World Health Organization
Western Pacific Region

WPSAR
Western Pacific Surveillance and Response Journal

Volume 7, Number 1, 2016, Pages 1–47
p-ISSN: 2094-7321 e-ISSN: 2094-7313

Western Pacific Surveillance and Response

Open access journal with continuous publication

Western Pacific Surveillance and Response (WPSAR) is an open access journal dedicated to the surveillance of and response to public health events. The goal of the journal is to create a platform for timely information sharing both within our region and globally to enhance surveillance and response activities. WPSAR is a continuous publication which means articles will be published online as soon as they have completed the review and editing process. Every three months articles will be batched for a print issue. It is a publication managed by the World Health Organization Regional Office for the Western Pacific.

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p-ISSN: 2094-7321
e-ISSN: 2094-7313

Hidden varicella outbreak, Luang Prabang Province, the Lao People's Democratic Republic, December 2014 to January 2015

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Background: In January 2015, the Lao People's Democratic Republic Ministry of Health received a report of 34 cases of fever and rash with one laboratory-confirmed measles case in Houitone village, Pakseng District of Luang Prabang Province. Between 21 and 27 January, we conducted a field investigation to determine the etiology, magnitude and severity of this outbreak.

Methods: We conducted active case findings in Houitone and neighbouring villages and collected information on age, location, date of rash onset, symptoms and measles vaccination status. We collected serum samples from cases with rash onset of less than 28 days and tested for measles and rubella IgM using enzyme-linked immunosorbent assay.

Results: Between 22 December 2014 and 23 January 2015, 190 fever and rash cases were identified in seven villages in Pakseng District with the majority of the cases in Houitone village. The most affected age group was between 1 and 9 years. The majority of the rashes were vesicular. Of the additional 43 serum samples collected, no samples tested positive for measles or rubella IgM. The clinical manifestation and epidemiology of the disease suggested a varicella outbreak.

Conclusion: The rapid response to a single laboratory-confirmed measles case did not identify a measles outbreak but suggested a varicella outbreak. Low measles vaccination coverage led us to recommend a routine catch-up vaccination campaign. We also recommend collecting information of rash types and photos of rashes in future fever and rash outbreaks to better differentiate potential etiologies.

Acute fever and rash outbreaks have a wide range of possible etiologies and can cause significant morbidity and mortality. Differential diagnosis includes measles that can cause fatality rates as high as 10–30% and relatively benign diseases such as varicella which rarely result in death (0.001% in 5–9 year-olds and 0.02% in adults).[1] Determining the etiology of a fever and rash outbreak can be complicated when there are outbreaks of different etiology occurring simultaneously in the community.[2]

Varicella, caused by the varicella zoster virus, is a common childhood disease characterized by fever and vesicular rash. It mostly affects children aged 1–9 years old and has a mild presentation except in neonates, pregnant women and immunocompromised individuals where varicella can be life-threatening.[1,3] In developed countries such as the United States of America and Germany, the introduction of varicella vaccination has reduced the disease incidence significantly.[4,5] However, in an unimmunized population such as the Lao People's Democratic Republic, outbreaks of varicella can be expected, especially during the cooler winter season.[6]

In January 2015, the National Center for Laboratory and Epidemiology (NCLE) of the Lao People's Democratic Republic received a report of 34 cases of fever and rash in the remote village of Houitone (population = 937) in Luang Prabang Province. Measles IgM enzyme-linked immunoabsorbent assay (ELISA) testing of 15 serum samples identified

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Submitted: 6 June 2015; Published: 12 January 2016
doi: 10.5365/wpsar.2015.6.2.010

one (6.7%) measles-positive result; however, reports of vesicular rash in the 34 cases suggested another disease, most likely varicella, may also be circulating. Measles is a high-priority disease in the Lao People's Democratic Republic. Two laboratory-confirmed measles outbreaks occurred a few months before this report resulting in 369 cases and 12 deaths in Huaphanh and Bolikhamxay Provinces. Following these outbreaks, a nationwide supplemental immunization activity (SIA) for measles and rubella (MR) was completed one month before the Houitone outbreak.

We conducted an outbreak investigation to determine the etiology, magnitude and severity of the Houitone outbreak.

METHODS

A team consisting of staff from the NCLE and World Health Organization (WHO) joined the provincial and district response teams to investigate the outbreak in Houitone village and neighbouring villages in Pakseng District, Luang Prabang Province between 21 and 27 January 2015.

The clinical case definition of this outbreak was any person presenting with fever and rash between 1 December 2014 and 24 January 2015 in Pakseng District. We conducted active case findings through a door-to-door survey in Houitone village; case findings in neighbouring villages were conducted through review of medical log books at the province and district hospitals and phone interviews with the heads of villages. We collected the name, age, residential location, date of rash onset, symptoms, measles routine and campaign vaccination status of the cases for analysis.

To differentiate between measles and varicella etiologies, information on rash types were collected with photographic documentation in 16 selected cases. Reinvestigation of the laboratory-confirmed measles case was also conducted. Cases were classified according to United States Centers for Disease Control and Prevention (US CDC) and WHO standard case definitions for varicella, measles and rubella (**Box 1**).[3,7]

Field investigators obtained serum samples from cases whose rash onset was less than 28 days – the optimal time frame for specimen collection to ensure test reliability.[8] The NCLE laboratory tested the sera for measles and rubella IgM using ELISA (Enzygnost® kits, Siemens, Erlangen, Germany).

Box 1. Case definitions of suspected measles, rubella and varicella (adapted from US CDC[3] and WHO[7])

Measles
Any person where a clinician suspects measles infection or any person with fever and non-vesicular maculopapular rash and cough/coryza/conjunctivitis.

Rubella
Any person with fever and non-vesicular maculopapular rash and adenopathy (cervical/suboccipital/postauricular) or arthralgia/arthritis.

Varicella
Any person with acute onset of diffuse maculopapulovesicular rash without other apparent cause.

Houitone village population data were provided by the head of the village for calculation of attack rates (AR). Data cleaning, recoding and descriptive analysis were conducted in Excel (Microsoft Excel, Redmond, USA). Relative risks with 95% confidence intervals were calculated in Epi-Info 7 (CDC, Atlanta, USA).

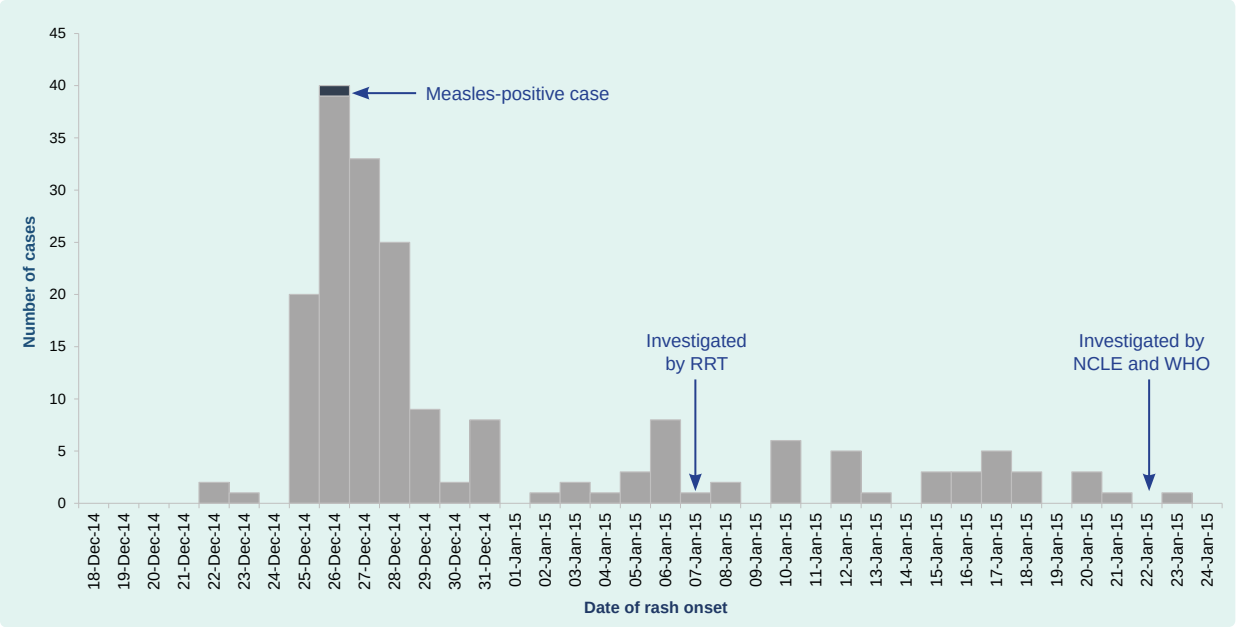
RESULTS

Epidemiological findings

Between 22 December 2014 and 23 January 2015, 190 cases with fever and rash were identified in seven villages in Pakseng District with the majority of the cases in Houitone village (94.2%). Response rate of the survey was 94.7% for those in Houitone village (178/188 households) given 10 absent households. The first two identified cases were an 8-year-old female and a 10-year-old male from the same household in Houitone village with rash onset on 22 December 2014. The case count peaked on 26 December 2014 with 40 cases and a secondary peak appeared on 6 January 2015. The last identified case was a 7-year-old male from Pakseng village with rash onset date of 23 January 2015 (**Figure 1**).

Ages of the 190 cases ranged from 1.6 months to 30 years (median: 5 years) with the majority between 1 and 9 years (n = 152, 80.0%); 75 cases (39.5%) were under 5 years with 10 (5.3%) under 1 year. There were 85 (44.7%) female cases. The overall AR in Pakseng District was 0.9%; the AR in Houitone village was 18.9%. Age-specific AR in this village were 3.7%

Figure 1. **Epidemic curve of fever and rash outbreak in Pakseng District, Luang Prabang Province, the Lao People's Democratic Republic, December 2014 to January 2015 (*n* = 190)**



NCLE, National Center for Laboratory and Epidemiology; RRT, Rapid Response Team; and WHO, World Health Organization.

for population who were aged 10 years or older and 69.7% for the population younger than 10 years (relative risk = 18.8, 95% confidence interval = 12.87–27.54).

Reinvestigation of the 5-year-old female case from Houitone village who tested positive for measles IgM revealed that her scars were evidence of vesicular rash characteristic of varicella. She developed a generalized vesicular rash on 26 December 2014 and had a fever soon after. According to her vaccination and MR campaign card, she had been vaccinated for measles through routine immunization on 12 December 2010 and during the SIA on 21 November 2014 (35 days before rash onset and 47 days before sample collection). Five contacts became ill near her symptom onset date (–1 to 16 days) with similar symptoms of vesicular rash and fever.

Clinical findings

The majority of the cases presented with vesicular rash (n = 189, 99.5%) at either the blistering, scabbing or scarring phase, which is characteristic of varicella (**Figure 2**), and met the US CDC standard case definition for varicella.[3] A single case manifested with a maculopapular rash (0.5%) without cough, coryza or conjunctivitis and met the WHO standard case definition for rubella.[7] No cases met the WHO standard case definition for measles.[7] The severity of the illness of the cases was uniformly mild with no complications, hospitalization or death.

Laboratory findings

Of the additional 43 serum samples collected, no (0%) samples tested positive for measles, and four (9.3%) were equivocal for measles IgM. No (0%) samples tested positive for rubella, and six (14.0%) were equivocal for rubella IgM.

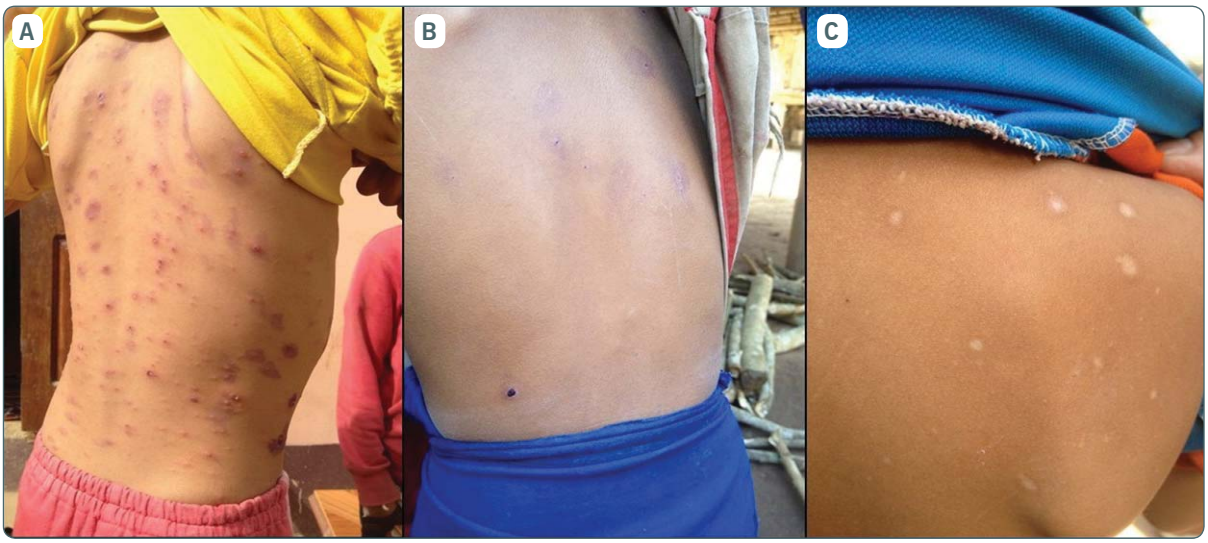
Measles vaccination coverage

Of the 190 cases, 84 (44.2%) had evidence of measles vaccination, including 30 (15.8%) verified by vaccination card and 54 (28.4%) by self-reporting. Among cases who were age-eligible (9 months to 10 years) to receive MR vaccination during the SIA (*n* = 152, 80.0%), 107 (70.4%) reportedly received the MR vaccination.

DISCUSSION

Despite the initial laboratory findings that suggested a measles outbreak, the epidemiological and clinical evidence suggested this outbreak was due to varicella. Evidence supporting this includes: (1) the nature of the rash in all but one case was vesicular; (2) the illness was mild and lacked complications; and (3) reinvestigation of

Figure 2. **Cases with different phases of vesicular rash in the fever and rash outbreak in Pakseng District, Luang Prabang Province, the Lao People's Democratic Republic, December 2014 to January 2015**



A: blistering phase; B: scabbing phase; and C: scarring phase.

the case with the positive measles IgM result identified inconsistent clinical presentation and epidemiological linkage to other vesicular rash cases. Given her recent MR vaccination, this most likely was a false positive.[9]

Varicella typically presents during the cooler winter season or in regions with temperate climate; the disease predominantly affects pre-adolescent children in temperate climates as opposed to appearing later in life in tropical climates.[6,10] The wide age range of the cases in this outbreak is consistent with this pattern and similar to other tropical South-East Asia countries such as Malaysia, the Philippines and Thailand where more than 90% seroconversion can only be seen in those older than 30 years.[11–13]

In a measles elimination setting, according to the *WHO Western Pacific Region Measles Elimination Field Guide*, a single laboratory-confirmed case requires immediate investigation and response.[14] The investigation conducted after the laboratory-confirmed measles case is a reflection of the adherence of NCLE to the WHO guidelines. In the Lao People's Democratic Republic, the national measles vaccination coverage was 87% in 2014 and 88% for the Pakseng District. The nationwide measles SIA conducted in November 2014 reported vaccination coverage of 100% nationwide and 105% in Pakseng District (Correspondence with the Lao People's Democratic Republic Ministry of Health, August 2015). Although the Houitone outbreak was not due to measles, we detected a suboptimal and much lower routine and campaign vaccination coverage, highlighting the importance to strengthen both routine immunization and SIA.

In some developing countries such as the Lao People's Democratic Republic, varicella vaccination has not been incorporated into routine immunization programmes as the cost of vaccine outweighs the public health benefit. However, there is some evidence of higher rates of complications in varicella outbreaks among rural South-East Asian populations with largely naïve populations.[15] In the following three months after this outbreak, at least 16 additional fever and vesicular rash outbreaks were documented with no reported deaths in the Lao People's Democratic Republic (unpublished data). Continued surveillance and investigation of fever and vesicular rash cases is necessary to monitor for severe health outcomes and reassess the need for varicella vaccination programmes.

There are several limitations in this study. First, the door-to-door survey was conducted only in Houitone village which may underestimate the scope of the outbreak. Second, during the door-to-door survey, we encountered 5.3% absent households which may underestimate the attack rate for the village. There may also be a certain level of recall bias regarding the rash onset date that could potentially limit the yield in ELISA IgM test if the true rash onset date was more than 28 days before the test.

In summary, the rapid response to a measles-positive laboratory result discovered a varicella outbreak. The low measles vaccination coverage detected in this setting led us to recommend a routine catch-up vaccination campaign. We recommend collecting detailed information of rash type and obtaining photo documentation of lesions to better differentiate potential etiologies of future fever and rash outbreaks.

Conflicts of interest

None declared.

Funding

This outbreak investigation was funded by WHO.

Acknowledgements

We would like to thank the following: Dr Gregory Jennings and Dr Manilay Phengxay from WHO for their input on the laboratory and epidemiological aspects of the investigation, respectively; and the Institute Pasteur of the Lao People's Democratic Republic for officially informing the Ministry of Health of the laboratory findings that confirmed the varicella etiology in this outbreak from their independent study, especially Dr Darouny Phonekeo, Ms Phonethipsavanh Nouanthong and Ms Keooudomphone Vilivong who conducted the varicella testing in their study. We would also like to thank the provincial and district health offices and hospitals for sharing their data and joining the investigation. Finally, we would like to thank the village heads and village volunteers who helped with translation and data collection.

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An outbreak investigation of scrub typhus in Western Province, Solomon Islands, 2014

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Objective: To identify the etiology and risk factors of undifferentiated fever in a cluster of patients in Western Province, Solomon Islands, May 2014.

Methods: An outbreak investigation with a case control study was conducted. A case was defined as an inpatient in one hospital in Western Province, Solomon Islands with high fever (> 38.5 °C) and a negative malaria microscopy test admitted between 1 and 31 May 2014. Asymptomatic controls matched with the cases residentially were recruited in a ratio of 1:2. Serum samples from the subjects were tested for rickettsial infections using indirect micro-immunofluorescence assay.

Results: Nine cases met the outbreak case definition. All cases were male. An eschar was noted in five cases (55%), and one developed pneumonitis. We did not identify any environmental factors associated with illness. Serum samples of all five follow-up cases (100%) had strong-positive IgG responses to scrub typhus. All but one control (10%) had a moderate response against scrub typhus. Four controls had low levels of antibodies against spotted fever group rickettsia, and only one had a low-level response to typhus group rickettsia.

Discussion: This outbreak represents the first laboratory-confirmed outbreak of scrub typhus in the Western Province of Solomon Islands. The results suggest that rickettsial infections are more common than currently recognized as a cause of an acute febrile illness. A revised clinical case definition for rickettsial infections and treatment guidelines were developed and shared with provincial health staff for better surveillance and response to future outbreaks of a similar kind.

Rickettsial infections classically present as an undifferentiated fever syndrome. Rash, eschars and lymphadenopathy occur at varying frequencies depending on the causative organism.[1] Scrub typhus, caused by *Orientia tsutsugamushi*, is spread by larval (chigger) trombiculid mites from a limited range of species. *O. tsutsugamushi* is maintained by transovarial transmission within the population of trombiculid mites.[1]

From 5 to 11 May 2014 there were nine admitted cases of an undiagnosed acute febrile illness at one hospital in Munda, Western Province of Solomon Islands. The cases tested negative on routine microscopy for malaria. These cases were from three villages, namely Dunde, Agagana and Rendova Harbour (**Figure 1**). Staff from the World Health Organization (WHO) Representative office in Solomon Islands were invited to review thee admitted cases. Finding of an eschar on examination of some of the cases suggested that rickettsial or related infections may be the disease etiology. As a high number of healthy patients having acute fever requiring hospitalization within a short period of time and in such confined areas is unusual, an outbreak investigation was conducted to reveal the etiology and associated risk factors of the illness.

METHODS

An outbreak investigation team consisting of a clinician from Honiara, a clinician from the study hospital, a WHO epidemiologist and staff from the Ministry of Health surveillance unit was formed. The team reviewed routine medical records to obtain demographics, clinical features and treatment outcomes for all suspected cases. A clinically suspected case of rickettsial or related infections was defined as an inpatient in the study

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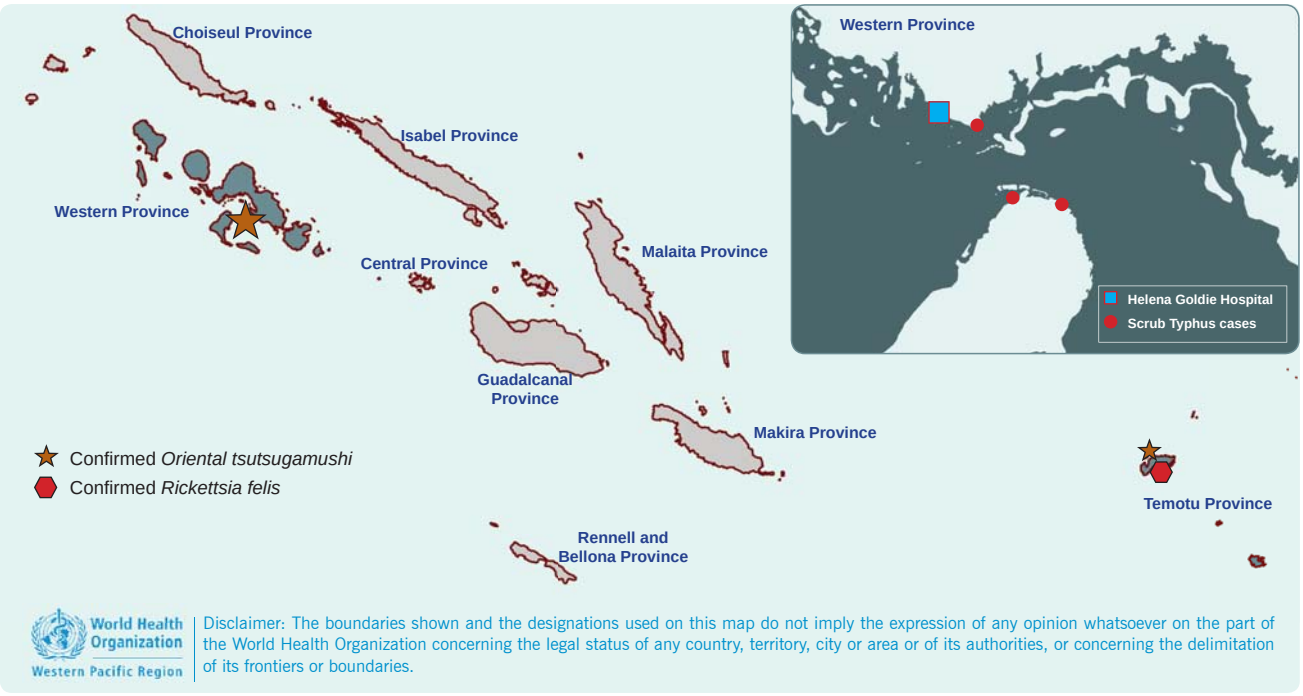
Submitted: 1 September 2015; Published: 26 January 2016
doi: 10.5365/wpsar.2015.6.3.007

Figure 1. **Rickettsial infections in Solomon Islands**



Note: The main map shows the proven cases of rickettsial infection in Solomon Islands from 1945 onwards. The inlay map shows the distribution of cases in the current 2014 outbreak.

hospital with high fever (> 38.5 °C) and a negative malaria microscopy test with an admission date between 1 and 31 May 2014.

The team visited communities from which cases arose between 15 and 16 June 2015. The purpose of the investigation was discussed with village chiefs who assisted in case identification and finding asymptomatic community volunteers as controls for analysis. In each community, the team attempted to locate the cases and recruit two residentially matched controls for each case. All subjects were interviewed using a standardized questionnaire developed by the investigation team, including information on clinical features, risk factors, animal exposure and treatment.

Serum samples were collected from the subjects by venipuncture for testing. Collected samples were transferred to Honiara within 24 hours and were cryopreserved at −80 °C at the National Referral Hospital for later testing. For rickettsial confirmation, serum samples were shipped at room temperature and were in transit for 72 hours before their arrival at the Australian Rickettsial Reference Laboratory that has accreditation for performing rickettsial diagnostics.[2] Samples were tested by indirect micro-immunofluorescence assay for total antibodies against six members of the spotted fever group (SFG) rickettsia (including *Rickettsia australis*, *R. honei*, *R. felis*, *R. conorii*, *R. africae* and *R. rickettsii*); typhus group (TG) rickettsia (*R. prowazekii* and *R. typhi*); and scrub typhus (ST) (*Orientia tsutsugamushi*, including Gilliam, Karp and Kato strains). The assay has been described previously.[3]

Descriptive analysis was conducted in Excel (Microsoft Excel, Redmond, WA, USA). All individuals from whom samples were collected provided informed written consent which was obtained in local dialect.

RESULTS

Nine suspected cases were identified by reviewing routine medical records. All cases were male. The median age of the cases was 25 years (interquartile range 18–41 years) with one aged 11 years. The mean duration from symptom onset to hospital admission was six days. All cases presented with an undifferentiated fever syndrome. An eschar, frequently in the groin area, was noted on examination in five cases (55%), and one case developed clinically significant pneumonitis (**Table 1**).

Eight cases were treated with doxycycline and one case was treated with chloramphenicol. Defervescence was reported to occur rapidly following treatment in all

Table 1. **Clinical symptoms presented in the nine suspected cases for rickettsial infections, Solomon Islands, 2014**

Clinical symptoms	*n* (%)
Fever (body temperature > 38.5 °C)	9 (100)
Myalgia	8 (89)
Lymphadenopathy	8 (89)
Headache	5 (56)
Cough	5 (56)
Eschar	5 (56)
Rash	2 (22)

cases. Three cases reported treatment with Coartem (Artemether-Lumefantrine) at local clinics before treatment at the hospital. The outbreak investigation team was able to follow up five of the nine cases (55%) and recruit 10 controls (median age 38.5 years, 90% male) for these five cases. Clinical features and demographics did not differ between the follow-up cases and those who were lost to follow-up.

All five cases and 10 controls reported that animals, including rats, were present in both their houses and gardens. There were no reported differences between the cases and controls in the habit of sleeping on the floor, use of mosquito nets and spending time in the bush. Serum samples were obtained from the cases at a median of two weeks following presentation to the hospital or three weeks following the onset of the febrile illness. All five cases (100%) had strong-positive IgG responses to ST (titre ≥ 1:512) which were consistent with a recent acute infection and were considered as confirmed cases of ST. One control (10%) had a moderate-strong total antibody response against ST (titre 1:256). Four controls (40%) had low levels of total antibodies against SFG rickettsia (mean titre 1:128) and one control had a low-level antibody response to TG rickettsia (titre 1:128), suggesting past exposure.

DISCUSSION

To our knowledge, these are the first laboratory-confirmed cases of ST identified in the Western Province of Solomon Islands. There have been previous laboratory-confirmed cases of both ST and SFG (*R. felis*) in Temotu Province; however Temotu is almost 1000 km across the ocean from Western Province (**Figure 1**).[4,5] We found some clinically suspected ST cases that were reported in United States of America soldiers during World War II in 'North Solomons' which might refer to Bougainville in Papua New Guinea or some regions of Solomon Islands.[6]

All nine ST cases in this study were male. It is unclear if this reflects gender differences regarding health-care access. The presence of eschar is pathognomonic of infection with a rickettsia, but this frequently may not be present. In this study, four cases (44%) did not have a documented eschar, including three of the five laboratory-confirmed cases. It is difficult to distinguish ST and other rickettsia from other causes of undifferentiated fever syndrome when eschars are absent.

Untreated ST has a case fatality ratio of more than 10%, but the disease normally responds well to treatment with doxycycline.[7] All cases responded clinically to doxycycline, providing evidence to support our diagnosis.

Solomon Islands Ministry of Health and Medical Services began conducting mass community treatment with azithromycin as part of a trachoma elimination programme shortly after this outbreak began,[8] which might have prevented further ST disease transmission in the community.

Rickettsial infections can be confirmed by polymerase chain reaction tests using blood or eschar sample in the acute phase of the disease or by serological methods to detect the rise of antibody titres against ST strains between acute and convalescent serum samples.[7] As samples for the acute phase were not available in this investigation, we were unable to perform the laboratory tests above. However, the typical clinical profile (including the presence of eschars) and the very high antibody titres confirmed that ST was the etiology. One control had a low-level antibody response to TG rickettsia, but this was most likely a cross-false positive as this control also had higher titres to the SFG antibodies.

The proportion of malaria that causes fever has been declining in some parts of Solomon Islands from 2008 to 2013.[9] Studies in nearby countries including West Papua, Indonesia have shown rickettsia infections are a common cause of acute infections that lead to hospitalization.[10] Results of our study may give some

Box 1. **Revised clinical case definition for rickettsial infections recommended by the Ministry of Health, Solomon Islands, June 2014**

Acute onset of fever (body temperature > 38.5 °C) AND either A or B	
Group A	Eschar
Group B	Malaria microscopy test negative AND two or more of the following: • Lymphadenopathy • Headache • Myalgia • Rash • Red eyes

insights for the incidence of rickettsia infections in Solomon Islands; however, in the absence of routine testing, the proportion of rickettsial infections that causes febrile illnesses in Solomon Islands is still unclear. A seroprevalence study for rickettsia infections is recommended. This may serve to estimate the incidence of rickettsia infections to help inform management of cases with undifferentiated fever syndromes.

As one of the study limitations, we were unable to obtain serum samples from four of the nine suspected cases; however, the presence of eschars in three of them, along with the results obtained from the other confirmed cases, suggested that the illness in these four cases was also due to ST. Given the small sample size in our study, it is difficult extrapolate these results to the wider population. Statistical analysis was also limited by case numbers. Further studies are recommended to confirm our findings.

In response to this outbreak, the clinical case definition for rickettsial infections was revised to "acute onset of fever (body temperature >38.5 °C) and having eschar OR having malaria microscopy test negative and two or more of the following: lymphadenopathy, headache, myalgia, rash or red eyes" (**Box 1**). Treatment guidelines for rickettsial infections were also developed. Solomon Islands Ministry of Health and Medical Services shared this information with provincial health staff throughout the country for combating future outbreaks of a similar kind.

Conflicts of interest

None declared.

Funding

Michael Marks is supported by a Wellcome Trust Clinical Research Fellowship (102807).

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An outbreak investigation of congenital rubella syndrome in Solomon Islands, 2013

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Introduction: During May 2012, a rubella outbreak was declared in Solomon Islands. A suspected case of congenital rubella syndrome (CRS) was reported from one hospital 11 months later in 2013. This report describes the subsequent CRS investigation, findings and measures implemented.

Methods: Prospective CRS surveillance was conducted at the newborn nursery, paediatric and post-natal wards, and the paediatric cardiology and ophthalmology clinics of the study hospital from April to July 2013. Retrospective case finding by reviewing medical records was also undertaken to identify additional cases born between January and March 2013 for the same wards and clinics. Cases were identified using established World Health Organization case definitions for CRS.

Results: A total of 13 CRS cases were identified, including two laboratory-confirmed, four clinically confirmed and seven suspected cases. Five CRS cases were retrospectively identified, including four suspected and one clinically confirmed case. There was no geospatial clustering of residences. The mothers of the cases were aged between 20 and 36 years. Three of the six mothers available for interview recalled an acute illness with rash during the first trimester of pregnancy.

Discussion: Additional CRS cases not captured in this investigation are likely. Caring for CRS cases is a challenge in resource-poor settings. Rubella vaccination is safe and effective and can prevent the serious consequences of CRS. Well-planned and funded vaccination activities can prevent future CRS cases.

Infection with rubella virus often causes mild disease characterized by fever and rash. Up to 50% of infections are asymptomatic.[1] Serious complications including fetal death and congenital rubella syndrome (CRS) may occur when women are infected early in pregnancy. CRS is characterized by congenital heart disease, deafness, glaucoma, cataracts, mental retardation and other disabilities. CRS may be observed in up to 90% of infants born to mothers infected during the first 10 weeks of gestation.[2]

CRS is a burden on countries with limited resources, particularly countries with low rubella vaccination coverage rates. In 2010, the reported rubella incidence in the Western Pacific Region was 26 per million population.[3] Available data from 2008 to 2010 indicate that more than 30% of female rubella infections were in the childbearing years from 15 to 44 years of age.[3] However, information on the burden of CRS in the Western Pacific Region and globally is scant.

Solomon Islands (population 515 870 in 2009) is an archipelago consisting of nine provinces and 992 islands located in the Western Pacific.[4] Eight provinces have access to a public hospital; in addition there are four private hospitals. In May 2012, a rubella outbreak was declared in Solomon Islands. Six of 10 suspected cases presenting with acute fever and rash (AFR) to a hospital located in the capital city, Honiara (population 64 609 in 2009),[4] were laboratory confirmed by rubella-specific immunoglobulin M (IgM) assay. Between May and September 2012, more than 440 cases of AFR were reported through the national syndromic surveillance system, a sentinel surveillance system with eight reporting sites in five provinces at that time (**Figure 1**). During April 2013, 11 months after the start of the rubella outbreak, a newborn infant with cataracts and thrombocytopenia was reported as a suspected case of CRS by a paediatrician at the hospital. This report describes the subsequent CRS investigation, findings and control measures implemented at the hospital.

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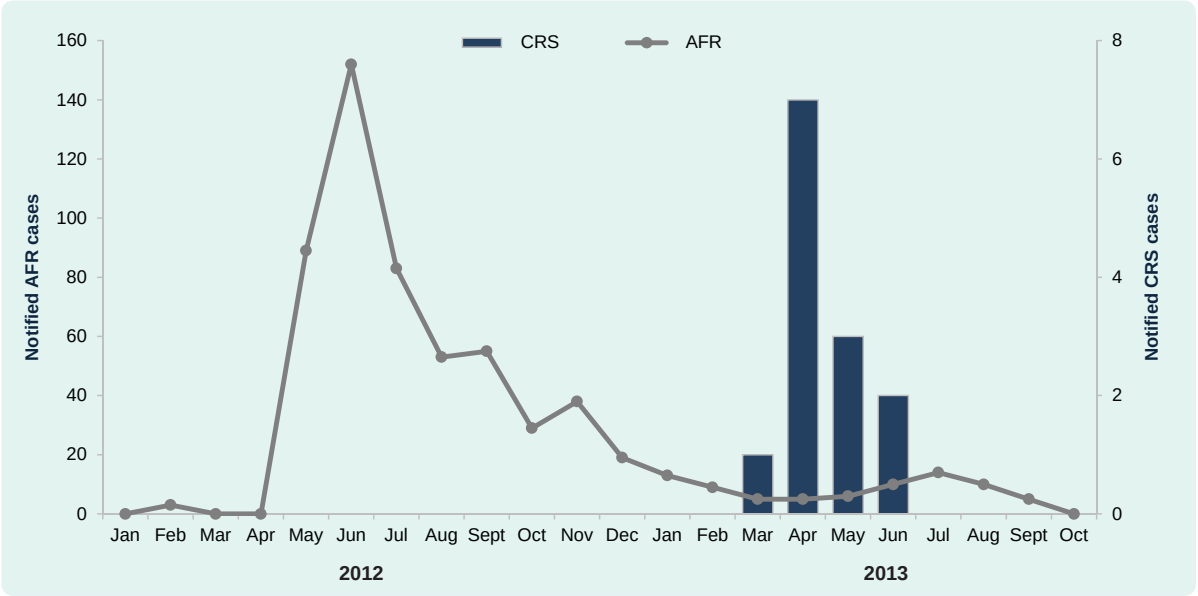
Submitted: 9 November 2015; Published: 3 February 2016
doi: 10.5365/wpsar.2015.6.4.005

Figure 1. **AFR and suspected or confirmed CRS cases by month, Solomon Islands, 2012–2013**



AFR, acute fever and rash; and CRS, congenital rubella syndrome.

METHODS

Prospective CRS surveillance was conducted at the study hospital in the newborn nursery, paediatric and postnatal wards and the paediatric cardiology and ophthalmology clinics from April to July 2013 using established World Health Organization (WHO) guidelines and case definitions.[5] We also conducted retrospective case finding from January to March 2013 by reviewing medical records for clinically compatible illnesses and demographics for the same wards and clinics using the same case definitions. The investigation period was based on the estimated gestational period of pregnant women who may have been infected during the 2012 rubella outbreak (1 May to 30 September 2012) as no routine rubella vaccination or CRS surveillance existed in Solomon Islands before this 2012 outbreak.

The following case definitions were used to identify and classify CRS cases. A suspected case of CRS was any infant less than one year of age in whom a health worker suspects CRS, including any infant with heart disease and/or suspicion of deafness and/or one or more of the following eye signs: cataract, diminished vision, nystagmus, squint, microphthalmus or congenital glaucoma. A clinically confirmed case of CRS was any infant less than one year with two complications in group A or one from A and one from B.

- Group A: cataract(s), congenital glaucoma, congenital heart disease, loss of hearing, pigmentary retinopathy; and
- Group B: purpura, splenomegaly, microcephaly, mental retardation, meningoencephalitis, radiolucent bone disease, jaundice with onset within 24 hours after birth.

A laboratory-confirmed case of CRS was a clinically confirmed CRS case with presence of serum anti-rubella IgM (Beckman Access, Lane Cove, Australia) or rubella-specific ribonucleic acid from pharyngeal swabs tested by reverse-transcriptase polymerase chain reaction (RT–PCR). Mothers were asked if they had illnesses with rash during their pregnancies. Infants had serum and pharyngeal swabs collected for testing. Serum was not available for the retrospectively identified cases and laboratory testing was not performed.

This investigation obtained WHO ethics approval (2015.16.SOL.2.ESR).

RESULTS

In total 13 CRS cases were identified during the investigation period. All CRS cases were born within a

Table 1. **Prospectively and retrospectively identified cases of suspected, clinically confirmed and laboratory-confirmed CRS patients at one hospital in Honiara, Solomon Islands, 2013**

Prospectively/ retrospectively identified	Sex	Age of case when examined	Birth weight (kg)	Clinical features	Anti-rubella IgM	Outcome	Birth year of mother	Fever and/or rash during first trimester	Classification
Prospective	Male	Day 0	1.50 FT	CC, TCP	Positive	Discharged	1993	Yes	Laboratory-confirmed
Prospective	Female	Day 0	2.73	TCP, PR	Negative	Discharged	1987	No	Suspected
Prospective	Female	Day 0	3.17 FT	CC, TCP, ENC	Negative	Death	1988	Yes	Clinically confirmed
Prospective	Male	Day 0	1.97	CC	Positive†	Discharged	1994	Yes	Laboratory-confirmed
Prospective	Male	Day 0	3.00 FT	CC, CHD	Negative	Discharged	1992	No	Clinically confirmed
Prospective	Female	Day 0	3.05 FT	CC, CHD	Sample not tested	Discharged	1977	Yes	Clinically confirmed
Prospective	Male	6 months*	N/A	CC	Negative	N/A	N/A	N/A	Suspected
Prospective	Male	6 months*	N/A	CC	Negative	N/A	N/A	N/A	Suspected
Retrospective	Male	Day 0	1.50 FT	TCP, IUGR	Not tested	Death	N/A	N/A	Suspected
Retrospective	Female	Day 0	N/A	N/A	Not tested	Death	N/A	N/A	Suspected
Retrospective	N/A	Day 0	N/A	TCP, PR	Not tested	Discharged	N/A	N/A	Suspected
Retrospective	N/A	Day 0	N/A	CC	Not tested	Discharged	N/A	N/A	Suspected
Retrospective	N/A	Day 0	N/A	CC, CHD	Not tested	Discharged	N/A	N/A	Clinically confirmed

CC, congenital cataracts; CHD, congenital heart disease [clinical diagnosis by the hospital paediatricians]; ENC, encephalitis; FT, full term; IGUR, intrauterine growth retardation; N/A, not available; PR, petechial rash; and TCP, thrombocytopenia.

* Sample collected at 6 months of age.

† Both IgM and RT-PCR positive.

gestational period from the rubella outbreak in 2012 (**Figure 1**). Eight CRS cases were prospectively identified including three suspected, three clinically confirmed and two laboratory-confirmed cases; six cases were identified in the nursery and two cases, who presented with cataracts, in the outpatient paediatric clinics. The two laboratory-confirmed CRS cases were anti-rubella IgM-positive (of which one was also RT–PCR-positive); the remaining six cases were anti-rubella IgM-negative (**Table 1**). The mothers were aged between 20 and 36 years. There was no geospatial clustering of residences. Three of the six (50%) mothers interviewed recalled an acute illness with rash during the first trimester of pregnancy; no other serious illness was reported during pregnancy.

Five CRS cases were retrospectively identified by medical record review and/or paediatricians' recall, including four suspected and one clinically confirmed case. The first suspected CRS case was born on 5 March 2013 and diagnosed with intrauterine growth retardation, overwhelming sepsis, thrombocytopenia, severe anaemia and asphyxia. From 5 March to 9 April, four newborns were admitted to the nursery with clinical characteristics of CRS, including purpuric rash, cataracts and/or congenital heart disease. Two of the five infants died shortly after birth (**Table 1**).

DISCUSSION

This is the first documented CRS outbreak in Solomon Islands. In 2012, the Solomon Islands Ministry of Health and Medical Services (MHMS) implemented indicator- and event-based early warning outbreak disease surveillance as part of the Pacific Syndromic Surveillance System that includes weekly reporting and investigation of AFR cases.[6] There were eight sentinel sites in five of nine provinces in 2012. From May to September 2012, unusual and substantial increases in AFR were documented from all sentinel sites. Given the absence of routine rubella vaccination, and given that six out of 10 (60%) samples tested from Honiara were confirmed for rubella, it is probable that widespread rubella transmission occurred during this period. Prior to implementation of the early warning surveillance system in 2012, the rubella outbreak would have likely gone unreported.

Despite the small number of laboratory-confirmed CRS cases, the timing of the CRS outbreak is consistent

with the previous rubella outbreak in 2012 (**Figure 1**). Suspected newborn CRS cases that test anti-rubella IgM negative should be re-tested one month later, as approximately 20% of infected infants may not have detectable titres before one month of age;[7] this diagnostic follow-up was not possible as the cases had returned to their villages. Given that substantial rubella transmission appears to have started in May 2012 and prospective CRS surveillance was only implemented from April 2013, it is probable that additional cases went undetected. Additional undetected cases in the other provinces where CRS surveillance was not conducted is also possible.

During 2013, a seroprevalence survey of 100 pregnant women attending the prenatal clinic at the same study hospital was conducted by the MHMS to assess for pre-existing immunity to rubella; 97% of the samples were positive for anti-rubella IgG (MHMS, unpublished data, 2013), demonstrating high rates of prior exposure and infection in this cohort. Given that rubella vaccination was not routinely administered in Solomon Islands until 2013, the high anti-rubella IgG positive proportion suggested substantial prior rubella virus transmission in Honiara. It is not possible to determine if these cases were infected during the 2012 rubella outbreak or during earlier, undocumented rubella transmissions.

CRS is a frequent complication of rubella infection in early pregnancy.[8] Preventing future rubella outbreaks and CRS cases in a resource-limited setting requires careful consideration and planning. The immunization coverage in the population should be greater than 80%, with at least one dose of vaccine, to prevent CRS outbreaks.[5] A vaccination strategy that achieves partial coverage may decrease but not eliminate rubella transmission, potentially shifting the average age of infection from childhood to adolescence and adulthood and increasing the risk of infection during the child-bearing years.[5]

Infants born with CRS are potentially infectious for up to one year.[9] In a setting where the susceptible population is unknown and vaccination coverage is low, implementing control measures to avoid the spread of disease is challenging. Important recommendations were implemented to minimize transmission of rubella within the hospital, including reinforcing hand-washing protocols, procuring and stocking hand sanitizing supplies within the nursery, temporarily relocating pregnant staff to other wards and isolating infectious cases.[10] Prior to hospital discharge, health-care workers must educate families about how to prevent transmission of rubella to others, in particular avoiding contact between pregnant women and the infectious infant.

Caring for CRS cases is a challenge in resource-poor settings. A CRS outbreak has a long-standing impact on vulnerable populations with minimal access to cardiac, auditory and ophthalmologic services. Rubella vaccination is safe and effective.[5] Well-planned and funded vaccination activities can prevent future CRS cases, including in resource-poor countries.

Conflicts of interest

None declared.

Funding

None.

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Effect of antiviral prophylaxis on influenza outbreaks in aged care facilities in three local health districts in New South Wales, Australia, 2014

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Background: There was a record number (n = 111) of influenza outbreaks in aged care facilities in New South Wales, Australia during 2014. To determine the impact of antiviral prophylaxis recommendations in practice, influenza outbreak data were compared for facilities in which antiviral prophylaxis and treatment were recommended and for those in which antivirals were recommended for treatment only.

Methods: Routinely collected outbreak data were extracted from the Notifiable Conditions Information Management System for two Local Health Districts where antiviral prophylaxis was routinely recommended and one Local Health District where antivirals were recommended for treatment but not routinely for prophylaxis. Data collected on residents included counts of influenza-like illness, confirmed influenza, hospitalizations and related deaths. Dates of onset, notification, influenza confirmation and antiviral recommendations were also collected for analysis. The Mann–Whitney U test was used to assess the significance of differences between group medians for key parameters.

Results: A total of 41 outbreaks (12 in the prophylaxis group and 29 in the treatment-only group) were included in the analysis. There was no significant difference in overall outbreak duration; outbreak duration after notification; or attack, hospitalization or case fatality rates between the two groups. The prophylaxis group had significantly higher cases with influenza-like illness (P = 0.03) and cases recommended antiviral treatment per facility (P = 0.01).

Discussion: This study found no significant difference in key outbreak parameters between the two groups. However, further high quality evidence is needed to guide the use of antivirals in responding to influenza outbreaks in aged care facilities.

Influenza is a notifiable condition in New South Wales (NSW), Australia. Aged care facilities (ACFs) are encouraged to notify influenza outbreaks to their local public health unit (PHU), where they are recorded in the NSW Notifiable Conditions Information Management System (NCIMS). There were 111 influenza outbreaks notified in NSW ACFs during 2014, the highest on record (**Figure 1**).[1] Notified influenza outbreaks require at least one laboratory-confirmed case. The predominant circulating influenza strain in 2014 was A(H3N2). As there was a relatively poor match between the circulating and the seasonal influenza vaccine strain in that year,[2] an effective antiviral intervention would have been particularly valuable for influenza outbreak control.

There is inconsistent international guidance on the role of antivirals during influenza outbreaks in ACFs, and practice varies both in Australia and internationally. The Communicable Disease Network of Australia guidelines note that "there is a potential role for antiviral medications in the management of influenza outbreaks in residential care facilities as an adjunct to other control measures",[3] and Victorian Health guidelines note that "prophylaxis may be recommended in some cases".[4] In contrast, antiviral treatment and prophylaxis are routinely recommended for ACF influenza outbreaks in Canada[5] and the United States of America[6] based mainly on the findings of observational studies[7–11] and a randomized controlled trial (RCT) of seasonal prophylaxis.[12]

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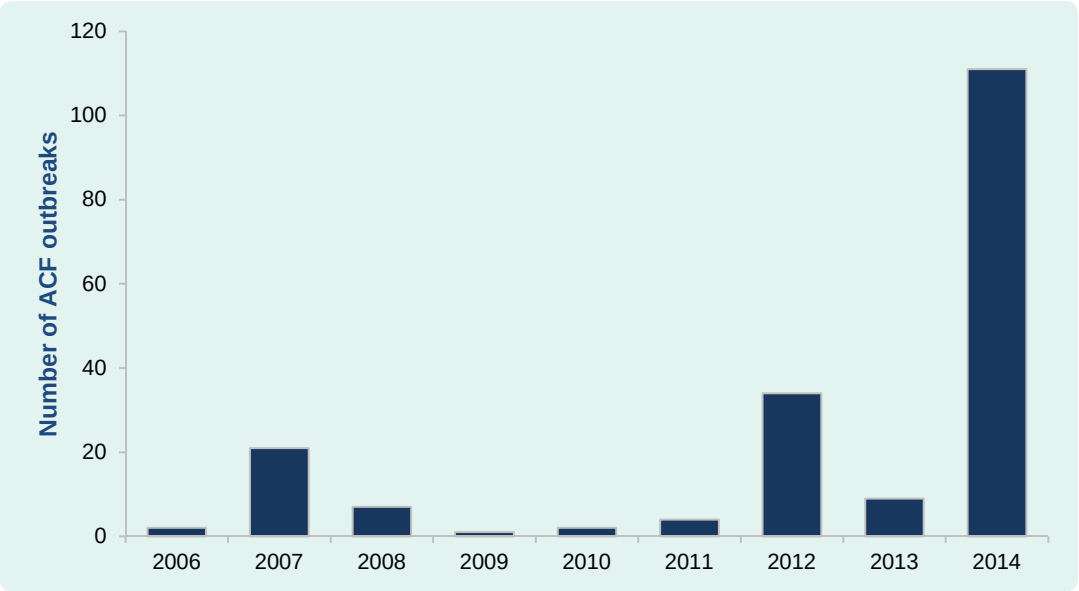
Submitted: 10 August 2015; Published: 19 February 2016
doi: 10.5365/wpsar.2015.6.3.005

Figure 1. **Reported aged care facility influenza outbreaks in New South Wales, Australia, 2006 to 2014**[1]



ACF, aged care facility.

The significant resource implications when considering antiviral prophylaxis, including the costs of health staff and medication, further support the need for a strong evidence base for prophylactic antiviral use. To determine the impact of antiviral prophylaxis recommendations in practice, influenza outbreak data were compared for facilities in which antiviral prophylaxis and treatment were recommended and for those in which antivirals were recommended for treatment only.

METHODS

Study sites

NSW is divided into 15 Local Health Districts (LHDs), each with a PHU. A convenience sample of two LHDs in which antivirals were routinely recommended to ACFs with influenza outbreaks for both treatment and prophylaxis (prophylaxis group) and one LHD in which antivirals were routinely recommended to ACFs for treatment only (treatment-only group) were included in the analysis.

Outbreak response procedures

All facilities were provided with routine outbreak management and infection control advice in accordance with Australian guidelines at the time of notification.[3] In the prophylaxis group, antiviral treatment and prophylaxis were recommended after the first influenza case was confirmed. The PHU sent a letter to the ACF to inform attending medical officers about the outbreak and to recommend oseltamivir treatment for symptomatic cases within 48 hours of onset. Prophylaxis was recommended to other residents for 10 days or until the outbreak was declared over, whichever was the longer period.[3] If the outbreak was confined to a section or wing that was reasonably separate from the remainder of the facility, a recommendation to offer prophylaxis only to residents in that area was made on some occasions. If ACFs did not have ready access to oseltamivir, a starter pack was provided by the PHU. Prophylaxis was routinely recommended for staff at one LHD.

In the treatment-only group, antiviral treatment of cases, in accordance with national guidelines,[3] was discussed with ACF staff when the first confirmed case was notified. Routine response measures for both groups included: isolation of ill residents, exclusion of ill staff, cohorting staff to work with either ill or well residents, limiting admission of new residents for the duration of the outbreak, use of appropriate personal protective equipment and enhanced cleaning.

Influenza outbreak data

All influenza outbreak data for 2014 were extracted from the NCIMS database, including the outbreak details, facility characteristics and key response features (**Table 1**). All confirmed influenza cases in the

Table 1. **Data extracted from the Notifiable Conditions Information Management System for each influenza outbreak in New South Wales, Australia, 2014**

Category	Data
Facility	Number of residents at risk Influenza vaccination coverage for residents Influenza vaccination coverage for staff
Outbreak	Influenza strain(s) Number of ILI cases (total cases) Number of confirmed influenza cases Onset dates for all ILI cases Number of cases hospitalized Number and onset date of related deaths
Response	Date of PHU notification Date of first positive influenza sample result Date of PHU visit to the facility Date of recommendation for use of antiviral prophylaxis Date of commencement of antiviral prophylaxis Number of residents recommended antiviral treatment Number of residents recommended antiviral prophylaxis

ILI, influenza-like illness; and PHU, public health unit.

outbreaks were positive by polymerase chain reaction at a laboratory accredited by the National Association of Testing Authorities.[13] Only illness in residents (but not in health-care workers) was included in the analysis.

Outbreak duration, attack rate, hospitalization rate and case fatality rate were calculated for each facility. Attack rate was further assessed for two time periods: before and after PHU notification. To assess the timeliness of PHU notification, the time from the earliest instance of three influenza-like illness (ILI) cases within a 72 hour period (a potential influenza outbreak)[3] to PHU notification was calculated. The time from notification to laboratory confirmation of influenza and the earliest time at which prophylactic antiviral use could be considered was also determined. When confirmation occurred before notification, this period was recorded as zero days. Definitions for the key analysis terms are listed in **Table 2**.

Statistical methods

Median and interquartile values were calculated for relevant outbreak parameters and the Mann–Whitney U test was used to assess the significance of differences between group medians. Differences are reported as significant for $P < 0.05$. Stata version 11 (StataCorp LP, Texas, USA) was used for all calculations.

RESULTS

Study population

The ACFs in the treatment-only and in the prophylaxis groups had comparable numbers of residents at risk (median 85.0 versus 87.5 residents, $P = 0.92$). Influenza vaccination rates for the two groups did not differ significantly for staff (50.0% versus 39.0%, $P = 0.11$) or for residents (95.6% versus 98.0%, $P = 0.23$) (**Table 3**).

Influenza outbreak profiles

A total of 41 outbreaks were included in the analysis. The treatment-only group had 29 confirmed influenza outbreaks notified during 2014, affecting 22.1% of the 131 ACFs in the district. Antiviral prophylaxis was used for three residents who shared a room with a confirmed case in one large outbreak in this group (with 22 cases and 120 residents at risk). This outbreak was retained as the antiviral prophylactic usage was minimal.

The prophylaxis group had a total of 13 confirmed influenza outbreaks in 2014, affecting 6.2% of the 210 ACFs in the two districts (6/63, 9.5% and 7/147, 4.8% in each LHD, respectively). In three outbreaks, prophylaxis was recommended for only part of the ACF

Table 2. **Terms and key analysis parameters used to compare the antiviral prophylaxis and treatment-only groups, New South Wales, Australia, 2014**

Term	Definition
Potential influenza outbreak	Three or more ILI cases in residents within a 72-hour period.
Confirmed influenza outbreak	Potential influenza outbreak plus laboratory-confirmed influenza in at least one case. Subsequent to an influenza outbreak being confirmed, further cases of ILI were considered to be related to the outbreak whether or not they were laboratory-confirmed.
Influenza-like illness	Sudden onset of fever and cough or other respiratory symptoms and one or more systemic symptoms.[1] In practice, ILI was loosely defined, and generally a resident was included as an outbreak ILI case if s/he had acute onset of any respiratory symptom(s) (for example, cough, rhinorrhoea or sore throat).
Residents at risk of infection	All residents in the same aged care facility during an influenza outbreak.
Outbreak duration	The period from first to last onset date in residents.
Linked death	Death in a resident who was included on an outbreak line list and had a death certificate that included influenza or respiratory disease as a cause of death or contributing factor.
Hospitalization rate	Total hospitalized residents/total resident cases (laboratory-confirmed and ILI).
Case fatality rate	Linked deaths/total resident cases (laboratory-confirmed and ILI).
Pre-notification attack rate	Total resident cases (laboratory-confirmed and ILI) up to and including date of PHU notification/total at-risk residents.
Post-notification attack rate	Total resident cases (laboratory-confirmed and ILI) with onset after date of PHU notification/total at-risk residents from the day following PHU notification.

ILI, influenza-like illness; and PHU, public health unit.

resident population. Twelve outbreaks were included in the analysis after excluding one outbreak that was notified too late for prophylaxis.

Influenza was laboratory confirmed in 47.3% and 41.2% of the ILI cases in the treatment-only and prophylaxis groups, respectively. The number of confirmed cases per facility was lower in the treatment-only group than the prophylaxis group (median 5 versus 7, $P = 0.06$) as was the number of ILI cases in each outbreak (median 13 versus 23, $P = 0.03$) (**Table 3**).

Both groups had a similar mix of implicated influenza strains. Influenza A was identified in all outbreaks. The predominant strain was A/H3N2. Influenza B was also identified in two outbreaks in the treatment-only group and one in the prophylaxis group (**Table 3**). Four outbreaks had two different influenza strains identified (two in the treatment-only and two in the prophylaxis group). All outbreaks in the prophylaxis group and 89.7% (26/29) of outbreaks in the treatment-only group occurred during the influenza season from July to September 2014. Oseltamivir was used for treatment and prophylaxis in all outbreaks.

The outbreak duration (median 9.0 days versus 11.5 days, $P = 0.41$), overall attack rate (18.3% versus 23.9%, $P = 0.15$), hospitalization rate (11.1% versus 14.1%, $P = 0.15$) and case fatality rate (0.0 versus 1.7, $P = 0.95$) were all lower in the treatment-only group than the prophylaxis group, but the differences were not statistically significant. There was also no significant difference between the two groups in pre- and post-notification attack rates or in outbreak duration after notification ($P > 0.05$) (**Table 3**).

Outbreak responses

The time from meeting the Communicable Disease Network of Australia's potential influenza outbreak criteria[3] to PHU notification was similar for the treatment-only and prophylaxis groups (median 1 day versus 2 days, $P = 0.23$), as was the time from notification to confirmation (median 1 day versus 1.5 days, $P = 0.77$). For three outbreaks in the prophylaxis group, influenza confirmation occurred before PHU notification. The median time from antiviral prophylaxis recommendation to medication commencing was 0.5 day (interquartile range, 0.0–1.0 day) for the prophylaxis group.

Based on the available data, antivirals were used for treatment in a lower proportion of facilities in the treatment-only group (68.8% versus 83.3%), and fewer cases per facility were treated with antivirals in the

Table 3. **Comparison of age care facility influenza outbreak parameters for the antiviral prophylaxis and treatment-only groups, New South Wales, Australia, 2014**

	Treatment-only group	Prophylaxis group	*P*-value*
ACF outbreaks included	29	12	NA
Antiviral prophylaxis recommended for all residents	0	12	NA
Total residents at risk:‡ median (IQR)	85.0 (52.0–123.0)	87.5 (66.5–99.5)	0.92
Staff vaccination coverage (%):† median (IQR)	50.0 (41.5–75.0)	39.0 (22.0–50.0)	0.11
Resident vaccination coverage (%):‡ median (IQR)	95.6 (86.5–98.4)	98.0 (95.0–100.0)	0.23
First outbreak onset date	2 January 2014	4 July 2014	NA
Last outbreak onset date	2 October 2014	8 September 2014	NA
Influenza A confirmed (H1, H3, unspecified)	29 (2, 18, 9)	12 (1, 7, 5)†	NA
Influenza B confirmed	2	1	NA
ILI outbreak to PHU notification in days:‡ median (IQR)	1.0 (0.0–2.0)	2.0 (0.5–4.5)	0.23
PHU notification to influenza confirmation in days:‡ median (IQR)	1.0 (0.0–3.0)	1.5 (0.0–2.5)	0.77
Total confirmed cases:‡ median (IQR)	5 (4.0–8.0)	7 (6.0–9.0)	0.06
Total ILI cases:‡ median (IQR)	13 (9.0–15.0)	23 (12.0–28.0)	0.03
Outbreak duration in days:‡ median (IQR)	9.0 (7.0–16.0)	11.5 (9.5–14.0)	0.41
Total attack rate (%):‡ median (IQR)	18.3 (9.8–25.0)	23.9 (17.3–30.6)	0.15
Attack rate (pre-notification) (%):‡ median (IQR)	9.5 (5.7–15.0)	10.9 (4.6–20.1)	0.76
Attack rate (post-notification) (%):‡ median (IQR)	7.8 (3.8–13.4)	15.1 (7.2–18.2)	0.11
Hospitalization rate (%):‡ median (IQR)	11.1 (0.0–20.0)	14.1 (12.8–25.5)	0.15
Case deaths:‡ median (IQR)	0 (0.0–1.0)	1 (0 – 2)	0.21
Case fatality rate (%):‡ median (IQR)	0.0 (0.0–8.3)	1.7 (0.0–7.8)	0.95
Total case deaths	15	12	NA
Duration after PHU notification in days:‡ median (IQR)	6.0 (3.0–8.0)	4.5 (4.0–8.5)	0.71
Antiviral treatment used in facility	11/16 (68.8%)	10/12 (83.3%)	NA
Resident cases recommended antiviral treatment:‡ median (range)	2.5 (0.0–12.0)	7.0 (0.0–29.0)	0.01
Antiviral prophylaxis used in facility	1/29 (3.4%)	12/12 (100%)	NA
Residents recommended antiviral prophylaxis:‡ median (IQR)	0 (0.0–3.0)	57.5 (7.0–94.0)	NA
Total residents recommended antiviral prophylaxis	3	544	NA
Time from antiviral prophylaxis decision to commencement days:‡ median (IQR)	NA	0.5 (0.0–1.0)	NA
Total deaths 24 hours or more after influenza confirmation	1	3	NA
Facilities with PHU onsite visit	3	3	NA

* Mann–Whitney U test was used.

† One outbreak had both influenza A H1 and H3 strains confirmed.

‡ Per facility.

ACF, aged care facility; ILI, influenza-like illness; IQR, interquartile range; NA, not applicable; and PHU, public health unit.

treatment only group (2.5 versus 7.0 cases, $P = 0.01$) (**Table 3**).

DISCUSSION

We found no significant difference in outbreak attack rate, duration, hospitalization or case fatality rate for those ACFs recommended antiviral treatment alone compared to those recommended antiviral treatment and prophylaxis. The facilities in the two groups had similar numbers of residents and comparable vaccination coverage for both residents and health workers. All outbreaks in the study occurred in NSW during 2014, with the majority in the three-month period between July and September.

The results are consistent with a recent European RCT in an aged care setting[14] that found no evidence that antiviral prophylaxis during an influenza outbreak reduced the risk of new infections over a four-year period; however, the European study was underpowered. In contrast, an Australian RCT concluded that there was

"some support for a policy of treatment and prophylaxis with oseltamivir in controlling influenza outbreaks in ACFs",[15] but the authors in that study also noted that the trial lacked power. Concerns were subsequently raised that one of the three control outbreaks in that study, in which there was a delayed and incomplete intervention, should be excluded. With that outbreak removed, the apparent beneficial effect of antiviral prophylaxis disappeared.[16] A subsequent review by the Academy of Medical Sciences in the United Kingdom in 2015 concluded that there was inadequate evidence to "inform a single approach for prophylaxis in care homes" and that "further research is needed to inform decisions on whether or not to use [antivirals] in prophylaxis in care homes".[17]

Some important potential confounding factors were considered in our analysis, including differences in the timeliness of notification, outbreak severity and the thoroughness of interventions between the two groups. No significant difference in the timeliness of PHU notification between the two groups was identified. Outbreak severity was assessed in several ways in this study. The attack rate for the period up to notification did not differ significantly between groups, which is consistent with the two groups having similar overall severity. However, there were some other indications that outbreaks may have been more severe in the prophylaxis group, with median values for overall attack rate and hospitalization rates higher than in the treatment-only group, although neither was significantly different.

A higher proportion of facilities in the treatment-only LHD reported having influenza outbreaks in 2014. There may have been more outbreaks in this district or there may have been relative underreporting of outbreaks in the prophylaxis districts. An audit of laboratory notifications for influenza in one LHD in the prophylaxis group identified seven ACFs with three or more linked cases of confirmed influenza and a further 15 facilities with one or two cases of confirmed influenza that did not report an outbreak to the PHU in 2014 (South Western Sydney LHD, unpublished data, 2014). Data were not available to assess whether non-reported outbreaks were less severe than those that were notified.

There was also limited capacity to assess the thoroughness of interventions. The same national response guidelines[3] were used for general infection control advice, but it was not possible to further explore the comparability and completeness of interventions at ACFs. Detailed data on non-antiviral outbreak measures and the extent to which antiviral recommendations were implemented by ACFs were not available. Additional information on antiviral use in future influenza seasons would enhance the analysis of routinely collected ACF outbreak data.

We found four outbreaks had two different influenza strains, indicating multiple importations into those facilities. Other outbreaks may have had unidentified multiple importations with potential impact on the course of the outbreak. Influenza was confirmed in less than half of the ILI cases in the treatment-only and prophylaxis groups. Some residents with ILI may have been infected with other pathogens that affected the analysis.

This was an observational study and is subject to several limitations. The use of antiviral prophylaxis was neither randomized nor blinded, and systematic differences between groups could have confounded the analysis. Notification timeliness, outbreak severity and thoroughness of intervention have been considered in detail, and the overall outbreak profile was similar for the two groups. However some parameters were not considered, including staff illness data, the outbreak setting (some occurred in high dependency units or semi-independent hostel settings), residents' demographics and co-morbidities and the overall resident acuity.

CONCLUSIONS

Our analysis did not find evidence that a policy of recommending prophylactic antivirals in ACF influenza outbreaks reduced attack rate, outbreak duration, hospitalization rate or case fatality rate during the 2014 influenza season in NSW. Despite the study limitations, the absence of any differences between groups suggests that any effect of antiviral prophylaxis in practice is likely to have been small or negligible. There is a need for further high quality evidence to guide use of antivirals in influenza outbreak response in ACFs.

Conflict of interest

None declared.

Funding

None.

Acknowledgments

The authors would like to acknowledge the many public health staff from the Hunter New England, Sydney and South Western Sydney Public Health Units and all of the aged care facility and laboratory staff who were involved in the identification and management of these outbreaks.

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Engaging the international community during the 2015 Middle East respiratory syndrome outbreak in the Republic of Korea

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The 2015 Middle East respiratory syndrome (MERS) outbreak in the Republic of Korea, which started with an imported case[1] and spread throughout the country with a total of 186 cases,[2] revealed the vulnerabilities of the health-care system of the country. The situation was compounded by the unique health-care settings in the Republic of Korea, including crowded emergency departments and large numbers of hospital visitors seeking care at multiple hospitals.[3] To assist with the outbreak response, the Ministry of Health and Welfare of the Republic of Korea hosted several international joint missions that provided valuable information and recommendations for MERS control and prevention of future outbreaks. This report briefly summarizes the missions' outcomes and discusses their positive impacts.

THE MISSIONS

The Republic of Korea–World Health Organization (WHO) Joint Mission on MERS aimed to provide technical recommendations on outbreak response measures; it was conducted between 9 and 13 June 2015.[4] The mission team was composed of 16 disease outbreak experts. On 16 June, the ninth International Health Regulation (IHR) Emergency Committee Meeting regarding Middle East respiratory syndrome coronavirus (MERS-CoV) was convened by teleconference.[5] On 19 June, the Director-General of WHO and the WHO Regional Director for the Western Pacific visited the Republic of Korea to provide recommendations to the leaders of the country.[6] Experts from Saudi Arabia also visited the Republic of Korea from 12 to 18 June to share their MERS experience. The Republic of Korea invited experts from the United States Centers for Disease Control and Prevention (US CDC) for technical cooperation on MERS during the period 21 June to 1 July. The Republic of Korea also invited experts from WHO and the United States of America during the period 23 to 26 June to assist with recommendations for communicable disease preparedness and response system reforms.

RESULTS

The Republic of Korea–WHO Joint Mission provided updates and assessments on the 2015 MERS outbreak. Technical recommendations on outbreak control measures were provided, including: (1) infection prevention and control measures should immediately be strengthened at all health-care facilities across the country; (2) close contacts of MERS cases should not travel during the period when they are being monitored for symptom development; (3) implementation of basic public health measures by all health authorities should be continued; (4) risk communications should be strengthen to increase domestic and international confidence and trust; and (5) selected hospitals should be designated for safe triage and assessment of suspected MERS cases.[3]

Based on the results of the Republic of Korea–WHO Joint Mission, the IHR Emergency Committee concluded that this MERS outbreak in the Republic of Korea did not constitute a Public Health Emergency of International Concern.[5] WHO leaders provided recommendations to Republic of Korea government officials; WHO also

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Submitted: 13 October 2015; Published: 1 February 2016
doi: 10.5365/wpsar.2015.6.4.003

announced its risk assessment results for this MERS outbreak and gave advice to the general public via a press conference.

The experts from Saudi Arabia shared MERS patient care experience with experts of the Republic of Korea. Epidemiological characteristics of MERS cases between the two countries were also compared. The experts concluded that the adjusted case fatality ratio (adjusted by secondary infection and co-morbidity) of MERS were similar for the two countries (also similar to the results of a previous study[7]). The Saudi Arabian experts also confirmed that MERS is transmitted mostly in droplets, reassuring airborne infections would be extremely rare.

Experts from the US CDC technical cooperation team conducted a comprehensive review of the epidemiological and clinical responses to the MERS cases. They also visited four hospitals to observe the triage system for suspected MERS cases. Infection prevention and control practices at emergency departments and isolation treatment units were also reviewed. The experts concluded that the Republic of Korea had done an extremely thorough and high-quality epidemiological investigation and contact-tracing.

The WHO and United States of America experts provided advice on strengthening the public health system and on establishing clear leadership for outbreak control and risk management. They also commended the strengthened response measures across all sectors of the government despite the limited early response efforts.

DISCUSSION

The information and advice provided by the joint missions helped the Republic of Korea to set clear directions and guidelines for the MERS outbreak response. The Republic of Korea government launched measures to reform their national infection prevention and control system and later revised it to strengthen their communicable disease outbreak response system.[8]

Based on the recommendations from the Republic of Korea-WHO Joint Mission, the Ministry of Health and Welfare reacted immediately by creating the MERS portal website[9] and multi-language, toll-free telephone hotline services for timely disease information sharing and effective risk communications.[10] These actions may have eased the mounting fear about MERS while restoring the public's trust in the local government's response measures. Using Google Trends data as a proxy for reflecting the level of concern in the public towards this MERS outbreak, we found Internet searches for MERS peaked during the week of the Republic of Korea–WHO Joint Mission and decreased substantially thereafter.[11]

These joint missions also fostered further scientific cooperation on MERS. The Saudi Arabian experts provided an opportunity to better understand the MERS coronavirus through sharing patient care experience. Joint research opportunities on sero-epidemiology for this outbreak were explored after the US CDC team visit. The Republic of Korea and WHO also jointly organized the 2015 International Symposium on MERS to share experience and new knowledge from recent MERS outbreaks and to discuss how to strengthen public health systems in response to future MERS outbreaks and other threats.[12]

Several limitations of the joint missions were noted, most related to the timing. The Republic of Korea–WHO Joint Mission and the Saudi Arabia mission occurred during the peak of the outbreak. This prevented a more comprehensive assessment with all relevant stakeholders as efforts were more focused on outbreak response at that time. The short duration of each mission was also an impediment for more in-depth situation analysis and review.

Engaging the international community allows the affected country to seek advice from world-class experts and also sends a strong message that local government is committed to sharing information and working together with the international community. Technical cooperation with international partners can produce useful outcomes for improving the communicable disease preparedness and response system. It also provides an opportunity to review the situation with external inputs from unbiased perspectives. Information sharing through collaborative activities helps allay fear in the international community. We found important benefits of international cooperation for combating infectious diseases, and it should be encouraged in future outbreaks.

Conflicts of interest

None declared.

Funding

None.

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Surveillance and response of hepatitis B virus in Hong Kong Special Administrative Region, 1988–2014

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The World Health Organization (WHO) Western Pacific Region with an estimated 160 million chronic hepatitis B virus (HBV) carriers in 2007 bears a significant burden of HBV-related mortality and morbidity.[1] Most Member States in the region have an estimated chronic HBV infection proportion of more than 8% in their adult population, which is the highest worldwide.[2] The WHO Regional Office for the Western Pacific published the first Regional Plan for Hepatitis B Control[1] in January 2003.This plan is updated periodically with a consistent ultimate goal of achieving a chronic HBV infection rate of less than 1% in the region.

Viral hepatitis is a statutorily notifiable disease in Hong Kong Special Administrative Region (SAR). The Central Notification Office of the Department of Health receives notifications with pre-defined case definitions.[3] In July 2011, Hong Kong SAR was verified by the WHO Regional Office for the Western Pacific as having successfully achieved the goal of hepatitis B control.[4]

Liver cancer was the third leading cause of cancer death in Hong Kong SAR in 2012,[5] and evidence showed that 75–80% of liver cancer cases were related to chronic HBV infection.[6] This report reviews the surveillance data of HBV infections in Hong Kong SAR from 1988 to 2014 and discusses the responses and existing gaps to achieve the WHO goal in the local context.

METHODS

Viral hepatitis has been a statutorily notifiable disease since 1974 in Hong Kong SAR. Collation and analysis of surveillance data obtained from various sources were compiled in the annual reports of surveillance of viral hepatitis by the Department of Health, Hong Kong SAR.[7] We extracted HBV-specific data from the reports, including acute HBV infection notification data for the period 1988 to 2014 and hepatitis B surface antigen (HBsAg) seroprevalence data from 1990 to 2014.

Acute hepatitis B

Data on acute HBV infections were obtained from the Department of Health Central Notification Office that centralizes communicable diseases notifications and monitoring in Hong Kong SAR. A case of acute hepatitis B is defined as a person having clinically compatible acute hepatitis illness with laboratory confirmation of hepatitis B core antibody immunoglobulin M positive result.[3]

Chronic hepatitis B

HBsAg seroprevalence data were obtained from various sources, including Hong Kong Red Cross Blood Transfusion Service; Family Planning Association of Hong Kong SAR, a nongovernmental organization providing screening for clients attending pre-marital and pre-pregnancy check-ups; Family Health Service; Public Health Laboratory Service; Tuberculosis and Chest Service; and HIV/AIDS Service of the Department of Health. Data were collected annually in 1990–2014. Data from Tuberculosis and Chest Service only covered data from March to May in 1990–2014.

Annual acute hepatitis B notification and HBsAg seroprevalence data were compared for trends. Data were stratified by sex for analysis. HBsAg seroprevalence data were also analysed among specific groups, including at-risk groups that are defined as groups with risk of blood-borne or sexual transmission of hepatitis B. All analysis was done by Excel (Microsoft Excel 2010, Redmond, USA).

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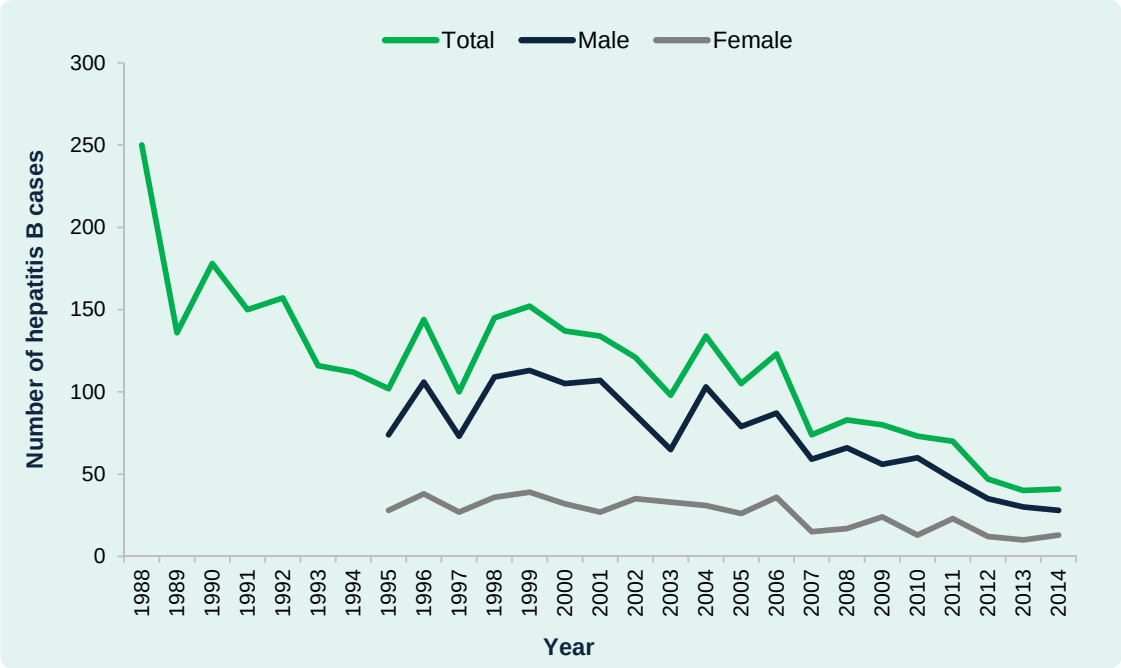
Submitted: 28 July 2015; Published: 3 February 2016
doi: 10.5365/wpsar.2015.6.3.003

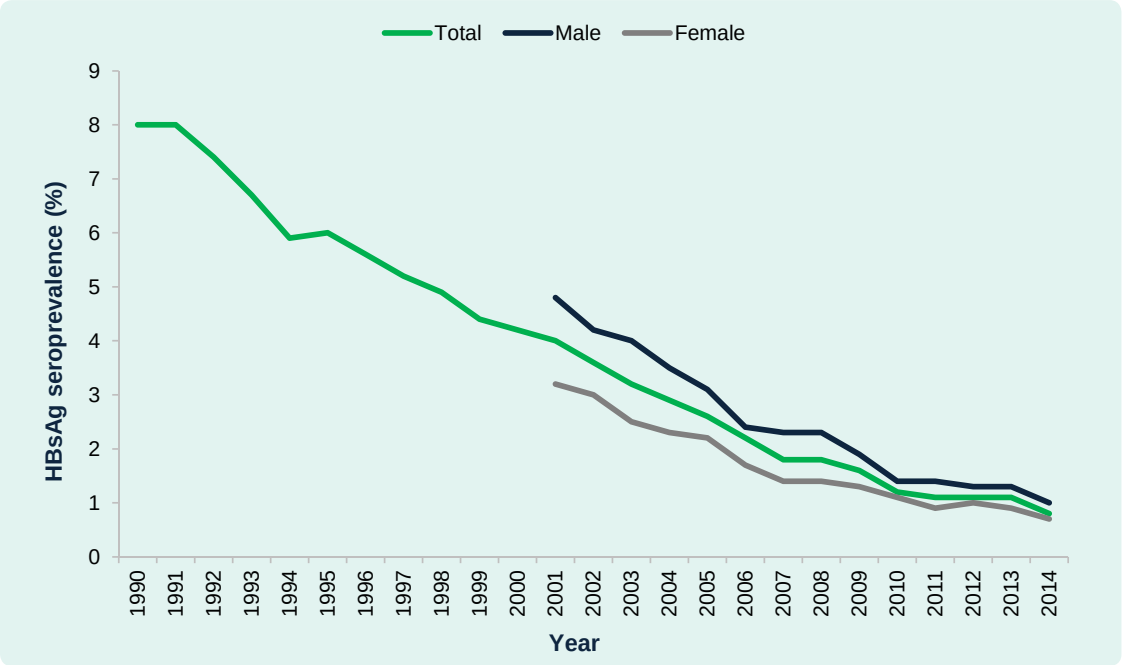
Figure 1. **Hepatitis B virus surveillance data, Department of Health, Hong Kong Special Administrative Region**

Panel A. Acute hepatitis B virus infection notification data, 1988–2014*



*Sex specific data are available since 1995.

Panel B. HBsAg seroprevalence (%) in new blood donors, 1990–2014*



*Sex specific data are available since 2001.

RESULTS

A downward trend was observed for both acute and chronic HBV infections. The reported number of acute HBV infections decreased steadily from 250 cases in 1988 to 41 cases in 2014 (**Figure 1**). For chronic HBV infections in new blood donors the rate dropped from 8.0% in 1990 to 0.8% in 2014 (1.0% for males and 0.7% for females). Among adults, the decreasing trend was also observed, albeit less prominently, in antenatal women (11.3% in 1990 to 6.2% in 2014), pre-marital/ pre-pregnancy screening clients (9.6% in 1990 to 5.5%

in 2014) and police officers (6.1% in 1996 to 2.6% in 2014). Based on the available data, the HBsAg seroprevalence was 9.5% and 7.5% in people living with HIV in 2000 and 2014, respectively and was 6.8% and 7.2% in female sex workers in 1995 and 2011, respectively.

DISCUSSION

The results show that Hong Kong SAR evolved from a region of high-intermediate to intermediate-low hepatitis B endemicity from 1988 to 2014. The decrease is probably due to concerted preventive efforts applied since the late 1980s, including community-based vaccination, public awareness programmes and measures such as antiviral subsidies and specialist referral for treatment, institution-based infection control to prevent occupational exposure and methadone treatment programmes for drug users to prevent infections of blood-borne pathogens.

Adequate vaccination policies in the past decades contributed significantly to reducing HBV infections. A local prospective study demonstrated the long-term protective effect of neonatal HBV vaccination for up to 30 years in high-risk infants borne to HBsAg-positive mothers.[8] Since 1988, the universal neonatal hepatitis B immunization programme has continued to record high birth dose coverage rates (99.1–99.6% in 2008 to 2013). For neonates of HBsAg-positive mothers, hepatitis B immunoglobulin was also given at birth to further reduce the risk of perinatal infection. The percentage of children aged 2 to 5 years who completed three doses of HBV vaccine exceeded 98.8% in 2012.[7] A supplementary hepatitis B vaccination programme for primary school students was introduced in 1998. From 2004 to 2014, the coverage of three-dose HBV vaccination among the students each year was 99% on average.[7] HBV immunization programmes were also in place for prioritized adult populations including health-care workers since 1983. High vaccine coverage provides sufficient individual and herd immunity against HBV infections.

Currently, the major burden of HBV infections in Hong Kong SAR lies in the adult population (aged 30 or above) who did not benefit from the universal neonatal hepatitis B immunization programme. While the risk of developing a chronic infection when contracting the virus in adulthood is generally low,[9] it is a public health priority to address the burden of morbidity and mortality from HBV infections among adults. At-risk groups, including health-care workers, injecting drug users, patients undergoing dialysis, and household contacts and sexual partners of persons with chronic hepatitis B, should be screened and referred to medical care. Currently, serological testing for HBV markers is implemented only in some of these targeted populations. Efforts should be extended for screening and linkage to medical care for the at-risk adult population who have not been screened and vaccinated. Meanwhile, territory-wide information of chronic HBV infection is essential for disease control. Robust data provided by different stakeholders and the potential use of mathematical modelling for disease and treatment burden estimation should be explored.

This study used only secondary data for analysis; the quality of some of the data from private agencies could not be controlled. In addition, there were missing data on specific groups that might have hindered the comparison, and more in-depth analysis could not be performed on these aggregated data. However, using official data from the government for analysis ensured data quality.

Hong Kong SAR has evolved from a region of high-intermediate to one with intermediate-low hepatitis B endemicity in the past decades. Adequate vaccination policies are likely to contribute to reducing HBV infections. Specific interventions should be conducted targeting the at-risk groups. More robust territory-wide HBV infection data should be collected and analysed for disease control.

Conflicts of interest

None declared.

Funding

None.

Acknowledgements

The authors would like to thank all colleagues and partners of the Department of Health, the Hospital Authority and the academic and private sector for their collaboration

and contributions to hepatitis B surveillance and control in Hong Kong SAR.

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Communicating about the Middle East respiratory syndrome outbreak to the international community and in-country foreigners, Republic of Korea, 2015

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Under the *International Health Regulations (2005)*, risk communication is one of the eight core capacities that are critical to effectively detect and respond to public health threats.[1] During outbreaks, international visitors and foreign residents may be poorly informed about the risk of infection and response measures due to language barriers. Specific strategies targeting these groups are needed for effective outbreak communications.

The Republic of Korea has a large number of international visitors annually and has a large population of foreign residents. In 2014, there were 14.3 million international visitors to the Republic of Korea. There were also 1.8 million foreign residents in the country in 2014, representing 3.6% of the total population. Among international visitors, China had the largest proportion (52.7%) followed by Japan (16.1%) and English-speaking countries (9.2%), including the United States of America, Canada, the United Kingdom, Australia and New Zealand. Among foreign residents, Chinese were also the largest group (52.3%, though 66% of them were Korean-Chinese) followed by people from the United States of America (7.6%) and Viet Nam (7.2%).[2]

During the Middle East respiratory syndrome (MERS) outbreak in 2015,[3] the Ministry of Health and Welfare (MOHW) of the Republic of Korea provided outbreak information targeting international visitors and foreign residents through multiple channels. The MOHW created a MERS portal website in Korean and English on 10 June 2015;[4] in addition, the existing MOHW website provided English-language press releases beginning 28 May.[5] A toll-free telephone hotline also started service in English on 12 June;[6] it expanded to include 18 other foreign languages on 15 June.[7] This report describes the usage of these multi-language communication channels during this MERS outbreak.

METHODS

Postings on the MOHW and the MERS portal website from 28 May to 5 July 2015 were screened using the keyword(s) "Middle East respiratory syndrome" or "MERS". Postings that contained these keywords were extracted and grouped into three categories: press release, statistics and other information for analysis. Website usage was evaluated by counting the total number of visits to the site and average visits per posting in the period of data collection. Hotline usage was evaluated by the number of calls received. Telephone hotline data from 12 June to 5 July 2015 were collected and stratified by day and by language for analysis. Data manipulation and analysis were conducted using Excel (Microsoft Excel, Redmond, USA).

RESULTS

There were 66 MERS-related postings on the MERS portal website and 61 related postings on the English-language MOHW website. For the MERS portal website, there were 25 press releases, 14 statistics postings and 27 postings of other MERS information. Similarly there were 24 press releases, 13 statistics postings and 24 postings for other information on the MOHW

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Submitted: 13 October 2015; Published: 24 February 2016
doi: 10.5365/wpsar.2015.6.4.002

Table 1. **Number of MERS-related postings provided on the MERS portal and English-language MOHW websites, Republic of Korea, 28 May to 5 July 2015**

Category	MERS portal website			English-language MOHW website		
	Number of postings	Number of site visits	Average site visits per posting	Number of postings	Number of site visits	Average site visits per posting
Press releases	25	18 272	731	24	11 409	475
MERS statistics	14	5534	395	13	5234	403
Other information	27	17 175	636	24	9146	381
Total	**66**	**40 981**	**621**	**61**	**25 789**	**423**

MERS, Middle East respiratory syndrome; and MOHW, Ministry of Health and Welfare.

website. The total number of site visits during the study period was 40 981 on the MERS portal website and 25 789 on the English-language MOHW website. On both websites, press releases had the highest number of visits with an average of 731 visits on the MERS portal website and 475 visits on the English-language MOHW website (**Table 1**).

The most popular postings were those related to the Republic of Korea–World Health Organization (WHO) joint mission conducted on 9–13 June 2015. The press release of the joint mission had 5447 visits on the MERS portal website and 1007 visits on the English-language MOHW website. The posting about high-level messages from the joint mission had 3409 visits on the MERS portal website and 388 visits on the English-language MOHW website.

In total, there were 787 MERS hotline calls using the foreign languages service from 12 June to 5 July 2015, representing 0.91% of the total calls (n = 86 826) in that period. The English-language hotline service received the most calls (n = 677) followed by the Japanese (n = 57) and Chinese (n = 50). The number of calls received was high at the beginning on 12 June 2015 and peaked on 16 June 2015 (n = 150), but it decreased to less than 20 calls per day from 20 June 2015 onwards.

DISCUSSION

The Republic of Korea government realized that outbreak information sharing in multi-languages is essential to communicate with the international community as recommended by the Republic of Korea–WHO joint mission.[8] The government responded immediately after the joint mission to provide daily press release summaries and statistics in English for the MERS outbreak situation. The information was disseminated through official websites.

Unlike the hotline call services, the MOHW and MERS portal websites provided information only in English. This might be a limitation, but sharing information in English should cover most of the foreign populations as we found English was the most commonly accessed language in the hotline service in this study. While Chinese accounts for the largest portion of international visitors and foreign residents in the Republic of Korea, utilization of the Chinese hotline was less than expected. This may be due to the fact that 66% of the Chinese residents were Korean-Chinese. They might not need the service as they are able to speak the Korean language or have Korean relatives who are able to translate the information for them.

While effective outbreak communication focuses on five key points: trust, early announcement, transparency, understanding the public and planning, it is essential to build, maintain and restore the public's trust during outbreak situations.[9] Establishing a hotline system has proved to be effective for building trust with the public.[10] This report gives evidence that dedicated English language MERS websites and multi-language hotlines were useful to share information with the international community for outbreak communications, although it is difficult to quantify the impact and effectiveness of these efforts.

Effective outbreak communication is essential to build the public's trust. Keeping the international community and foreign residents well informed is

important to streamlining implementation of timely and effective response measures during outbreaks.

Conflicts of interest

None declared.

Funding

None.

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Underreporting of influenza outbreaks in aged care facilities in South Western Sydney, Australia, 2014

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In 2014, influenza activity was high in New South Wales (NSW), Australia, and 21 443 people were hospitalized with a diagnosis of influenza-associated pneumonia. This translates to a rate of 252.4 cases per 100 000 population. More than 18 000 cases of laboratory-confirmed influenza were reported in NSW. The majority were influenza A, dominated by A/H3N2 subtype. There were also 111 influenza outbreaks in aged care facilities (ACFs) reported in NSW in 2014, the highest number on record.[1]

Elderly residents in ACFs experience high rates of morbidity and mortality during influenza outbreaks. They are at increased risk of developing complications due to underlying diseases.[2] These residents also have an increased risk of infection because of the institutional environment they share with many other residents and staff. Furthermore, impaired oral intake, limited dexterity and altered consciousness may limit treatment options when they are infected.[3]

The Australian Government's Department of Health and Ageing (DHA) has issued specific guidelines for prevention and control of influenza outbreaks in residential care facilities.[4] While ACFs have primary responsibility for managing outbreaks, Public Health Units (PHUs) are required to promote ACF compliance with these guidelines and facilitate delivery and administration of antivirals. However, effective influenza prophylaxis and other timely interventions can only occur if PHUs are notified in a timely manner.[5]

DHA guidelines indicate influenza outbreaks in ACFs are to be reported to PHUs.[4] However, under NSW public health legislation, reporting of outbreaks in ACFs is not mandatory.[6] In this report we investigated whether there were outbreaks that were not reported to the South Western Sydney Local Health Districts PHU during the 2014 influenza season.

METHODS

New South Wales Notifiable Conditions Information Management System (NCIMS)

Influenza is a laboratory-notifiable disease in NSW.[7] Influenza cases are confirmed by viral culture or polymerase chain reaction from nasopharyngeal aspirates or nose and throat swabs. In ACFs, samples are taken by either nursing staff or attending medical officers or taken during hospital admission. Results are electronically notified to the NCIMS from corresponding laboratories.

Definition of influenza outbreak

DHA guidelines[4] define an influenza outbreak as:

- three or more epidemiologically linked cases of influenza-like illness (ILI) in residents or staff of the facility within a period of 72 hours, plus
- at least one case having a positive laboratory test, or
- at least two having a positive point-of-care test.

ILI is defined as sudden onset of fever (body temperature ≥38 °C) plus cough and/or other respiratory

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Submitted: 9 July 2015; Published: 18 March 2016
doi: 10.5365/wpsar.2015.6.3.001

Table 1. **Number of ACFs (and cases) reporting and not reporting influenza outbreaks to the South Western Sydney Local Health District PHU for laboratory-confirmed cases of influenza (age 65 years or above), Australia, 2014**

	ACFs reporting (cases)	ACFs not reporting (cases)	Total ACFs (cases)
Non-outbreak (fewer than three influenza confirmed cases)	1 (2)	17 (20)	18 (22)
Outbreak (three or more influenza confirmed cases)	7 (72)	7 (45)	14 (117)
Total	**8 (74)**	**24 (65)**	**32 (139)**

ACFs, age care facilities; PHU, public health unit.

symptoms (e.g. shortness of breath) plus one or more systemic symptom(s) (fatigue, muscle soreness, headache).

For a conservative estimate, we use three or more confirmed cases of influenza in residents or staff of the facility (by either laboratory or point-of-care test) to define an influenza outbreak for analysis.

Study population and data analysis

Notifications of influenza among residents of South Western Sydney Local Health District that were reported to the NCIMS during 2014 were extracted and stratified by age. Those aged 65 years or above were selected for further analysis. The selected cases with residential addresses corresponding to the ACFs in NSW were identified. These ACFs were then cross-referenced with a database of influenza outbreaks reported to the PHU in 2014 for comparison. Data analysis was conducted using the Statistical Analysis Software (SAS Institute, Cary, North Carolina, USA).

Qualitative assessment

Informal interviews with facility managers were conducted by PHU staff on an ad hoc basis to understand the managers' knowledge of outbreak recognition and what factors should trigger a notification.

RESULTS

The results revealed that 139 of 549 laboratory-confirmed influenza cases aged 65 years or above had originated from 32 known ACFs. Eight ACFs with one or more confirmed cases (range 2–16 cases) reported their cases to the PHU. Twenty-four ACFs with one or more confirmed cases did not report their cases to the PHU (range 1–16 cases). There were 14 ACFs with three or more confirmed cases of influenza. Only seven of them (50%) reported the influenza outbreaks appropriately (**Table 1**). A delay of one to four days occurred between onset of ILI and notification to the PHU.

Informal interviews were conducted with managers from five ACFs that reported ILI among residents before June 2015. Results revealed that although all managers (n = 5) were aware of the need to report an outbreak, some were unsure what number of cases constituted an outbreak and others did not know when to report. In some cases, managers believed they had to wait for the laboratory confirmation before notifying the PHU. High workload was also a reason given for delays in reporting.

DISCUSSION

The results revealed that half of ACFs that should have reported an influenza outbreak did not do so. This is similar to a British survey where only 20% (n = 34) of all local Health Protection Units were formally notified of ILI occurring within ACFs.[8]

It is unclear whether ACFs were cognizant of the influenza outbreak definition in the DHA guidelines.[4] Feedback from facility managers indicated that various factors could have contributed to delays in notification. Nonetheless, delays in identification and notification of influenza outbreaks in ACFs have led to difficulties in containing the spread of influenza. These challenges with influenza outbreak reporting are not unique to the South Western Sydney Local Health District. Other PHUs have reported fear of bad publicity as another reason for delays in notification by ACFs.[9] Factors such as awareness of outbreak definitions and the assumption that laboratory confirmation should occur before notification can be corrected with improved education and training provided by the PHU before the annual influenza season.

Limitations of the study include the reliance on information provided by facility managers with potential recall bias and laboratory reporting. Unreported outbreaks of ILI may have occurred for which laboratory testing was never done. Also, reported ACF outbreaks of ILI may never be classified as influenza outbreaks because of insufficient testing. PHU staff do not have the resources to routinely conduct onsite investigations and testing for every reported ACF outbreak of ILI.

The study suggests that PHUs should ensure that ACFs understand the DHA guidelines, specifically the importance of the epidemiological link between cases and influenza outbreaks. Reminders and education sessions should be issued to ACFs before the beginning of influenza seasons to ensure ACF facility managers are able to recognize outbreaks and provide timely notifications to PHUs. Furthermore, it may be useful for PHUs to conduct influenza preparedness activities, possibly in the form of desktop exercises.

Conflicts of interest

None declared.

Funding

None.

Acknowledgements

The authors would like to acknowledge all PHU staff involved in managing ACF-based influenza outbreaks.

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Using the two-source capture–recapture method to estimate the incidence and case ascertainment of congenital rubella syndrome in Australia, 1993–2013

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In 2009, the Technical Advisory Group on Immunization and Vaccine Preventable Diseases in the World Health Organization (WHO) Western Pacific Region endorsed the 2015 targets for accelerating control of rubella and preventing congenital rubella syndrome (CRS).[1] The global goal outlined in the Global Vaccine Action Plan is for five of six WHO regions, including the Western Pacific Region, to achieve rubella elimination by 2020.[2]

Current evidence suggests that rubella is well controlled and may already be eliminated in Australia.[3] CRS is now rare, with an average of one case reported annually over the past decade, occurring mostly in infants of unimmunized immigrant mothers.[4] Rubella and CRS have been nationally notifiable since 1991 with all states and territories notifying confirmed and probable cases to the National Notifiable Diseases Surveillance System (NNDSS). NNDSS is a passive surveillance system, managed by the Commonwealth Department of Health, which collects de-identified data from all Australian states and territories on nationally notifiable diseases. The Australian Paediatric Surveillance Unit (APSU) undertakes active surveillance by child health clinicians who report monthly de-identified clinical laboratory and epidemiological data on a range of conditions, including CRS, since 1993.

To verify rubella and CRS elimination, countries need to ensure that their surveillance systems are sufficiently sensitive to capture almost all cases. This study aims to estimate the incidence of CRS in Australia and the sensitivity of CRS case ascertainment in the NNDSS.

METHODS

The two-source capture–recapture method[5] was used to estimate the incidence of CRS and to evaluate the sensitivity of case ascertainment by the NNDSS. Data on infants born between 1993 and 2013 from NNDSS and APSU were collected and were used to estimate the total number of cases (N) based on the expression $N = ab/c$, where a is the total number of cases ascertained from NNDSS (the primary source), b is the total number ascertained from APSU (the secondary source) and c is the number of cases common to both sources. A modified formula for small numbers[5,6] was used to estimate CRS incidence between 1993 and 2013:

$$N = \left[\frac{(a+1)(b+1)}{(c+1)}\right] - 1$$

Estimates were made for the entire 21-year period and additionally stratified by single years and by two time periods, 1993–2003 and 2004–2013, with 95% confidence intervals (CI) calculated for the estimated incidence using the formulas:[6]

$$var(N) = \frac{[(a+1)(b+1)(b-c)(a-c)]}{(c+1)^2(c+2)};$$

$$95\%\ CI = N \pm Z\sqrt{var(N)}$$

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Submitted: 9 November 2015; Published: 29 March 2016
doi: 10.5365/wpsar.2015.6.4.006

Cases were matched based on date of birth, sex and state or territory of residence. Where cases were matched but their notification dates spanned different years, they were attributed to the earlier of the two notification years. The estimated annual incidence rate (per million live births) was calculated as the sum of reported cases over the sum of the reported live births for the relevant period between 1993 and 2013.[7] Both confirmed and probable cases, according to the national case definition,[8] were included in the analysis. Analysis was conducted using Excel (Microsoft Excel 2010, Redmond, WA, USA).

The APSU congenital rubella surveillance study was approved by the Royal Alexandra Hospital for Children (The Children's Hospital at Westmead, New South Wales, Australia) Human Research Ethics Committee. Ethics committee approval was not required for the NNDSS data as the de-identified, aggregated data provided are already available in the public domain.

RESULTS

Twenty-five cases were identified through the primary source (NNDSS), including 23 confirmed and two probable cases. Thirty-four cases were identified through the secondary source (APSU) and 16 cases were common to both systems for infants born between 1993 and 2013. There were five duplicate notifications identified in the APSU data that were excluded. Three of the 16 cases were mismatched for sex but matched on other parameters. Further investigation found one of the three cases had an incorrectly recorded sex status and another one was further matched by hospital of birth. Both cases were included in the analysis. No further details could be determined for the third case and it was excluded.

An estimate of 56 CRS cases (95% CI: 44–68) were expected for the entire 21-year period (1993–2013), assuming 15 cases common to both sources, representing an overall 45% case ascertainment for NNDSS. The average birth prevalence in the period 1993 to 2013 was estimated as 9.3 per million live births. When stratifying the data by the two time periods, an average of 18.3 cases per million live births was estimated from 1993 to 2003 compared with 2.2 per million live births from 2004 to 2013. Case ascertainment by NNDSS was 35% in 1993–2003 compared with 100% in 2004–2013 (**Table 1**).

DISCUSSION

This study indicates that CRS incidence in Australia has been low during the 21-year study period with a marked reduction in incidence after 1996. The significant decrease in incidence is most likely due to introducing a second dose of measles-mumps-rubella vaccine to the National Immunisation Program schedule in 1994, and improved vaccination coverage and population immunity achieved as a result of the Measles Control Campaign in 1998.[9] Case ascertainment by the NNDSS was poor during the first 11 years of this study but improved substantially to 100% in all years from 2003 onwards.

The two-source capture–recapture method allows detection of cases by two independent sources to estimate the total number of cases in a given population. This method is based on animal population studies and has been used in epidemiological studies to evaluate completeness of case ascertainment and to estimate the incidence and prevalence of diseases in both human and animal populations.[5] It has previously proved valuable to validate the sensitivity of acute flaccid paralysis surveillance in Australia.[5] The use of this method assumes that the primary and secondary sources are independent, all cases have an equal probability of inclusion, cases have been diagnosed accurately and appropriate matching between sources has occurred.[10] The small number of cases and clinical presentation of CRS combined with a nationally consistent case definition applied by both sources since 2004 assured that most of these assumptions are likely to be met, except that it is difficult to ensure the two sources are completely independent. Nevertheless, they have distinct reporting parthways. While the APSU captures cases reported directly by child health clinicians, the NNDSS is notified of laboratory- or clinically confirmed cases reported to state or territory health departments.

Our analysis reveals CRS incidence in Australia was low and has a marked reduction after 1996. Currently, the NNDSS is sensitive to monitor CRS occurrence and elimination of CRS in Australia.

Table 1. **Estimated annual incidence of CRS and case ascertainment, Australia, 1993–2013**

	Total from NNDSS (primary source) (*a*)	Total from APSU (secondary source) (*b*)	Total from both sources (*c*)	Estimated total number of cases (*N*)	95% confidence intervals for *N*	Estimated completeness of ascertainment (%)	Estimated incidence of CRS per million live births
Total	25	34	15	56	44–68	45	9.3
Year range							
1993–2003	18	29	10	51	36–66	35	18.3
2004–2013	7	5	5	7	7–7	100	2.2
Year							
1993	2	4	0	14	0–29	14	53.8
1994	4	6	3	8	6–10	52	30.0
1995	1	4	0	9	0–18	11	35.0
1996	5	6	2	13	6–20	38	37.2
1997	0	1	0	1	1–1	0	3.9
1998	0	1	0	1	1–1	0	4.0
1999	1	1	1	1	1–1	100	4.0
2000	0	0	0	0	0–0	–	0.0
2001	0	0	0	0	0–0	–	0.0
2002	2	3	1	5	2–8	40	19.9
2003	3	3	3	3	3–3	100	11.9
2004	1	1	1	1	1–1	100	3.9
2005	1	0	0	1	1–1	100	3.8
2006	0	0	0	0	0–0	–	0.0
2007	1	0	0	1	1–1	100	3.5
2008	1	1	1	1	1–1	100	3.4
2009	0	0	–	0	0–0	–	0.0
2010	0	0	–	0	0–0	–	0.0
2011	0	0	–	0	0–0	–	0.0
2012	1	1	1	1	1–1	100	3.2
2013	2	2	2	2	2–2	100	6.5

APSU, Australian Paediatric Surveillance Unit; CRS, congenital rubella syndrome; and NNDSS, National Notifiable Diseases Surveillance System.

Conflicts of interest

None declared.

Funding

The activities of the APSU are funded in part by the Australian Government Department of Health, National Health and Medical Research Council (NHMRC) Practitioner Fellowship No: 1021480 (EE) and an Australian Research Council Linkage Project Grant (LP110200277). Gulam Khandaker is supported by NHMRC Health Practitioners' Early Career Fellowship (1054414) and Cheryl Jones by NHMRC Centres of Research Excellence in Critical Infections (1001021).

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Vector-control response in a post-flood disaster setting, Honiara, Solomon Islands, 2014

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Problem: The close quartering and exposed living conditions in evacuation centres and the potential increase in vector density after flooding in Solomon Islands resulted in an increased risk of exposure for the occupants to vectorborne diseases.

Context: In April 2014, Solomon Islands experienced a flash flooding event that affected many areas and displaced a large number of people. In the capital, Honiara, nearly 10 000 people were housed in emergency evacuation centres at the peak of the post-flood emergency. At the time of the floods, the number of dengue cases was increasing, following a record outbreak in 2013.

Action: The National Vector Borne Disease Control Programme with the assistance of the World Health Organization implemented an emergency vector-control response plan to provide protection to the at-risk populations in the evacuation centres. The National Surveillance Unit also activated an early warning disease surveillance system to monitor communicable diseases, including dengue and malaria.

Outcome: Timely and strategic application of the emergency interventions probably prevented an increase in dengue and malaria cases in the affected areas.

Discussion: Rapid and appropriate precautionary vector-control measures applied in a post-natural disaster setting can prevent and mitigate vectorborne disease incidences. Collecting vector surveillance data allows better analysis of vector-control operations' effectiveness.

PROBLEM

There was concern that the large populations of displaced people in evacuation centres in Honiara, Solomon Islands were vulnerable to several communicable diseases (including vectorborne diseases such as malaria and dengue) after severe flooding in April 2014. The risk for dengue transmission in the evacuation centres was considered high due to several contributory factors: the increasing dengue circulation among the general population before the floods; large populations living in close, confined conditions; locations of evacuation centres that were covered but were unscreened open-air structures; and optimal environmental conditions with widespread availability of *Aedes* (and potentially *Anopheles*) breeding sites.

This paper describes the vectorborne disease risk assessment conducted in the affected areas of Honiara and Guadalcanal Province and the application of rapid response interventions to reduce the level of exposure of those living in the evacuation centres.

CONTEXT

Solomon Islands has a history of dengue outbreaks with several recorded dengue epidemics since the 1970s.[1] Two dengue vectors are now present in Honiara, namely, *Aedes aegypti* and *Aedes albopictus*. The country experienced its largest documented dengue outbreak in 2013 (type 3), with nearly 8000 cases and eight deaths. *Aedes aegypti* re-emerged in Honiara during 2013 after last being identified in the 1980s. The even

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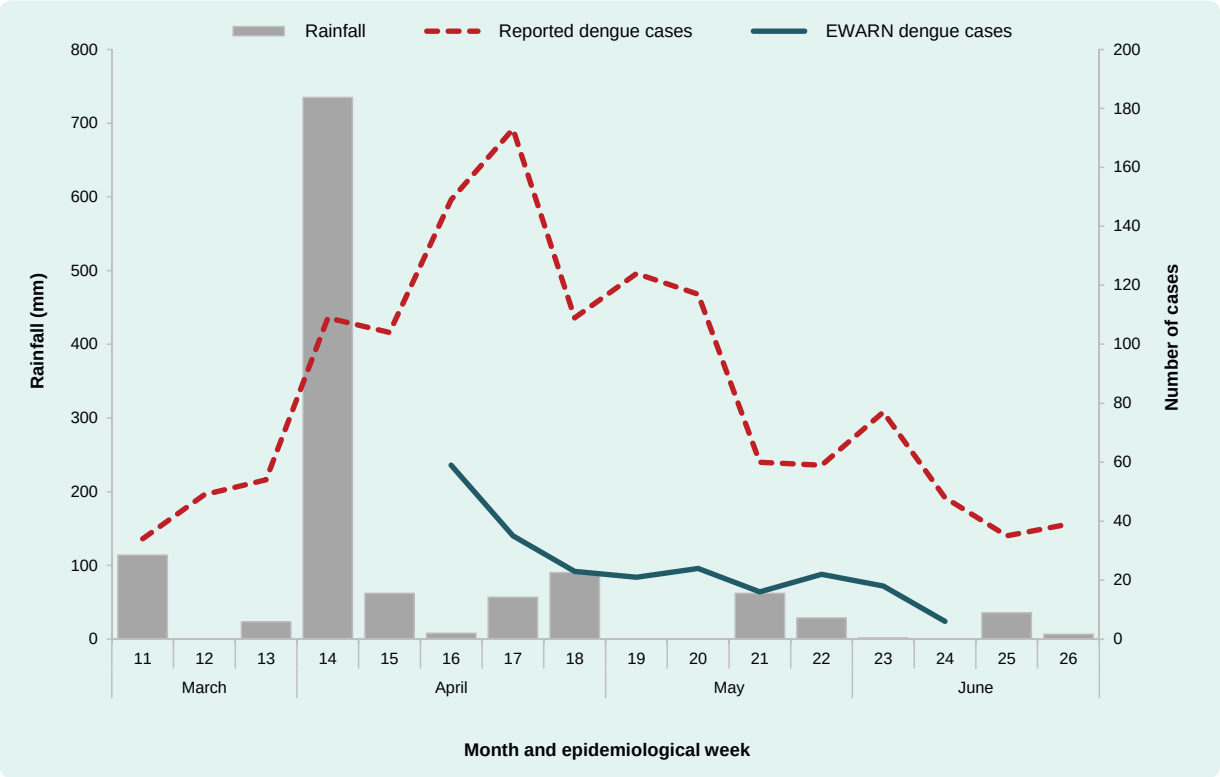
Submitted: 30 July 2015; Published: 21 January 2015
doi: 10.5365/wpsar.2015.6.3.004

Figure 1. **Reported dengue cases, EWARN dengue cases and rainfall during pre- and post-flood periods, March–June 2014, Honiara, Solomon Islands**



EWARN, Early Warning Alert and Response Network.

distribution of infections across age groups suggested that type 3 dengue had not circulated in the country for several years.[2] Due to this absence of immunity in the population, the outbreak continued into early 2014, with cases increasing in March 2014 as environmental conditions became more favourable for vector production.

In early April 2014, a tropical depression formed a trough over Solomon Islands causing 732.5 mm of rain to fall between 2 and 5 April (**Figure 1**). This triggered severe flooding in the capital and many other provinces, especially in Guadalcanal Province. The flooding resulted in the death of 23 people and the displacement of approximately 50 000 people. The majority of the affected people came from Guadalcanal Province and Honiara. At the peak of the crisis, nearly 10 000 people were being housed in 31 evacuation centres within Honiara.

The Guadalcanal plains to the east of Honiara, and the peri-urban areas on the eastern and western margins of Honiara historically experience high levels of malaria transmission between March and June. Epidemic risk of both malaria and dengue in evacuation centres located in these areas was high during the April 2014 post-flood period.

ACTION

Risk assessment

As requested by the Ministry of Health and Medical Services of the Solomon Islands, a post-disaster outbreak risk assessment was conducted by the World Health Organization (WHO) four days after the flood event. A WHO epidemiologist visited the major evacuation centres, the National Referral Hospital and other health facilities in Honiara and Guadalcanal Province to assess the post-disaster epidemic risk factors, including sanitation, water quality, living conditions of displaced populations, exposure to flood water and exposure to disease vectors using standard WHO guidelines.[3]

Establishment of Early Warning Alert and Response Network (EWARN)

The risk assessment recommended implementing an early warning disease surveillance system to monitor

epidemic diseases; therefore, a paper-based EWARN system was implemented after the floods. The EWARN system was an enhancement of the existing routine syndromic surveillance system, coordinated by the National Surveillance Unit (NSU), and used the same data collection methods which involves weekly visits to sentinel sites (permanent health clinics) to collect and aggregate tallies that are manually recorded by facility staff for the targeted syndromes. The existing NSU system collects weekly disease data on five syndromes (dengue-like illness, acute fever and rash, diarrhoea, influenza-like illness and prolonged fever) from four sentinel sites in Honiara and five sites in other provinces. The EWARN system collected data from an additional six sentinel sites within Honiara and 12 health facilities in Guadalcanal Province. EWARN monitored eight diseases and syndromes that included the five routine syndromes plus malaria, bloody diarrhoea and acute jaundice. Positive case detection for EWARN was based on clinical definitions of the targeted syndromes. In addition, some samples were also collected for laboratory and/or rapid diagnostic tests confirmation (for example, dengue, malaria and rotavirus).

Data for EWARN were collected weekly and analysed using Excel (Microsoft Excel, Redmond, USA) by the NSU. Thresholds were set for each of the syndromes which, if exceeded, triggered verification and investigation. The thresholds for dengue and malaria were set at "twice the average number of cases seen in the previous three weeks".

Vector-control responses for high-risk transmission sites

Precautionary preventative strategies were implemented by the National Vector Borne Disease Control Programme (NVBDCP). Interventions were primarily focused on larger evacuation centres due to limited resources. These included:

(1) minimizing exposure to adult vector activity through reducing the density and the age of adult populations by targeted application of interior residual spraying (IRS) and peri-focal spraying (active ingredient: lambda-cyhalothrin), application of ultra-low volume fog (ULV) (active ingredient: deltamethrin) and distribution of long-lasting insecticide-treated nets (LLINs) (active ingredient: deltamethrin);

(2) reducing juvenile vector populations through manual removal or mitigation of all potential *Aedes* breeding sites in evacuation centres and applying larvicide (pyriproxyfen granules) to all other potential *Aedes* breeding sites and all positive *Anopheles* breeding sites in the eastern and western fringes of Honiara; and

(3) providing barriers between hosts and vectors through distribution of LLINs to all residents in the major evacuation centres.

OUTCOME

Risk assessment

The risk assessment revealed that several conditions were increasing the risk of communicable disease outbreaks in the community, in particular poor sanitation, limited and poor water quality, displaced populations living in dirty and densely populated evacuation centres, exposure to flood water and increased exposure to disease vectors.

Heavy rains would have flushed *Aedes* larvae from breeding sites while also flooding many receptacles and hatching dormant reserves of *Aedes* eggs.[4] This could lead to increases in adult dengue vector populations within 7–10 days, and it was therefore realistic to expect dengue transmission to potentially increase within 3–4 weeks.[5,6]

The flood waters could also have created large tracts of suitable breeding sites for *Anopheles farauti*, the major endemic malaria vector species.[7–9] In coastal areas where rivers and creeks had burst their banks and formed temporary pools, flood water could potentially form suitable breeding sites. Increases in mosquito productivity from these sites could be expected to take between 2–4 weeks and 6–8 weeks before affecting malaria incidence.[8–10]

EWARN

EWARN helped the NVBDCP to track potential epidemic outbreaks of key vectorborne diseases in Honiara and Guadalcanal Province in the wake of the floods. The EWARN system was initiated on 14 April and operated for nine weeks after the floods. Weekly reporting of geographical coverage rates varied from

Table 1. **Coverage of vector-control interventions for the estimated population who were displaced in Honiara, Solomon Islands, 2014 (n = 8080)**

	LLINs	Residual spraying	ULV
Displaced population covered (%)	6499 (80%)	6188 (77%)	6188 (77%)
Material/area coverage	4180 nets	12 062 m^2	8 780 000 m^2 (878 hectares)
Activity date range (2014)	7 to 10 April	9 to 15 April	8 April to 11 June

LLINs, long-lasting insecticide-treated nets; and ULV, ultra-low volume.

73% to 91%. Lack of coverage was due to either flood-damaged health facilities or failure to submit reports. The EWARN system's alert threshold was triggered once for vectorborne diseases in Honiara with malaria exceeding the defined threshold in late April.

Vector-control responses

A total of 4180 LLINs were distributed to the evacuation centres, providing coverage to 6499/8080 (80%) of the estimated displaced population (**Table 1**). The LLINs were considered the highest priority intervention for protection against malaria vectors, so delivery of all LLINs was completed within five days of the mass evacuations to the evacuation centres.

Residual and ULV space spraying were the next priority interventions with IRS and peri-focal spraying applied to potential indoor and outdoor mosquito-resting sites in all structures and to potential *Aedes* breeding sites (excluding potable water sources) at 11 of the largest evacuation centres. This provided additional protection to 6188/8080 (77%) of the estimated displaced population (**Table 1**). Interior wall surfaces in the evacuation centres were mainly exposed or painted dressed timber, so the encapsulated suspension formulation of the IRS chemical would have provided an effective treatment. ULV space spraying was conducted using backpack foggers at the same 11 evacuation centres. Spraying was done in the late afternoon or early evening to target the peak activity times of the two major dengue vectors. ULV space spraying was also conducted using a truck-mounted fogger (LECO 1800E, Clarke, St Charles, Illinois, USA) in high transmission suburbs/areas around Honiara, focusing on those areas having evacuation centres. During the first two weeks after the floods, all evacuation centres were treated with backpack ULVs twice a week. ULV treatments in evacuation centres were stopped as residents were relocated. Ongoing truck-mounted ULV treatments targeting high transmission areas, which were identified using data from the dengue line list, were applied weekly. A total of 878 hectares were treated with ULV from 8 April to 11 June (**Table 1**).

The responses successfully minimized the exposure of at-risk displaced populations to vector activity, reduced juvenile vector populations and provided barriers between hosts and vectors.

DISCUSSION

The number of dengue cases detected by EWARN was generally lower than the reported dengue cases. This may be because the EWARN site at the National Referral Hospital included only cases from the emergency department but not admitted cases. However the general trend of dengue transmission was reflected in both systems (**Figure 1**). While the number of malaria cases exceeded the threshold set within EWARN in epidemic week 18 (last week of April 2014), this incidence level was consistent with the annual pattern of malaria transmission in Honiara over the past three years as reported in the national routine malaria information system (**Table 2**). This result indicates that although EWARN is sensitive for monitoring disease incidence against a baseline projection, it can be misleading if the baselines are set without referencing the historical disease trends.

The displacement of large populations of people into evacuation centres plus flood waters potentially generating an increase of disease vectors was a combination of circumstances that presented a clear vectorborne disease epidemic risk. While it is not able to be determined from the disease surveillance data the level of protection that was afforded to these at-

Table 2. **Historical trend of March to June clinical malaria cases in Honiara, 2012–2014 and EWARN malaria cases in Honiara, Solomon Islands during the same months in 2014**

	Clinical malaria cases*			EWARN malaria cases†
	2012	2013	2014	2014
March	770	930	637	–
April	617	836	705	326
May	768	772	605	398
June	501	461	763	174‡

EWARN, Early Warning Alert and Response Network.

* Monthly clinical malaria cases data were extracted from the routine malaria information system, National Vectorborne Disease Control Programme.

† Aggregated weekly EWARN data for clinical malaria cases.

‡ EWARN data only collected for first two weeks of June 2014.

risk populations, it is likely that the rapid precautionary vector-control measures that were put in place prevented larger numbers of vectorborne-disease cases in the evacuation centres. Although a high level of intervention coverage was achieved, several problems were faced by the teams when implementing these interventions. Data availability on evacuation centres' populations and locations and the coordination of emergency services were inherent problems, especially immediately after the floods. These issues affected the operational planning and quantification of interventions required for vector control and other essential emergency services. Delivering emergency control interventions to displaced populations was more efficient when the lists of designated evacuation centre locations and their populations were provided. The information is extremely important for rapid and effective emergency public health interventions.

Unfortunately, no vector surveillance data was collected during this period, which would have complemented the disease surveillance and intervention data and allowed better guidance and analysis of the vector-control operations.[11–13] This highlights the importance of collecting routine data on vector populations as well as conducting pre- and post-control surveillance of targeted vectors. Since the floods, a routine adult *Aedes* surveillance programme is now being conducted in Honiara with BG-Sentinel traps (BioQuip Products, Inc., Rancho Dominguez, CA, USA) set at 20 sentinel sites in the city. Data are collected and analysed every two weeks. Monthly monitoring of larval density in major *Anopheles* breeding sites close to high population areas around Honiara is also conducted. These activities can help inform the NVBDCP on the effectiveness of their vector-control interventions.

The public health responses to the 2014 Honiara floods highlighted several important lessons in providing vector-control interventions in a disaster setting. Rapid epidemic disease risk assessment and ongoing disease alert networks can provide evidence to prioritize public health interventions. Also it is necessary to implement the interventions in a timely and effective manner. Furthermore, it is important for public health officials to work closely with the disaster management bodies and to share vital information on vulnerable populations so as to help better targeted interventions.

Conflicts of interest

None declared.

Funding

None.

Acknowledgements

The authors would like to acknowledge the assistance by the Solomon Islands Department of Health and Medical Services staff as well as the Office of the WHO Representative in Solomon Islands staff during the manuscript writing stage.

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Preparedness for Zika virus testing in the World Health Organization Western Pacific Region

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On 1 February 2016, the World Health Organization (WHO) declared that clusters of microcephaly cases and other neurological disorders occurring in Zika virus (ZIKV)-affected areas constituted a public health emergency of international concern. Increased surveillance of the virus, including the requirement for laboratory confirmation of infection, was recommended. The WHO Regional Office for the Western Pacific therefore initiated a rapid survey among national-level public health laboratories in 19 countries and areas to determine regional capacity for ZIKV detection. The survey indicated that 16/19 (84%) countries had capacity for molecular detection of ZIKV while others facilitated testing through referral. These results suggest that robust laboratory capacity is in place to support ZIKV surveillance in the Western Pacific Region.

Initially identified in a rhesus monkey from Uganda's Zika forest in 1947 and subsequently isolated from humans in 1968 in Nigeria,[1] Zika virus (ZIKV) is a flavivirus transmitted by *Aedes* mosquitoes, the same vector transmitting other arboviruses of public health impact such as yellow fever virus, dengue virus (DENV) and chikungunya virus (CHIKV).[2] The first known ZIKV outbreak occurred in 2007 in Yap state of the Federated States of Micronesia[1] in the World Health Organization (WHO) Western Pacific Region followed by a 2013–2014 outbreak in French Polynesia with an estimated 32 000 cases.[3] The virus has gone on to cause outbreaks in multiple Pacific island countries and has spread throughout the Americas.[1] In November 2015, Brazil began reporting substantial increases in the number of children born with microcephaly in ZIKV-affected areas.[4] That evidence, coupled with reports of Guillain-Barré syndrome cases in other ZIKV outbreaks, particularly in French Polynesia, led WHO on 1 February 2016 to declare that the cluster of microcephaly cases and other neurological disorders constituted a public health emergency of international concern (PHEIC).[5] Among the recommendations from that meeting of the International Health Regulations (2005) Emergency Committee were that "surveillance for ZIKV infection should be enhanced, with the dissemination of standard case definitions and diagnostics to at-risk areas".[6]

Laboratory testing is a critical component of surveillance for ZIKV infection due to co-circulation of DENV and CHIKV that cause similar symptoms.[7,8] To determine regional capacity for ZIKV detection, the WHO Regional Office for the Western Pacific initiated a voluntary, rapid survey among national-level public health laboratories in its countries and areas (areas are non-sovereign jurisdictions within a WHO region;[9] countries and areas are together referred to as "countries" in this article). The survey sought to assess preparedness for ZIKV testing in the context of co-circulating DENV and CHIKV. Questions primarily addressed in-country capacity for molecular and serological detection of the three arboviruses, additional laboratory capacities specific for ZIKV and testing-related services to other countries.

The 19-question, email-based survey was administered between 2 and 23 February 2016, immediately following the PHEIC declaration. A total of 28 surveys to national-level laboratories likely to be tasked with ZIKV testing were distributed to 19 countries in the Region (omitting resource-limited countries with

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Submitted: 21 March 2016; Published: 31 March 2016
doi: 10.5365/wpsar.2016.7.1.007

Table 1. **Responses to an email-based survey assessing national-level public health laboratory testing capacity for ZIKV and other priority arboviruses among 19 countries and areas* in the WHO Western Pacific Region, 2–23 February 2016**

Category	Proportion of countries	%
In-country molecular testing (PCR) available		
PCR for DENV	17/19	89.5
PCR for CHIKV	17/19	89.5
PCR for ZIKV	16/19	84.2
Related ZIKV techniques available		
Sequencing of ZIKV	14/16	87.5
Isolation of ZIKV	14/16	87.5
Differential diagnostic PCR algorithm†		
Concurrent (US CDC algorithm[7])	9/15	60.0
Sequential (AMRO algorithm[13])	5/15	33.3
Case-by-case	1/15	6.7
In-country serological testing available		
IgM and/or IgG for DENV	17/19	89.5
IgM and/or IgG for CHIKV	16/19	84.2
IgM and/or IgG for ZIKV	6/19	31.6

* Countries and areas covered under the survey were: Australia, Brunei Darussalam, Cambodia, China, Fiji, French Polynesia (France), Hong Kong Special Administrative Region (China), Japan, the Lao People's Democratic Republic, Macau Special Administrative Region (China), Malaysia, Mongolia, New Caledonia (France), New Zealand, Papua New Guinea, the Philippines, the Republic of Korea, Singapore and Viet Nam.

† Data unavailable from one country with PCR testing capacity for ZIKV.

AMRO, World Health Organization Regional Office for the Americas; CHIKV, chikungunya virus; DENV, dengue virus; PCR, polymerase chain reaction; US CDC, United States Centers for Disease Control and Prevention; ZIKV, Zika virus.

basic laboratory capacity known to rely on specimen referral). The survey was completed by 23 laboratories in 18 countries. For the country not responding, information from other sources such as recent peer-reviewed publications was used where possible to augment the data set and cover all 19 countries.

Table 1 summarizes the main findings of the survey. Polymerase chain reaction (PCR)-based detection of ZIKV was in place for 16/19 (84.2%) countries. Of the remaining three, two were using specimen referral to neighbouring countries (similar to Pacific island countries without PCR capacity), while the other has been working closely with the WHO Regional Office for the Western Pacific to obtain materials and reagents to enable in-country testing. Of the 16 countries with PCR test capacity for ZIKV, 14 could additionally sequence the virus and isolate it in culture. Serological diagnosis of ZIKV infection by immunoglobulin M (IgM) and/or immunoglobulin G (IgG) detection was also surveyed in the 19 countries, with less than one third (6/19) reporting having this capacity. Twelve countries indicated that they were willing to accept international specimens to supplement the capacity in other countries or for confirmation testing (data not shown).

Given the similarity of disease presentation,[1] co-circulation and increasing prevalence of infection,[10–12] differential diagnosis for DENV, CHIKV and ZIKV is crucial. Molecular detection of DENV and CHIKV was in place in 17/19 (89.5%) countries, and a similarly large majority could perform serological diagnosis of DENV (17/19, 89.5%) and CHIKV (16/19, 84.2%) infection by IgM and/or IgG detection. The algorithm followed for differential diagnosis should take into consideration the endemic circulation of DENV, CHIKV and ZIKV.[8] Among 15 countries detailing their algorithm, 9 (60%) indicated they tested suspected samples for all three arboviruses concurrently, similar to the algorithm recommended by the United States Centers for Disease Control and Prevention;[7] 5/15 (33.3%) attempted to rule out each virus sequentially as outlined in the WHO Regional Office

for the Americas guidance.[13] The remaining country indicated that the epidemiological circumstances of each case drove the specific algorithm followed.

This survey, conducted immediately following the WHO declaration of a PHEIC surrounding clusters of microcephaly and neurological disorders in the context of ZIKV infection, suggests that robust coverage for molecular detection of priority arboviruses is in place in the Region. Molecular detection by PCR is the critical differential diagnostic tool in this public health event as serology is problematic due to antibody cross-reactivity in regions with multiple circulating flaviviruses and/or use of vaccines against those viruses (for example, Japanese encephalitis virus).[7,8] Other methodologies, such as the plaque reduction neutralization test (PRNT), exist for the specific serological discrimination among the flaviviruses but require significant technical expertise for accurate execution and would not be practical for large-scale surveillance. Only three of the countries responding to the survey reported they could perform PRNT (data not shown).

As in our previous survey of regional PCR testing capacity for Middle East respiratory syndrome coronavirus,[14] most (13/16) of the national-level public health laboratories supporting PCR testing of ZIKV in their countries functioned as National Influenza Centres in the Global Influenza Surveillance and Response System, showing the versatility of this network. A similar proportion (12/16) participated in the external quality assessment (EQA) for DENV and CHIKV diagnostics, which has a substantial PCR-based component. This EQA, conducted by the WHO Regional Office for the Western Pacific[15,16] in 2013 and 2015, showed robust proficiency for diagnosis of these viruses in the Region.

While the Region seems prepared overall for testing of ZIKV, it is important to continue strengthening the apparatus for detection particularly through ensuring testing proficiency by EQA participation and enhancing referral mechanisms and International Air Transport Association certification where needed. It should be noted that while the EQA for DENV and CHIKV diagnostics gives confidence about regional testing proficiency for those arboviruses,[16] proficiency of ZIKV diagnostics remains untested. Note also that by omitting countries known to rely mainly on specimen referral, the study's geographic coverage only included countries of the Asian sub-region and larger countries or referral hubs of the Pacific sub-region such as Australia and French Polynesia.

The laboratory plays an important role in improving our understanding of ZIKV epidemiology. While this survey reveals a broad availability of molecular diagnostics to support surveillance of ZIKV in the Western Pacific Region, further key roles remain for laboratories in helping to unravel the pathogenicity of the virus and its potential causal role in the observed cases of microcephaly and other neurological disorders.

Conflicts of interest

None declared.

Funding

None.

Acknowledgements

The authors are grateful to the participating laboratories and countries that shared their information and took the time to complete the survey. We would also like to thank the other members of the Zika Incident Management Team, including: Christopher Lowbridge, Katherine Russell, May Chiew, Cong Ze, Joy Caminade, Jun Nakagawa, Thierry Cordier-Lassalle, Janet Mina, Meg Dichoso, Takuya Yamagishi, Rabindra Abeyasinghe, Babatunde Olowokure and Li Ailan.

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