# Seroprevalence and prevention of hepatitis B, measles and rubella among healthcare workers in Dili, Timor-Leste

Celia Gusmao,[a] Maria Y. Tanesi,[b] Nelia Gomes,[b] Sarah L. Sheridan,[c] Nevio Sarmento,[b] Tessa Oakley,[b] Michael David,[d,e] Johanna Wapling,[b] Lucsendar Alves,[b] Salvador Amaral,[b] Anthony D. K. Draper,[b,f] Bernardino Cruz,[g] Danina Coelho,[g] Helio Guterres,[a] Nicholas S. S. Fancourt,[b] Jennifer Yan,[b] Kristine Macartney,[c,h] Joshua R. Francis,[b,j] and Paul Arkell[b,i,j,*]

[a]Hospital Nacional Guido Valadares, Dili, Timor-Leste
[b]Menzies School of Health Research, Charles Darwin University, Darwin, Northern Territory, Australia
[c]National Centre for Immunisation Research and Surveillance, Westmead, NSW, Australia
[d]Daffodil Centre, The University of Sydney, A Joint Venture with Cancer Council New South Wales, Sydney, NSW, Australia
[e]School of Medicine & Dentistry, Griffith University, Gold Coast, QLD, Australia
[f]Northern Territory Centre for Disease Control, Darwin, Northern Territory, Australia
[g]Ministry of Health, Dili, Timor-Leste
[h]Faculty of Medicine and Health, University of Sydney, Sydney, New South Wales, Australia
[i]Imperial College, London, United Kingdom

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## Summary

**Introduction** The World Health Organisation recommends that healthcare workers (HCWs) are immune to measles and rubella, and those at risk of exposure are offered the hepatitis B vaccine. No formal programme for occupational assessment and provision of vaccinations to HCWs currently exists in Timor-Leste.

**Methods** A cross-sectional study was undertaken to determine the seroprevalence of hepatitis B, measles and rubella among HCWs in Dili, Timor-Leste. All patient-facing employees at three healthcare institutions during April–June 2021 were invited to participate. Epidemiological data were collected by interview-questionnaire and a serum sample was collected by phlebotomy and analysed at the National Health Laboratory. Participants were contacted to discuss their results. Relevant vaccines were offered to seronegative individuals and those with active hepatitis B infection were referred for further assessment and management in a hepatology clinic as per national guidelines.

**Results** Three-hundred-and-twenty-four HCWs were included (representing 51.3% of all eligible HCWs working at the three participating institutions). Sixteen (4.9%; 95% CI: 2.8–7.9%) had active hepatitis B infection, 121 (37.3%; 95% CI: 32.1–42.9%) had evidence of previous (cleared) hepatitis B infection, 134 (41.4%; 95% CI: 35.9–46.9%) were hepatitis B seronegative, and 53 (16.4%; 95% CI: 12.5–20.8%) had been vaccinated. Two-hundred-and-sixty-seven (82.4%; 95% CI: 77.8–86.4%) and 306 (94.4%; 95% CI: 91.4–96.7%) individuals exhibited antibodies to measles and rubella, respectively.

**Interpretation** There are significant immunity gaps and a high prevalence of hepatitis B infection among HCWs in Dili Municipality, Timor-Leste. Routine occupational assessment and targeted vaccination of this group would be beneficial and should include all types of HCWs. This study provided an opportunity to develop a programme for the occupational assessment and vaccination of HCWs and forms the template for a national guideline.

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**Keywords:** Healthcare worker; Hepatitis B; Measles; Occupational health; Rubella; Serological surveillance; Vaccination; Vaccine preventable diseases

*Corresponding author. Menzies School of Health Research, Timor-Leste Office, Apartment 203-204B, Plaza Hotel, Rua 30 de Agosto No. 72, Bairro dos Grilos, Dili, Timor-Leste.
*E-mail address:* paul.arkell@menzies.edu.au (P. Arkell).
[j]Joint senior authors.

## Research in context

### Evidence before this study

To identify seroepidemiological studies of vaccine-preventable diseases (VPDs) in Timor-Leste, Pubmed was searched on 1st October 2022 with the terms (("vaccin*" [title/abstract]) OR ("hepatitis B" [title/abstract]) OR ("measles" [title/abstract]) OR ("rubella" [title/abstract])) AND "Timor-Leste". One single-centre cross-sectional study was published in 2015, which found that 2.8% of women accessing antenatal care were hepatitis B surface antigen positive. No studies including healthcare workers (HCWs) were identified.

### Added value of this study

This is the first study to estimate the seroprevalence of hepatitis B, measles and rubella among HCWs in Timor-Leste. Out of 324 participants, 16 (4.9%; 95% CI: 2.8–7.9%) had active hepatitis B infection, 121 (37.3%; 95% CI: 32.1–42.9%) had evidence of previous (cleared) hepatitis B infection, and 134 (41.4%; 95% CI: 35.9–46.9%) were hepatitis B seronegative (i.e. susceptible). Immunity gaps to measles and rubella were also identified. Overall, 171 (52.8%; 95% CI: 47.2–58.3%) HCWs were eligible for either hepatitis B and/or measles-rubella vaccination and at the time of writing there was high uptake of first doses.

### Implications of all the available evidence

HCWs in Timor-Leste are at risk of VPDs. Occupational assessment and provision of vaccines is feasible and should be implemented in this setting.

## Introduction

Healthcare workers (HCWs) are at a higher risk of certain infectious diseases including vaccine-preventable diseases (VPDs). The World Health Organisation (WHO) recommends that all HCWs should be immune to measles and rubella, and those at risk of blood exposure should be offered hepatitis B vaccine. These vaccines provide protective immunity and therefore also reduce the risk of onward transmission from HCWs to patients or other HCWs.[1–3]

Timor-Leste is a nation located between Australia and Indonesia which regained independence from Indonesia in 2002. There are approximately 7000 HCWs, with almost 50% working within Dili Municipality, including the capital city (Dili, population = 222,000).[4] While some HCWs have sporadically received vaccines during government-sponsored overseas training programmes, there is currently no formal programme for occupational assessment of HCWs or healthcare students working or training in Timor-Leste. Despite this, HCWs were assigned the highest priority for vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and a programme of vaccine delivery in hospitals and other healthcare facilities between April–June 2021 resulted in high uptake.[5,6]

This study aimed to determine the seroprevalence of hepatitis B, measles and rubella among HCWs in Dili, Timor-Leste, and to assess the feasibility of providing occupational assessment and vaccines for these infections in this setting.

## Methods

### Participant recruitment

HCWs were recruited during a parallel project investigating SARS-CoV-2 seroprevalence, between April and June 2021.[5] All HCWs working in patient-facing and/or clinical sample-processing roles at the referral hospital in Dili (Hospital Nacional Guido Valadares, HNGV), the national health laboratory in Dili (Laboratório Nacional de Saúde, LNS), and the regional ambulance service in Dili (Servico Nacional Ambulancia e Emergencia Medica, SNAEM) were eligible.

### Sample analysis

Samples were analysed at LNS for rubella IgG (quantitative, positive if >10 IU/mL) hepatitis B surface antigen (HBsAg, qualitative), hepatitis B core total (IgG and IgM) antibody (HBcAb, qualitative) and hepatitis B surface antibody (HBsAb, positive if >10 mIU/mL) using Ortho Clinic Diagnostics® chemiluminescent assays on the Vitros ECiQ® platform, and for measles IgG using the Eurimmun® ELISA assay (semi-quantitative, positive if >250 IU/L). Samples which were positive for HBsAg were forwarded for hepatitis B envelope antigen (HBeAg, qualitative) and hepatitis B envelope antibody (HBeAb, qualitative) testing using Ortho Clinic Diagnostics chemiluminescent assays on the Vitros ECiQ platform, and hepatitis B viral load (HBVL, quantitative) using the Cepheid® assay on the geneXpert platform. All testing was carried out according to manufacturers' instructions and cited serological cut-off values. Samples with borderline/indeterminate results were repeated one time and the second result was used for analysis. The sample was assigned negative when the second result was also borderline/indeterminate.

### Analysis

Demographic data, clinical data and self-reported vaccine status were collected using a bespoke structured interview-questionnaire. This was not formally validated but was piloted on HCWs within the research team prior to being finalised. A serum sample was collected

by phlebotomy. Participants were categorised as being seropositive or seronegative to measles and rubella. They were categorised as either having active hepatitis B (HBsAg and HBcAb positive), having evidence of previous (cleared) hepatitis B (HBcAb positive but HBsAg negative), being hepatitis B seronegative (HBcAb, HBsAb and HBsAg negative) or having evidence of hepatitis B vaccination (HBsAb positive but HBcAb and HBsAg negative). Percentage seropositivity was determined for each VPD and compared across demographic (age group, gender, occupation), clinical (history of infection), and vaccine-related (history of vaccination) variables. Fisher's exact test was used to assess associations between hepatitis B surface antigen, measles and rubella seropositivity and categorical outcomes. Where association between occupation and seroprevalence was observed, its independence was assessed using multivariable binary logistic regression which included age and gender as a priori confounders. Stata version 17 (StataCorp, College Station, USA) was used for all statistical analyses. Results were considered significant if $p < 0.05$.

### Participant follow-up

Participants were contacted by telephone to discuss their results and were managed according to standard-operating procedures which were developed with input from local and international members of the research team with expertise in laboratory analysis, vaccines, and the management of infectious diseases including hepatitis B. Those who were determined to be measles and/or rubella seronegative (or whose serology remained borderline/indeterminate after repeat testing) were offered two doses of MR vaccine (Measles and Rubella Vaccine, Live, Attenuated, Serum Institute of India, PVT, Ltd), with the second dose being given at least 28 days after the first. Those who were hepatitis B seronegative were offered three doses of hepatitis B vaccine (Hepatitis B Vaccine (rDNA), Adult, Serum Institute of India, PVT, Ltd), with the second and third doses being given 28 days and 6 months after the first dose, respectively. Those diagnosed with active hepatitis B infection were referred to a hepatology clinic in Dili for clinical assessment, which included biochemical and radiological assessment of liver function and consideration of antiviral treatment in-line with international clinical guidelines.[7] They were also assessed for occupational risk, with advice to abstain from exposure-prone procedures if applicable. Vaccines were procured internationally using study funds and were delivered by local research nurses in a bespoke study clinic.

### Ethical considerations

This study received ethical approval from the Research Ethics and Technical Committee of the Instituto Nacional da Saude, Timor-Leste (Reference: 265/MS-INS/DE/III/2021) and the Human Research Ethics Committee of the Northern Territory Department of Health and Menzies School of Health Research, Australia (Reference: 2020–3925). All participants provided informed written consent. Participants were assigned a study ID number at enrolment which was used to de-identify all samples and data. Personally identifiable information (name, date-of-birth and contact details) were collected separately and stored in a master study file in a secure filing cabinet (alongside consent forms). Once available, de-identified results were sent electronically to one of only two researchers with access to the study master file. These individuals re-identified the results and managed all participant follow-up activities. When referral for vaccination and/or assessment in the hepatology clinic was required, a referral was only made if the participant gave explicit verbal permission for this to occur (via telephone or face-to-face).

### Role of funding source

None.

## Results

A total of 324 HCWs participated in the study, with 263 participants (81.2%) working at HNGV, 30 (9.2%) working at LNS and 31 (9.6%) working at SNAEM. This represented 51.3% of all eligible HCWs registered as working at the three participating institutions. One-hundred-and-one (31.2%) were nurses, 64 (19.8%) cleaners, 51 (15.7%) doctors, 37 (11.4%) laboratory scientists, 18 (5.6%) midwives, and 13 (4.0%) ambulance staff. Forty (12.3%) were classified as miscellaneous healthcare staff which included administrative staff (16), assistants (8), students (8), physiotherapists (4), nutritionists (2), a safety officer (1) and a driver (1). One-hundred-and-ninety-one (59.0%) were female and the median age was 29 years (interquartile range (IQR) 34–43 years). Table 1 shows VPD serostatus across different groups of individuals. Demographic data for HCWs who did not participate was unavailable. As such, this group could not be compared to participants in order to assess for potential sampling bias.

### Hepatitis B seroprevalence

Serology showed that 16 (4.9%; 95% CI: 2.8–7.9%) participants had active hepatitis B infection, 121 (37.3%; 95% CI: 32.1–42.9%) had evidence of previous (cleared) hepatitis B infection, 134 (41.4%; 95% CI: 35.9–46.9%) were hepatitis B seronegative, and 53 (16.4%; 95% CI: 12.5–20.8%) had evidence of vaccination. No statistically significant association between active hepatitis B and any measured demographic variable, such as age or occupation, was observed.

| | Hepatitis B status | | | | | | | | | Measles IgG positive[a] | | | Rubella IgG positive[b] | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Active | | No active infection | | | | | | p[c,d] | | | p[c] | | | p[c] | |
| | | | Previous | | Susceptible | | Vaccinated | | | | | | | | | |
| Gender | | | | | | | | | | | | | | | | |
| Female | 6 | 3.1% | 64 | 33.5% | 88 | 46.1% | 33 | 17.3% | | 155 | 81.2% | | 178 | 93.2% | | **191** |
| Male | 10 | 7.5% | 57 | 42.9% | 46 | 34.6% | 20 | 15.0% | 0.115 | 112 | 84.2% | 0.554 | 128 | 96.2% | 0.326 | **133** |
| Age Group (years) | | | | | | | | | | | | | | | | |
| 17–30[e] | 6 | 5.5% | 29 | 26.4% | 65 | 59.1% | 10 | 9.1% | | 73 | 66.4% | | 104 | 94.5% | | **110** |
| 31–40 | 6 | 5.1% | 45 | 38.5% | 38 | 32.5% | 28 | 23.9% | | 100 | 85.5% | | 107 | 91.5% | | **117** |
| 41–50 | 4 | 6.8% | 23 | 39.0% | 23 | 39.0% | 9 | 15.3% | | 57 | 96.6% | | 57 | 96.6% | | **59** |
| >50 | 0 | 0.0% | 24 | 63.2% | 8 | 21.1% | 6 | 15.8% | 0.492 | 37 | 97.4% | **<0.001** | 38 | 100.0% | 0.211 | **38** |
| Occupation | | | | | | | | | | | | | | | | |
| Ambulance staff | 0 | 0.0% | 5 | 38.5% | 7 | 53.8% | 1 | 7.7% | | 13 | 100.0% | | 12 | 92.3% | | **13** |
| Cleaner | 6 | 9.4% | 22 | 34.4% | 33 | 51.6% | 3 | 4.7% | | 55 | 85.9% | | 63 | 98.4% | | **64** |
| Doctor | 2 | 3.9% | 19 | 37.3% | 10 | 19.6% | 20 | 39.2% | | 47 | 92.2% | | 48 | 94.1% | | **51** |
| Laboratory scientist | 1 | 2.7% | 10 | 27.0% | 13 | 35.1% | 13 | 35.1% | | 29 | 78.4% | | 35 | 94.6% | | **37** |
| Midwife | 0 | 0.0% | 8 | 44.4% | 6 | 33.3% | 4 | 22.2% | | 13 | 72.2% | | 16 | 88.9% | | **18** |
| Nurse[e] | 3 | 3.0% | 46 | 45.5% | 42 | 41.6% | 10 | 9.9% | | 85 | 84.2% | | 94 | 93.1% | | **101** |
| Other | 4 | 9.8% | 11 | 27.5% | 23 | 57.5% | 2 | 5.0% | 0.361 | 25 | 62.5% | **0.005** | 38 | 95.0% | 0.567 | **40** |
| History of vaccination | | | | | | | | | | | | | | | | |
| Yes | 3 | 3.5% | 29 | 33.7% | 21 | 24.4% | 33 | 38.4% | | 36 | 75.0% | | 19 | 100.0% | | - |
| No/DK | 13 | 5.5% | 92 | 38.7% | 113 | 47.5% | 20 | 8.4% | 0.574 | 231 | 83.7% | 0.153 | 287 | 94.1% | 0.612 | - |
| History of infection | | | | | | | | | | | | | | | | |
| Yes | 5 | 71.4% | 1 | 14.3% | 1 | 14.3% | 0 | 0.0% | | 56 | 90.3% | | 0 | 0.0% | | - |
| No/DK | 11 | 3.5% | 120 | 37.9% | 133 | 42.0% | 53 | 16.7% | **<0.001** | 211 | 80.5% | 0.093 | 306 | 94.4% | | - |
| Total | **16** | **4.9%** | **121** | **37.3%** | **134** | **41.4%** | **53** | **16.4%** | | **267** | **82.4%** | | **306** | **94.4%** | | **324** |

DK = Don't know, IgG = Immunoglobulin G. Bold indicates statistical significant value. [a]Assigned measles IgG positive if >250 IU/L. [b]Assigned rubella IgG positive if >10 IU/mL. [c]Fisher's exact test was used to assess associations between VPD seropositivity and other categorical variables. [d]Hepatitis B serostatus was treated as a binary variable (level 1 = active hepatitis B infection, level 2 = all other categories). [e]Reference for variables with multiple categories.

***Table 1:*** **Vaccine preventable disease (VPD) serostatus among healthcare workers of differing gender, age-group, occupation and self-reported vaccination and infection status.**

| Participant | HBsAg | HBcAb | HBsAb | HBeAg | HBeAb | HBVL (IU/ml) | Serum AST (normal range: 14–36 U/L) | Liver USS | Clinical management/outcome |
|---|---|---|---|---|---|---|---|---|---|
| 1 | + | + | – | – | + | ND | 33 | Normal | Active monitoring |
| 2 | + | + | – | – | + | 45 | | | |
| 3 | + | + | – | + | – | 5,950,000 | 61 | Nodular mass | Died of HCC |
| 4 | + | + | – | – | + | 596 | | | |
| 5 | + | + | – | – | + | 102 | 18 | Normal | Active monitoring |
| 6 | + | + | – | – | + | 5410 | 40 | Normal | Active monitoring |
| 7 | + | + | – | – | + | 544 | 39 | Normal | Active monitoring |
| 8 | + | + | – | – | + | 37 | 24 | Normal | Active monitoring |
| 9 | + | + | – | – | + | <10 | | | |
| 10 | + | + | – | – | + | 994 | 25 | Normal | Active monitoring |
| 11 | + | + | – | – | + | 2050 | | | |
| 12 | + | + | – | + | – | >1,000,000,000 | 64 | Increased echogenicity | Started TDF 300 mg OD |
| 13 | + | + | – | + | – | 96,800 | | | |
| 14 | + | + | – | – | + | <10 | | | |
| 15 | + | + | – | – | + | <10 | | | |
| 16 | + | + | – | + | – | IS | | | |

HBsAg = hepatitis B surface antigen, HBcAb = hepatitis B core antibody, HBsAb = hepatitis B surface antibody, HBeAg = hepatitis B envelope antigen, HBeAb = hepatitis B envelope antibody, HBVL = hepatitis B viral load, ALT = alanine aminotransferase, USS = ultrasound scan, ND = not detected, HCC = hepatocellular carcinoma, TDF = tenofovir disoproxil fumarate, OD = once daily, IS = insufficient sample.

*Table 2:* **Laboratory and clinical features of healthcare workers with active hepatitis B.**

Of those who had active hepatitis B infection, 11/16 (68.8%) did not report a diagnosis prior to this study. Of the 16 people with active hepatitis B infection, 4 (25.0%) were HBeAg positive (and HBeAb negative), and 12 (75.0%) were HBeAg negative (and HBeAb positive). Fifteen out of 16 individuals underwent HBVL testing (with one individual's sample being of insufficient volume for this test). The median HBVL in copies/mL (range) was 570 (<10 to >1 × $10^9$). In 8/15 (53.3%) cases HBVL was >200 IU/mL (the threshold which would prohibit participation in exposure prone procedures according to international guidelines for HCWs[8,9]), and in 5/15 (33.3%) cases HBVL was >2000 IU/mL (a treatment threshold in international guidelines[7]). At the time of writing, as shown in Table 2, 8/16 (50.0%) had attended hepatology clinic for review; 4/8 (50.0%) had biochemical evidence of liver inflammation; and 2/8 (25.0%) were assessed as requiring treatment based on elevated viral load (>2000 IU/mL). Of those recommended treatment, one was started on antiviral therapy (tenofovir disoproxil fumarate 300 mg once daily) and the other refused treatment, opting instead for active follow-up and re-consideration of treatment in six months. One participant had developed hepatocellular carcinoma as a complication of their hepatitis B infection and died shortly after review.

### Measles seroprevalence

Two-hundred-and-sixty-seven (82.4%; 95% CI: 77.8–86.4%) individuals were measles seropositive. Univariate analysis showed that increasing age was associated with measles seropositivity, with seropositivity increasing from 66.4% among 17–30-year-olds to 97.4% among people aged over 50 years. Point measles prevalence varied by occupation ranging from 62.5% of health care workers with 'Other' occupations to 100% of ambulance staff. On multivariable analysis including age group, gender and occupation, age group remained significantly associated with seropositivity (OR = 2.909 [95% CI: 1.858–4.555], p < 0.001). Additionally, those with occupation 'other' (OR = 0.355 [95% CI: 0.144–0.874], p = 0.024), were significantly less likely to be seropositive than nurses (the reference category).

### Rubella seroprevalence

Three-hundred-and-six (94.4%; 95% CI: 91.4–96.7%) individuals were rubella seropositive. Of the 18 (5.6%) individuals who were rubella seronegative, 10 (55.6%) were female whose median (IQR) age in years was 33 (31–37). No statistically significant association between rubella seropositivity and any measured demographic variable, nor measles seropositivity, was observed.

### Provision of vaccines

Overall, 171 participants were eligible to receive one or more vaccine types. One-hundred-and-thirty-four participants were eligible to receive a course of hepatitis B vaccination. Uptake of first dose of hepatitis B vaccine was 72.4%, ranging from 67.3% at HNGV to 100.0% at LNS and SNAEM. Fifty-seven participants were eligible to receive a course of MR vaccine. Uptake of first dose of MR vaccine was 63.2%, ranging from 56.8% at HNGV

| | Hospital Nacional Guido Valadares | Laboratório Nacional de Saúde | Servico Nacional Ambulancia e Emergencia Medica | Total |
|---|---|---|---|---|
| Eligible to receive hepatitis B vaccination | 113 | 8 | 13 | 134 |
| Not yet received any doses | 37 (32.7%) | 0 (0.0%) | 0 (0.0%) | 37 (27.6%) |
| Received first dose | 76 (67.3%) | 8 (100.0%) | 13 (100.0%) | 97 (72.4%) |
| Received second dose | 62 (54.9) | 7 (87.5%) | 12 (92.3%) | 81 (60.4%) |
| Received third dose | 48 (42.5) | 7 (87.5%) | 8 (61.5%) | 63 (47.0%) |
| Eligible to receive measles and/or rubella vaccination | 44 | 8 | 5 | 57 |
| Not yet received any doses | 19 (43.2%) | 2 (25.0%) | 0 (0.0%) | 21 (36.8%) |
| Received first dose | 25 (56.8%) | 6 (75.0%) | 5 (100.0%) | 36 (63.2%) |
| Received second dose | 20 (45.5%) | 6 (75.0%) | 3 (60.0%) | 29 (50.9%) |

*Table 3:* **Participants eligible for vaccination and doses received (at the time of writing).**

to 100.0% at SNAEM. Numbers of participants who received subsequent doses (which are still ongoing at the time of writing) are shown in Table 3.

## Discussion

This is the first study to estimate the seroprevalence of VPDs among HCWs in Dili, Timor-Leste. Sixteen (4.9%) individuals were found to have active hepatitis B, including two who required treatment and another who suffered a fatal complication of their hepatitis B infection. There was a high prevalence of previous (cleared) hepatitis B (37.3%) and only a minority had evidence of vaccination (16.4%). One-hundred-and-thirty-four (41.4%) were susceptible, most of whom (72.4%) initiated a course of hepatitis B vaccination as part of this study. Although there are not yet any population-representative studies in Timor-Leste, hepatitis B is recognised as a significant health issue and likely causes most chronic liver disease and hepatocellular carcinoma in the country. These sequalae are likely to have resulted from hepatitis B transmission occurring at birth in many individuals. Birth dose hepatitis B vaccine was introduced in Timor-Leste in 2016. Prevalence of active infection is similar to other studies which have assessed HCWs in the Southeast Asian region, including Indonesia,[10] Thailand,[11] Vietnam,[12] and Laos.[13,14] A nationwide population-representative VPD serosurvey has been initiated and will provide accurate, high-resolution estimates of HBcAb and HBsAb seropositivity in Timor-Leste.[15]

Measles seroprevalence was 82.4%, below what is required to prevent outbreaks through herd immunity.[16] Thirty-six out of 57 (63.2%) eligible individuals initiated a course of MR vaccination. An association of age with measles seropositivity is consistent with many other settings and likely represents natural infection-derived seropositivity among older participants who were infected when measles was endemic and before the implementation of the measles vaccine. In Timor-Leste, this was relatively late (circa 1989, during Indonesian occupation). Additionally, there was significant disruption of healthcare infrastructure, including the near cessation of childhood vaccine delivery between 1999 and 2002. These factors are likely to have adversely affected population immunity to measles. After independence was regained in 2002, single-dose measles vaccine was reinstated as part of a national vaccination programme, and combined measles and rubella vaccination (2 doses) was introduced in 2016.[17] While Timor-Leste was declared by the WHO in 2018 to have eliminated endemic measles transmission, there is a global risk of measles resurgence, emphasising the need to assess and address population immunity gaps, including via the national population-representative VPD serosurvey currently underway.

Limitations of this study include its relatively small, convenience sample from three healthcare institutions in one municipality, potentially reducing the generalisability of our findings. It is possible that access/uptake of vaccination among HCWs has been higher in Dili than the rest of Timor-Leste, because healthcare infrastructure is relatively developed and there has been more consistent access to medicines. Similarly, occupational exposure of HCWs to pathogens may be reduced because personal protective equipment is more readily available. Serological assays for VPDs are not 100% accurate in determining individual immunity to pathogens. While antibody concentrations associated with protective immunity are reasonably well defined for HBsAb and rubella IgG, a reliable correlate of protection is not well defined for measles.[18] Furthermore, in cases where vaccination (or natural infection) occurred a long time ago, the concentration of antibodies can wane close to assay limits of quantification. A previous study showed wide variation in the performance of different rubella IgG assays in this situation.[19]

During this study, local researchers developed standard operating procedures for engaging HCWs, collection of samples by phlebotomy, serological analysis, and the provision of vaccines. Strict protocols were developed to maintain participant confidentiality. A

programme of occupational assessment was developed and implemented across three institutions, forming a template for a national guideline on this topic. While HCWs broadly supported this programme, there were some anecdotal concerns around hepatitis B testing, confidentiality, and the potential for diagnoses to lead to restrictions on working conditions (for example for those who undertake exposure prone procedures). Uptake of first doses of vaccines was less than 100%, and was lower at HNGV (which was the biggest participating institution and has higher staff turnover). Uptake may be improved by taking a universal approach, as opposed to targeted delivery using pre-assessment with serological testing (as was achieved in this study). These issues should be explored further using qualitative methods during the design and implementation of a national guideline, to ensure that there is ultimately high uptake among HCWs in Timor-Leste.

This study identified significant immunity gaps and a high prevalence of hepatitis B infection among HCWs in Dili Municipality, Timor-Leste. Occupational assessment and provision of vaccines to HCWs is feasible and should be implemented in this setting.

#### Contributors

CG, MYT, SLS, NS, LA, SA, JY, KM, JRF, and PA conceived and designed the study. CG, MYT, NS, SA, BC, DC, HG, and PA enrolled participants and collected epidemiological data. NG, NS, TO, JW, LA, and PA performed serological analysis. CG, SLS, MD, ADKD, NSSF, and PA were responsible for statistical analysis. CG, ADKD, JRF, JY, and PA drafted the manuscript, with all authors having significant contribution to revisions, finalisations for submission and decision to submit.

#### Data sharing statement

Data in this manuscript have been presented to collaborators at the Ministry of Health, Timor-Leste to assist with local outbreak response. They were presented at the Australasian Society of Infectious Diseases 2022 Annual Scientific Meeting.

#### Declaration of interests

Authors do not have any commercial or other associations that might pose conflicts of interest. PA is paid by Menzies as a Technical Advisor for work on the ARIA-RISE Timor-Leste Project. This is a portfolio of sero-surveillance studies investigating vaccine-preventable disease seroepidemiology in Timor-Leste, including the one reported in this manuscript. He is paid according to a consultancy agreement. ADKD is an honorary fellow at the Menzies School of Health Research who provides technical advice and support to surveillance and epidemiology activities in Timor-Leste.

#### References


1 World Health Organisation. WHO position paper–July 2020. https://apps.who.int/iris/bitstream/handle/10665/332952/WER9527-306-324-eng-fre.pdf?sequence=1&isAllowed=y; 2020. Accessed April 20, 2022.

2 World Health Organisation. Measles vaccines: WHO position paper–April 2017. http://apps.who.int/iris/bitstream/handle/10665/255149/WER9217.pdf?sequence=1; 2017. Accessed April 20, 2022.

3 World Health Organisation. Hepatitis B vaccines: WHO position paper–July 2017. http://apps.who.int/iris/bitstream/handle/10665/255841/WER9227.pdf;jsessionid=8030BFA23A94854FBC5AB2C3A51D5982?sequence=1; 2017. Accessed April 20, 2022.

4 National Directorate for Human Resource, Ministry of Health DR of T-L. National Strategic Plan for Human Resources for Health (NSPHRH) 2020–2024. https://fliphtml5.com/nkhca/lomh/basic. Accessed April 20, 2022.

5 Arkell P, Gusmao C, Sheridan SL, et al. Serological surveillance of healthcare workers to evaluate natural infection- and vaccine-derived immunity to SARS-CoV-2 during an outbreak in Dili, Timor-Leste. *Int J Infect Dis*. 2022;119:80–86.

6 Ministry of Health DR of T-L. Novel Coronavirus (2019-nCoV) situation reports. https://www.who.int/timorleste/emergencies/novel-coronavirus-2019/novel-coronavirus-(2019-ncov)-situation-reports; 2022. Accessed September 8, 2022.

7 Lampertico P, Agarwal K, Berg T, et al. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. *J Hepatol*. 2017;67:370–398.

8 Australian Health Ministers' Advisory Council. Australian national guidelines for the management of healthcare workers living with blood borne viruses and healthcare workers who perform exposure prone procedures at risk of exposures to blood borne viruses. https://www1.health.gov.au/internet/main/publishing.nsf/Content/cda-cdna-bloodborne.htm; 2018. Accessed June 22, 2022.

9 UK Health Security Agency. *Integrated guidance on health clearance of healthcare workers and the management of healthcare workers living with bloodborne viruses (hepatitis B, hepatitis C and HIV) UK Advisory Panel for Healthcare Workers Living with Bloodborne Viruses (UKAP)*. 2021.

10 Wijayadi T, Sjahril R, Ie SI, et al. Seroepidemiology of HBV infection among health-care workers in South Sulawesi, Indonesia. *BMC Infect Dis*. 2018;18:279. https://doi.org/10.1186/S12879-018-3190-X.

11 Luksamijarulkul P, Watagulsin P, Sujirarat D. Hepatitis B virus seroprevalence and risk assessment among personnel of a governmental hospital in Bangkok. *Southeast Asian J Trop Med Public Health*. 2001;32:459–465.

12 Nguyen T, Pham T, Tang HK, et al. Unmet needs in occupational health: prevention and management of viral hepatitis in healthcare workers in Ho Chi Minh City, Vietnam: a mixed-methods study. *BMJ Open*. 2021;11:e052668. https://doi.org/10.1136/bmjopen-2021-052668.

13 Black AP, Vilivong K, Nouanthong P, Souvannaso C, Hübschen JM, Muller CP. Serosurveillance of vaccine preventable diseases and hepatitis C in healthcare workers from Lao PDR. *PLoS One*. 2015;10:e0123647. https://doi.org/10.1371/JOURNAL.PONE.0123647.

14 Mangkara B, Xaydalasouk K, Chanthavilay P, et al. Hepatitis B virus in Lao dentists: a cross-sectional serological study. *Ann Hepatol*. 2021;22:100282. https://doi.org/10.1016/J.AOHEP.2020.10.010.

15 Arkell P, Sheridan SL, Martins N, et al. Vaccine Preventable Disease Seroprevalence In a Nationwide Assessment of Timor-Leste (VASINA-TL) - study protocol for a population-representative cross-sectional serosurvey. medRxiv. 2022; 2022.12.23.22283897.

16 Moss WJ, Shendale S, Lindstrand A, et al. Feasibility assessment of measles and rubella eradication. *Vaccine*. 2021;39:3544–3559.

17 National Verification Committee. *Annual country report on progressing toward measles elimination and rubella/CRS control*. Dili: Timor-Leste Ministry of Health; 2021.

18 Bolotin S, Hughes SL, Gul N, et al. What is the evidence to support a correlate of protection for measles? A systematic review. *J Infect Dis*. 2020;221:1576–1583.

19 Dimech W, Grangeot-Keros L, Vauloup-Fellous C. Standardization of assays that detect anti-rubella virus IgG antibodies. *Clin Microbiol Rev*. 2015;29:163. https://doi.org/10.1128/CMR.00045-15.