	
No. of return antenatal visits							
<3	27 (9.1)	24 (9.0)	3 (10.3)		11 (6.4)	16 (13.0)	
≥3	209 (70.6)	205 (76.8)	4 (13.8)	<0.001	138 (79.8)	71 (57.7)	<0.001
Unknown	60 (20.3)	38 (14.2)	22 (75.9)		24 (13.9)	36 (29.3)	
Maternal HBV status							
Negative	276 (93.2)	248 (92.9)	28 (96.6)	0.705	159 (91.9)	117 (95.1)	0.351
Positive	20 (6.8)	19 (7.1)	1 (3.5)		14 (8.1)	6 (4.9)	
Maternal knowledge (out of 10)							
Good, ≥6	153 (51.7)	137 (51.3)	16 (55.2)	0.845	91 (52.6)	62 (50.4)	0.725
Poor, <6	143 (48.3)	130 (48.7)	13 (44.8)		82 (47.4)	61 (49.6)	
Maternal attitude (out of 6)							
Positive, ≥4	286 (96.6)	257 (96.3)	29 (100)	0.606	165 (95.4)	121 (98.4)	0.203
Negative, <4	10 (3.4)	10 (3.8)	0		8 (4.6)	2 (1.6)	

HBV: hepatitis B virus.

[a] For the purposes of analysing the participants as mother–child pairs, the two sets of twin children in this study were assumed to have the same vaccination status. The total reflects the number of mother–child pairs, rather than the number of children.

[b] Includes those born in hospitals outside Kwajalein Atoll such as Majuro Hospital and hospitals in other countries.

[c] Includes all dispensaries outside Ebeye.

Table 4. **Knowledge and attitudes toward HBV infection and vaccination among mothers on Kwajalein Atoll, 2016–2017 (*N* = 360)**

Question topic	Proportion of "yes" answers % (95% CI)
Knowledge items:	
HBV infection	84.2 (80.0–87.8)
Complications such as liver cancer	44.2 (39.0–49.5)
Transmission through blood transfusion	50.3 (45.0–55.6)
Transmission through unprotected sexual intercourse	50.3 (45.0–55.6)
Mother-to-child transmission	60.8 (55.6–65.9)
Prevention of transmission through timely HBV vaccine birth dose	51.7 (46.4–56.9)
Asymptomatic nature of HBV infection	53.1 (47.8–58.3)
Ability to cause jaundice	73.3 (68.4–77.8)
Long-term complications for children infected perinatally	46.4 (41.1–51.7)
Availability of treatment for HBV infection	38.3 (33.3–43.6)
Total with:	
Good knowledge (knowledge score ≥6)	53.1 (47.8–58.3)
Poor knowledge (knowledge score <6)	46.9 (41.7–52.2)
Mean score	5.5 (SD = 3.3)
Attitude items (positive attitude):	
Vaccination	95.8 (93.2–97.6)
Recommending vaccination to others	96.1 (93.6–97.9)
Being screened during pregnancy (antenatal visit)	96.7 (94.2–98.2)
Allowing child to be vaccinated	97.5 (95.3–98.9)
Allowing child to receive immunoglobulin treatment	96.3 (93.9–98.1)
Allowing child to be screened for HBV infection postnatally (first 12 months)	96.7 (94.2–98.3)
Total with:	
Positive attitude (attitude score ≥4)	96.9 (94.6–98.5)
Negative attitude (attitude score <4)	0.03 (0.02–0.05)
Mean score	5.9 (SD = 0.94)

CI: confidence interval; HBV: hepatitis B virus; SD: standard deviation.

interventions for HBV disease control have since been implemented, the estimates presented here are likely to be higher than present-day levels. Use of school records to identify study participants excludes children who are not enrolled in school, which may limit the generalizability of the results. However, this is not likely to be significant as enrolment rates on the atoll are higher than national estimates. For mothers with no antenatal record for the pregnancy of interest, the serostatus during subsequent pregnancies was used. This may have resulted in some misclassification as the serostatus may have changed between pregnancies. In addition, antenatal records for women from the outer islands were more likely to be missing than those for mothers from the main atoll, which may have introduced confounding by place of residence. Interviews for the knowledge and attitudes survey were conducted by public health nurses, which may have created some social desirability bias in the responses, particularly those relating to attitudes.

Conclusion

This study showed significant progress towards regional targets for hepatitis B control on Kwajalein Atoll of the Marshall Islands and a reduction in the mother-to-child transmission of HBV through the timely administration of HBV vaccine birth dose. To ensure ongoing timely completion of HBV vaccination schedules, greater vaccine accessibility is required, and it is recommended that consideration be given to the use of out-of-cold-chain HBV vaccines in the national immunization programme. Reduction of disease prevalence among adults will require culturally appropriate public education activities and innovative approaches focused on women with poor vaccine uptake and low levels of knowledge. Prenatal visits provide a critical opportunity for screening, vaccination and education. Policies and integrated approaches for improving prenatal vaccination coverage and expanded screening should be considered to improve vaccination uptake among adults on Kwajalein Atoll and the Marshall Islands. Further research is needed to explore barriers to vaccination in adults.

Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

Ethical approval for this study was obtained from the Kwajalein Atoll Health Care Bureau as no national health research ethics committee existed at the time of the study. The Fiji National University College of Medicine and Health Sciences Human Health Research Ethics

Committee provided approval for the study methodology (ID 22.18).

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A test-based strategy for early return to work for health-care workers with COVID-19 during the Omicron wave, Brunei Darussalam, 2022

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Objective: This paper summarizes and evaluates a test-based strategy for early return to work for health-care workers (HCWs) with mild coronavirus disease in Brunei Darussalam during the Omicron wave in February 2022 and compares the characteristics of HCWs by how long it took them to return to work.

Methods: The early return-to-work strategy involved testing on day 3 of infection with reverse transcription–polymerase chain reaction and with a rapid antigen test on days 5 and 6 or days 5 and 7. Data about infected HCWs were extracted from the Ministry of Health's public health surveillance database. Percentages and proportions were used for descriptive statistics, and Pearson's χ^2 test and the paired *t*-test were used to compare return-to-work patterns with demographic factors and vaccination status of the HCWs, as well as between cycle threshold (Ct) values and occupational groups of HCWs.

Results: From 15 February to 15 March 2022, a total of 1121 HCWs were notified as being infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Of these, 175 (15.6%) were able to return to work on day 4 of their infection, 153 (13.6%) on day 6 and 268 (23.9%) on day 7; 525 (46.8%) required 10 days of home isolation. Statistically significant associations were observed between return-to-work periods and occupational group ($P < 0.01$) and Ct value ($P < 0.01$), but not between return to work and age, sex or vaccination status.

Discussion: This test-based strategy ensured a balance between mitigating a shortage of HCWs and enabling them to return to work early without compromising their safety and that of their patients.

Since the start of the coronavirus disease (COVID-19) pandemic in early 2020, many countries have faced either their third or fourth wave of the outbreak, mainly due to new variants and subvariants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Health-care workers (HCWs), therefore, were at the highest risk for COVID-19 as a direct consequence of their occupational exposure to the virus.[1] With the health-care sector experiencing staffing shortages as a result of the increasing number of cases occurring with each wave, health-care facilities faced challenges in managing the pandemic while maintaining essential health services.[1] This burden was further compounded by the absence of HCWs due to them becoming infected with SARS-CoV-2, experiencing the psychological effects of the pandemic, being unable to attend work if they were the main caregivers for infected and ill family members, and being in quarantine or self-isolation as a result of close contact with someone with COVID-19.[2,3]

Health services required additional staffing during the pandemic to maintain appropriate functioning but still had to consider how to maintain a safe work environment for HCWs.[4] During the pandemic, several strategies were implemented by countries to avoid shortages of essential HCWs. This included hiring additional staff, limiting non-essential health services, restricting non-essential annual leave, implementing early return-to-work (RTW) policies for HCWs with COVID-19 and enforcing strict workplace surveillance for asymptomatic HCWs who are in close contact with patients confirmed or suspected to have COVID-19.[4–6]

Following the first case of COVID-19 in Brunei Darussalam on 9 March 2020, the country had three waves of outbreaks. There were 337 cases during the first wave, from 9 March to 31 July 2021; 16 139 cases during the second wave (Delta variant), from 1 August 2021 to 31 January 2022; and 124 066 cases during

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the third wave (Omicron variant), from 1 February to 20 April 2022, at the time of this report.[7–9] There was no confirmed local transmission to HCWs during the first wave; however, during the second wave, 394 HCWs were infected.[10] The number increased significantly during the third wave, such that in the first 2 weeks of the third wave, in February 2022, 474 HCWs were infected. This number rose to 2345 infected HCWs by 20 April 2022.

The Ministry of Health (MOH) saw a need to step up mitigation measures to detect cases early and to break the onward chain of transmission.[10] One of these was a test-based early RTW strategy for HCWs. During the first and second waves, HCWs with COVID-19 followed the same testing and isolation protocol as the community. However, due to the significant number of HCWs affected during the third wave, a revised strategy was implemented for HCWs beginning on 15 February 2022 (**Fig. 1**). The revised HCW protocol was circulated to all health-care facilities through the heads of departments or services and supervisors. Infected HCWs were to undergo reverse transcription–polymerase chain reaction (RT-PCR) testing on day 3 of infection, and if they were negative or positive with a Ct value of ≥30, they could end isolation and return to work by day 4. If their Ct value was <30 on day 3, they needed to continue isolation and perform exit tests as per the community health protocol.

The third-wave community health protocol required infected individuals to undergo mandatory home self-isolation for a minimum of 6 days or a maximum of 10 days, depending on the outcome of their exit tests. If the individual had two consecutive negative rapid antigen test results on days 5 and 6, they could end isolation. If they were positive on day 5, they took another test on day 7. If they were negative on day 7, they could end isolation. If their day 6 or day 7 result was positive, they needed to complete 10 days of isolation.

To ensure compliance with self-testing using the rapid antigen test during home isolation, results from the test were uploaded onto the MOH web portal via the BruHealth mobile application, a one-stop mobile platform used for contact tracing and identifying positive cases of COVID-19 in Brunei Darussalam. This electronic platform also featured access to a self-assessment health tool, entry and exit QR code to be scanned for accessing public premises, access to online personal health records and updates on the national and global situation of the COVID-19 pandemic, among others.[11,12] On uploading their negative exit test result or completion of 10 days of isolation, the BruHealth code would change colour from purple (indicating a positive case and therefore barring the individual from entering public premises) to green (indicating the individual was negative for COVID-19 and had no underlying medical conditions) or yellow (indicating the individual was negative for COVID-19 but had underlying chronic medical conditions).

The objective of this study is to summarize the outcomes of the test-based early RTW strategy of HCWs in Brunei Darussalam and compare the characteristics of the HCWs by their RTW period.

METHODS

Data about infected HCWs were extracted from the MOH public health surveillance database. This national database was updated daily and contained data about HCWs with COVID-19 who had been diagnosed by RT-PCR or rapid antigen testing. Data on HCWs who were diagnosed from 15 February to 15 March 2022 were analysed until the end of their isolation period.

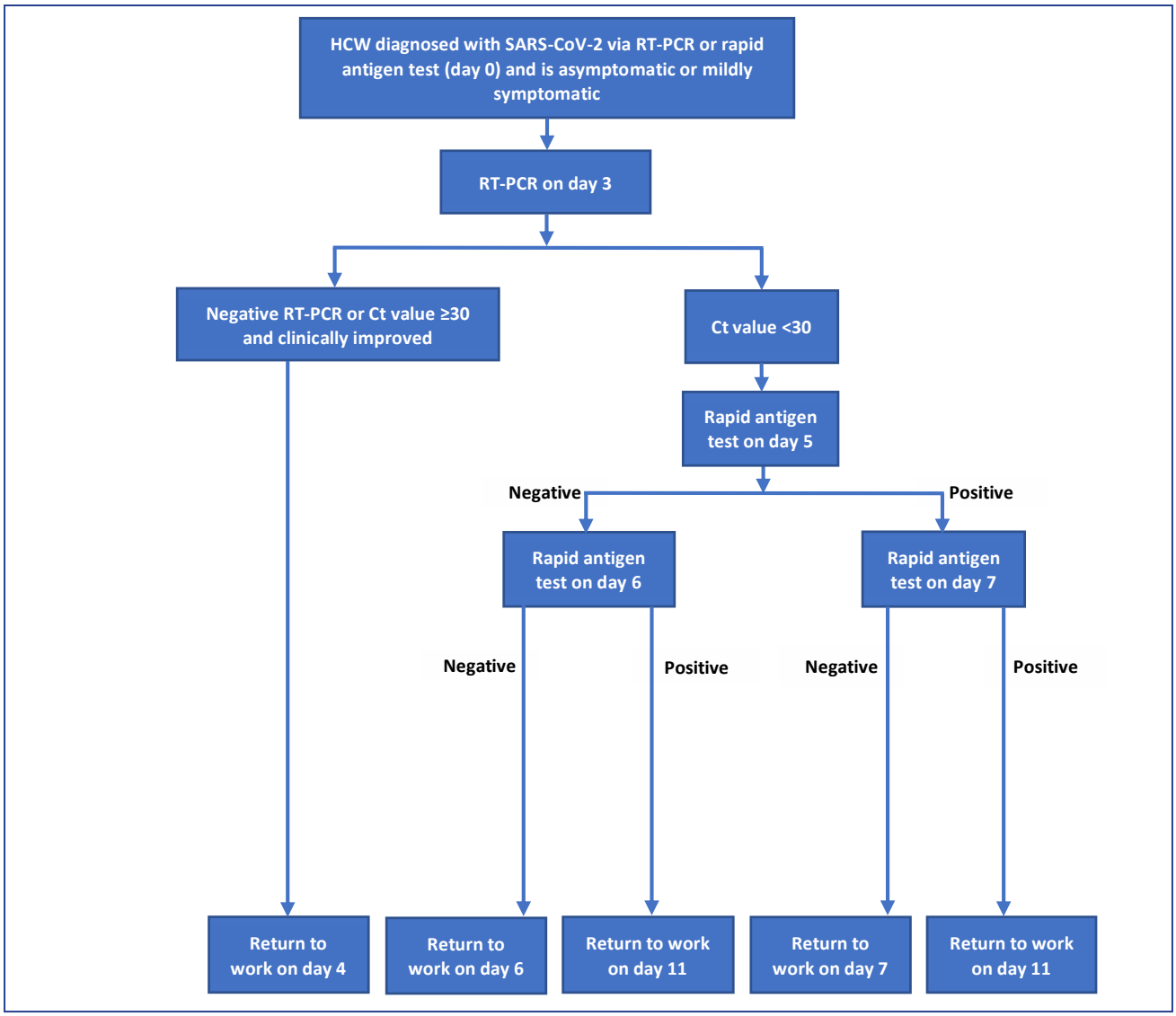
For infected HCWs, testing by RT-PCR on day 3 was carried out at any MOH-designated swab facility; MOH-approved kits for self-testing with the rapid antigen test were distributed through a coordinated, multisectoral COVID-19 relief agency.

Data were analysed using Epi Info version 7.2.0.1 (Centers for Disease Control and Prevention, Atlanta, GA, USA). Percentages and proportions were used for descriptive statistics, and Pearson's χ^2 test and the paired *t*-test were used to compare RTW patterns with demographic factors and vaccination status, as well as Ct values and occupational groups of HCWs.

RESULTS

A total of 1643 HCWs from government and private health-care facilities were diagnosed with COVID-19 during the study period. Of these, 522 were excluded from the study due to missing information for the day 3 RT-PCR test or the day 5, 6 or 7 rapid antigen test. Of the 1121 infected HCWs included, 139 (12.4%) had a negative RT-PCR result and 36 (3.2%) had a Ct value of ≥30 on their day 3 test. Therefore, 175 (15.6%) HCWs

Fig. 1. **Flowchart of the test-based strategy for early return to work for health-care workers, Brunei Darussalam, effective 15 February 2022**



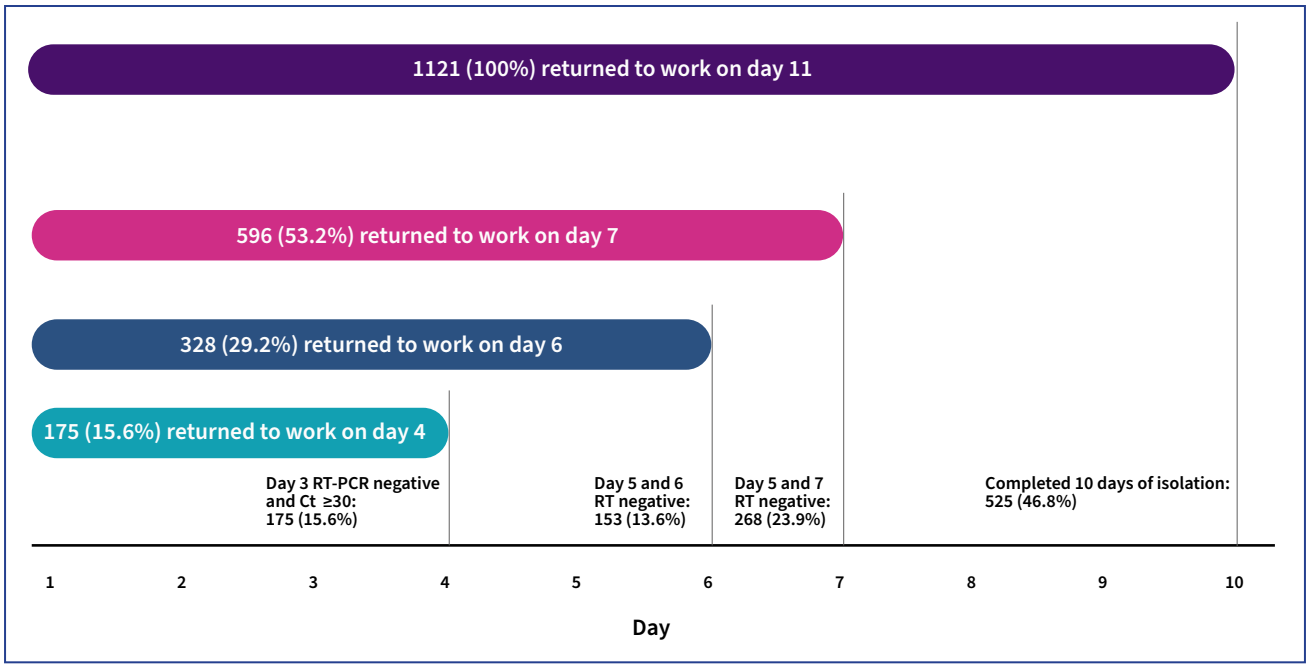
Ct: cycle threshold; HCW: health-care worker; RT-PCR: reverse transcription–polymerase chain reaction; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

were able to return to work after 3 days of isolation (**Fig. 2**). A further 153 (13.6%) were able to return to work on day 6 and 268 (23.9%) on day 7. The remaining 525 (46.8%) HCWs were required to complete 10 days of isolation.

The majority of infected HCWs were female (68.1%, 763), and more than one third were in the 31–40-year age group (34.3%, 384), with a mean age of 38 ± 12 years (**Table 1**). Nurses were the occupational group most affected (45.9%, 514), followed by support staff (i.e. health technicians, porters, attendants, voluntary health workers, at 21% [235]) and allied health professionals (i.e. radiographers, physiotherapists and occupational therapists, optometrists and laboratory staff, at 10.8% [121]).

Statistically significant associations were observed between RTW periods and occupational group ($P < 0.01$) and Ct value ($P < 0.01$); however, there were no significant associations between RTW periods and age, sex or vaccination status. A higher proportion of HCWs with direct clinical contact – such as medical practitioners (65.9%, 58), allied health professionals (52.1%, 63), nursing staff (48.4%, 249), paramedic staff (42.9%, 15) and support staff (40.9%, 96) – had a

Fig. 2. **Number of health-care workers with COVID-19, by the day they returned to work, Brunei Darussalam, 15 February to 15 March 2022**



Ct: cycle threshold; RT: rapid antigen testing; RT-PCR: reverse transcription–polymerase chain reaction.

positive result on day 7 and completed 10 days of isolation compared with those who had indirect or no clinical contact with patients. Similarly, a significant association was observed between RTW patterns and baseline Ct values: 49% (123) of HCWs with high baseline Ct values of ≥30 were able to return to work by day 4, while those with Ct values <30 spent longer in isolation ($P < 0.01$).

At the time of diagnosis, 93% (1042) had received three doses of COVID-19 vaccine, while 6.9% (77) had received two doses. Among those who had three doses, 54.7% (570) had their third dose more than 3 months prior to infection, while 41.5% (432) had theirs 1–3 months prior and 3.8% (40) had theirs within 1 month prior to infection. There was no significant difference between RTW pattern and vaccination status (whether the HCW had two or three doses) or the booster period (i.e. the time between the third dose of COVID-19 vaccine and COVID-19 diagnosis) (**Table 1**).

In a comparison of Ct values at baseline and at day 3, 83.4% (116/139) of HCWs who had a high Ct value of ≥30 at diagnosis transitioned to a negative RT-PCR result by day 3. There were no significant associations between vaccination status and booster period and a change in Ct value from baseline to day 3 (**Table 2**).

DISCUSSION

The adoption of a test-based strategy incorporating RT-PCR testing on day 3 for HCWs with asymptomatic or mild COVID-19 infection enabled essential HCWs to return to work safely and with minimal risk of disease transmission to their patients. This also mitigated issues of staffing shortages for HCWs. Altogether, 15.6% of infected HCWs cleared high infectivity levels by their day 3 RT-PCR testing and, therefore, were able to return to work early. More than half (53%) of the HCWs were deemed safe to return to work after day 7, whereas 47% still had a positive rapid antigen test result at day 7 and required a longer duration of isolation. A study in the United States of America reported a similar proportion of HCWs (43%) with a positive result on rapid antigen testing from day 5 to day 10 during the Omicron wave (Landon E, Bartlett AH, Marrs R, Guenette C, Weber SG, Mina MJ, University of Chicago, unpublished data, 2022.

Our findings showed a significant association between a HCW's occupational group and RTW period in that HCWs who had direct clinical contact (high-risk HCWs) took longer to recover from COVID-19 compared with those who had indirect (moderate-risk HCWs) or no

Table 1. **Demographic characteristics, cycle threshold values and vaccination status of health-care workers with COVID-19, by day of return to work, Brunei Darussalam, 15 February to 15 March 2022 (N = 1121)**

Characteristic	Day returned to work[a]				Total	P[b]
	4	6	7	11		
Age group (years)						
≤20	3 (27.3)	3 (27.3)	1 (9.1)	4 (36.3)	11 (1.0)	0.30
21–30	46 (15.0)	49 (15.9)	72 (23.5)	140 (45.6)	307 (27.4)	
31–40	63 (16.4)	45 (11.7)	80 (20.8)	196 (51.1)	384 (34.3)	
41–50	42 (16.4)	33 (12.9)	73 (28.5)	108 (42.2)	256 (22.8)	
>50	21 (12.9)	23 (14.1)	42 (25.8)	77 (47.2)	163 (14.5)	
Sex						
Female	128 (16.8)	108 (14.1)	179 (23.5)	348 (45.6)	763 (68.1)	0.32
Male	47 (13.1)	45 (12.6)	89 (24.9)	177 (49.4)	358 (31.9)	
Occupational group						
Medical practitioner	16 (18.2)	8 (9.1)	6 (6.8)	58 (65.9)	88 (7.9)	<0.01
Nursing staff	73 (14.2)	66 (12.8)	126 (24.5)	249 (48.4)	514 (45.9)	
Paramedic staff	7 (20.0)	4 (11.4)	9 (25.7)	15 (42.9)	35 (3.1)	
Dental practitioner or staff	9 (27.3)	4 (12.1)	9 (27.3)	11 (33.3)	33 (2.9)	
Allied health professional	18 (14.8)	11 (9.1)	29 (24.0)	63 (52.1)	121 (10.8)	
Administrative staff	7 (9.5)	16 (21.6)	25 (33.8)	26 (35.1)	74 (6.6)	
Support staff	42 (17.8)	40 (17.0)	57 (24.3)	96 (40.9)	235 (21.0)	
Security staff and cleaners	3 (14.3)	4 (19.0)	7 (33.3)	7 (33.3)	21 (1.9)	
Results of diagnostic test						
RT-PCR cycle threshold value						
≥30	123 (49)	8 (3.2)	26 (10.4)	94 (37.6)	251 (22.4)	<0.01
21–30	32 (11.7)	35 (12.8)	70 (25.6)	136 (49.8)	273 (24.4)	
11–20	14 (3.1)	85 (19.0)	133 (29.8)	215 (48.1)	447 (39.8)	
Rapid antigen test positive	6 (4.0)[c]	25 (16.7)	39 (26.0)	80 (53.3)	150 (13.4)	
Vaccination status						
Complete[d]	14 (18.2)	15 (19.5)	20 (25.9)	28 (36.4)	77 (6.9)	0.15
Complete plus booster[e]	160 (15.4)	137 (13.1)	248 (23.8)	497 (47.7)	1042 (93.0)	
Incomplete	1 (50.0)	1 (50.0)	0	0	2 (0.2)	
Booster (n = 1042)						
Within <1 month	11 (27.5)	4 (10.0)	8 (20.0)	17 (42.5)	40 (3.8)	0.13
Within 1–3 months	72 (16.7)	56 (13.0)	91 (21.1)	213 (49.2)	432 (41.5)	
Within >3 months	76 (13.3)	76 (13.3)	150 (26.3)	268 (47.1)	570 (54.7)	

RT-PCR: reverse transcription–polymerase chain reaction.

[a] Values are number (%).

[b] P values were calculated using Pearson's χ^2 test.

[c] These are health-care workers who underwent rapid antigen testing instead of RT-PCR.

[d] This refers to having completed two doses of a WHO-approved COVID-19 vaccine.

[e] A booster is an additional dose beyond the primary two-dose series of a WHO-approved COVID-19 vaccine.

clinical contact (low-risk HCWs). This can be attributed to an increased risk of disease transmission in the high-risk occupational groups who were managing COVID-19 cases or suspected cases in a hospital setting, treating cases with influenza-like illness in outpatient clinics or performing RT-PCR testing at swab centres, and who had more frequent surveillance testing for SARS-CoV-2. This surveillance testing occurred thrice weekly and

Table 2. **Change in cycle threshold values from baseline to day 3 and association of the change with vaccination status for health-care workers with COVID-19, Brunei Darussalam, 15 February to 15 March 2022**

Change in Ct values	No. of HCWs	Ct value at day 3[a]			
		10–20	21–30	>30	Negative
Ct value at day 0					
10–20	447	154 (34.5)	279 (62.4)	9 (2.0)	5 (1.1)
21–30	273	132 (48.4)	109 (39.9)	19 (7.0)	13 (4.8)
≥30	251	87 (34.7)	41 (16.3)	7 (2.8)	116 (46.2)
Rapid antigen test positive	150	71 (47.3)	73 (48.6)	1 (0.7)	5 (3.3)
Total	1121	444	502	36	139
Change in Ct values and association with vaccination	**No. of HCWs**	**Ct value[b]**		***P*[c]**	
		Day 0	**Day 3**		
Total	975	20.9 (12.9)	21.5 (7.3)	0.74	
Vaccination status					
2 doses	54	22.1 (11.3)	22.35 (8.3)	0.48	
3 doses	921	20.9 (12.9)	21.5 (7.1)	0.56	
Booster period					
Within <1 month	36	22.5 (15.9)	24.7 (11.8)	0.74	
Within 1–3 months	393	21.3 (14.4)	21.9 (7.5)	0.85	
Within >3 months	546	20.7 (11.9)	20.9 (6.9)	0.41	

Ct: cycle threshold; HCW: health-care worker.

[a] Values are number (%).

[b] Values are median (interquartile range).

[c] *P* values were calculated using the paired *t*-test.

comprised one RT-PCR test and two rapid antigen tests for HCWs who were at high risk of infection, compared with the protocol for those at moderate risk, which was RT-PCR testing twice a month and rapid antigen testing twice a week, and the protocol for those considered to be at low risk, which was RT-PCR testing once a month and rapid antigen testing once a week.[13] This testing strategy allowed for early detection of COVID-19 in presymptomatic HCWs, which subsequently also resulted in a longer period of isolation. A similar finding was observed in a study in the United States of America, in which positivity on rapid antigen testing and a longer duration of isolation were reported among frequently screened university students compared with infrequently screened groups.[14]

Our study also reported an early RTW pattern among a substantial proportion of HCWs (49%) who had Ct values of ≥30 at diagnosis. This could have been due to the virus being detected at a later stage of infection, particularly among the low-risk group of HCWs who underwent less stringent regular surveillance and SARS-CoV-2 testing.[13] No significant association was observed between the RTW pattern and vaccination status or booster period after primary vaccination. Similarly, no association was seen between vaccination status or booster period and Ct value on day 0 and day 3. This is similar to findings from two studies in the United States of America that looked at HCWs and university students during the Omicron wave, whereby primary COVID-19 vaccination did not have any protective effect on rapid antigen test positivity beyond day 5, and boosted individuals needed a longer duration of isolation (Landon E, Bartlett AH, Marrs R, Guenette C, Weber SG, Mina MJ, University of Chicago, unpublished data, 2022).[14]

In conclusion, the introduction of RT-PCR testing on day 3 resulted in 15.6% of HCWs being able to return to work by day 4. Although this proportion may appear low, it had a significant and positive impact on the health workforce crisis during the pandemic when every contribution by a HCW was most welcome. Such a test-based RTW strategy also helped maintain a balance between infection prevention and control measures and

mitigation of staff shortages, particularly during the Omicron wave, which saw higher transmissibility and immunity evasion properties of the virus, and resulted in a large number of HCWs becoming infected as a result of occupational exposure and community exposure.

Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

This report describes a new health protocol implemented in the midst of the COVID-19 pandemic, for which secondary data analyses were conducted. Therefore, no ethics review was needed.

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High SARS-CoV-2 attack rates in areas with low detection after community transmission established in Port Vila, Vanuatu, April 2022

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Objective: On 4 March 2022, the first community-acquired case of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was reported in Vanuatu, with community transmission occurring subsequently. It was expected that the number of notified SARS-CoV-2 cases would be an underestimate of the true infection rate of this outbreak; however, the magnitude of underreporting was unknown. The purpose of this study was to provide a population-based estimate of SARS-CoV-2 infection shortly after the first reports of community transmission, to understand the level of underdetection and undernotification in Vanuatu and thus to inform ongoing prevention and response activities.

Methods: We conducted a cross-sectional SARS-CoV-2 prevalence study in two geographical administrative areas in Port Vila, Vanuatu in April 2022. All residents in selected areas were eligible. Trained teams conducted demographic and behavioural interviews and collected nasal specimens. Specimens were tested by polymerase chain reaction. The primary outcomes were the rates of SARS-CoV-2 attack (point prevalence) and cumulative attack, underdetection, notification and household secondary attack.

Results: A total of 252 people from 84 households participated. Among 175 people who had a sample collected, 91 were SARS-CoV-2-positive (attack rate 52.0%). Most cases had not been detected before the study (underdetection rate 91.5%). More than half of previously detected cases were notified (notification rate 65.2%).

Discussion: Within the first few weeks of community transmission, more than half of participants in the selected areas had evidence of SARS-CoV-2 infection; however, most infections had been undetected. This study provides important information about the rapid spread of novel infectious diseases in Vanuatu.

At the end of 2021, the Pacific island country of Vanuatu was one of about 10 countries globally that had not yet experienced community transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease (COVID-19).[1] Between 2020 and 2021, Vanuatu (which comprises 83 islands and has a population of 302 000) implemented stringent and successful policies to prevent importation and community transmission of SARS-CoV-2, and only seven border cases were detected among over 8000 returning citizens until the end of 2021.[2,3]

The highly transmissible B.1.1.529 (Omicron) variant of SARS-CoV-2 was first identified globally in November 2021.[4] Between December 2021 and January 2022, Vanuatu paused all repatriation flights for returning citizens and residents. Repatriation flights resumed on 16 February 2022; from 17 February to 4 March, 39 cases were detected among travellers (n = 27) and front-line border workers (n = 12).[5]

On 4 March 2022, the first locally acquired case of SARS-CoV-2 was detected in the capital city, Port Vila, in a person who had not undertaken international travel.[5] This case was asymptomatic and detected through routine screening at Vila Central Hospital. An additional 13 community cases, all symptomatic, were subsequently identified after they presented to the hospital-based testing clinic on 5 March 2022, indicating

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community transmission.[5] The test positivity rate in Port Vila increased from 16% on 7 March to a peak of 52% on 26 March (data not publicly available, personal communication with the authors from the National Surveillance, Research & Emergency Response Unit [NSRERU]).

The Vanuatu Ministry of Health implemented several surveillance-strengthening activities between 2020 and 2021, including developing standard operating procedures (SOPs) for managing suspected and confirmed cases, training health-care workers on SOPs and implementing electronic notifications for new SARS-CoV-2 diagnoses.[2,6] However, gaps remained; for example, there was limited awareness of notification requirements among health-care workers. Owing to limited access to SARS-CoV-2 tests (antigen and polymerase chain reaction [PCR]) and an expected high number of infections due to high-density housing, it was anticipated that the number of notified SARS-CoV-2 cases would underestimate the true infection rate in Vanuatu during a community outbreak. However, the magnitude of this underreporting was unknown. The purpose of this study was to provide a population-based estimate of SARS-CoV-2 infection shortly after community transmission was first reported, to understand the level of underdetection and undernotification in Port Vila to inform ongoing prevention and response activities.

METHODS

Study design

We conducted a cross-sectional SARS-CoV-2 prevalence study and triangulated data with notification data.

Study setting

Two geographically defined administrative units in Port Vila, Vanuatu were purposively selected based on a population size of about 300 people and at least one confirmed case notified to the NSRERU by 25 March 2022. The administrative units were defined by the Vanuatu National Statistics Office, and the population of about 300 people was deemed to be a manageable sample size.

Study population

The eligible population included all residents (defined as those whose main dwelling was in one of the administrative areas) who were at home in the two selected administrative areas at the time of fieldwork. A stay-at-home order was in effect during the study period;[7] therefore, it was expected that most residents would be at home. Where possible, residents who were not present during data collection were approached to participate by field research teams within 2–3 days of fieldwork. Unattended households were not included. Any nonresidents present during the study were not eligible to participate; nonresidents were identified by field teams asking, "Is this your usual place of residence?"

Recruitment and consent

A three-stage process was used to invite eligible people to participate. The first stage was liaison and approvals with key local stakeholders, known locally as the municipality secretary and area administrator of the selected communities, and the second was through the village chief and community leaders. Finally, once approval for the study had been granted by the village chief and community leaders, community engagement teams went door-to-door to all households listed on the administrative maps to explain the study, address any concerns and obtain informed consent. Data collection teams then visited households to interview residents and collect nasopharyngeal samples.

Data collection

Data were collected by trained interviewers, most of whom were health professionals or nursing students. The questionnaire collected demographic information, symptom history, health-care seeking behaviour and compliance with prevention measures. Demographic information included sex, age, country of nationality and household size. Symptoms experienced during the previous 2 weeks included cough, fever, headache, aches and pains, runny nose, sore throat, fatigue, loss of smell, nausea, shortness of breath, vomiting, diarrhoea or chest pain; a period of 2 weeks (rather than the 4 weeks since

the beginning of the outbreak) was used to increase the accuracy of participant recall.

Health-care seeking behaviour included SARS-CoV-2 vaccination status and testing history. At the time of the study, public testing for SARS-CoV-2 was only available at a limited number of government-run testing clinics and at Vila Central Hospital. Some workplaces and individuals had privately procured point-of-care SARS-CoV-2 antigen tests; however, these tests were not widely available for purchase in Vanuatu. "Fully vaccinated" was defined as having received two doses of a COVID-19 vaccine that had received World Health Organization (WHO) emergency use listing as of 2 March 2022.[8] The two vaccines available in Vanuatu at this time were BBIBP-CorV (Sinopharm) and AstraZeneca, and 44% of the adult population was considered fully vaccinated on 23 January 2022.[9] Compliance with prevention measures such as mask use, staying home except for essential movements and practising hand hygiene was assessed using a three-point Likert scale (always, sometimes or never).

Trained nursing students collected SARS-CoV-2 nasopharyngeal swabs. Participants reporting a positive SARS-CoV-2 test within the previous 2 weeks chose whether to be retested; when a previous positive SARS-CoV-2 test was reported, this test was searched for in the national surveillance dataset using a name, date of birth and address. Questionnaires were entered into a custom Google form and transferred to Microsoft Excel and Stata for analysis.

Laboratory testing

Specimens collected for this study were transported to Vila Central Hospital in a temperature-controlled vaccine carrier box for laboratory testing. Specimens were tested using the GeneXpert SARS-CoV-2 assay, a reverse transcription PCR (RT-PCR) based assay for the detection of SARS-CoV-2. Meta-analyses have consistently reported high pooled sensitivity (>98%) and pooled specificity (>95%) for this assay.[10,11]

Data analysis

The primary outcomes were rates of SARS-CoV-2 attack (point prevalence) and cumulative attack, underdetection, notification and household secondary attack, all of which were expressed as percentages.

The attack rate was calculated by dividing the number of SARS-CoV-2-positive participants identified through the study by the number of participants who had a specimen collected for SARS-CoV-2 testing. The cumulative attack rate was calculated by dividing the total number of all SARS-CoV-2-positive participants (including participants with verified positive test results from the previous 2 weeks who did not have a specimen collected in the study) by the total number of participants with known test results. The underdetection rate was defined as the proportion of SARS-CoV-2-positive participants who did not self-report having a recent positive SARS-CoV-2 test result or were not identified in the notification database. The undernotification rate was defined as the proportion of SARS-CoV-2-positive participants – both those detected during the study and those who self-reported testing positive in the previous 2 weeks – who had a corresponding notification. The household secondary attack rate was defined as the number of secondary cases within a household with at least one case divided by the total number of participants within that household.

Secondary outcomes included symptoms reported during the previous 4 weeks, the number of participants who had a specimen tested for SARS-CoV-2 since the start of community transmission, the secondary household attack rate in households and associations with SARS-CoV-2 positivity. Univariate associations with SARS-CoV-2 positivity assessed included sex, age, vaccination status and prevention measures adhered to (coughing into elbow, handwashing, mask wearing, maintaining physical distance and staying home). Data were analysed using Microsoft Excel and Stata version 17 (StataCorp 2021; Stata Statistical Software, Release 17; College Station, TX, USA).

Ethical considerations

Ethical approval was obtained from the Chair of the Vanuatu Ministry of Health Research and Ethics Committee. Written consent was obtained from all adults aged over 18 years. For those aged under 18 years, parental or caregiver written consent was obtained. Participants were informed of their results via a phone call and information on isolation was provided as per existing Ministry of Health protocols. Cases were advised of the symptoms of severe disease and to call an ambulance or travel to their closest health facility if they developed severe disease. Strict infection control

procedures were in place during the survey process, including routine testing of fieldwork staff, wearing of appropriate personal protective equipment, outdoor data collection and maintenance of optimal physical distance at all times while collecting specimens.

RESULTS

Participation rate

The cross-sectional survey was conducted over 3 days on 7, 8 and 14 April 2022; data collection was delayed because of the time required to ensure local authority and chief approvals and because of a funeral in one area. In total, 363 people were eligible across the two study sites and 252 people participated (69.4% participation rate). Sixteen empty houses were not included in the denominator.

Description of participants

Most participants were aged 18–34 years (range 0–81 years, average 32 years), and 60% were female (**Table 1**). Over half (66.3%) of adult participants were fully or partially vaccinated. There was no statistical difference between study sites for age or sex, but self-reported receipt of a COVID-19 booster shot and having a previous positive SARS-CoV-2 test differed between the two groups ($P < 0.05$). A total of 84 households participated, with a mean of 7.1 people per house (range 1–13 people); household size did not differ significantly between study sites.

Primary outcomes

A total of 175 participants had a specimen collected in this study (69% of all participants), with 89 having a positive SARS-CoV-2 test result, giving an attack rate of 50.9% (95% confidence interval [CI]: 43.2–58.5%; **Table 2**). The cumulative attack rate was 55.3% (95% CI: 47.9–62.6%), because 104 participants were positive for SARS-CoV-2 infection, including 15 participants who had positive results notified to the NSRERU but who did not have a specimen collected in the study. Among the 104 SARS-CoV-2-positive participants, 15 self-reported having a positive SARS-CoV-2 test before the study, giving an underdetection rate of 85.6% (95% CI: 77.3–91.7%).

An additional 10 participants who reported having received a previous positive SARS-CoV-2 test result did not have a specimen collected in this study. The 23 participants who self-reported a positive SARS-CoV-2 test result before the study had the test conducted at the hospital ($n = 10$), provincial health clinic ($n = 4$), private clinic ($n = 4$), workplace ($n = 3$) or home ($n = 2$, data not shown). Among these 23 participants, a corresponding notification was identified for 15, giving a notification rate of 65.2% (95% CI: 42.7–83.6%).

Over half of the 84 households ($n = 50$, 59.5%) had at least one SARS-CoV-2 case, giving a secondary household attack rate of 47.7% (95% CI: 33.2–62.2%) (**Table 2**).

Secondary outcomes

Most participants who were positive for SARS-CoV-2 reported recent COVID-19 symptoms ($n = 83$, 80.6%, 95% CI: 63.0–98.2%). **Fig. 1** shows the epidemic curve of symptom onset in such participants. A total of 31 participants (12.3%, 95% CI: 8.5–17.0%) reported having a specimen collected for SARS-CoV-2 testing within the previous month. Among participants positive for SARS-CoV-2, 22 (20.1%, 95% CI: 13.6–30.0%) reported having a specimen collected for SARS-CoV-2 testing in the previous month (**Table 2**).

In univariate analysis, the odds of SARS-CoV-2 infection were significantly higher for participants who reported wearing a mask sometimes or never compared to always (odds ratio [OR]: 5.21, 95% CI: 1.47–18.45), or maintaining physical distancing sometimes or never compared to always (OR: 1.83, 95% CI: 1.01–3.36) (**Table 3**).

DISCUSSION

This study is one of the first to publish evidence for the rapid community transmission of SARS-CoV-2 in a Pacific island country. It provides novel evidence that 52% of the study population were SARS-CoV-2-positive within a few weeks of the first community case being identified in Vanuatu. This, and a high secondary attack rate, reflected a short incubation period and serial interval. The underdetection rate of 91.5% suggests that, at the time of the study, about 9 in 10 cases of SARS-CoV-2 had not been diagnosed. Optimistically, the results suggest that over half of detected cases had been notified to the NSRERU.

Table 1. **Description of participants in two administrative areas of Port Vila, Vanuatu, April 2022**

Characteristic	Study site 1		Study site 2		Total		*P*
	n	%	n	%	n	%	
Total	127	50.4	125	49.6	252	100	
Age (years)							
<5 years	6	4.7	10	8.0	16	6.3	>0.05
5–17 years	19	15.0	24	19.2	43	17.1	
18–34 years	53	41.7	35	28.0	88	34.9	
35–54 years	27	21.3	33	26.4	60	23.8	
≥55 years	21	16.5	21	16.8	42	16.7	
Unknown	1	0.8	2	1.6	3	1.2	
Sex							
Male	51	40.2	48	38.4	99	39.3	>0.05
Female	75	59.1	77	61.6	152	60.3	
Unknown	1	0.8	0	0.0	1	0.4	
Vaccination status							
Fully or partially vaccinated	84	66.1	83	66.4	167	66.3	**0.001**
Not vaccinated	43	33.9	40	32.0	83	32.9	
Missing	0	0.0	2	1.6	2	0.8	
Description of households							
Number of households	38	45	46	55	84	100	
Average household size (range)	7.1	(3–13)	7.2	(1–12)	7.1	(1–13)	>0.05

Bold *P* values are statistically significant.

The high rates of underdetection suggest insufficient testing. WHO recommends minimizing the test positivity rate to less than 5% to indicate comprehensive surveillance of suspected cases;[12] however, the test positivity for the study was high at 52%. The reasons for these low testing rates are multifaceted and involve structural, health system and psychosocial factors. Private car ownership is low in Vanuatu, with most of the population using an informal system of privately owned minibuses. Restricted bus services and road barriers prevented movement of people into and within Port Vila; also, loss of income during the COVID-19 pandemic reduced capacity to pay for bus fares. At the time of the study, the main location with free community-based testing was in the grounds of Vila Central Hospital. Government policy at the time was for people testing positive to be immediately taken in buses to a community isolation centre. Anecdotally, there was considerable fear of testing in Port Vila because of this requirement. There was also hesitancy towards testing owing to caregiver and family responsibilities. Further community-based research may be warranted to fully understand barriers to testing, because these are critical for pandemic preparedness and response activities.

The initial community cases in Port Vila were of the BA.1 and BA.2 sublineage of the Omicron variant. Compared with the Delta variant, the Omicron variant had higher transmissibility,[13] a shorter incubation period and serial interval,[21] a higher rate of asymptomatic infection[22] and a lower rate of severe infection.[23] These factors intrinsic to the Omicron variant are likely to have driven the high attack rate and high underdetection rate in Port Vila, in addition to sociocultural and housing factors. Relatively few studies have been conducted to investigate underdetection of the Omicron sublineage; studies conducted in France[14] and South Africa[15] reported similar underdetection rates of 90–95%. The level of underdetection reported here demonstrates the importance of using a range of surveillance data when interpreting case-based surveillance data such as the case-fatality rate or hospitalization rate.

Table 2. **SARS-CoV-2 positivity, underdetection and undernotification among participants from two administrative areas of Port Vila, Vanuatu, April 2022**

Outcome	*n*	%	95% CI
SARS-CoV-2 positivity			
Attack rate (point prevalence)	89	50.9[a]	43.2–58.5
Cumulative attack rate	104[b]	55.3[c]	47.9–62.6
SARS-CoV-2 underdetection			
Number of positive participants that were not detected prior to the study (self-reported and verified)	89	85.6[d]	77.3–91.7
SARS-CoV-2 notification rate			
Participants self-reporting previous positive test result	23	9.2[e]	3.2–15.1
Participants self-reporting previous positive test result with corresponding notification to surveillance unit	15	65.2[f]	49.4–81.0
SARS-CoV-2 testing			
Participants reporting having had a specimen tested for SARS-CoV-2 during the previous month	31	12.3[e]	5.4–19.2
Positive participants reporting having had a specimen tested for SARS-CoV-2 during the previous month	22	20.4[d]	11.5–29.2
Household attack rate			
Number of households with at least one case	50	59.5[f]	44.4–74.6
Secondary household attack rate	–	47.7[g]	34.2–61.2

CI: confidence interval; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

[a] Denominator includes all 175 participants who had a specimen collected in the study.

[b] Numerator includes 89 participants detected in this study plus 15 participants with verified previous infection.

[c] Denominator includes 188 participants with known SARS-CoV-2 test result, excluding those with no testing history.

[d] Denominator includes all 104 SARS-CoV-2-positive participants.

[e] Denominator includes all 252 participants.

[f] Denominator includes all 84 households.

[g] Rate is only calculated for 50 households with at least one case.

Fig. 1. **Epidemic curve of symptom onset of SARS-CoV-2-positive participants in two administrative areas of Port Vila, Vanuatu, March–April 2022**

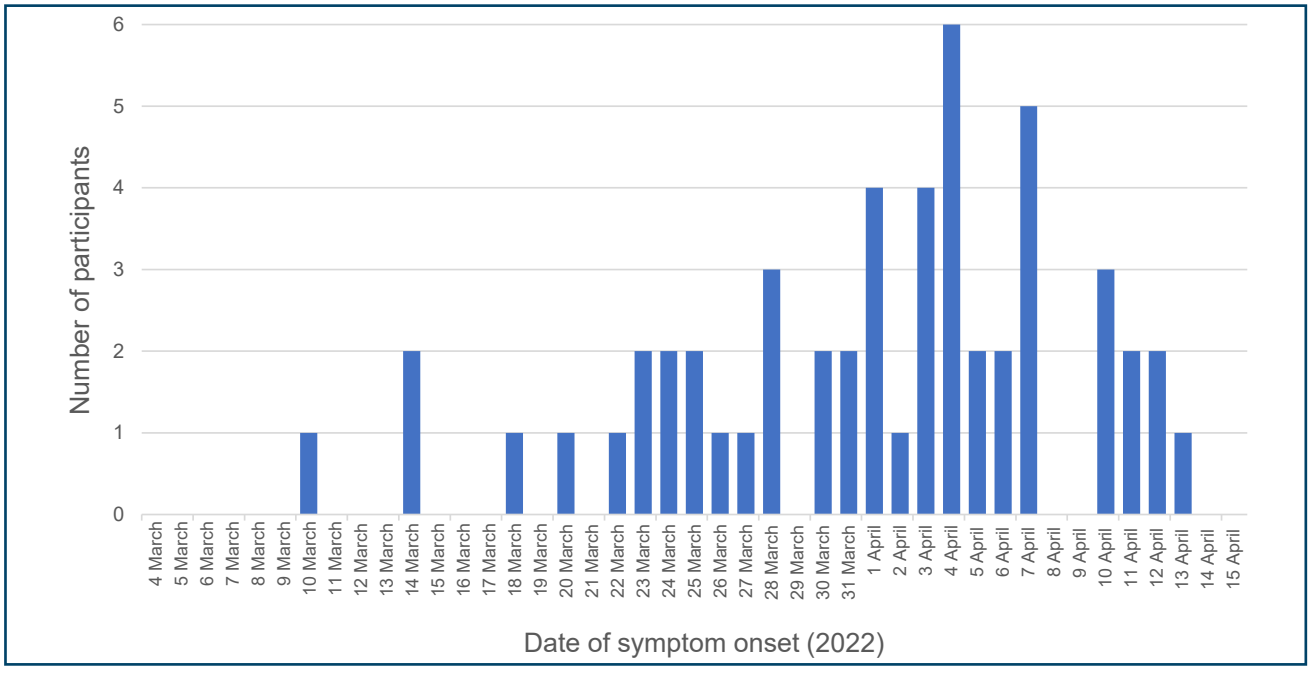

Table 3. **Associations with SARS-CoV-2 positivity in two administrative areas of Port Vila, Vanuatu, April 2022**

Predictors of SARS-CoV-2 positivity	Odds ratio	*P*	95% CI
Demographics			
Male (ref. female)	0.96	>0.05	0.53–1.72
Age (ref. each additional year of age)	0.99	>0.05	0.98–1.01
Not vaccinated (ref. any vaccination)	1.22	>0.05	0.67–2.27
Prevention measures			
Coughed into elbow sometimes or never (ref. Always)	1.72	0.07	0.96–3.07
Handwashing sometimes or never (ref. Always)	1.77	0.101	0.89–3.53
Wore a mask sometimes or never (ref. Always)	5.21	**<0.01**	1.47–18.45
Maintained physical distancing sometimes or never (ref. Always)	1.83	**<0.05**	1.01–3.36
Stayed home except for essential movements (ref. Always)	1.08	0.45	0.46–2.55

CI: confidence interval; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

Bold *P* values are statistically significant.

The findings suggest that health-care workers were diligent in notification requirements during the study period. Until 2022, Vanuatu had a paper-based notification system whereby medical officers submitted notifications to surveillance officers via phone, email or in person. An informal assessment among health-care workers in 2021 revealed poor knowledge about notification requirements and processes for COVID-19. Therefore, the NSRERU conducted activities such as rapid development and roll-out of an electronic notification form and brief training of health-care workers on notification processes to undertake once a case was identified. The notification rate reported here is a positive reflection of these surveillance-strengthening activities; however, further work is required to ensure notification of all notifiable diseases beyond SARS-CoV-2, to facilitate case investigation and response.

The reported household secondary attack rate of 48% was high compared with similar reports internationally; an updated systematic review in March 2022 reported a pooled household secondary attack rate of 43% for the Omicron variant.[16] The secondary household attack rate reported is likely to underestimate the true household attack rate because some households may have been experiencing within-household transmission at the time of the study; therefore, some secondary cases may not yet have occurred. Household attack rates in other Pacific island countries are not known but are expected to be similarly high owing to a range of social, cultural and environmental factors (e.g. large household sizes due to extended families sharing housing, cooking, water and sanitation facilities across many families, low health literacy and higher density housing).[17]

Our analysis suggests that consistent mask wearing and physical distancing were protective against infection, and that mask wearing was the most protective public health and social measure (PHSM) identified. This is consistent with international evidence[18,19] and is the first evidence for effectiveness of PHSMs in community settings based in a Pacific island country. The Ministry of Health messaging of wearing a mask and physical distancing was therefore warranted and successful in Vanuatu, and should be retained for future respiratory virus outbreaks.

The findings of this study may be considered generalizable across Port Vila and to Vanuatu's second small urban centre of Luganville in the north of the country, which had similar housing, commercial and government hubs, transportation and road access and implementation of COVID-19 containment policies such as stay-at-home orders. The age and sex structure of the sample was broadly similar to that reported for Port Vila in the 2020 census, although the average household size reported here was higher (7.1 compared with 4.7 people per household).[20] Similar definitions of a household were used in this study and the 2020 Vanuatu census, and thus the higher household size reported here may be due to households temporarily living together during the stay-at-home order period. The results may also be considered generalizable to small urban centres in other Pacific island countries, but are less generalizable to rural areas and small islands that do not have government or commercial hubs or road access, and where communication on containment policies were not easily delivered owing to limited communication infrastructure. In these settings, transmission and secondary attack rates may have been greater; however, there are insufficient data to demonstrate this.

Some limitations should be considered. Misclassification of true cases not detected due to insufficient viral load may have occurred due to older infection or new infection; however, RT-PCR has high sensitivity with a long period of detection (up to 90 days).[11] Participants who reported having a positive test but for whom a notification was not identified may be underestimated owing to the common practice of both formal names and nicknames in Vanuatu. We attempted to minimize this bias by using a recently introduced national identification number; however, many participants did not report their number in interviews. Recent intra-household transmission may not have been captured, underestimating household secondary attack rates. In addition, biases may have been associated with self-reported health-care seeking behaviours and recall; however, the interviewers were trained to ensure accurate recall and reporting. Usual residents may have been excluded owing to not being home on the day of fieldwork; however, this is anticipated to be low because of the stay-at-home orders in effect and the use of road blockages. Finally, and as described above, the results cannot be considered generalizable to the whole of Vanuatu.

Despite these limitations, this study provides important evidence for the rapid spread of novel respiratory diseases in Vanuatu and the findings are potentially useful for pandemic preparedness and response across the Pacific, particularly for small urban areas. Surveillance systems are fundamentally important to the monitoring and control of infectious diseases; however, a high level of underdetection and undernotification may be expected and should be anticipated when planning for future outbreak detection and control activities.

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Conflicts of interest

CvG holds an Early Career Research Fellowship, funded by the Australian National Health and Medical Research Council. The other authors have no conflicts of interest to declare.

Ethics approval

Ethical approval was obtained from the Chair of the Vanuatu Ministry of Health Research and Ethics Committee.

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Feral pigs as a reservoir for zoonotic and transboundary diseases in the Western Pacific Region

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Over the last century, the global human population has more than quadrupled, leading to anthropogenic and environmental impacts that have disrupted the interactions between pathogens, humans and animal hosts. More than 60% of emerging infectious diseases affecting humans are considered zoonotic, with >70% of these originating from wild animals.[1]

Feral pigs (*Sus scrofa*) are one of the most prevalent invasive species worldwide, with an estimated population size of over half a billion.[2] Feral pigs are regarded as a "triple threat pest" due to: 1) their propensity to be reservoirs for important transboundary diseases; 2) the serious threats they pose to native flora and fauna; and 3) the massive impacts they have on agricultural production and practices.[3] The rapid reproduction rate of feral pigs, their omnivorous, flexible and opportunistic diet, the absence of predators in many areas, and their ability to thrive in anthropogenic landscapes are all factors driving ongoing expansion of their geographic range.[4] Human activities are key to the expansion of the feral pig population, as anthropogenic modifications to the ecosystems that support feral pigs can boost population densities over the natural carrying capacity.

To date, limited research or monitoring activities have been conducted to determine the risk that feral pigs pose as reservoirs for zoonotic or veterinary pathogens. As the number of feral pigs increases, they encroach into human habitats in search of feed, thus amplifying the risk of zoonotic disease transmission.[4] Feral pig hunters, farmers, slaughterhouse workers and animal health workers are at increased risk of contracting zoonotic diseases associated with feral pigs. In a study from northern Australia, 90% of brucellosis cases were reported in feral pig hunters.[5] More broadly in the Western Pacific Region, other emerging threats associated with feral pigs include Japanese encephalitis (JE), African swine fever (ASF), foot and mouth disease (FMD), influenza A and Nipah viruses. In addition, feral pigs may act as reservoirs for endemic pathogens with possible impacts on human and livestock health such as hepatitis E virus, *Coxiella burnetii* (Q fever), *Brucella suis* (brucellosis), *Streptococcus suis* and *Leptospira spp.* (leptospirosis). In the Western Pacific Region, feral pigs are widely distributed and are speculated to play a key role in the maintenance and spread of several pathogens of international concern. Other pig species are also found in the Western Pacific (such as the threatened *Sus barbatus* and *Porcula salvania*), but not much is known about the threats to conservation due to the diseases carried by feral pigs.

The recent emergence of JE in mainland Australia (February 2022) has highlighted the risk that once the virus has been introduced, feral pigs may act as an amplifier and/or reservoir host for the establishment of the virus in new geographic areas.[6] JE is a complex zoonotic transboundary arboviral infection involving both vertebrates (pigs, birds) as reservoirs/amplifying hosts and arthropod vectors (*Culex* mosquitoes).[7] Recent modelling studies have highlighted the role of feral and domestic pigs in the epizootic and epidemic risk of JE in the natural cycle of transmission in Australia.[6] Studies in other settings have reported pig-to-pig transmission (non-

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vector transmission), mediated by the high replication of the JE virus in swine tonsils, allowing oronasal spread between animals, implying higher risks of enzootic establishment associated with pig populations.[8]

ASF is an arboviral haemorrhagic disease caused by the ASF virus, which can be transmitted through various mechanisms including *Ornithodoros* ticks, oronasal contact, swill feeding and contaminated fomites. The World Organisation for Animal Health designated ASF a notifiable disease due to its globally devastating economic impacts on the pig industry following the rapid expansion of the disease across eastern Europe and Asia from 2018.[9] To date, ASF has spread to over 19 countries in the Western Pacific Region. Feral pigs may be infected with ASF due to spillover from domestic piggeries, as observed in some parts of Asia and Europe. In Romania, for example, the proximity of feral pigs to domestic piggeries has been documented as the source of ASF. This suggests dual transmission between domestic and feral pig populations, leading to further amplification and geographic spread of the virus. The abundance, distribution and density of feral pigs are considered major factors driving the introduction of ASF into naïve areas.

FMD is caused by the FMD virus, a highly contagious transboundary viral disease of artiodactyls, with severe epidemics in susceptible animals affecting the socioeconomic livelihoods of affected communities through trade embargoes of livestock and their products. FMD is enzootic in Africa, Asia, the Middle East and South America. *In vivo* studies have demonstrated the persistence of the virus in the tonsils of feral pigs for over 30 days post-inoculation, which is characterized by the presence of vesicles in the oral cavity, interdigital spaces, and coronary bands of the hoof and udder.[10] Illegal trading and movement of animals from one place to another is considered a high-risk activity associated with the introduction of FMD into an area, as is swill feeding. Countries with large feral pig populations may have difficulty eradicating the disease, as it can circulate cryptically and may become endemic. Many countries in the Western Pacific Region that are FMD-free have instituted strict import policies and biosecurity measures at seaports and airports and have set up surveillance in livestock populations to prevent (or mitigate) possible incursions.

We suggest the establishment of surveillance programmes for monitoring the circulation of pathogens of zoonotic and veterinary concern amongst feral pigs, in addition to the expansion on the use of sentinel domestic pig herds as a system for the early detection of diseases that could potentially spill over to humans and other animals of economic importance. This would entail a joint regional One Health collaborative effort by all stakeholders from diverse fields, including risk communicators, modellers, ecologists, biosecurity experts, epidemiologists, virologists and anthropologists. Feral pig ethology should also be further studied to advance programmes for effective population control.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

Ethics approval was not required as no original research was conducted for this report.

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Delays in health seeking, diagnosis and treatment for tuberculosis patients in Mongolia: an analysis of surveillance data, 2018–2021

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Early diagnosis and treatment of infectious tuberculosis (TB) is essential to the attainment of global targets specified in the End TB Strategy. Using case-based TB surveillance data, we analysed delays in health seeking, diagnosis and treatment among TB patients in Mongolia from 2018 to 2021. We calculated the median and interquartile range (IQR) for "diagnostic delay", defined as the time from symptom onset to diagnosis, subdivided into "health-seeking delay" (time from symptom onset to first visit to a health facility) and "health facility diagnostic delay" (time from first health facility visit to diagnosis), and for "treatment delay", defined as the time from diagnosis to start of treatment. We also calculated "total delay", defined as the time from symptom onset to treatment start. Based on data for 13 968 registered TB patients, the median total delay was estimated to be 37 days (IQR, 19–76). This was mostly due to health-seeking delay (median, 23 days; IQR, 8–53); in contrast, health facility diagnostic delay and treatment delay were relatively short (median, 1 day; IQR, 0–7; median, 1 day; IQR, 0–7, respectively). In 2021, health-seeking delay did not differ significantly between men and women but was shorter in children than in adults and shorter in clinically diagnosed than in bacteriologically confirmed TB cases. Health-seeking delay was longest in the East region (median, 44.5 days; IQR, 20–87) and shortest in Ulaanbaatar (median, 9; IQR, 14–64). TB treatment delay was similar across sexes, age groups and types of TB diagnosis but slightly longer among retreated cases and people living in Ulaanbaatar. Efforts to reduce TB transmission in Mongolia should prioritize decreasing delays in health seeking.

Early diagnosis and prompt treatment of infectious tuberculosis (TB) cases reduce TB transmission and incidence and thus are crucial components of the End TB Strategy.[1] However, multiple barriers to early diagnosis and treatment exist and delays are common. Timely diagnosis requires individuals to recognize the symptoms of the disease and seek treatment. As TB symptoms such as cough and fever are common to other minor illnesses, individuals may delay seeking care until their symptoms become persistent or they develop additional symptoms (e.g. weight loss, night sweats). Diagnosing TB early is especially challenging in people with subclinical disease, who represent a potentially important subgroup to target, given recent evidence suggesting that half of bacteriologically confirmed TB cases are subclinical.[2]

People with TB symptoms often visit multiple informal and formal health services before a TB diagnosis is established. If a bacteriological test of a sputum specimen is positive, the case is confirmed, but if it is negative or the person cannot produce sputum, the diagnostic process can take longer because either a repeat sputum test or other evidence is required to establish a diagnosis. Limited access to health facilities and low levels of health knowledge and literacy are additional factors that can delay health seeking and diagnosis.[3]

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Once a diagnosis has been made, prompt treatment is necessary to cure the disease and reduce transmission to others. Treatment initiation delays can arise because of poor health system organization, inefficient supply chains and lack of human resources. A global systematic review of studies found considerable heterogeneity in patient and health system delays for TB,[4] suggesting that time delays are setting-specific.

At 452 cases per 100 000 population, Mongolia has one of the highest TB incidence rates in the world.[5] Surveillance is conducted by the Mongolia National TB Programme and has established that in 2015–2019, the TB burden was heterogeneously distributed, with the country's capital city, Ulaanbaatar, notifying more than half of all cases.[6] High notification rates among younger age groups suggest recent transmission, emphasizing the need to expand and accelerate case detection.[6] Previous studies have suggested that there is scope for improving TB diagnosis and treatment times across the country. A study in Ulaanbaatar conducted in 1996 reported that health-seeking delays averaged 29 days and health facility diagnostic delays averaged 35 days.[7] A later study, based on national data from 2016 and 2017, found that only 34% of patients were diagnosed and treated within 30 days of symptom onset.[8] Recent expansion of Xpert MTB/RIF testing nationwide in 2021 is expected to enhance case detection and reduce diagnostic delays.

In this report, we use national surveillance data for 2018–2021 to describe the time lapse between TB symptom onset and diagnosis, and between diagnosis and treatment initiation, in Mongolia. We also report diagnostic and treatment delays at the subnational level for 2021. Subnational analysis of diagnostic and treatment delays is needed to guide the planning of effective interventions tailored to local dynamics, as well as to monitor progress towards national and End TB Strategy targets and milestones.

METHODS

Description of the surveillance system

In Mongolia, details of all registered TB cases are recorded on a patient treatment card by health-care workers at all health facilities that offer TB care. The card contains information such as the date of symptom onset (as reported by the patient), the date of diagnosis (defined as the date of bacteriological confirmation or the date on which a physician established a clinical–radiological TB diagnosis), and the date of TB treatment initiation. Most data from the patient treatment card are entered by health-care workers into TUBIS, an electronic case-based TB surveillance information system. The first version of TUBIS was implemented nationwide in 2012 and has since undergone significant development. Data quality is reviewed in quarterly meetings; oversight is provided by a data manager dedicated to TUBIS. Alongside TUBIS, the National TB Programme continues to operate its traditional aggregated data system, which provides quarterly reports on all notified cases of TB, from the basic management unit upwards. Over 95% of the aggregate data system notifications are also included in TUBIS. Patients treated for TB at the public hospital are not included in TUBIS.

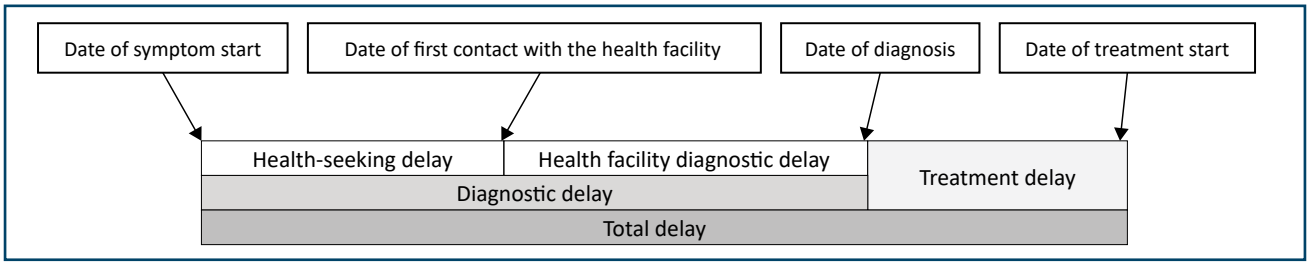
Analysis of surveillance data

For drug-susceptible TB cases captured by TUBIS from 2018 to 2021, we calculated the "diagnostic delay" (the time from symptom onset to diagnosis), the "treatment delay" (the time from diagnosis to treatment), and the "total delay" (the overall time from symptom onset to treatment). Diagnostic delay was further divided into "health-seeking delay", defined as the time from symptom onset to first contact with a health facility, and "health facility diagnostic delay", defined as the time from first health facility visit to diagnosis (**Fig. 1**).

In the absence of standard definitions of TB symptoms, specification of the time of symptom onset relied on inquiry by health staff. For asymptomatic cases identified by active case finding (i.e. through contact tracing or screening), the date of the screening test (sputum sample or chest X-ray) was used as the date of symptom onset. The date of diagnosis was the date of a positive bacteriological result or the date of a clinical or radiological diagnosis. Thus, for some cases the date of symptom onset and the date of diagnosis were the same.

Median and interquartile range (IQR) were calculated for each type of delay (in number of days) for the study period overall and for each of the four calendar years, 2018–2021. The statistical significance of yearly trends in each delay type was examined using the Mann–Kendall test. For 2021 cases, median delays were disaggregated by demographic (age, sex, place of

Fig. 1. **Definition of delays related to tuberculosis health seeking, diagnosis and treatment used in the study**



residence) and clinical characteristics (type of diagnosis, type of case [new, relapse, other retreatment]). Mann–Whitney U and Kruskal–Wallis tests were used to compare differences in delays between groups of patients defined by these characteristics. Statistical significance was defined as $P < 0.05$.

Multivariable linear regression models were used to determine which patient characteristics were independently associated with longer diagnostic and treatment delays using a backwards stepwise strategy, starting with a model that included all the variables that were significant in univariate analysis. Models were compared using the F test. Cases with implausible dates were excluded, i.e. cases in which the diagnosis date was before the time of symptom onset and those in which the treatment date was before the date of diagnosis. There were no records with missing dates. Data analysis was performed using STATA 17/SE software (Stata Corp, College Station, TX, USA).

RESULTS

After excluding 1779 (11.3%) case registrations with implausible dates (1634 for health-seeking delay and 145 for treatment delay), case-based data for 13 968 registered TB patients in Mongolia from 2018 to 2021 were analysed. There were 2718 registered TB cases in 2021, which represented 90.4% of all notified TB cases for that year.

Overall, the median (IQR) time lapse between symptom onset and initiation of treatment (total delay) was 37 (19–76) days. The median total diagnostic delay was 31 (14–66) days, whereas the median treatment delay was just 1 (0–7) day. Health-seeking delays (median, 23; IQR, 8–53) represented the greater contributor to diagnostic delays. There was no significant difference across the years in health-seeking delay ($P = 0.89$), nor was there any evidence of a trend in the total diagnostic delay ($P = 0.12$) (**Table 1**). However, there were significant upward trends over time in health facility diagnostic delay ($P < 0.001$), in treatment delay ($P = 0.001$) and in total delay ($P = 0.009$). The upward trend was most apparent in 2020 onwards and likely related to the impact of the COVID-19 pandemic.

In 2021, the total diagnostic delay was <15 days in 35.7% of TB cases, 15–30 days in 23.4% of cases, 31–60 days in 17.1% of cases and >60 days in 23.1% of cases. Total delay was <15 days in 15.9% of TB cases; around a quarter of cases experienced total delays of 15–30 days (24.5%), another quarter had delays of 31–60 days (24.8%) and 34.8% of cases experienced delays of >60 days (**Table 1**).

Diagnostic delay

Ulaanbaatar had the shortest median total diagnostic delay (29 days), followed by the West region (33 days) (**Table 2**). Both the East and Khangai regions had diagnostic delays higher than the national average (44.5, 41.5 and 31 days, respectively). There was heterogeneity in diagnostic delay within regions (**Fig. 2**). Fifteen provinces (five in Central, four in Khangai, three in East and three in West) had median diagnostic delays of 40 or more days from symptom onset.

In the multivariable analysis of health-seeking delays, both age and place of residence were significantly associated with time to first visit to a health-care facility; sex was not. Children (aged 0–4 and 5–14 years) had shorter delays than adults aged 25–34 years ($P < 0.001$ for both). Patients with bacteriologically confirmed pulmonary TB had a longer health-seeking delay compared with patients with clinically or radiologically diagnosed TB ($P < 0.001$); patients classified as "other retreatment" had longer delays than those classified as "new" cases ($P < 0.001$). All regions had longer median health-seeking delays than Ulaanbaatar, but

Table 1. **Tuberculosis diagnostic and treatment delays, Mongolia, 2018–2021**

Year	Delay[a] (days)					Proportion with total delay >60 days (%)
	Health seeking	Health facility diagnostic	Total diagnostic	Treatment	Total	
Overall	23 (8–53)	1 (0–7)	31 (14–66)	1 (0–7)	37 (19–76)	32.6
2018	22 (8-–54)	1 (0–7)	30 (14–68)	1 (0–6)	36 (18–76)	32.2
2019	23 (9–52)	1 (0–8)	31 (14–64)	1 (0–7)	37 (19–74)	32.1
2020	23 (8–51)	2 (0–8)	31 (14–63)	2 (0–7)	38 (19–74)	31.9
2021	24 (9–56)	2 (0–8)	31 (15–69)	1 (0–7)	38 (21–82)	34.8
***P* test for annual trend[b]**	0.89	<0.001	0.12	0.001	0.009	

[a] Values are median (interquartile range) unless otherwise indicated.

[b] *P* values were calculated using the Mann–Kendall test.

Fig. 2. **Median tuberculosis diagnostic delay (days) by province, Mongolia, 2021**

UB: Ulaanbaatar.

this difference was only significant in the multivariable analysis for the East and Khangai regions (P = 0.024 and 0.013, respectively). Similar patterns were observed in the case of the multivariable analysis of total diagnostic delays.

Treatment delay

Treatment delay did not differ significantly by sex or type of TB diagnosis (**Table 3**) and was less heterogeneous across provinces than was diagnostic delay (**Fig. 3**). Four provinces had median treatment delays of 3 or more days (Bayan-Ulgii, Selenge, Tuv and Zavkhan). The multivariable analysis of treatment delays suggested that children and young adults were more likely to start treatment sooner than older adults (P = 0.025). In addition, the time between diagnosis and treatment was significantly longer among "relapsed" cases (P = 0.016) and "other retreatment" cases (P < 0.001) than in "new" cases. Compared with Ulaanbaatar, treatment delays were significantly shorter in the East region (P = 0.012) and in the Khangai region (P = 0.049).

Table 2. **Tuberculosis diagnostic delay by patient characteristics and place of residence, Mongolia, 2021 (*N* = 2718)**

Characteristic[a]	Health-seeking delay (days), median (IQR)	*P*[b]	Health facility diagnostic delay (days), median (IQR)	*P*[b]	Diagnostic delay (days), median (IQR)	*P*[b]
Total	24 (9–56)		2 (0–8)		31 (15–69)	
Sex						
Female (*n* = 1161)	22 (7–55)	**0.008**	2 (0–9)	0.251	31 (14–67)	0.11
Male (*n* = 1557)	25 (10–56)		2 (0–7)		31 (17–70)	
Age group						
0–4 (*n* = 70)	4.5 (1–20)	**0.0001**	1 (0–7)	**0.048**	11.5 (3–26)	**0.0001**
5–14 (*n* = 223)	10 (3–23)		2 (0–8)		16 (6–31)	
15–24 (*n* = 512)	19 (7–41.5)		2 (0–7)		26 (13–55)	
25–34 (*n* = 655)	27 (10–62)		2 (0–7)		34 (17–79)	
35–44 (*n* = 442)	30 (10–63)		2 (0–9)		35 (20–78)	
45–54 (*n* = 411)	28 (11–68)		2 (0–7)		39 (19–86)	
55–64 (*n* = 270)	25 (11–66)		1 (0–8)		35 (20–90)	
≥65 (*n* = 133)	28 (11–53)		4 (0–14)		39 (22–77)	
Type of diagnosis						
Bacteriologically confirmed pulmonary TB (*n* = 1453)	28 (11–61)		2 (0–6)		35 (18–73)	
Clinically diagnosed pulmonary TB (*n* = 317)	18 (6–50)	**0.0001**	2 (0–12)	0.085	27 (12–69)	**0.0001**
Extrapulmonary (*n* = 946)	19 (6–46)		2.5 (0–11)		28 (14–59)	
Patient type						
New (*n* = 30)	23 (8–53)		2 (0–8)		30 (15–67)	
Relapse (*n* = 332)	25.5 (10–57)	**0.0003**	2 (0–9.5)	0.815	33 (18–64)	**0.0001**
Other retreatment (*n* = 114)	37 (15–92)		2 (0–16.5)		60.5 (31.5–180.5)	
Place of residence						
Ulaanbaatar (*n* = 1829)	22 (8–52)	**0.0004**	2 (0–8)	0.152	29 (14–64)	**0.0001**
Khangai	28 (10–65)		2 (0–10.5)		41.5 (18–91)	
Arkhangai (*n* = 48)	25 (7.5–42)		0 (0–10)		27 (12–60.5)	
Bayankhongor (*n* = 36)	31.5 (14–74.5)		2 (2–10.5)		42 (24.5–88)	
Bulgan (*n* = 31)	57 (18–153)		4 (0–15)		66 (26–164)	
Khuvsgul (*n* = 59)	13 (4–42)		8 (2–37)		49 (25.5–110)	
Orkhon (*n* = 50)	31 (10–58)		1 (0–2)		18 (31.5–66)	
Uvurkhangai (*n* = 32)	51.5 (25–115)		1 (0–4.5)		61.5 (25.5–115.5)	
Central	29 (8–54)		2 (0–7.5)		35 (14.5–72.5)	
Darkhan-Uul (*n* = 96)	21.5 (7–47.5)		1 (0–4.5)		30.5 (14–63)	
Dornogovi (*n* = 44)	29.5 (7–57.5)		1.5 (1–7.5)		32.5 (11.5–66.5)	
Dundgovi (*n* = 26)	37.5 (11–83)		5.5 (3–20)		49 (36–101)	
Govisumber (*n* = 10)	29.5 (0–120)		1.5 (0–11)		61 (11–121)	
Selenge (*n* = 85)	22 (5–46)		2 (0–9)		31 (12–63)	
Tuv (*n* = 62)	35.5 (15–59)		0 (0–1)		40.5 (20–65)	
Umnugobi (*n* = 21)	31 (9–43)		8 (3–21)		38 (22–74)	
East	30 (13–75)		1 (0–8)		44.5 20–87	
Dornod (*n* = 64)	24.5 (9–55)		3.5 (1–16.5)		41 (19–86)	
Khentii (*n* = 74)	28.5 (17–72)		1 (0–15)		38 (19–80)	
Sukhbaatar (*n* = 48)	50 (16–94.5)		0 (0–1.5)		58.5 (24.5–105.5)	
West	27 (9–52)		4 (1–8)		33 (14–77)	
Bayan-Ulgii (*n* = 33)	24 (7–71)		3 (0–13)		33 (16–85)	
Gobi-Altai (*n* = 4)	47 (36–79)		0.5 (0–3)		47.5 (39–79)	
Khovd (*n* = 28)	42 (17–76.5)		7 (3–15)		49 (25.5–110)	
Uvs (*n* = 22)	19 (10–38)		1 (0–4)		22 (10–40)	
Zavkhan (*n* = 12)	8 (5–17.5)		4 (1.5–8)		16 (11–26.5)	

IQR: interquartile range.

[a] The Mann–Whitney U test was used to compare median delays between males and females; the Kruskal–Wallis test was used to compare median delays between groups of people categorized by age group, type of diagnosis, patient type and place of residence.

[b] Significant *P* values (<0.05) are in bold.

Table 3. **Tuberculosis treatment and total delays by patient characteristics and place of residence, Mongolia, 2021 (*N* = 2718)**

Characteristic[a]	Treatment delay (days), median (IQR)	*P*[b]	Total delay (days), median (IQR)	*P*[b]
Total	1 (0–7)		38 (21–82)	
Sex				
Female (*n* = 1161)	1 (0–7)	0.358	39 (19–79)	0.187
Male (*n* = 1557)	1 (0–7)		38 (22–85)	
Age group				
0–4 (*n* = 70)	1 (0–3)		15.5 (5–27)	
5–14 (*n* = 223)	1 (0–7)		24 (12–44)	
15–24 (*n* = 512)	1 (0–7)		32 (17–65)	
25–34 (*n* = 655)	2 (0–8)	**0.025**	45 (23–90)	**0.0001**
35–44 (*n* = 442)	2 (0–7)		45 (23–90)	
45–54 (*n* = 411)	2 (0–7)		50 (24–93)	
55–64 (*n* = 270)	2 (0–8)		46.5 (26–101)	
≥65 (*n* = 133)	1 (0–5)		48 (26–82)	
Type of diagnosis				
Bacteriologically confirmed pulmonary TB (*n* = 1453)	1 (0–6)		42 (24–86)	
Clinically diagnosed pulmonary TB (*n* = 946)	1 (0–7)	0.757	34 (18–82)	**0.0001**
Extrapulmonary (*n* = 317)	1 (0–8)		33 (18–69)	
Patient type				
New (*n* = 30)	1 (0–7)		36 (20–78)	
Relapse (*n* = 332)	2 (0–8)	**0.0001**	45 (26–78.5)	**0.0001**
Other retreatment (*n* = 114)	4 (0–22)		123.5 (39.5–222.5)	
Place of residence				
Ulaanbaatar (*n* = 1829)	2 (0–8)	**0.0001**	36 (21–78)	0.054
Khangai	1 (0–3)		46 (21–100)	
Arkhangai (*n* = 48)	0.5 (0–8.5)		36 (20.5–75.5)	
Bayankhongor (*n* = 36)	1 (0–7)		42.5 (24.5–93.5)	
Bulgan (*n* = 31)	0 (0–6)		103 (28–164)	
Khuvsgul (*n* = 59)	1 (0–3)		52 (17–100)	
Orkhon (*n* = 50)	1 (0–2)		39.5 (21–67)	
Uvurkhangai (*n* = 32)	0 (0–0)		67 (25.5–140)	
Central	1 (0–5)		42 (20–82)	
Darkhan-Uul (*n* = 96)	1 (0–2)		35 (17–72)	
Dornogovi (*n* = 44)	1 (0–2)		41 (16.5–73)	
Dundgovi (*n* = 26)	0 (0–4)		59 (40–136)	
Govisumber (*n* = 10)	1 (1–7)		63 (19–122)	
Selenge (*n* = 85)	3 (1–7)		34 (18–76)	
Tuv (*n* = 62)	3 (0–13)		50.5 (31–101)	
Umnugobi (*n* = 21)	2 (1–4)		46 (24–75)	
East	1 (0–3)		48.5 (23–93)	
Dornod (*n* = 64)	1 (0–3)		44 (19–90)	
Khentii (*n* = 74)	0.5 (0–5)		41.5 (27–88)	
Sukhbaatar (*n* = 48)	0 (0–1.5)		65 (28–111)	
West	1 (0–5)		43 (19–90)	
Bayan-Ulgii (*n* = 33)	3 (1–23)		54 (21–104)	
Gobi-Altai (*n* = 4)	2 (0.5–90)		79.5 (49–159.5)	
Khovd (*n* = 28)	0 (0–0)		49 (25.5–110)	
Uvs (*n* = 22)	1 (0–1)		29 (12–44)	
Zavkhan (*n* = 12)	6.5 (2.5–12)		23.5 (19.5–54)	

IQR: interquartile range.

[a] The Mann–Whitney U test was used to compare median delays between males and females; the Kruskal–Wallis test was used to compare median delays between groups of people categorized by age group, type of diagnosis, patient type and place of residence.

[b] Significant *P* values (<0.05) are in bold.

Fig. 3. **Median tuberculosis treatment delay (days) by province, Mongolia, 2021**

UB: Ulaanbaatar.

DISCUSSION

Our analysis revealed that during the period of 2018–2021, the average time from symptom onset to treatment initiation for TB in Mongolia was 37 days. This was compounded mostly by diagnostic delay (median, 31 days), which in turn was mainly caused by health-seeking delay (median, 23 days). Health facility diagnostic delays contributed little to the overall diagnostic delay (median, 1 day). In 2021, time to diagnosis was shorter among children, but bacteriological diagnoses took longer than clinical and radiological diagnoses. Treatment delays were generally short (median, 1 day) but significantly longer among retreated TB cases. The East and Khangai regions had longer diagnostic delays but shorter treatment delays relative to Ulaanbaatar.

Our finding that delay in health seeking was the greatest contributor to the total delay is consistent with other studies, both global systematic reviews[4,9,10] and individual studies conducted in England,[11] Ethiopia[12] and India.[3] Our results are also similar to those obtained by a previous analysis of data from Mongolia for 2016–2017, which reported an average health-seeking delay of 28 days and an average health system delay (defined as health facility diagnostic delay plus treatment delay) of 7 days.[8] In addition, the proportion of TB patients with a health-seeking delay of more than 2 months (60 days) was similar to that reported in a 10-year analysis conducted in Japan (18% vs 21%, respectively).[13]

We attribute the shorter health-seeking delay that we observed among children to the fact that paediatric TB is frequently diagnosed through investigation of contacts and active case finding. We also found that among pulmonary cases, those that were clinically or radiologically diagnosed had shorter health-seeking delays than those that were bacteriologically diagnosed, suggesting that the former tend to present at an earlier stage of the disease; conversely, people whose TB disease takes longer to develop and who eventually become a bacteriologically confirmed case are more likely to delay seeking health care. This result is similar to that reported for Mongolia in 2016–2017,[8] and suggests that introduction of the sensitive rapid Xpert MTB/RIF test has yet to make a significant impact on both the number of bacteriologically confirmed cases and the length of diagnostic delays.

Our findings of similar delays in men and women, even after controlling for other variables, are consistent with a global systematic review that also found no differences by sex.[4] Other studies have identified low literacy[12,14,15] and first seeking care at informal providers[4,15] as factors that increase health-seeking delays, but we were not able to investigate these factors in our study.

We found that both health-seeking delays and treatment delays differed by geographical location. Generally speaking, health-seeking delays were shorter and treatment delays were longer in Ulaanbaatar compared with the rest of the country; these patterns were also evident in the earlier analysis of Mongolian surveillance data for 2016–2017.[8] It is likely that the shorter health-seeking delays in Ulaanbaatar, which were shorter in 2021 than in 1996 (22 and 29 days, respectively[7]), relate to easier access to health facilities and higher literacy rates in the capital. Such spatial heterogeneity is common in many countries regardless of income level, and multiple studies have shown that living in a rural area is associated with longer health-seeking delays.[4,12,16] Increasing access to health care through initiatives that deliver more patient-centred services (e.g. use of mobile teams in rural areas, adopting clinic opening hours that match patients' preferences) has proven to reduce delays in health seeking.[17]

TB treatment delay in Mongolia was relatively short and similar to that reported by a study conducted in India.[3] Treatment delay was longer among relapsed and retreated cases, which may be explained by the need to first rule out drug resistance. The small but nevertheless significant longer treatment delay observed in Ulaanbaatar in 2021 compared with most regions and provinces may be a consequence of greater caseloads and more complex clinical and/or administrative steps and processes, resulting in longer wait times for treatment initiation. Outside the capital, where clinics are less busy, these might be completed more quickly. Only four provinces had median treatment delays longer than 2 days (Zavkhan, 6.5 days; Bayan-Ulgii, Selenge and Tuv, 3 days).

Use of routinely collected case-based data enabled us to analyse delays in TB diagnosis and treatment at both the national and subnational level. However, our study was limited by the lack of standardized definitions of TB symptoms and absence of data on a number of factors that are known to affect diagnostic delay, such as socioeconomic status and geographical access to health facilities. In addition, as data on treatment outcomes were rarely entered into TUBIS, we were unable to assess the impact of diagnostic and treatment delays on treatment outcomes. Finally, we did not include drug-resistant TB cases, which may have longer delays.

In sum, this study found that the lapse in time between initial symptom onset and start of treatment for TB (total delay) was dominated by the time taken by an individual to seek health care (health-seeking delay). Estimated median health-seeking delays were either comparable or lower than those documented in other settings and to those reported in Mongolia in 2016–2017 and in the 1990s. However, evidence of persistent longer health-seeking delays at regional and provincial levels highlights the need to increase access to TB diagnostic health facilities. Strategies such as community education and awareness programmes, same-day diagnosis and effective use of specimen transportation mechanisms and mobile heath teams could help reduce diagnostic delays in rural areas. Enhanced or active case finding of bacteriologically confirmed cases, including increasing the availability of Xpert MTB/RIF tests, could help reduce diagnostic delays and transmission. Finally, including data on socioeconomic and other factors that affect health-seeking behaviours in routine TB surveillance would improve our understanding of the causes of delays.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

Ethics clearance was not required as the analysis was based on routine data with no identifiable information.

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Epidemiology of and programmatic response to tuberculosis in Solomon Islands: analysis of surveillance data, 2016–2022

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Objective: To identify progress and challenges in the national response to tuberculosis (TB) in Solomon Islands through an epidemiological overview of TB in the country.

Methods: A descriptive analysis was conducted using the national TB surveillance data for 2016–2022. Case notifications, testing data, treatment outcomes and screening activities were analysed.

Results: The number of case notifications was 343 in 2022, with an average annual reduction of the case notification rate between 2016 and 2022 of 4.7%. The highest case notification rate was reported by Honiara City Council (126/100 000 population) in 2022. The number of people with presumptive TB tested by Xpert® rapidly increased from zero in 2016 to 870 in 2022. Treatment success rate remained consistently high between 2016 and 2022, ranging from 92% to 96%. Screening for HIV and diabetes mellitus (DM) among TB patients in 2022 was 14% and 38%, respectively. Most patients (97%) were hospitalized during the intensive phase of treatment in 2022; in contrast, during the continuation phase, the proportion of patients treated at the community level increased from 1% in 2016 to 63% in 2022. Despite an increase in household contact investigations, from 381 in 2016 to 707 in 2021, the uptake of TB preventive treatment (TPT) was minimal (7% among eligible child contacts).

Discussion: This epidemiological analysis in Solomon Islands reveals both notable achievements and challenges in the country's TB programme. One major achievement is a potential actual reduction in TB incidence. Challenges identified were potential underdetection of cases in rural areas, suboptimal community-based care, and insufficient contact tracing and uptake of TPT. It is crucial to address these challenges (e.g. by optimizing resources) to advance the national TB response.

Tuberculosis (TB) is one of the most important infectious diseases globally, with an estimated 10.6 million people developing the disease and 1.6 million people dying from it in 2021.[1] The coronavirus disease (COVID-19) pandemic greatly disrupted TB case detection, resulting in a reduction in global case notifications of 18% in 2020 and 10% in 2021.[2]

Solomon Islands was classified as a country with upper-moderate TB incidence in 2021.[3] Passive case finding is the primary method of case finding; it is supplemented by systematic screening, including contact investigation and cross-referral of people with suspected TB from clinics for HIV and diabetes mellitus (DM). Xpert® MTB/RIF has been used as a primary TB diagnostic test, and there were nine sites using Xpert in 2023. If Xpert testing is unavailable, sputum smear tests are used. TB treatment is centralized either at the National Referral Hospital or provincial hospitals, with a minimum of 2 months of hospitalization required during the intensive phase. After discharge, treatment for the continuation phase is provided, with the support of the clinic nearest to the patient's residence. Patients can opt for facility-based ambulatory care, community-based care or self-administration of TB medicines.

The national TB response is guided by the Tuberculosis National Strategic Plan 2021–2023.[4] Various activities have been planned and implemented to detect, treat and prevent TB, with considerable financial support from international donors.

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This paper describes the epidemiology of TB in Solomon Islands, and highlights programmatic achievements and challenges through the analysis of national surveillance data collected by the National TB Programme (NTP). Beyond addressing the country's concerns, this analysis contributes valuable insights to the broader understanding of TB challenges in other island countries with similar conditions.

METHODS

This descriptive analysis included the trend of TB case notifications, age and sex distributions, type of diagnosis, laboratory data, treatment outcomes, HIV screening, DM screening, contact investigation, TB preventive treatment (TPT) and mode of care. Data were sourced from quarterly TB reports submitted by provincial TB coordinators to the NTP. Province-level analysis was performed for the case notifications, treatment outcomes, and HIV and DM screening.

In Solomon Islands, case information is recorded on the TB patient registry at the provincial hospital, and the area or rural health centre. The information is compiled into both aggregated and case-based Microsoft Excel® reports by a provincial TB coordinator on a quarterly basis. Laboratory data are reported from the Chronic Cough Register. The quarterly reports are then submitted to the NTP for programme monitoring and evaluation.

The definitions of cases and treatment outcomes are in accordance with the World Health Organization (WHO) reporting framework for TB.[5] Data analysis and visualization were conducted with the statistical software package R-4.3.1 (Comprehensive R Archive Network: https://cran.r-project.org/).

RESULTS

TB case notifications

In 2022, there were 343 cases and the rate of case notifications was 44 per 100 000 population (**Fig. 1**, **Table 1**). The average annual reduction in the case notification rate between 2016 and 2022 was 4.7%. Among nine provinces and the national capital, in 2022, the highest number of cases was reported by Honiara City Council (n = 119), the capital city, followed by Malaita province (n = 89) and Makira province (n = 34), which accounted for 71% of total cases (**Fig. 2A**). The highest rate was also reported in the same three provinces, at 126, 49 and 62 per 100 000 population, respectively (**Fig. 2B**).

Age and sex distribution

Among 343 new and relapse cases reported in 2022, the male-to-female ratio was 1.0 (n = 170 to n = 173). Of these 343 cases, 10% (n = 35) were children aged 14 years or below and 8% (n = 28) were adults aged 65 years or above. Between 2015 and 2022, relatively consistent trends and patterns by age group and sex were observed (**Fig. 3**). Notably, more females were diagnosed between the ages of 15–34 years, and more males were diagnosed among those aged over 55 years. The case notification rate was low for both sexes aged 14 years or below, at 9–41 cases per 100 000 population.

Diagnosis category and type of TB

In 2022, the proportion of pulmonary bacteriologically confirmed, pulmonary clinically diagnosed and extrapulmonary TB cases was 52%, 20% and 27%, respectively (**Fig. 4**). The proportion of bacteriologically confirmed cases increased from 32% in 2016.

Laboratory testing and drug-resistant TB

The number of people with presumptive TB who underwent Xpert testing rapidly expanded from zero in 2016 to 951 in 2019. It then decreased to 571 in 2020 and further to 322 in 2021. However, it increased to 870 in 2022 (**Fig. 5A**). Conversely, the number of people presumed to have TB who were tested with smear microscopy increased by 124% in 2020 (n = 605) compared with 2019 (n = 270). Of those tested with Xpert between 2016 and 2022, one had rifampicin-resistant TB. The population testing rate was fairly stable, ranging from 0.13% to 0.18% between 2016 and 2022 (**Fig. 5B**).

Treatment outcomes

Treatment success rates for new and relapse cases ranged from 92% to 96% between 2016 and 2022 (**Fig. 6**, **Table 2**). In 2022, there were no cases whose treatment outcome was not evaluated, and only one case (0.3%) lost to follow-up, with 14 deaths (4%) reported. The cure

Fig. 1. **Number of TB notifications and rate per 100 000 population, Solomon Islands, 2016–2022**

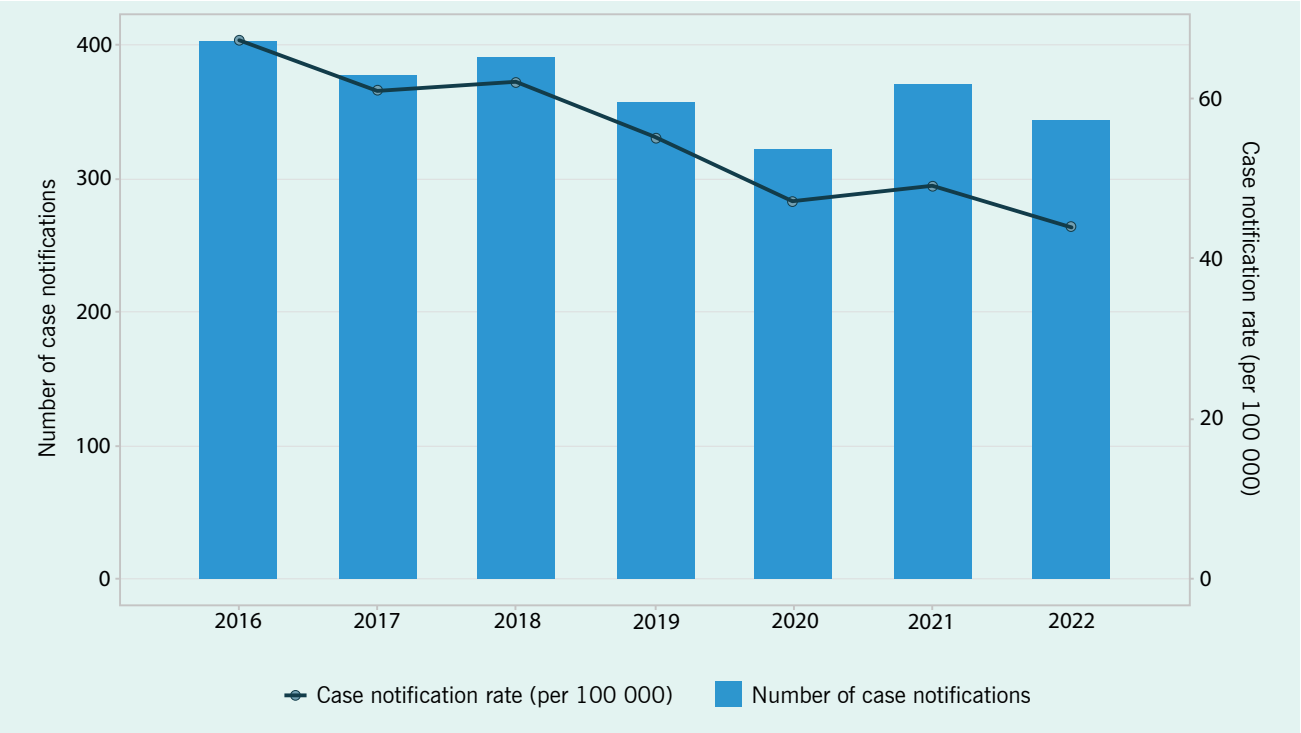


Table 1. **Number of TB case notifications and case notification rate (CNR) per 100 000 population, Solomon Islands, 2016–2022**

Year	2016	2017	2018	2019	2020	2021	2022
Case notifications	402	377	391	357	321	370	343
CNR per 100 000 population	67	61	62	55	47	49	48

rate among bacteriologically confirmed pulmonary TB was low, at 44%, between 2016 and 2022. By province, most cases (80%) had a treatment success rate of more than 90% in 2022, except for Central province (67%) and Western province (86%) (**Fig. 7**).

Indicators of collaborative TB/HIV activities

The proportion of TB cases with known HIV status – including those newly tested for HIV – increased between 2016 and 2019, from 14% to 56%, whereas it decreased in 2020 and 2021, and fell back to 14% in 2022 (**Table 3**). The number of reported TB cases coinfected with HIV was low, with two cases reported between 2016 and 2022 (0.1% [*n* = 2/2561] of total notified cases). The antiretroviral therapy (ART) coverage among coinfected cases was 100% during the same period.

Indicators of collaborative TB/DM activities

Between 2016 and 2022, of the total new and relapse TB cases, 28% (*n* = 706/2561) were screened for DM. Among the individuals screened, 5% (*n* = 33/706) were diagnosed with DM. The number of patients with DM screened for TB varied by year between 2016 and 2022, ranging from 0 to 34 (**Table 4**). The proportion of patients with DM also diagnosed with TB was high, at up to 67% of those screened during the same period.

Contact tracing and TPT

The number of household contacts aged under 5 years varied by year, ranging from 32 in 2019 to 85 in 2021 (**Fig. 8A**). Contact tracing activities were expanded until 2021, but then reduced by 56% compared with the previous year (*n* = 37). Of the contacts identified, most

Fig. 2. **Number of TB notifications (A) and rate per 100 000 population (B) by province, Solomon Islands, 2022**

(78–100%) were screened. However, among the 359 children eligible for TPT, only 7% (n = 24) started on TPT. The number of household contacts identified from all age groups increased (with some fluctuation), from 381 in 2016 to 707 in 2021, followed by a reduction to 508 in 2022 (**Fig. 8B**).

Mode of care

In 2022, 97% of the patients with TB were hospitalized during the intensive phase. During the continuation phase, the proportion of patients who underwent facility-based ambulatory care decreased from 95% in 2016 to 15% in 2022, while community-based care increased from 1% in 2016 to 63% in 2022. The rest of the patients were either hospitalized (0.3%) or self-administered (22%) in 2022.

DISCUSSION

Our epidemiological analysis highlighted multiple programmatic achievements and challenges in Solomon Islands. The major achievements include declining case notifications despite sustained case finding efforts, consistently high treatment success rates, expansion of contact investigation initiatives and the decentralization of treatment during the continuation phase. The challenges included disruptions in TB services caused by the COVID-19 pandemic, suboptimal screening of HIV and DM among TB cases, and low uptake of TPT.

Fig. 3. **Age and sex distribution of TB notifications (new and relapse) per 100 000 population by year, Solomon Islands, 2016–2022**

Fig. 4. **Proportion of TB notifications by year and type of diagnosis, Solomon Islands, 2016–2022**

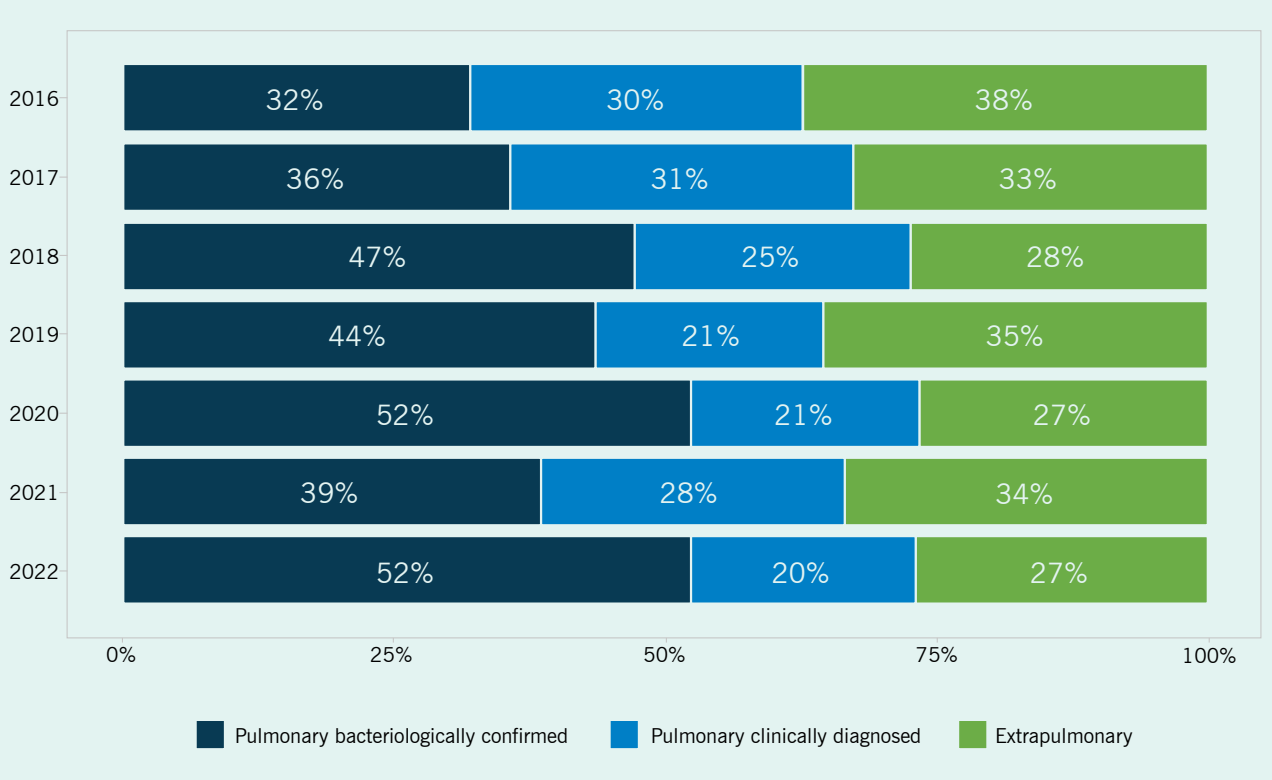


Fig. 5. **Number of presumptive TB cases on the Chronic Cough Register who were tested with smear microscopy and Xpert (A) and population testing rate (B), Solomon Islands, 2016–2022**

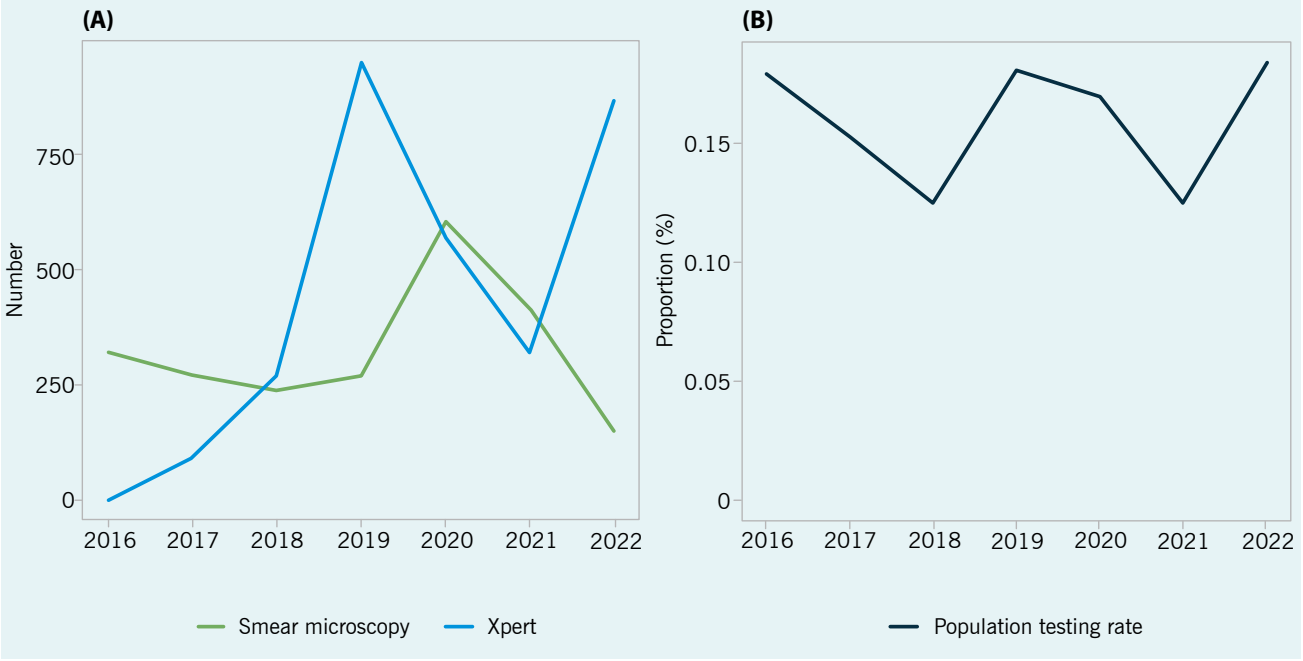
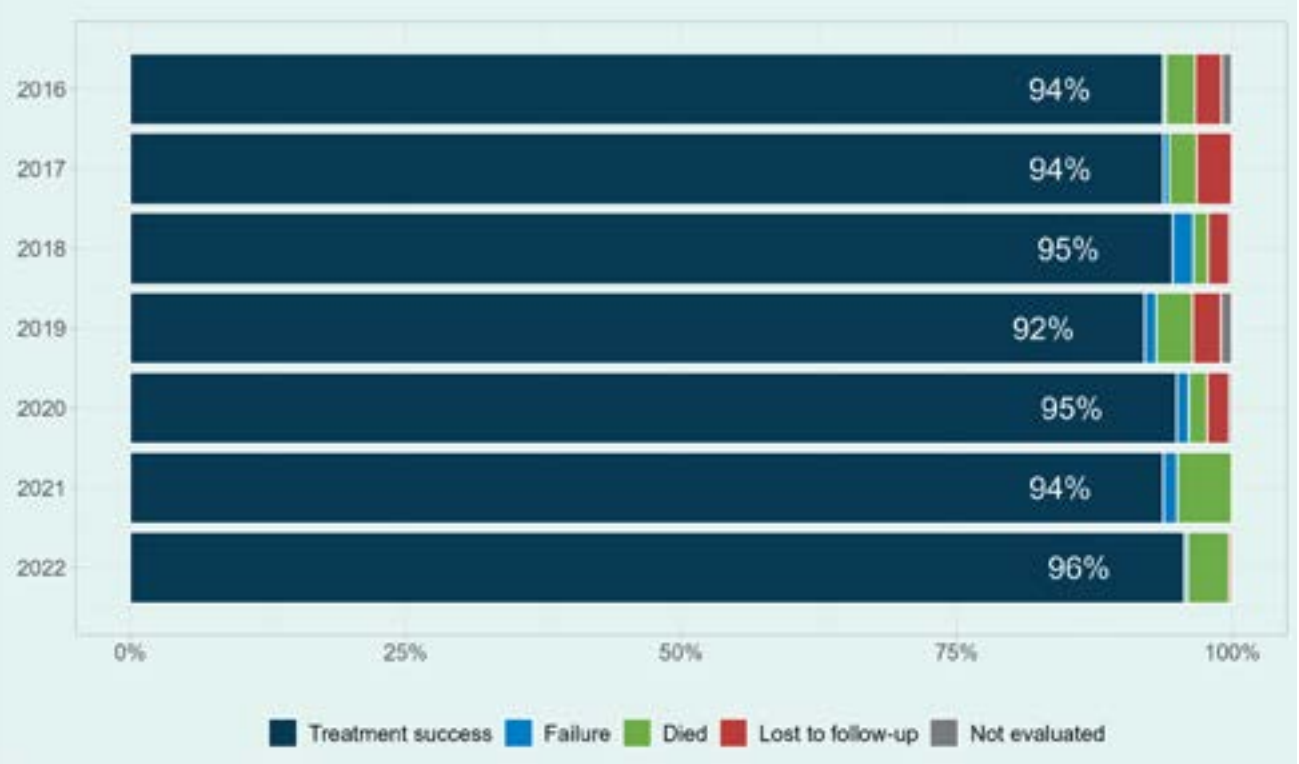


Fig. 6. **Treatment outcomes among new and relapse cases by year, Solomon Islands, 2016–2022[a]**



[a] Year of evaluation (e.g. 2022 in the figure shows the cohort in 2021).

Table 2. **Treatment outcomes among new and relapse TB cases by year, Solomon Islands, 2016–2022**

Year[a]	2016	2017	2018	2019	2020	2021	2022
Treatment cohort	415	402	370	391	357	321	379
Cure	118	81	44	72	50	83	70
Treatment completed	271	296	306	288	289	218	284
Failure	1	2	7	4	4	4	1
Died	11	10	5	13	6	16	14
Lost to follow-up	10	13	7	10	7	0	1
Not evaluated	4	0	1	4	1	0	0
Treatment success rate	94%	94%	95%	92%	95%	94%	96%

[a] Year of evaluation (e.g. 2022 in the table shows the cohort in 2021).

Fig. 7. **Treatment outcomes among new and relapse TB cases by province and year, Solomon Islands, 2016–2022[a]**

[a] Year of evaluation (e.g. 2022 in the figure shows the cohort in 2021).

In Solomon Islands, the case notification rate consistently declined over the years of the study. Considering the sustained population testing rate observed in our analysis, the reduction of TB cases in Solomon Islands could potentially be due to the reduction in underlying TB incidence. This is supported by improving socioeconomic indicators and declining prevalence of risk factors for TB in the country,[6] although further epidemiological evidence is needed.

Honiara City Council reported the highest case notification rate. In general, higher density and overcrowded living conditions in populated cities contribute to transmission of TB, increasing the TB burden. However, the finding in Honiara could suggest better access to health care in the capital compared with rural provinces, indicating significant geographic disparities across provinces. The country's geography, lack of public transport and resource constraints in

Table 3. **Known HIV status, HIV prevalence in TB patients and antiretroviral therapy (ART) coverage for TB/HIV patients by year, Solomon Islands, 2016–2022**

	Year	2016	2017	2018	2019	2020	2021	2022	Total
TB/HIV	New and relapse cases	402	377	391	357	321	370	343	2561
	TB patients tested for HIV	57	111	109	201	123	170	49	820
	TB with HIV+	0	0	0	1	1	0	0	2
	HIV started on ART	0	0	0	1	1	0	0	2
	% of TB with HIV+	0%	0%	0%	0.5%	0.8%	0%	0%	0.2%
	Coverage of HIV screening for TB	14%	29%	28%	56%	38%	46%	14%	32%

Table 4. **People with diabetes mellitus (DM) screened for TB and people with TB screened for DM by year, Solomon Islands, 2016–2022**

	Year	2016	2017	2018	2019	2020	2021	2022	Total
TB/DM	New and relapse cases	402	377	391	357	321	370	343	2561
	TB screened for DM	65	74	142	86	110	100	129	706
	TB with DM	2	6	6	3	6	1	9	33
	% of TB with DM	3%	8%	4%	3%	5%	1%	7%	5%
	Coverage of DM screening for TB	16%	20%	36%	24%	34%	27%	38%	28%
	DM screened for TB	15	22	28	5	11	34	0	115
	DM with TB	10	11	3	3	5	12	2	46
	% of DM with TB	67%	50%	11%	60%	45%	35%	-	40%

health care pose a considerable challenge in population health access and cause severe financial hardship for TB-affected families.[7] Thus, it is critical to address potential underdetection of TB cases in rural areas.

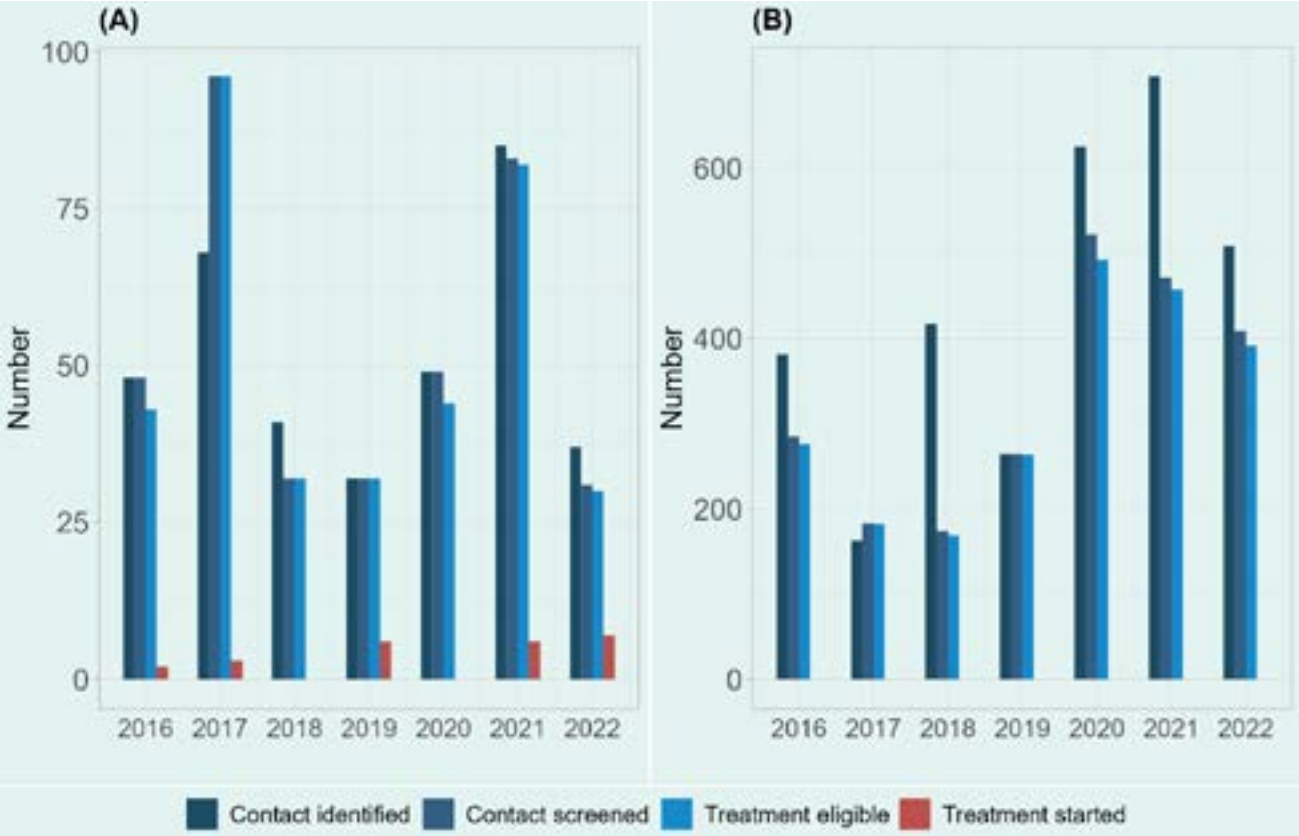
A further important finding is the potential underdetection of specific groups, particularly elderly males. Given the global increase of male-to-female ratios in older age, there is a likelihood of underdetection among males.[8] This could be attributed to concerns about catastrophic costs or difference in health-seeking behaviour between males and females.[7,9] Also, there is the possibility of underreporting across the country. Some people could be identified and treated in the private sector, but the extent of the private sector's contribution to diagnosis remains uncertain.

Our analyses demonstrated the impact of the COVID-19 outbreak on various TB activities in the country. It is likely that border controls caused interruptions to the supply of laboratory consumables including Xpert cartridges and smear reagents, which resulted in the reduction in laboratory testing in 2021. The number of Xpert tests undertaken increased to pre-pandemic levels in 2022, but case detection was affected in that year, mostly because of the reallocation of human resources, particularly during the first half of 2022 when community transmission of COVID-19 was reported.[10]

In recent years, facility-based ambulatory care during the continuation phase has rapidly been replaced by community-based care. This could have contributed to the increased adherence to treatment and seems to be a positive transition towards patient-centred care. However, the low cure rate among bacteriologically confirmed cases raises concerns about inadequate treatment follow-up, and evaluation during and at the end of treatment. At present, hospitalization ensures adherence to and monitoring of treatment but causes a financial burden for the affected families. To overcome this contradiction, further strengthening of community-based care by empowering communities and engaging local authorities is essential.

Our analysis suggested that screening for HIV and DM among TB patients was suboptimal. In Solomon

Fig. 8. **Number of TB contacts identified, screened, eligible for TB preventive treatment (TPT), and TPT started by year among household contacts aged under 5 years (A) and household contacts of all age groups (B), 2016–2022**



Islands, HIV testing among TB cases might often be undervalued, given the low HIV prevalence in the general population.[11] Other factors (e.g. insufficient supply of test kits and people's hesitancy around screening) might have contributed to this, which requires further investigation. Given that screening is not systematically conducted, the proportion of positive cases reported in this analysis does not represent the national prevalence; for example, the proportion of DM among screened TB cases (5% for 2016–2022) was lower than the estimated DM prevalence among the general population aged 20–79 (19.8% in 2021).[12] Although the number of DM patients screened for TB was limited, the high proportion of TB cases detected demonstrated the effectiveness of screening for TB among DM patients in this context. They might be prescreened by TB symptoms or other TB risk factors.

Although contact investigation activities were expanded, the number of people who started on TPT was low, representing a missed opportunity to intensify TB prevention. Anecdotal evidence suggested that clinicians were hesitant to prescribe TPT owing to uncertainty about eligibility, and that this was coupled with lack of acceptance by eligible populations. To counteract this situation, it is necessary to train the health-care providers and provide education to eligible patients. At the same time, systematic recording and reporting of TPT implementation from treatment initiation to completion is required to inform corrective actions.

Our analysis was limited by the relatively small number of cases included because of the small population size. This makes it challenging to determine definitive trends and patterns, especially in age- and sex-disaggregated data analysis and province-level analysis. Additionally, the quality of the surveillance data was heavily dependent on local facility and staff capacity. Manual data entry using paper-based records and reports might have led to inconsistencies in some of the data reported. In particular, the data from the Chronic Cough Register that were used to describe the

trends of laboratory testing did not fully match the data from the laboratory records.

Despite these limitations, our analyses provided a comprehensive insight into TB epidemiology and programmatic performance in Solomon Islands. For the country to stay on track to achieve the goal of ending TB by 2035, it is imperative to address the identified challenges through the efficient use of existing resources. Moreover, concerted national efforts to build resilient health systems, expand health service coverage and address social determinants of health are crucial in advancing the national TB response in Solomon Islands.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics statement

Ethics approval was not required as routinely collected and anonymized surveillance data were used.

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Letter to the Editor: Pathogens detected from patients with acute respiratory infections negative for SARS-CoV-2, Saitama, Japan, 2020

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Dear Editor,

We read with interest the article by Miyashita et al.[1] and commend them for conducting syndromic acute respiratory infection (ARI) surveillance during 2020, a challenging year for surveillance. The COVID-19 pandemic reminded us that the number of cases detected directly relates to testing intensity, and that test data (the number of tests performed) and positivity (the proportion of tests that are positive for a given pathogen or pathogens) should be considered when interpreting trends in surveillance data.[2–5] The data from Miyashita et al. provide an empirical illustration of the importance of test data.

For instance, when comparing the respiratory pathogen data (excluding SARS-CoV-2 and influenza, as per the study design) among the 10 age groups, test data enable the interpretation of the number of test-positive cases *accounting* for the number of tests performed (Miyashita et al., Table 2). As the authors noted, while those aged 80–89 years had the most tests (n = 389 samples), positivity ranked seventh, at only 8.7%; although case detections ranked second (n = 30), this was probably the result of more testing and ignoring the test and positivity data would have conveyed a misleading picture. In contrast, those aged 0–9 years had the highest case detections (n = 77) *and* positivity (40.5%). Compared to those aged 80–89 years, the paediatric group had more than double the number of detections despite having only half the number of tests (n = 192 samples), thus the high detection counts cannot be explained by more testing. The fact that children were most affected is also suggested when restricted to lower respiratory tract infections (Miyashita et al., Table 4, collapsed to three age groups). While 0–14-year-olds had fewer detections (n = 39) compared to 15–64-year-olds (n = 69) and ≥65-year-olds (n = 59), they had a substantially higher positivity at 52.0%, 15.9% and 6.9%, respectively. Taken together with the much smaller underlying paediatric population (age distribution of Saitama Prefecture's 2020 population:[1] 11.7% 0–14 years, 62.0% 15–64 years, 26.3% ≥65 years), the test data strongly suggest that children were the age group most burdened by respiratory pathogens.

Test data can also help with temporal interpretations of surveillance data. As the authors comment, fewer detections in the latter half of 2020 could be due to a reduced number of samples. Reduced testing in November (n = 28) and December (n = 9)—combined with high positivity—supports this interpretation, suggesting that ARI surveillance sensitivity may have been lower compared to April, when test frequency was highest (n = 521), resulting in more detections but with low positivity (Miyashita et al., Fig. 1). In contrast, during June and September, while there were also fewer tests

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(n = 114) resulting in fewer detections, *positivity* was also at its lowest; less testing alone generally does not lead to lower positivity, and the observed pattern rather suggests a genuine reduction in respiratory pathogen prevalence. Again, all else being equal, accounting for test data allows for more confident assessments of detected case numbers.

To summarize, when comparing across "person", "time" or "place", explicitly accounting for testing helps address testing bias and improve data interpretation, in ways not possible with numerator case data alone.[2–5] Surveillance workers should recognize that appropriate interpretation of data has real public health implications, as surveillance data directly inform situational awareness, risk assessment and response.

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Conflicts of interest

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Ethics statement

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