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IN THIS ISSUE

Surveillance Report

Epidemiology of drowning deaths in the Philippines, 1980–2011

Martinez RE, Go JJ, and Guevarra J

1

Surveillance System Implementation / Evaluation

Syndromic surveillance in Vanuatu since Cyclone Pam: a descriptive study

Worwor G, Harries AD, Merilles OE, Viney K, Rory JJ, Taleo G, and Guyant P

6

Original Research

The changing epidemiology of measles in an era of elimination: Lessons from healthcare setting transmissions of measles during an outbreak in Australia, 2012

Pillsbury A, Chiew M, Bag S, Hope K, Norton S, Conaty S, Sheppeard V, and McIntyre P

12

A Q fever cluster among workers at an Abattoir in South Western Sydney, Australia

Lord H, Fletcher-Lartey S, Weerasinghe G, Chandra M, Egana N, Schembri N, and Conaty S

21

Rotavirus Vaccine and Healthcare Utilization for Rotavirus Gastroenteritis in Tsu City, Japan

Asada K, Kamiya H, Suga S, Nagao M, Ichimi R, Fujisawa T, Umemoto M, Tanaka T, Ito H, Tanaka S, Ido M, Taniguchi K, Ihara T, and Nakano T

28

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Epidemiology of drowning deaths in the Philippines, 1980 to 2011

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Drowning kills 372 000 people yearly worldwide and is a serious public health issue in the Philippines. This study aims to determine if the drowning death rates in the Philippine Health Statistics (PHS) reports from 1980 to 2011 were underestimated. A retrospective descriptive study was conducted to describe the trend of deaths caused by drowning in the Philippines from official and unofficial sources in the period 1980 to 2011. Information about deaths related to cataclysmic causes, particularly victims of storms and floods, and maritime accidents in the Philippines during the study period were reviewed and compared with the PHS drowning death data.

An average of 2496 deaths per year caused by drowning were recorded in the PHS reports from 1980 to 2011 (range 671–3656). The average death rate was 3.5/100 000 population (range 1.3–4.7). An average of 4196 drowning deaths were recorded from 1980 to 2011 (range 1220 to 8788) when cataclysmic events and maritime accidents were combined with PHS data. The average death rate was 6/100 000 population (range 2.5–14.2).

Our results showed that on average there were 1700 more drowning deaths per year when deaths caused by cataclysms and maritime accidents were added to the PHS data. This illustrated that drowning deaths were underestimated in the official surveillance data. Passive surveillance and irregular data management are contributing to underestimation of drowning in the Philippines. Additionally, deaths due to flooding, storms and maritime accidents are not counted as drowning deaths, which further contributes to the underestimation. Surveillance of drowning data can be improved using more precise case definitions and a multisectoral approach.

Drowning is the process of experiencing respiratory impairment from submersion/immersion in liquid. It is a serious and neglected public health threat that claims the lives of 372 000 people per year worldwide.¹ It is the third leading cause of unintentional injury death, accounting for 7% of all injury-related deaths. More than 90% of these deaths occur in low- and middle-income countries.¹ In the Philippines, there were 3044 reported deaths due to drowning in 2010.² The profile of drowning deaths is expected to vary significantly across the Philippines since the country has diverse hazards, population densities and levels of development.

In the Philippines, there are two national databases that capture accidental drowning: the National Civil Registry and the Online National Electronic Injury Surveillance System (ONEISS). The National Civil Registry captures deaths from accidental drowning

and submersion from all health authorities. Both the public and private sectors report to this system as it is required by law. These data are published regularly in the Philippine Health Statistics (PHS) reports. On the other hand, both fatal and non-fatal drownings are captured by the ONEISS, and data in this system are collected only by hospitals (both public and private) that are registered in the system. ONEISS is maintained by the Department of Health. Drowning deaths in the PHS reports include those coded under the category of “accidental drowning and submersion” in the National Civil Registry but not those categorized as cataclysm, including flood, storm and tsunami, intentional drowning deaths or water-transport-related incidents.² In addition, there are drowning deaths that are not reported or classified due to the remoteness of the incidents. Deaths caused by drowning are likely to be underestimated in the Philippines. This study aims to provide a more comprehensive documentation of drowning deaths in the Philippines from 1980 to 2011.

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METHODS

Study design

A retrospective descriptive study was conducted to describe the number and trend of deaths caused by drowning in the Philippines from official and unofficial sources from 1980 to 2011.

Data collection

Data about deaths caused by drowning in the Philippines were retrieved from the PHS reports from 1980 to 2011.³ For the deaths related to cataclysmic causes and maritime accidents in the Philippines during this period, a Google search retrieved related literature and reports online. Keywords used for the search include “Philippine typhoons”, “Pacific typhoons”, “Philippine storms”, “capsize ship Philippines”, “maritime accidents” and “maritime disaster in the Philippines”. The search was performed in English. The same search strategy was also applied to retrieve posts specifically on the Wikipedia website. The first 10 hits in the search results were reviewed by the authors. Related information from these resulting web pages was extracted for analysis. In addition, news from two Philippines local online news agencies^{4,5} was reviewed to retrieve drowning-related information. Information extracted includes the number of deaths related to drowning; cataclysmic events (including flood, storm, typhoon, storm surge and all water-related disasters); and maritime accidents. Only information from 1980 to 2011 was extracted for analysis.

Data analysis

Data analysis for the deaths caused by drowning was conducted. The estimated number of actual drowning deaths was calculated by summing PHS data with additional deaths from cataclysmic storm, typhoon and maritime accident retrieved from Wikipedia, Google search and news agencies. The estimated death rates were computed based on the projected population retrieved from PHS in the given year.

All analyses were conducted using Excel version 2010 (Microsoft Excel, Redmond, WA, USA).

This paper does not breach issues of confidentiality. All information was validated and considered to be true.

RESULTS

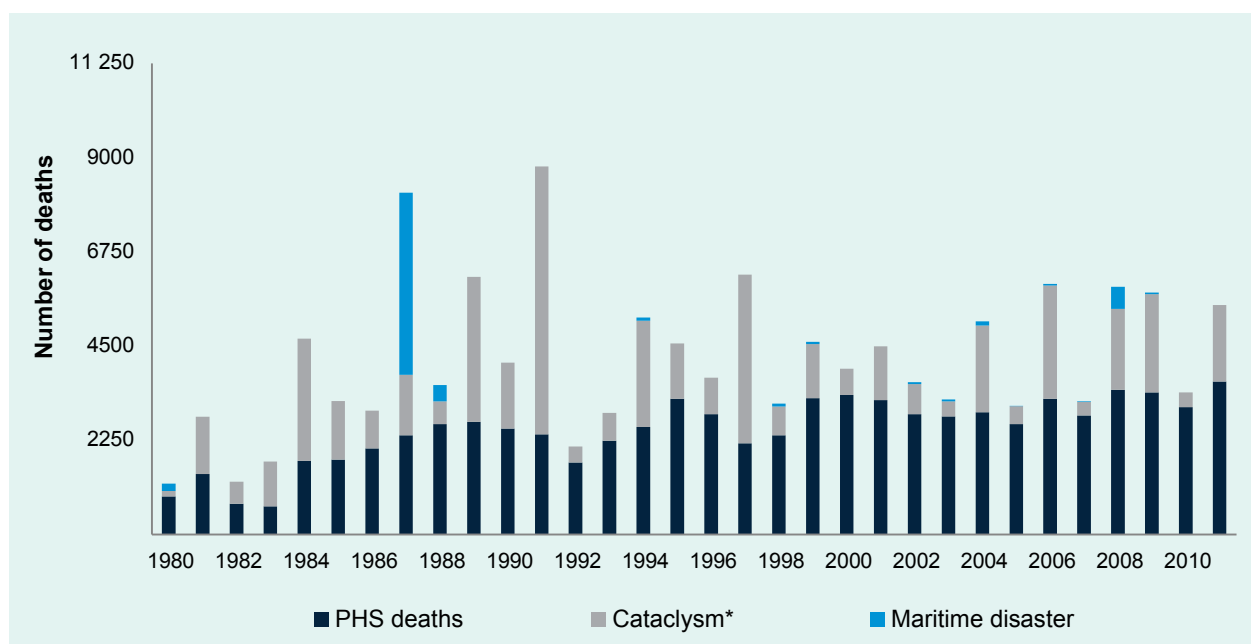
An average of 2496 deaths caused by drowning per year were recorded in PHS from 1980 to 2011 (range 671–3656) (**Fig. 1**). The average death rate was 3.5/100 000 population (range 1.3–4.7). The highest peak of drowning death rates was in 1995 with the death rate of 4.7 per 100 000 population, followed by 1988 and 1989 (rate = 4.5/100 000 population) and 1999 and 2000 (rate = 4.4/100 000 population) (**Fig. 2**). The death rate plateaued from 2002 to 2011; in 2011, 3656 deaths were caused by drowning (death rate = 3.9/100 000 population).

When PHS data were combined with the number of deaths caused by water-related cataclysmic events and maritime accidents, an average of 4196 deaths per year (range 1220–8788) from 1980 to 2011 was revealed. The average death rate was 6.0/100 000 population (range 2.5–14.2). The highest peaks of death rate for the combined drowning death data were in 1987 and in 1991 (**Fig. 2**). The average number of deaths due to cataclysm was 1515 per year from 1980 to 2011 (range 131–6397), and the average number of deaths due to maritime accidents was 185 per year (range 0–4352) (**Fig. 1**). On average there were 1700 deaths per year from water-related cataclysm and maritime accidents with an average death rate of 2.5/100 000 population. When water-related cataclysmic causes and maritime accidents were added, the average number of annual deaths due to drowning (4196 deaths per year) is 1.68 times the PHS estimate (2496 deaths per year).

DISCUSSION

Our results showed that on average there were 1700 deaths per year in addition to the PHS data of drowning deaths when cataclysm and maritime accidents deaths data retrieved from other sources were included. This clearly illustrated that drowning deaths were underestimated in the official report. An underestimated report of drowning reflected by the PHS data is likely contributed to neglecting drowning as a serious public health issue. The lack of a comprehensive national drowning prevention strategy also adds to the neglect of this public health issue. The World Health Organization (WHO) Global Report on Drowning (2014)¹ recommends that collection of drowning rates and circumstances surrounding drowning are necessary in drowning

Figure 1. Combined number of drowning and other water-related deaths, Philippines, 1980 – 2011



PHS, Philippine Health Statistics

* include tsunami, cataclysmic storm, flood, exposure to other and unspecified forces of nature (e.g. tidal wave)

prevention. Likewise, a strict implementation of death registration is necessary. Use of the WHO verbal autopsy instrument is also useful when underestimation is suspected.¹

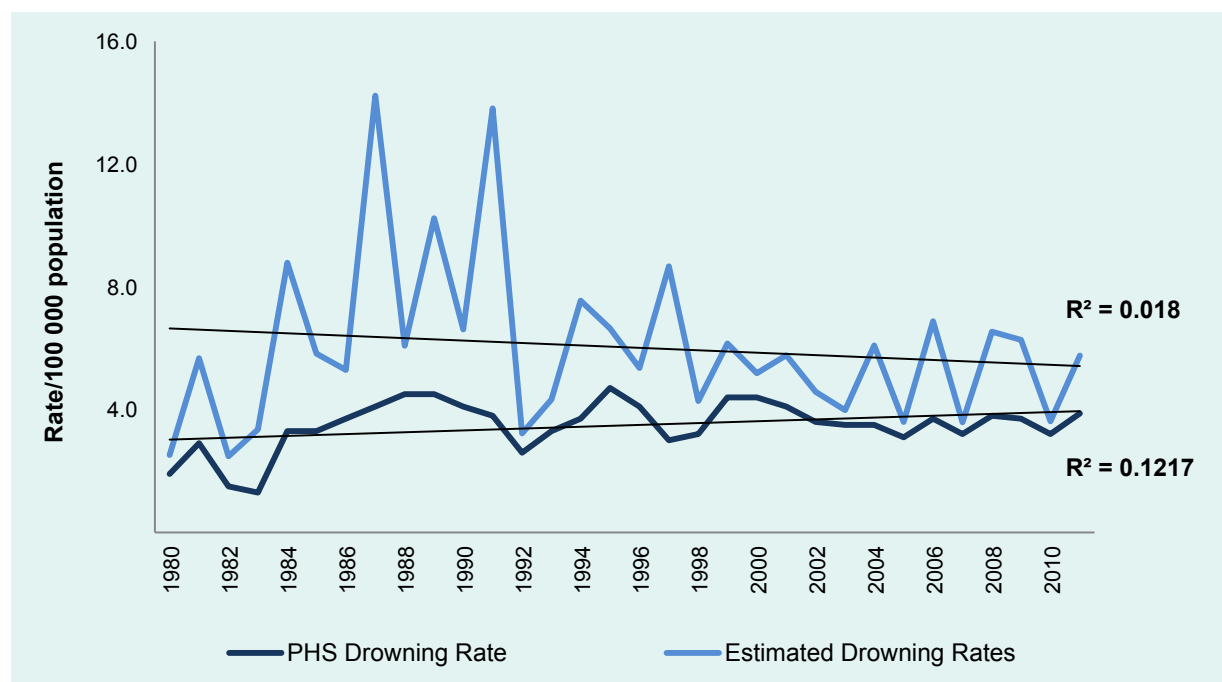
One reason for the underestimation is that the definition of drowning deaths in PHS is not comprehensive. The National Civil Registry followed the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) to classify drowning cases.⁶ In ICD-10, the whole range of conditions is classified into mutually exclusive categories. Accidental drowning and submersion were coded as W65-W74, but this category excludes water-transport-related drowning and submersion (coded as V90 and V92) and drowning and submersion caused by cataclysm (coded as X34-X39). Victims of cataclysmic storms (X37), victims of floods (X38) and victims of tsunamis (X34.1) are combined into the category of cataclysm (X34-X39) in PHS but not in the category of drowning and submersion in PHS. Additionally, intentional self-harm by drowning and submersion (X71) is combined into the category of self-harm, and assault by drowning or submersion (X92) is combined into the category of assault. In the future, consolidation of the above-mentioned drowning-related codes into a single category would facilitate estimation

of all drowning-related deaths.

Drowning (fatal and non-fatal) is also captured by ONEISS in the Philippines. ONEISS data can be used as the source of information in determining primary cause and risk factors of drowning.⁷ However, there are limitations for using the ONEISS data as (1) the data are collected by selected hospitals; (2) the system is web-based and hospitals with no or poor access to the Internet will have problems in using the system; (3) drowning events captured by local health clinics are not usually reported; (4) cataclysmic events and water transport accidents are not included; and (5) like other countries in Asia, misclassification of cases could be a problem.⁸ We did not include ONEISS data in the analysis as basically all the drowning deaths in ONEISS were captured in the National Civil Registry. ONEISS can be improved by considering other sources to collect drowning incidence data.⁹ Also it is necessary to avoid double-entry of patients referred or transferred from one health facility to another. Additional variables for patient coding can avoid this issue and should be considered.^{10,11}

This study has several limitations. First, the data were limited only to available information collected from the PHS reports and information online.³ Additional

Figure 2. **Drowning death rate of the PHS data only and the combined drowning deaths rate*, Philippines, 1980–2011**



PHS, Philippine Health Statistics

* include deaths from tsunami, cataclysmic storm, flood, exposure to other and unspecified forces of nature (e.g. tidal wave)

drowning death data such as accidental drowning, submersion and other non-specific water-related deaths may have been missed. The results are only a conservative estimate and the actual number of drowning deaths may be even higher. Second, this study only provided yearly data due to the availability of information. With data of higher resolution, trends for drowning deaths could be better presented to determine if seasonality is a contributing factor for drowning deaths. Third, the reliability of data from online media and grey literature was not examined. The deaths captured in media reports may not be the final death tolls as the situations evolved. Some natural disasters and maritime accidents might have been missed.

CONCLUSION

When cataclysmic and maritime deaths data from online sources were combined with PHS data, the number of deaths due to drowning per year is 1.68 times the PHS estimate in the Philippines in 1980–2011. This clearly showed that drowning deaths were underestimated in the official surveillance data. Surveillance of drowning data can be improved using more precise case definitions and a multisectoral approach.

Conflict of Interest

None declared.

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None.

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Syndromic surveillance in Vanuatu since Cyclone Pam: a descriptive study

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In 2012, Vanuatu designed and implemented a syndromic surveillance system based on the guidelines developed by the Pacific Community and the World Health Organization to provide early warning of outbreaks and other important public health events. Four core syndromes were endorsed for surveillance: acute fever and rash, prolonged fever, influenza-like illness and acute watery diarrhoea. In March 2015, Vanuatu was struck by Cyclone Pam, after which several important changes and improvements to the country's syndromic surveillance were made. To date, there has been no formal evaluation of whether regular reports are occurring or that core syndromes are being documented. We therefore carried out a descriptive study in the 11 sentinel sites in Vanuatu conducting syndromic surveillance between July and December 2015. There was a total of 53 822 consultations which were higher in the first 13 weeks ($n = 29\,622$) compared with the last 13 weeks ($n = 24\,200$). During the six months, there were no cases of acute fever and rash or prolonged fever. There were cases with influenza-like illness from week 27 to 35, but no case was reported after week 35. Acute watery diarrhoea occurred in one or two cases per week during the whole study period. For these two core syndromes, there were generally more females than males, and about one third were children aged under 5 years. In conclusion, Vanuatu implemented changes to its new syndromic surveillance system from July to December 2015, although laboratory components had not yet been incorporated. The laboratory components are working in 2016 and will be the subject of a further report.

A central and historic responsibility for the World Health Organization (WHO) has been the management and control of the international spread of disease. To this end, International Health Regulations were formulated by WHO and adopted by the World Health Assembly in 1969.¹ In 2005, the World Health Assembly approved a second edition of the International Health Regulations in response to growth in international travel and trade and the emergence of the severe acute respiratory syndrome, the first global public health emergency of the 21st century.² Within this framework, Member States are mandated to collect information regarding public health events through surveillance activities and to assess the potential of these events to cause international spread of disease and possible interference with international travel and trade.

In recent decades, new diseases have emerged around the world that pose serious threats to regional and

global security. The Asia Pacific Strategy for Emerging Diseases was developed in 2005, updated in 2010 and again in 2016 to meet the challenges of emerging diseases and acute public health threats in the Asia Pacific region.³ From this strategy came a work plan for the Asia Pacific region with eight focus areas that included surveillance, risk assessment and response linked with accurate laboratory diagnosis.³ In 2010, WHO and the Pacific Community (SPC) developed guidelines for the Pacific island countries and areas to design and implement a syndromic surveillance system to provide early warning of outbreaks and other important public health events so that immediate action could be taken to deal with epidemic infectious diseases.⁴ Four core syndromes, along with case definitions and important diseases to consider, were endorsed for surveillance: acute fever and rash, prolonged fever, influenza-like illness and acute watery diarrhoea.

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Vanuatu is a Y-shaped chain of islands located in the Pacific Ocean between the equator and the tropic of Capricorn. In 2012, syndromic surveillance based on the WHO PICTs guidelines was established and set up initially in three sentinel sites in the capital city, Port Vila. Five months later, the number of sentinel sites increased to eight. In March 2015, the island country was hit by Cyclone Pam.^{5,6} There were several outbreaks and public health events after the cyclone that led to important changes and improvements in syndromic surveillance, including:

1. an increased number of trainings on syndromic surveillance from the SPC;
2. an increase in the number of sentinel surveillance sites to 11 by June 2015;
3. better appreciation from front-line health workers of the importance of syndromic surveillance;
4. a re-design of the sentinel site paper-based collection forms to record daily consultations (these data were not previously collected) and for ease in recording core syndromes;
5. introduction of a new weekly reporting template for use by the central unit, based on WHO surveillance reports;⁷
6. introduction of rapid diagnostic tests for malaria, dengue and leptospirosis; and
7. algorithms for sentinel sites to collect and send blood samples to the central unit for polymerase-chain-reaction (PCR) diagnosis which is done overseas.

By May 2015, and based on the surveillance system that was in place, the number of outbreaks and public health events had decreased in Vanuatu to the number before Cyclone Pam.

Since the introduction of the improvements to the syndromic surveillance system, there has been no formal evaluation of whether this system works for regular reports of patient consultations or counts of the four core syndromes. We therefore carried out a descriptive study in the 11 sentinel sites in Vanuatu conducting syndromic surveillance between July and December 2015 to determine the numbers of weekly consultations and

the number of patients presenting with core syndromes of acute fever and rash, prolonged fever, influenza-like illness and acute watery diarrhoea along with data on gender and age group.

METHODS

Study design

This was a descriptive study using already collected routine surveillance data.

Setting

General setting

Vanuatu has 83 islands divided into six provinces with an estimated population of about 240 000.⁸ It is classified as a lower middle income country according to the World Bank with an annual gross national income of US\$ 1006–3975 per capita.⁹ In each province there is a provincial hospital staffed by doctors and nurses, and the peripheral health care in the country is provided by 32 health centres, 99 dispensaries and 222 aid posts. Health care in the government sector and in the provincial hospitals is free of charge. There is one private health facility which is situated in Port Vila and serves a population of 10 000–15 000.

Syndromic surveillance at the sentinel sites

The surveillance unit in the Ministry of Health was established in June 2012 with the purpose of early detection and reporting of unusual cases and clusters of disease to the Ministry of Health and WHO and to respond rapidly to limit the impact of outbreaks. The 11 sentinel sites include six hospitals, one in each province, and five health centres located in five islands in three provinces selected because of remoteness, population sizes or damage from Cyclone Pam. The population sizes in the catchment areas of the sentinel sites varied from 2600 to 15 000. At each sentinel site, doctors and/or nurses record the number of outpatient consultations each day on specially designed forms. Any patient who has one or more core syndromes has details entered into the syndromic data form along with appropriate clinical and laboratory action taken (see [Table 1](#)).⁴ Whenever possible, a clinical diagnosis is made, laboratory confirmation is attempted, treatment is given, isolation is

Table 1. Core syndromes, case definitions, other important diseases to consider and laboratory actions

Core syndromes identified during syndromic surveillance	Case definition	Important diseases to consider	Laboratory action that should take place
Acute fever & rash	Sudden onset of fever* PLUS acute non-blistering rash	Measles, dengue, rubella, meningitis, leptospirosis	Blood sample sent to the central unit for transmission to New Caledonia for polymerase chain reaction investigation
Prolonged fever	Any fever* lasting 3 or more days	Typhoid fever, dengue, leptospirosis, malaria, other communicable diseases	Blood sample sent to the central unit for transmission to New Caledonia for polymerase chain reaction investigation
Influenza-like illness	Sudden onset of fever* PLUS: cough and/or sore throat	Influenza, other viral or bacterial respiratory infections	Naso-pharyngeal swab sent to the central unit for transmission to New Caledonia for polymerase chain reaction investigation only if the number of cases at sentinel sites exceeds a certain number
Acute watery diarrhoea	3 or more loose or watery stools in 24 hours	Viral and bacterial gastroenteritis, including cholera, food poisoning and ciguatera fish poisoning	Stool sample sent to the central unit for investigation at the central hospital, Port Villa, Vanuatu

* Fever is defined as 38 °C/100.4 °F or higher. If no thermometer is available, fever or chills reported by the patient or the caregiver are also acceptable.

Source: adapted from World Health Organization and Secretariat of the Pacific Community.⁴

recommended as appropriate and as agreed between staff of the sentinel sites and the central unit and notification is made to the director of public health and WHO in line with guidelines in the Pacific Outbreak Manual.¹⁰

Syndromic surveillance at the central unit

The consultations for one week at each of the 11 sentinel sites are sent routinely on Monday of every week to the central unit. If an alert threshold is exceeded in any of the four core syndromes at a sentinel site, the officer in charge of the central unit is immediately informed by telephone and initiates an in-depth investigation to confirm the alert. Syndromic data forms and laboratory samples, if available, are either collected by the officer in charge from nearby sentinel sites or sent to him by courier. The officer in charge then enters data for each core syndrome into the syndromic database. Data variables include the sentinel site, the name and contact details of the patient, age, sex, core syndrome, date of reporting of the core syndrome, clinical diagnosis, and, if available, details of the laboratory samples received at the central unit. If sentinel sites observe an unusual increase in the number of cases with a core syndrome, it is reported to the central unit within 24 hours and the central unit then recommends an investigation.

The syndromic surveillance situational report and follow-up action

The syndromic surveillance report is generated on a weekly basis from the central unit and sent in Vanuatu to all Ministry of Health cluster members, the national disaster management office and other government ministries. The report also goes to provincial health authorities who disseminate it to health centres, dispensaries and community-aid posts. An Epi-net response team then uses standardized procedures, as described in the Pacific Outbreak Manual,¹⁰ to carry out field investigations. The syndrome data are shared weekly with WHO upon which the Pacific Syndromic Surveillance Report is generated and posted on PacNet. The syndromic surveillance reports highlight countries where thresholds for core syndromes are exceeded.

Patient population

The study population included all patients presenting for consultation and identified with a core syndrome at 11 sentinel sites in Vanuatu between 1 July and 31 December 2015.

Data variables, sources of data and data collection

Data variables included the sentinel site, the week of the year, the number of consultations in each week, the counts of the core syndromes, and for those with core syndromes the gender and the age (categorized as 0–4 years and 5 years and above). The source of data was the Excel electronic database maintained by the officer in charge of the central unit.

Analysis and statistics

Data were single-entered from the Excel database into Epi Info™ Version 7.0 (Centers for Disease Control and Prevention, Atlanta, GA, USA). A descriptive analysis was performed using absolute numbers, frequencies and proportions.

Ethics

Permission for the study was given by the Ministry of Health as part of routine surveillance. Ethics approval for the writing and publication of the study was obtained from the Ethics Advisory Group, International Union Against Tuberculosis and Lung Disease (The Union), Paris, France. Patient consent was not required as this was anonymized secondary data.

RESULTS

Weekly consultations along with the number with core syndromes of influenza-like illness, acute watery diarrhoea, acute fever and rash, and prolonged fever between week 27 (1 July) and week 53 (31 December) 2015 are shown in [Fig. 1](#). There was a total of 53 822 daily consultations which were higher in the first 13 weeks (weeks 27–40, $n = 29\,622$) compared with the last 13 weeks (weeks 41–53, $n = 24\,200$). During the six-month period, there were no cases of acute fever and rash or prolonged fever. However, there were cases with influenza-like illness and acute watery diarrhoea. Cases with influenza-like illness presented from week 27 to 35 and then stopped. There were generally one or two cases with acute watery diarrhoea for most of the weeks during the study period. Demographic characteristics of patients presenting with influenza-like illness and acute watery diarrhoea are shown in [Table 2](#). There were generally more females than males, and about one third of the patients were children aged less than 5 years.

Table 2. Demographic characteristics of patients presenting with influenza-like illness and acute watery diarrhoea

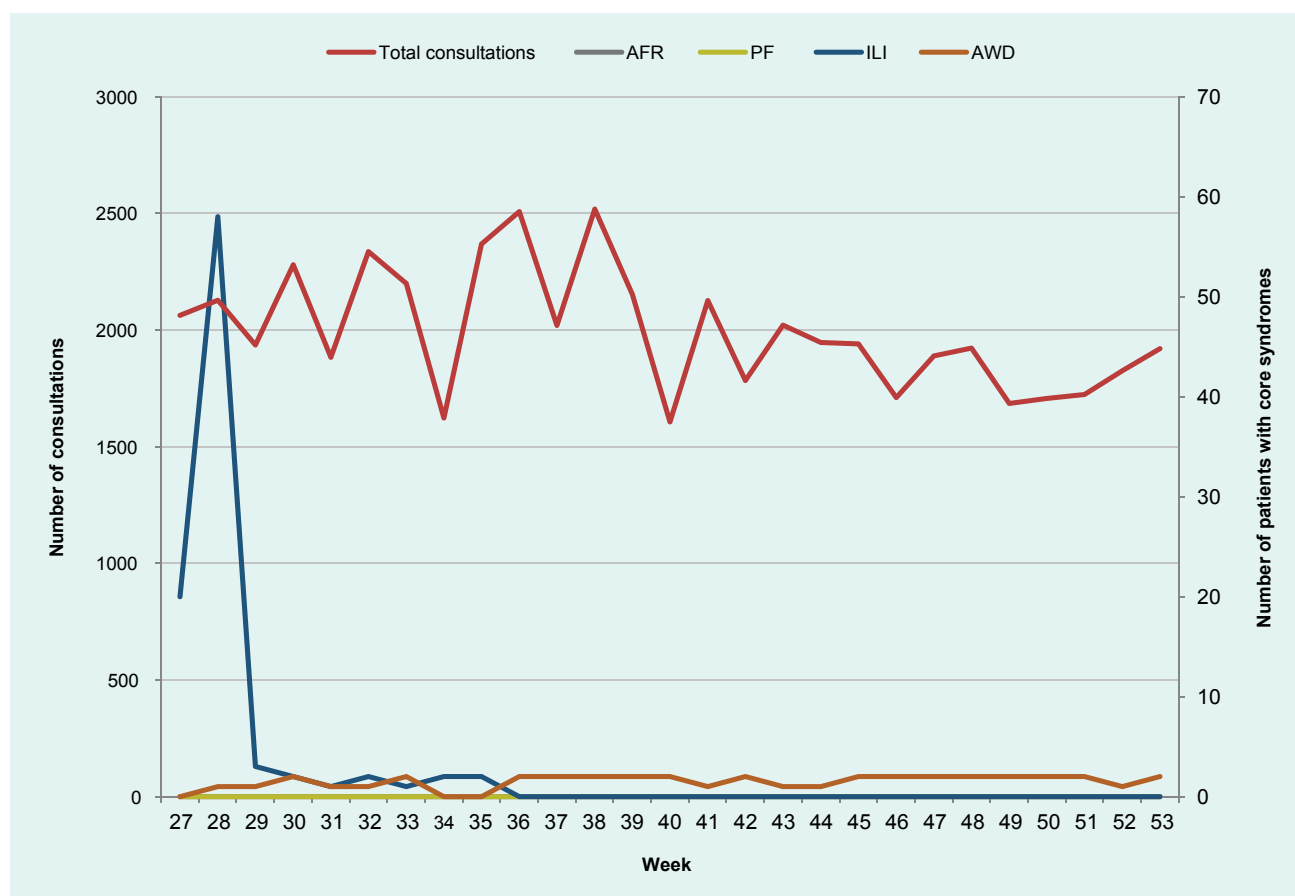
Characteristics	Influenza-like illness Number (%)	Acute watery diarrhoea Number (%)
All patients	91	40
Gender:		
Male	45 (49)	17 (42)
Female	46 (51)	23 (58)
Age group in years:		
0 – 4	34 (37)	13 (32)
5 and above	57 (63)	27 (68)

DISCUSSION

This study shows that the new syndromic surveillance system in Vanuatu set up to document the number of weekly consultations and the number of the four core syndromes worked with data being collated and produced in the electronic Excel database by the central unit. The main findings were a gradual decrease in weekly consultations in the fourth quarter of 2015 compared with the third quarter, reports of influenza-like illness in the third quarter that stopped completely in the fourth quarter, and one to two cases of acute watery diarrhoea that generally continued throughout the observation period. Thirty-seven per cent of patients with influenza-like illness and 32% of patients with acute watery diarrhoea were children aged less than 5 years.

An important finding was the large number of weekly consultations and yet the relatively small number of these presenting with one or more of the core syndromes. On reflection, this was probably due to several factors: 1) many of the focal officers in the sentinel sites who had been trained in syndromic surveillance were transferred to other facilities after Cyclone Pam leaving generally untrained personnel to do the reporting – hence it is likely that cases with core syndromes were missed; 2) poor telecommunication infrastructure after the cyclone especially with respect to mobile phones and email access hindered reporting from peripheral sites to the centre; and 3) poor transportation also hindered reporting. These obstacles are in the process of being resolved, and for 2016, it is expected that reporting of core syndromes will improve.

Figure 1. **Weekly consultations along with the number of patients with core syndromes of influenza-like illness, acute watery diarrhoea, acute fever rash and prolonged fever in the 11 sentinel sites, Vanuatu, July to December 2015**



AFR = acute fever and rash, PF = prolonged fever, ILI = influenza-like illness, AWD = acute watery diarrhoea. Zero cases have been reported for AFR and PF.

There were some limitations to the study. The system reports only on those less than 5 years and those 5 years and above with no further categorization of this older age group. This needs to be modified. At least the age strata of 5–9 years, 10–19 years and over 20 years should be included as incidence of the syndromes may differ between these groups. In the second half of 2015, there were no operational systems in place for laboratory investigation and, therefore, no reports on recommended tests done, the time for samples to get to the central unit, the ease or difficulty of overseas sample testing or the time taken for results to get back to Vanuatu. Since 2016, however, the laboratory component has been started and gradually strengthened, although we have no collated data to report in this current study.

Since Cyclone Pam struck in March 2015, Vanuatu has implemented changes to its syndromic surveillance system. From July to December 2015, there were regular

weekly reports of consultations along with reports of the number of people with one or more of the four core syndromes. Laboratory components had not yet been incorporated although work has been done in 2016 and will be the subject of a further report.

Conflict of interest

No conflict declared.

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The changing epidemiology of measles in an era of elimination: lessons from health-care-setting transmissions of measles during an outbreak in New South Wales, Australia, 2012

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Introduction: In countries where measles is rare, health-care-setting transmissions remain problematic. Australia experienced its largest measles outbreak in 15 years in 2012 with 199 cases reported nationally; 170 cases occurred in the state of New South Wales (NSW) with symptom onset between 7 April and 29 November 2012.

Methods: A descriptive study was conducted using measles case data obtained from metropolitan Sydney local health districts in NSW in 2012. Characteristics of measles source and secondary cases were described. Details of health-care presentations resulting and not resulting in measles transmission were also analysed.

Results: There were 168 confirmed and two probable cases resulting in 405 documented health-care presentations. Thirty-four secondary cases acquired in health-care settings were identified, including 29 cases resulting from 14 source cases and 5 cases whose source could not be identified. Health-care-acquired cases accounted for 20% of all cases in this outbreak. Source cases were more likely to be of Pacific Islander descent ($p = 0.009$) and to have had more presentations before diagnosis ($p = 0.012$) compared to other cases. The percentage of presentations to emergency departments was higher for presentations that resulted in transmission compared to those that did not (71.4% and 37.6%, respectively, $p = 0.028$). There were no significant differences between transmission and non-transmission presentations with respect to presence of rash and infection control measures ($p = 0.762$ and $p = 0.221$, respectively), although the power to detect these differences was limited. Rash was reported at 66% of the presentations.

Conclusion: Development of and adherence to protocols for the management of patients presenting to hospitals with fever and rash will minimize secondary transmission of measles.

Although Australia had been near measles elimination since 2005¹ and was declared to have officially eliminated measles in 2014,² Australia experienced its largest measles outbreak in 15 years in 2012 with a total of 199 cases reported nationally. The number of cases has remained high since then with 340 confirmed cases (14.39 per 1 000 000 population) in 2014.³ There were 170 cases in the state of New South Wales (NSW, Australia's most populous state) in the 2012 outbreak with the index case having symptom onset on 7 April and the last case on 29 November, among whom 168 were confirmed.⁴ Western

Sydney, where the majority of outbreak cases resided, is culturally diverse. Over a third of its two million population were born overseas, and it also includes a very large urban population of Aboriginal and Torres Strait Islander people.^{5–7}

In countries where measles is rare, transmissions in health-care facilities have been important in amplifying outbreaks^{8,9} and challenging retention of measles elimination status. Although numerous measles outbreak reports have been published describing health-care transmissions,^{10–12} many lack details of case

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demographics and transmission characteristics that are crucial for improving control and response guidelines for post-elimination settings.

The 2010 NSW Public Health Act requires all measles patients to be notified to local public health units by doctors and laboratories.¹³ Health-care-setting transmissions of measles in NSW were well documented in the 2012 Australian outbreak. This study describes key characteristics of health-care transmissions in this NSW outbreak, including the clinical setting and timing of presentations, the ability of clinicians to efficiently identify a probable measles case and the stage of illness of presenting cases.

METHODS

A descriptive routine-database study was conducted to compare characteristics of the measles cases who met the definition of a source case and cases who presented to a health-care facility and did not transmit illness. Characteristics of individual presentations to health-care facilities were also described.

Data source

Case series data describing both confirmed and probable measles cases, as defined by Australian national guidelines,¹⁴ with symptom onset between 7 April and 29 November 2012 were obtained from metropolitan Sydney local health districts (LHDs) that conducted case interviews in NSW. Collected data included age, sex, ethnicity and/or country of origin, second language, number of health-care presentations before diagnosis and vaccination status. Vaccination status was categorized as fully vaccinated, partially vaccinated, not vaccinated, too young to be vaccinated or unknown, according to the data recorded by the public health units in the NSW Notifiable Conditions Information Management System (NCIMS). For most cases, their vaccination status relied upon self- or parental-recall. Where complete, details in the vaccination validation field in NCIMS that documented written evidence of vaccination history, such as Australian Childhood Immunization Register (ACIR) or health records, were used to assist categorization of vaccination status. Data regarding time of arrival and discharge from health-care facilities were obtained from emergency department (ED) records or from

general practice (GP) clinic records where available.

Definitions of study parameters

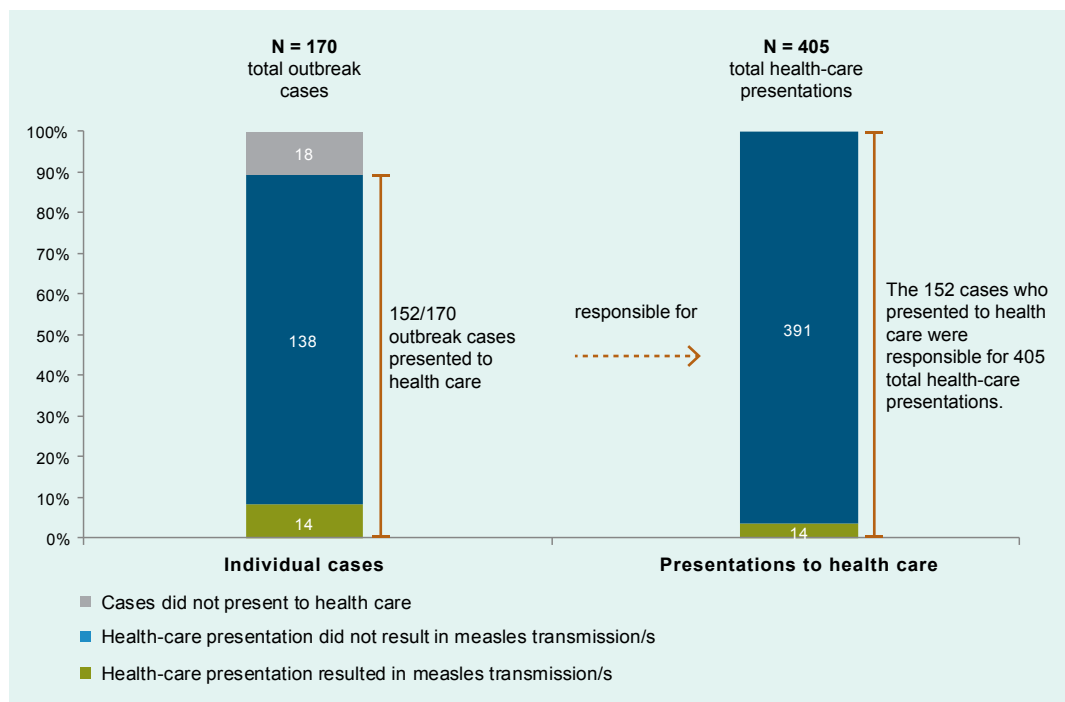
A health-care facility was defined as any premise that delivers health-care services including hospital EDs, inpatient wards and GP clinics. A presentation was defined as a case who sought care at a health-care facility. A transmission event in a health-care setting was defined by the discovery of a measles case arising 7–18 days after a visit to the same health-care setting at approximately the same time as an infectious case. A (known) source case was defined as a measles-infected individual who transmitted the disease to another previously uninfected individual. A secondary case was defined as a previously uninfected individual who was infected by a source case in a health-care facility. If more than one case had symptom onset at the same time and presented in the same health facility on the same day with likely overlap in time and location, these cases were also considered as secondary cases even though the source cases could not be determined. Secondary cases were only classified as having been infected in a health-care setting if there was no other more likely source of transmission (e.g. household).

Data analysis

Demographic details of the measles cases in the outbreak were summarized. Characteristics of the measles source cases and cases who presented to a health-care facility and did not transmit illness were compared. Characteristics of individual health-care presentations were described to compare health-care presentations that led to transmission events and those that did not.

Overlap times in health-care facilities for presentations that resulted in transmission with the presentation times of their subsequent secondary cases were estimated by calculating the difference in minutes between recorded arrival and discharge times. χ^2 tests were conducted to compare categorical variables, including age group distribution, sex and vaccination status between those cases or presentations that resulted in transmission events and those that did not. A p -value of less than 0.05 was considered statistically significant. All analyses were done using Stata version 12 (StataCorp LP, College Station, TX, USA). When conducting χ^2 tests comparing presentations, we used survey commands to

Figure 1. Overview of the total number of measles cases and presentations analysed, NSW, Australia, 2012



adjust for clustering of observations within patients. A Mann–Whitney test was used for all analyses comparing medians of numbers of presentations before diagnosis between cases who transmitted and those who did not. For medians of time spent in a health-care setting and day of illness when presenting to health care, no statistical test was conducted to compare presentations that led to transmissions to those that did not due to the complexity of clustering effect.

Ethics

Ethics approval was not required for this study as it was part of the public health outbreak response conducted under the NSW Public Health Act.¹³

RESULTS

Characteristics of the measles cases

From 7 April to 29 November 2012 in NSW, there were 168 confirmed and two probable measles cases.¹⁴ Of these 170 cases, 152 presented a total of 405 times to various health-care settings during the outbreak (Fig. 1). Of the total presented cases, 43 (28.3%) were aged 10–19 years and 80 (52.6%) were

male. Thirty-four (22.4%) were of Pacific Islander descent. Twenty-six (17.1%), were reported as fully vaccinated and eight (5.3%) as partially vaccinated (Table 1). Only seven (20.6%) of those reported to be fully or partially vaccinated were noted in the NCIMS database as having documented evidence of their vaccination status including written health record or inclusion in the ACIR. Fourteen (9.2%) cases met the definition of source case and were linked to 29 health-care-acquired secondary cases; two unknown source cases were linked to a further five health-care-acquired cases, resulting in a total of 34 identified secondary cases. This represents 20.2% of all laboratory confirmed cases.

Health-care-acquired (secondary) cases

The median age of the health-care-acquired cases ($n = 34$) was 5.5 years (range: 0–37 years). Ten cases (29.4%) were infants too young to be vaccinated, nine (26.5%) were unvaccinated, two (5.9%) were partially vaccinated and eight (23.5%) were fully vaccinated. The vaccination status for the remaining five cases was unknown (Table 1). One case (2.9%) was a health-care worker. Three secondary cases (8.8%) were documented as Pacific Islanders (Table 1).

Table 1. **Demographics of total measles outbreak cases who presented to health-care facilities and total health-care-acquired measles cases, NSW, Australia, 2012**

	Total outbreak cases who presented to a health-care facility* (n = 152)		Total health-care-acquired (secondary) cases (n = 34)	
	Number	Proportion	Number	Proportion
Age group				
< 1 year	36	23.7%	12	35.3%
1–9 years	23	15.1%	7	20.6%
10–19 years	43	28.3%	3	8.8%
20–59 years	49	32.2%	12	35.3%
≥ 60 years	1	0.7%	-	-
Sex				
Male	80	52.6%	21	61.8%
Female	72	47.4%	13	38.2%
Vaccination status				
Fully vaccinated	26	17.1%	8	23.5%
Partially vaccinated	8	5.3%	2	5.9%
Ineligible (aged < 12 months)	38 [†]	25.0%	10	29.4%
Not vaccinated	52	34.2%	9	26.5%
Unknown	28	18.4%	5	14.7%
Pacific Islander status				
Pacific Islander	34	22.4%	3	8.8%

* Of 170 total cases, 152 presented a total of 405 times to various health-care settings during the outbreak.

[†] These included two cases who had just reached 12 months of age at symptom onset and health-care staff decided they were “too young to be vaccinated”.

Comparison of source cases and cases who did not transmit measles

The median age of the 14 known source cases (15.5 years; range: 0–38 years) was not statistically different from the median age of those 138 cases who presented to a health-care facility but did not transmit infection (14.5 years; range: 0–61 years). Similar proportions in both groups were unvaccinated (35.7% versus 34.1%) or too young to be vaccinated (21.4% versus 25.4%) (Table 2). Though Table 2 indicates that 26 total cases were fully vaccinated, only three of these cases had their vaccination status validated by a written health record or inclusion in the ACIR; all of these were non-transmitters. A significantly higher percentage of source cases were of Pacific Islander descent compared to cases that did not lead to health-care-acquired transmission (50.0% versus 19.6%, $p = 0.009$).

All cases who resulted in transmission presented on more than one occasion before successfully receiving a diagnosis (range: 2–5 presentations). The median number of presentations among cases that resulted in transmission was statistically higher than those who did not (3.5 presentations versus 2.0 presentations, $p = 0.012$).

Presentations

Of the 405 presentations, 14 (3.5%) resulted in transmission. Two hundred and sixty-nine presentations (67.8%) included a rash at presentation and 377 (96.2%) included a cough. A total of 104 presentations occurred on weekends (26.1%). There were 157 (39.2%) presentations to an ED and 195 (48.6%) to a GP. In 148 (39.6%) presentations, infection control measures were reported by physicians, including giving patients masks, locating them in a single room and others.

Table 2. Demographics of measles cases presenting to health-care facilities that resulted in transmission (source cases) versus no transmission, NSW, Australia, 2012

Total number of cases presenting to a health-care facility (n = 152 [†])					
	Transmission (n = 14)		No transmission (n = 138)		P-value
	Number	Proportion	Number	Proportion	
Age group					
< 1 year	3	21.4%	35	25.4%	0.290
1–9 years	2	14.3%	19	13.8%	
10–19 years	5	35.7%	38	27.5%	
20–29 years	3	21.4%	15	10.9%	
30–39 years	1	7.1%	25	18.1%	
≥ 40 years	-	-	6	4.4%	
Sex					
Male	8	57.1%	72	52.2%	0.723
Female	6	42.9%	66	47.8%	
English as a second language					
Yes	1	7.1%	3	2.2%	0.327
No	11	78.6%	101	73.2%	
Unknown [§]	2	14.3%	34	24.6%	
Vaccination status					
Fully vaccinated	3	21.4%	23	16.7%	0.973
Partially vaccinated	1	7.1%	7	5.1%	
Ineligible (aged < 12 months)	3	21.4%	35	25.4%	
Not vaccinated	5	35.7%	47	34.1%	
Unknown [§]	2	14.3%	26	18.8%	
Pacific Islander					
Yes	7	50.0%	27	19.6%	0.009*
No	7	50.0%	111	80.4%	
Number of presentations before diagnosis					
	Median: 3.5 presentations (range: 2–5 presentations)		Median: 2.0 presentations (range: 1–7 presentations)		0.012*

[†] Of 170 total cases, 152 presented a total of 405 times to various health-care settings during the outbreak.

* Indicates statistical significance.

[§] Unknowns not included in the χ^2 analysis.

Presentations resulting in transmissions versus those that did not

Presentation setting

In presentations that led to transmission, ED visits were significantly over-represented (71.4% versus 37.6%) and GP visits significantly under-represented (14.3% versus 49.4%) compared with presentations not resulting in transmission ($p = 0.028$; **Table 3**).

Presentation time

The median time of presentations which resulted in transmission was longer than those presentations which did not result in transmission (15.0 hours versus 4.9 hours). While 42.9% of presentations that resulted in transmission occurred on a weekend, 25.1% of those that did not result in transmission occurred on a weekend, although the difference was not significant ($p = 0.141$). Of the presentations that resulted in transmission, those

Table 3. Information by health-care presentations that resulted in measles transmission versus no transmission, NSW, Australia, 2012

Total number of health-care presentations (n = 405)					
	Transmission (n = 14)		No transmission (n = 391)		P-value
	Number	Proportion	Number	Proportion	
Rash at presentation					
Yes	10	71.4%	259	66.2%	0.762
No	4	28.6%	124	31.7%	
Unknown [§]	-	-	8	2.1%	
Day of week					
Weekday	8	57.1%	287	73.4%	0.141
Weekend	6	42.9%	98	25.1%	
Unknown [§]	-	-	6	1.5%	
Cough at presentation					
Yes	14	100.0%	363	92.8%	0.565
No	-	-	15	3.8%	
Unknown [§]	-	-	13	3.3%	
Health-care setting					
Emergency department	10	71.4%	147	37.6%	0.028*
General practice	2	14.3%	193	49.4%	
Hospital ward	2	14.3%	47	12.0%	
Unknown [§]	-	-	4	1.0%	
Infection control measures					
Yes	3	21.4%	145	37.1%	0.221
No	10	71.4%	216	55.2%	
Unknown [§]	1	7.1%	30	7.7%	
Median time spent in a health-care setting (hours)					
	15.0 [†] (range: 2.3–2212.0 hours)		4.9 [‡] (range: 0–10080.8 hours)		-
Day of illness when presenting to health-care					
	Median: 3.5 days (range: 1–8 days)		Median: 3.0 days (range: 0–15 days) [‡]		-

[§] Unknowns not included in the χ^2 analysis.

* Indicates statistical significance.

^{||} Statistical tests not conducted for continuous variables.

[†] Time unknown for one presentation.

[‡] Time unknown for 153 presentations.

[‡] Day of illness unknown for 10 presentations.

on weekends had a median time of 33.1 hours (range: 6.6–2212.0 hours) while those on weekdays had a median time of 4.6 hours (range: 2.3–108.8 hours) (data not shown).

Stage of illness of presenting case

The median day of illness for presentations resulting in transmission was 3.5 (range: 1–8 days)

compared with 3.0 days (range: 0–15 days) for those presentations which did not (Table 3). Rash was reported at 71.4% presentations that resulted in transmission, compared to 66.2% of those that did not ($p = 0.762$). On average, 2.3 secondary cases resulted from presentations with rash compared with 1.5 secondary cases for presentations without rash (data not shown).

Overlap time for secondary infections

The overlap time between presentations that resulted in transmission and their subsequent secondary cases was estimated for 10 of the 12 transmission events in hospital (ED and wards) for which the source cases could be identified; the median was 4.4 hours (range: 59 minutes – 35.5 hours). All secondary cases were present at the same time as the case who was the source of their infection. For one of the two transmission events for which a source case could not be identified, the four resultant secondary cases each overlapped in time. For the other transmission event with no identifiable source case, the secondary case was present in the ED at the same time as two source cases so we could not ascertain which source case was responsible for the infection. Overlap times for presentations that resulted in transmission in GP clinics could not be estimated because arrival and departure times of patients were not typically recorded; however, one of the three secondary cases acquired in a GP clinic reported that a measles case was known to be present during a concurrent visit.

DISCUSSION

In countries where measles is rare and most clinicians have not experienced a case first hand,^{9,15} measles may go undiagnosed and outbreaks may result. A recent review found that up to 50% of cases in developed countries, particularly where measles elimination was established, had been acquired in a health-care setting.¹⁶ In the 2012 NSW outbreak, we found approximately 20% of cases were infected in health-care facilities.

The reasons for the predominance of health-care-setting transmissions are obvious. Cases are contagious from four days before to four days after the rash appears.¹⁴ At first presentation, few cases are suspected of having measles because clinically distinguishing it from other viral systemic illnesses is problematic.¹⁷ A patient in the early stages of measles may present with a combination of non-differential symptoms, including fever and perhaps only one of the following: cough, coryza and conjunctivitis. Differential diagnoses include influenza and other common respiratory viral infections and allergic rhinitis. Even with the characteristic maculopapular rash, a measles diagnosis may be overlooked because of the disease's rareness and similarities to adeno- and enteroviral infection, other exanthema of childhood and

drug allergy.^{9,18} In this outbreak, unable to obtain a successful diagnosis on first presentation, most source cases presented multiple times. Cases who transmitted measles were more likely to have multiple presentations compared with those who did not transmit the virus and were more likely to be of Pacific Islander descent.

In ED settings where ill individuals congregate in close proximity, often for long periods of time, transmission is particularly problematic. In this outbreak, presentations that resulted in measles transmission were significantly more likely to be in an ED. This could be influenced by the fact that particularly vulnerable individuals such as young infants and the immunocompromised may be more likely to present to an ED as compared to a GP for their illness. Our data demonstrated that transmissions were also more likely to have occurred among presentations that lasted longer.

In addition to documenting the lengthiness of presentation times, our data also revealed that all transmissions for which a source case could be identified occurred during a direct overlap in time between the presentation of source and secondary cases, echoing similar findings from a 2011 NSW outbreak.¹⁹ This evidence influenced the Communicable Diseases Network of Australia to amend its Series of National Guidelines for measles control. It is now recommended that contact tracing only be conducted for contacts present in a location for up to 30 minutes after the source case is known to have departed, rather than for two hours as was previously advised.¹⁴ As previous Australian research estimated the expenses associated with managing 75 contacts of one measles case in a 2011 outbreak as 2433 Australian dollars,²⁰ reduction in contact-tracing expenditure in future outbreaks could be substantial.¹⁹

Our results identified that even during the 2012 outbreak's peak, when multiple public health alerts had been disseminated to health-care facilities, several measles cases despite presenting with rash were not suspected of having measles at the first presentation. The need for clinicians to maintain a high suspicion of measles during times of outbreaks cannot be overemphasized.²¹ In the future, more innovative approaches may be required to improve such control efforts, including establishing alerts that are triggered when 'fever' and 'rash' are entered into electronic medical records. Such

measures, however, have yet to be evaluated.^{22,23} In addition to improving timely recognition and diagnosis of measles cases, control of the 2012 outbreak could have benefited from consistent and standardized infection control measures.¹⁴ Although several source cases were recorded as having been subjected to infection control measures, efforts were ineffective or enacted too late to prevent transmission. Infection control was documented to have differed not only between hospitals but also within hospitals. Admittedly, measures may not have been rigorously documented in this outbreak.

As is common with studies based on retrospectively collected data, data completeness and quality presented significant limitations to the interpretations we could draw from our analysis and to the analyses we were able to conduct. Accuracy of routine clinical documentation limited our ability to compare transmission risk between source and non-source cases. While hospital data systems allow accurate recording of measures such as arrival and departure time, given the extremely long periods of time that some patients were determined to have been present in hospital, it is possible that even these measures are not always accurate. Other infection control measures are not uniformly reported and could range from actions that haven't been proved to be effective such as giving a patient a mask to locating them in a single room with negative pressure ventilation. Vaccination status is rarely confirmed against medical records by assessing clinicians, and there is known underreporting of vaccination to the ACIR, limiting public health units' ability to confirm vaccination histories; vaccination histories of cases born overseas are particularly difficult to verify. Improved recording of clinical details of cases during times of outbreak could improve our understanding of measles infectiousness and better inform our outbreak response and control efforts.

As more countries progress towards measles elimination, transmission in health-care facilities assumes increasing importance as a remaining obstacle. Though imported measles cases will continue to challenge countries that have achieved elimination status,²¹ health-care-setting transmissions can be addressed more effectively to ensure that health-care facilities are not contributing to outbreaks. Describing characteristics of health-care-setting outbreaks such as this one may assist in improving appropriate and targeted response and control efforts.

Conflicts of interest

None to declare.

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A Q fever cluster among workers at an abattoir in south-western Sydney, Australia, 2015

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Background: In September 2015, the Public Health Unit of the South Western Sydney Local Health District was notified of two possible Q fever cases. Case investigation identified that both cases were employed at an abattoir, and both cases advised that co-workers had experienced similar symptoms. Public Health Unit staff also recalled interviewing in late 2014 at least one other Q fever case who worked at the same abattoir. This prompted an outbreak investigation.

Methods: The investigation incorporated active case finding, microbiological analysis, field investigation and a risk factor survey. Included cases were laboratory definitive or suspected cases occurring from October 2014 to October 2015, residing or working in south-western Sydney. A suspected case had clinically compatible illness, high-risk exposure and was epidemiologically linked to another confirmed case. A confirmed case included laboratory detection of *C. burnetii*.

Results: Eight cases met the case definition with seven confirmed (including a deceased case) and one suspected. The eight cases were all males who had been employed at an abattoir in south-western Sydney during their incubation period; symptom onset dates ranged from November 2014 to September 2015. Field investigation identified multiple potential risk factors at the abattoir, and the majority (75%) of employees were not vaccinated against Q fever despite this high-risk setting.

Conclusion: This cluster of Q fever in a single abattoir confirms the significance of this zoonotic disease as an occupational hazard among persons working in high-risk environments. Implementation of Q fever vaccination programmes should eliminate Q fever in high-risk occupational settings.

Q fever is a zoonotic disease caused by *C. burnetii*.¹⁻⁷ The main reservoirs for transmission of Q fever are cattle, sheep and goats.⁸⁻¹⁰ Humans are predominately infected through inhalation of airborne dust or droplets containing *C. burnetii* bacterium.⁵⁻⁷ The Q fever incubation period is 14 to 21 days. Q fever cases can present as either acute or chronic clinical manifestations; however, approximately 60% of Q fever infections are asymptomatic.⁵⁻⁷ During the acute phase, symptoms are generally limited to a febrile illness with associated headaches, fatigue and chills.¹⁻³ Diagnosis of Q fever is predominantly through serological testing.^{1,3}

In Australia, human infection with Q fever has been largely attributed to close contact with cattle, sheep and goats, particularly their reproductive organs and secretions. Those at greatest risk of Q fever are people employed at abattoirs, cattle farms and veterinarian

clinics.^{1,7} There have been 12 significant reported outbreaks of Q fever since 1959 with 9 of these associated with abattoirs, meatworks and cattle/goat/sheep farms.¹¹ In 2012–2014, a large outbreak of Q fever in Victoria was linked to a goat and sheep dairy farm with 18 confirmed cases over the period.¹² A safe and effective Q fever vaccine has been available in Australia since 1989.⁴ It is recommended in the Australian Immunization Handbook¹³ and mandated by SafeWork NSW (a New South Wales [NSW] government agency for work health and safety regulations)¹⁴ for those employed in high-risk occupations.

In NSW, Q fever is a notifiable condition under the Public Health Act 2010 and notifiable to the local Public Health Unit (PHU). In September 2015, the South Western Sydney Local Health District (SWSLHD) PHU was notified of two possible Q fever cases. Both cases

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were interviewed and followed up according to NSW Health control guidelines for Q fever.¹⁵ These interviews revealed that they had been employed at the same abattoir during their incubation period with no other likely risk exposures identified. These cases reported that co-workers had experienced similar symptoms. PHU staff recalled interviewing at least one other Q fever case in late 2014 who worked at the same abattoir. The interviews prompted further investigation to identify any additional possible or confirmed Q fever cases not notified to the PHU. This paper describes the approaches used in the Q fever cluster investigation and the findings that can inform Q fever surveillance and future investigations.

METHODS

The two Q fever cases notified to PHU were investigated. In addition, active case finding was conducted through (1) the line listing of abattoir employees, (2) routine case notifications, (3) local facsimile back system (facsimile sent to medical practices by PHU and sent back to PHU by the general practitioner (GP) with required information completed), (4) retrospective review of clinical pathology submissions from September to November 2015 together with field investigation around the abattoir, and (5) a risk factor survey. The additional cases identified through active case finding were investigated.

Active case finding

1. The abattoir provided a list of all persons employed at the facility during the suspected exposure period. Further information including employees' Q fever vaccination status (if not vaccinated, reason for not being immunized), occupation, duration of employment, and whether employees had a history of illness consistent with Q fever were recorded in the form of a line listing.
2. A retrospective review of Q fever cases notified to the PHU through electronic and paper-based reporting from the laboratories was conducted. The notifiable conditions database and all cases notified to PHU throughout the study period were reviewed. Review of symptom profile, possible risk exposures and laboratory methods were included.
3. General practitioners in the local government area surrounding the abattoir in south-western Sydney

were contacted and asked to review any possible Q fever cases who presented to their practices. This process was implemented through a local facsimile back system. Written permission to contact these cases for investigation was provided by the GP.

4. A retrospective review of Q fever clinical pathology submissions during the study period for a resident of SWSLHD (identified using residential postcodes) was performed with the assistance of the State reference laboratory, NSW Pathology West, previously Institute for Clinical Pathology and Medical Research (ICPMR).

Additional cases were identified via cross-referencing of the above line listing with cases already notified to the PHU.

Case definition

We referenced the NSW Control Guidelines for Q fever to define the cases in this investigation:¹⁵

1. A suspected case was defined as any person who had clinical evidence of Q fever (fever, headaches, fatigue, chills), a high-risk exposure to *C. burnetii* and was epidemiologically linked with other suspected or confirmed cases in the cluster.
2. A confirmed case was defined as any person who had:
 - a. laboratory-definitive evidence:
 - i. detection of *C. burnetii* by nucleic acid testing, or
 - ii. seroconversion or significant increase in antibody level to Phase II antigen of *C. burnetii* in paired sera tested in parallel in the absence of recent Q fever vaccination, or
 - iii. detection of *C. burnetii* by culture; or
 - b. laboratory-suggestive evidence (i.e. detection of specific IgM in the absence of recent Q fever vaccination) and clinical evidence of Q fever disease.

Laboratory methods

Commercial enzyme immune assays were used for initial serological testing by detecting Q fever IgM and IgG antibodies. Results of NSW Pathology West laboratory testing were requested to reach a definitive diagnosis. NSW Pathology West tested acute and convalescent specimens using immunofluorescent antibody testing and complement fixation testing for both Phase 1 and 2 antigens.

Risk factor survey

A modified risk assessment section of the standard Q fever investigation question package¹⁵ was developed, which included additional questions to capture potential risk factors for Q fever. Cases were asked about symptom profile, occupational risks, vaccination and exposure to animals outside of their occupational setting.

Field investigation

An inspection of the affected abattoir conducted on 13 October 2015 involved review of abattoir documentation encompassing standard operating procedures for new staff inductions, work health and safety regulations and vaccination for Q fever; gathering information on species slaughtered and wholesalers who provide them to the abattoir; inspection of the kill floor, holding yards and layout and design of the abattoir; and review of cleaning practices. Staff knowledge of Q fever was also assessed by asking questions about transmission, vaccination, symptoms and their understanding of abattoir management reporting requirements for Q fever.

RESULTS

In total, we identified eight cases of Q fever (seven confirmed and one suspected cases) with onset dates ranging from 24 November 2014 to 9 September 2015 (**Table 1**). All cases were males employed at the implicated abattoir during their incubation period. Most cases had fever (7/8), followed by lethargy and malaise (6/8), headache (5/8), chills or rigors (5/8) and nausea and vomiting (5/8) (**Table 2**). Case 7 was seen by a GP and was deceased on arrival to a hospital three weeks after onset of symptoms. A coronial inquest into his death indicated that Q fever was a significant condition contributing to his death but not the condition causing his death.

Six cases were identified after active case finding; four cases through retrospective review of laboratory reporting to PHU and two through the abattoir line listing. Furthermore, one potential case was identified through GP facsimile back. However, this case did not meet the confirmed or suspected case definition for Q fever and was excluded.

Risk factor surveys were conducted between October 2015 and November 2015, which revealed that only 25% (2/8) of cases had previously received a Q fever vaccination (**Table 3**). All eight cases had high-risk exposures during their current employment: handling the carcasses/slaughtering of pregnant animals, contact with animals giving or having given birth recently, and handling of animal fetuses and waste containers used for collection and disposal of birthing products. None of the cases identified other potential risk factors outside their occupational setting. Numerous attempts to interview or have asymptomatic staff complete the risk factor survey were unsuccessful.

Field investigation at the abattoir identified that there were 33 staff currently employed at the abattoir – 23 were employed to slaughter animals; the other 10 staff had roles in management, maintenance and stock handling. Management advised that there was a high turnover of staff. High turnover of staff and the ongoing pressure of needing to start employees immediately was certainly a concern for the abattoir management and could have potentially contributed to the problem of occupational vaccination for Q fever. Liaison with abattoir management was challenging, and low compliance with appropriate work health and safety obligations was evident. The field investigation revealed that management and staff were lacking in knowledge and awareness of Q fever infection. Abattoir management were not compliant in reporting to SafeWork NSW.

Possible high-risk exposures included animals aborting/giving birth in the holding yards and at the evisceration point where a fetus (if identified) would be pulled out and dumped into a slops chute; however, it was difficult to ascertain where these infectious materials were stored or disposed. All staff on the kill floor would have potentially been exposed to the aerosolization of the birthing products. Additionally, staff were observed smoking during their break times, indicating a possible hand-to-mouth exposure if strict

Table 1. **Summary of confirmed and suspected cases in the Q fever cluster, south-western Sydney, Australia, 2015**

Case No.	Age, Sex	Onset date	Notification date	Laboratory evidence	Investigation classification	Method used to identify case
1	17, M	24/11/2014	10/12/2014	Definitive seroconversion	Confirmed	RR*
2	28, M	27/11/2014	09/01/2015	Definitive – nucleic acid testing	Confirmed	RR
3	28, M	28/11/2014	08/09/2015	Definitive seroconversion	Confirmed	I
4	22, M	11/01/2015	13/10/2015	Suspected case (no convalescent sample available)	Suspected case	RR
5	27, M	27/07/2015	30/11/2015	Definitive seroconversion	Confirmed	RR
6	17, M	31/08/2015	21/10/2015	Definitive seroconversion	Confirmed	A
7	60, M	7/09/2015 (deceased 30/9/2015)	18/09/2015	Definitive seroconversion	Confirmed	I
8	45, M	7/09/2015	21/10/2015	Definitive seroconversion	Confirmed	A

Note: A: Abattoir line listing, I: Initial case/s that prompted the investigation, RR: Retrospective Review of Laboratory Reporting.

* Public Health Unit staff recalled being notified of this case after being notified of cases 3 and 7.

Table 2. **Symptoms reported by confirmed and suspected cases in the Q fever cluster, south-western Sydney, Australia, 2015**

Symptom/Abnormal investigation findings	Number of cases	%
Abnormal liver function tests	4	50
Endocarditis	0	0
Fever	7	87.5
Headache	5	62.5
Chills or rigors	5	62.5
Lethargy and malaise	6	75
Abdominal pain	1	12.5
Nausea/Vomiting	5	62.5
Arthralgia/Myalgia	4	50

personal protective equipment (PPE) and hand hygiene practices were neglected.

In keeping with NSW Health Q fever control guidelines, the SWSLHD PHU made a formal notification of the Q fever cluster to SafeWork NSW, the enforcing body for Work Health and Safety Regulations. Further follow-up with SafeWork NSW confirmed that the abattoir was issued a strict warning and a recommendation to implement a vaccination programme for existing and future staff.

DISCUSSION

This was a significant cluster of Q fever in a high-risk setting. This outbreak in south-western Sydney compares with several previous outbreaks in both size and case finding but particularly the abattoir outbreak in South Australia in 2007 with five confirmed cases and one possible fatality.¹⁶ This investigation has confirmed the significance of this zoonotic disease as an occupational hazard for people working in high-risk settings and underscores the need for accurate diagnosis and timely reporting. It has also highlighted the challenges of a public health investigation in an area where the legislative enforcement authority lies with other agencies and demonstrates the need for improved interagency communication.

The application of active case finding strategies created the opportunity to identify potential cases in the community and within the vicinity of the abattoir – especially given that the field investigation identified various vulnerable groups (a school and residential properties) within close proximity to the abattoir. This was important since Q fever infection, which can be prevented by controlling the disease at its source, can be asymptomatic in approximately 60% of cases. An outbreak in the Netherlands in 2007–2010 was thought to be associated with intensive dairy goat farming that reported an increased number of abortions in the years before the first human cases.^{17,18} Cases were found to

Table 3. Summary of findings from the risk factor survey among confirmed and suspected cases in the Q fever cluster, south-western Sydney, Australia, 2015

Assessment criteria	Number of cases
1. Current occupation at an abattoir	8/8
2. Experienced Q fever symptoms in past 12 months (combination of the symptoms including fever, severe head-aches, muscle aches, extreme fatigue, joint pain, sweating and chills)	8/8
3. Received Q fever vaccine in the past	2/8
4. Tested positive for Q fever – blood test only	8/8
5. Doctor has advised ongoing check-ups/scans or blood tests	4/8
6. Worked in a high-risk occupation in the month before onset of symptoms (Yes = abattoir)	8/8
7. GP or hospital doctor ever requested an echocardiogram or heart scan due to symptoms	3/8
8. Still have problems/symptoms related to Q fever	5/7 [#]
9. Type of work done in abattoir	
a. Slaughtering	8/8
b. Boning	2/8
c. Packing	2/8
d. Inspecting meat	1/8
10. Types of animals* in contact with as part of abattoir work	
a. Cattle	8/8
b. Sheep	8/8
c. Goats	8/8
d. Pigs	8/8
11. Contact with fluids from pregnant animals or animals giving birth	
a. Animals giving birth	4/8
b. Handled carcass/slaughtering of pregnant animal	6/8
c. Handling of animal fetus or slops bucket	3/8
12. Family member living in the same house as case working in an abattoir	3/8
13. Time lapse before seeing a doctor after first symptoms developed	
a. Immediately to within two weeks	6/8
b. Between two weeks and six weeks	2/8

* Only these species are processed at this abattoir.

[#] Does not include a response from the deceased.

be residing within close proximity to the farms (5 km radius) that were thought to be the primary source of infection precipitated by the dry weather aerosolizing *C. burnetti*.^{17,19,20} This demonstrates the necessity for surveillance and active case finding in the area surrounding an abattoir. It is important to note that only looking for symptomatic cases may grossly underestimate the number of exposures associated with an outbreak as was demonstrated by the Dutch experience.

Although the PHU was notified of the first case in December 2014, limitations in the surveillance process may have inadvertently prevented the detection of other

cases in a more timely fashion. Timely notification of positive results from laboratories and an alert system in the notifiable conditions database may have notified PHU staff to the cluster earlier.

Issues in this study arose with the absence of clear guidelines to notify, collaborate with or provide recommendations for interagency communication. This investigation also revealed the alarming lack of knowledge among abattoir management and staff about the risk of Q fever. Equally disconcerting was the absence of a prescreening and vaccination programme. The abattoir has a responsibility to ensure all staff,

before commencement of employment, attend a health-care provider to carry out the prescreening process that requires checking immunization records for evidence of Q fever vaccination or screening for previous exposure to Q fever through skin and blood testing to rule out contraindications for vaccination. Such programmes are imperative not only for detecting possible exposure/cases, but also for identifying persons for which the Q fever vaccine is contraindicated because of previous infection or vaccination.¹³ Poor recordkeeping at the abattoir made it difficult to identify previous staff and the roles they occupied during their period of employment at the abattoir. This issue also made establishing the immunization status of current or previous employees at the abattoir extremely challenging. A lack of cooperation from asymptomatic staff to complete surveys or be interviewed also limited the information that could be collected.

The abattoir has a duty of care and legal obligation to their employees given the high-risk occupational setting. Other outbreaks have demonstrated that the optimal time period for Q fever vaccination is two weeks before possible occupational exposure.^{14,21} SafeWork NSW guidelines indicate an employer must implement safe work practices to minimize risk and notify SafeWork NSW if one of their employees has Q fever.¹⁴ This case investigation concluded that despite abattoir management being aware of several employees with Q fever symptoms, not even the death of an employee linked to Q fever prompted appropriate notification. Although a warning and compliance order was issued to the abattoir, this action is not comparable to restrictions placed on abattoirs in previous outbreaks and may not mitigate any ongoing risk to employees. In previous abattoir outbreaks, restrictions had been placed on the abattoir operation (including access restriction to those who could not show evidence of vaccination, erection of biosecurity signage on all access roads to the abattoir/farm, introduction of vehicle wash stations and foot baths, changes to work health and safety policy at the facility and introduction of uniforms with laundering onsite with a longer-term plan to develop showering facilities onsite) along with recommendations for a mandatory vaccination programme for all staff in these high-risk settings.^{14,22} Increased monitoring by

agencies responsible for work health and safety may be necessary to ensure prescreening and vaccination programmes and other necessary restrictions and policies are implemented for employees in high-risk occupations. An area of further research would be to assess the level of noncompliance with work health and safety legislation in abattoirs across NSW.

Limitations

This study had several limitations. The risk assessment survey was conducted 12 months after the initial onset of symptoms in some of the cases with the possibility of recall bias due to the time lapsed. Lack of resources and time constraints prevented the expansion of the investigation to neighbouring residences and schools, which might have resulted in an underestimation of the scope of the outbreak. However, the retrospective review of the pathology results was used as a proxy for this. While this investigation demonstrated great collaboration between human and animal health experts, reliance on one agency for the field investigation may have limited the information obtained from the abattoir. Development of a checklist for future field investigations could be explored to alleviate this limitation. The study is also limited due to the inability to access information on other abattoir workers who were not diagnosed or tested to provide a comparison. This study must therefore be interpreted in the context of a case series.

CONCLUSION

This investigation revealed that Q fever is a significant zoonotic disease, especially among abattoir workers, and underscores the need for accurate diagnosis and timely reporting. In high-risk settings, prescreening and vaccination programmes are imperative prevention strategies, which require close collaboration between public health and agencies responsible for work health and safety to ensure maximum compliance.

This investigation highlights the need for multiagency review of the management of Q fever in these high-risk settings, especially in regards to notifications to PHUs and adherence to work health and safety regulations.

Conflicts of interest

None declared.

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Rotavirus vaccine and health-care utilization for rotavirus gastroenteritis in Tsu City, Japan

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Background: Rotavirus vaccines were introduced in Japan in November 2011. We evaluated the subsequent reduction of the health-care burden of rotavirus gastroenteritis.

Methods: We conducted active surveillance for rotavirus gastroenteritis among children under 5 years old before and after the vaccine introduction. We surveyed hospitalization rates for rotavirus gastroenteritis in children in Tsu City, Mie Prefecture, Japan, from 2007 to 2015 and surveyed the number of outpatient visits at a Tsu City clinic from 2010 to 2015. Stool samples were obtained for rotavirus testing and genotype investigation. We assessed rotavirus vaccine coverage for infants living in Tsu City.

Results: In the pre-vaccine years (2007–2011), hospitalization rates for rotavirus gastroenteritis in children under 5 years old were 5.5, 4.3, 3.1 and 3.9 cases per 1000 person-years, respectively. In the post-vaccine years (2011–2015), the rates were 3.0, 3.5, 0.8 and 0.6 cases per 1000 person-years, respectively. The hospitalization rate decreased significantly in the 2013–2014 and 2014–2015 seasons compared to the average of the seasons before vaccine introduction ($p < 0.0001$). In one pre-vaccine year (2010–2011), the number of outpatient visits due to the rotavirus infection was 66. In the post-vaccine years (2011–2015), the numbers for each season was 23, 23, 7 and 5, respectively. The most dominant rotavirus genotype shifted from G3P[8] to G1P[8] and to G2P[4]. The coverage of one dose of rotavirus vaccine in Tsu City was 56.5% in 2014.

Conclusion: After the vaccine introduction, the hospitalization rates and outpatient visits for rotavirus gastroenteritis greatly decreased.

In young children, the single most important cause of severe dehydrating diarrhoea is rotavirus infection.¹ Some patients need fluid therapy at the hospital for severe dehydration. Even in small numbers, death from rotavirus infection does occur in developed countries, including Japan.² Complications of rotavirus infection include seizure, prerenal or postrenal kidney failure and encephalitis/encephalopathy.^{3–5} A study in Japan suggested rotavirus is the third leading pathogen of infections that proceed acute encephalopathy nationally after influenza virus and human herpesvirus-6.⁵ Therefore, rotavirus vaccine would help reduce severe acute gastroenteritis and its complications.

In Japan, monovalent rotavirus vaccine (RV1) was introduced in November 2011 and pentavalent rotavirus vaccine (RV5) in July 2012. Currently, the rotavirus vaccine is not included in the National Immunization Programme in Japan, and the cost of vaccination including an administration fee is covered by parents and guardians. RV1 is administered at 2 and 4 months of age. RV5 is administered at 2, 3 and 4 months of age.

Previously, we studied the disease burden of rotavirus infection in children under 5 years old retrospectively in two cities (Tsu City, Ise City) from

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2003 to 2007 in Mie Prefecture, Japan.⁶ The annual hospitalization rate for rotavirus gastroenteritis in the two cities was estimated to be 3.8 and 4.9 per 1000 person-years, respectively.

Since then, we have been conducting active surveillance for rotavirus gastroenteritis hospitalization in children under 5 years old in three cities (Matsusaka City in addition to the two cities mentioned above) in Mie.⁷ The annual hospitalization rate for rotavirus gastroenteritis in the three cities from 2007 to 2009 was estimated to be 2.8 to 4.7 per 1000 person-years.

In this study, we report monitored trends in the hospitalization rate and the number of outpatient visits due to rotavirus gastroenteritis, and prevalent rotavirus genotypes in Tsu City, Mie, Japan before and after the introduction of rotavirus vaccine.

METHODS

Data source and case definition

We conducted active surveillance for rotavirus gastroenteritis among children under 5 years old in Tsu City, Mie, Japan before and after the vaccine introduction. In Japan, November to July is considered to be the rotavirus peak season and August to October is the rotavirus off-season. We defined one season as November of one year to October of the next year.

From November 2007 to October 2015, we surveyed hospitalization rates for rotavirus gastroenteritis in children under 5 years old. Two hospitals in Tsu City were included in this study because there are no other hospitals in the city that admit children with severe dehydration. In addition, we asked surrounding city hospitals to notify us if rotavirus acute gastroenteritis patients under 5 years old who reside in Tsu City were admitted to their hospitals.

From November 2010 to October 2015, we concurrently surveyed outpatient visits of children under 5 years old who were diagnosed with rotavirus gastroenteritis at one walk-in clinic in the same city. We selected this clinic in Tsu City because it has the most outpatient visits.

All patients under 5 years old who were hospitalized with a diagnosis of acute gastroenteritis were tested for rotavirus at the two hospitals. For patients from whom we were unable to collect stool samples at the time of admission, we attempted to collect samples during hospitalization. We did not use enema and rectal swab to collect samples. For the outpatient clinic, parents and guardians were asked to submit their child's stool sample.

We used a commercially available enzyme immunoassay (Rota-Adeno Dry; Sekisui Medical Co., Tokyo, Japan) for rotavirus antigen detection in the stool specimens; the sensitivity and specificity of this test are approximately 94% and 99%, respectively, when compared with electron microscopy (data from package insert). Rapid inspection using this assay for rotavirus is broadly implemented in Japan. Positive cases by this testing were diagnosed as rotavirus gastroenteritis. Patients living outside Tsu City were excluded from this study.

Genotype investigation

For rotavirus-positive stool samples, G and P genotypes were investigated. Stool suspension was prepared in Eagle's minimum essential medium; rotavirus RNA was extracted for the determination of G and P types by nested reverse transcription polymerase chain reaction (RT-PCR) carried out in two steps, first and second amplifications, as described previously.^{8,9} For G typing, the full-length VP7 gene was amplified using a pair of primers, 5'-GGCTTTAAAAGAGAGAATTTCCGTCTGG-3' (T31) and 5'-GGTCACATCATAAATTCTAATCTAAG-3' (T32), corresponding to the common 5' and 3' ends of the VP7 gene, respectively. In the second PCR amplification, the T32 primer was used along with G1, G2, G3, G4, G8 and G9 genotype-specific primers to identify G types. For P typing, a pair of primers, 5'-TGGCTTCGTTTCATTATAGACA-3' and 5'-CTAAATGCTTTTGAATCATCCCA-3', corresponding to the common sequences of the VP4 gene, including nucleotides 11 to 32 and 1072 to 1094, respectively, were used for the first amplification. A mixture of primers specific to each of the variable regions P[8], P[4], P[6] and P[9], along with a primer corresponding to nucleotides 11 to 32, were used for the second amplification. PCR products were electrophoresed in 1% agarose gels and stained with ethidium bromide.

Estimation of rotavirus vaccine coverage

We defined the period from 2007 to 2011 as pre-vaccine years because the rotavirus vaccine was not commercially available until late November 2011; the period from 2012 to 2015 was defined as post-vaccine years. However, because the rotavirus vaccine is not routinely recommended in Japan, there is no official method to obtain the vaccine coverage rate for Tsu City. Thus, we estimated the rotavirus vaccine coverage rate using child health check-up data.

In Japan, all children are obliged to have periodic health check-ups by the government at 3 to 4, 18 and 36 months of age. We assessed rotavirus vaccine coverage at the 18-month check-up from January to March of 2014. We checked the immunization records of the mother–child handbook of these children to obtain the rotavirus vaccine coverage among children born in mid- to late 2012.

Data analysis

We summarized the demographic characteristics of hospitalized cases and outpatient visits for rotavirus gastroenteritis using a standardized abstraction form. For hospitalizations, we calculated the annual incidence rate for each year using the total number of rotavirus-positive cases during the study period as the numerator and the population of those aged under 5 years as the denominator. We obtained population data from the statistics office in Mie every year for the number of children under 5 years old in the city.

We performed χ^2 tests using the software GraphPad Prism version 6.0 (GraphPad Software Inc., San Diego, CA, USA). A p -value of less than 0.05 was considered statistically significant.

Ethics

This study was approved by the Institutional Review Board of National Hospital Organization Mie Hospital.

RESULTS

Trends in hospitalization for rotavirus gastroenteritis

Table 1 and **Fig. 1a** summarized the yearly hospitalization rates for rotavirus gastroenteritis from 2007 to 2015. The average hospitalization rate in pre-vaccine years for children under 5 years old (2007–2011) was 4.2 cases per 1000 person-years (95% confidence interval, 3.7–4.8). The hospitalization rates in the post-vaccine years (2011–2012, 2012–2013, 2013–2014 and 2014–2015) were 3.0, 3.5, 0.8 and 0.6 cases per 1000 person-years, respectively. The hospitalization rate declined by 85.7% in 2014–2015 compared to the average of pre-vaccine years (0.6 and 4.2 cases per 1000 person-years, respectively). In the 2013–2014 and 2014–2015 seasons, the rate of hospitalizations was significantly lower compared with the seasons before vaccine introduction from 2007 to 2011 ($p < 0.0001$). There was no case admitted to surrounding city hospitals during the study period. No death or serious complication was observed during this study period.

Age distribution of hospitalizations

Fig. 2 shows hospitalization rates by age group. In the pre-vaccine years, 205 children were hospitalized for rotavirus gastroenteritis. Hospitalization rates per 1000 population were 5.2 among children aged under 1 year, 7.9 among children aged 1–2 years, 5.2 among children aged 2–3 years, 1.6 among children aged 3–4 years and 1.2 among children aged 4–5 years. In the post-vaccine years, 92 children were hospitalized. Hospitalization rates per 1000 population were 1.1 among children aged under 1 year, 3.8 among children aged 1–2 years, 2.6 among children aged 2–3 years, 1.1 among children aged 3–4 years and 1.1 among children aged 4–5 years. The hospitalization rates in the three age groups (under 1 year old, 1–2 years old and 2–3 years old) in the post-vaccine years decreased significantly compared with the pre-vaccine years ($p < 0.0001$, $p = 0.0003$ and $p = 0.0062$, respectively), while the hospitalization rates in the other age groups (3 years old or older) did not change significantly.

Table 1. Hospitalization data for rotavirus gastroenteritis in Tsu City

	Pre-vaccine years				Post-vaccine years			
	2007–2008	2008–2009	2009–2010	2010–2011	2011–2012	2012–2013	2013–2014	2014–2015
No. of hospitalizations	68	53	38	46	35	41	9	7
Tsu City population (< 5 years old)	12 270	12 339	12 279	11 755	11 775	11 794	11 687	11 598
Hospitalization rate (per 1000 person- years)	5.5	4.3	3.1	3.9	3.0	3.5	0.8*	0.6*
95% confidence interval	4.4–7.0	3.3–5.6	2.3–4.2	2.9–5.2	2.1–4.1	2.6–4.7	0.4–1.5	0.3–1.2

* Statistically significant decrease compared to the average hospitalization rate before introduction of rotavirus vaccine (2007–2011).

Figure 1a. Number of hospitalizations for rotavirus gastroenteritis

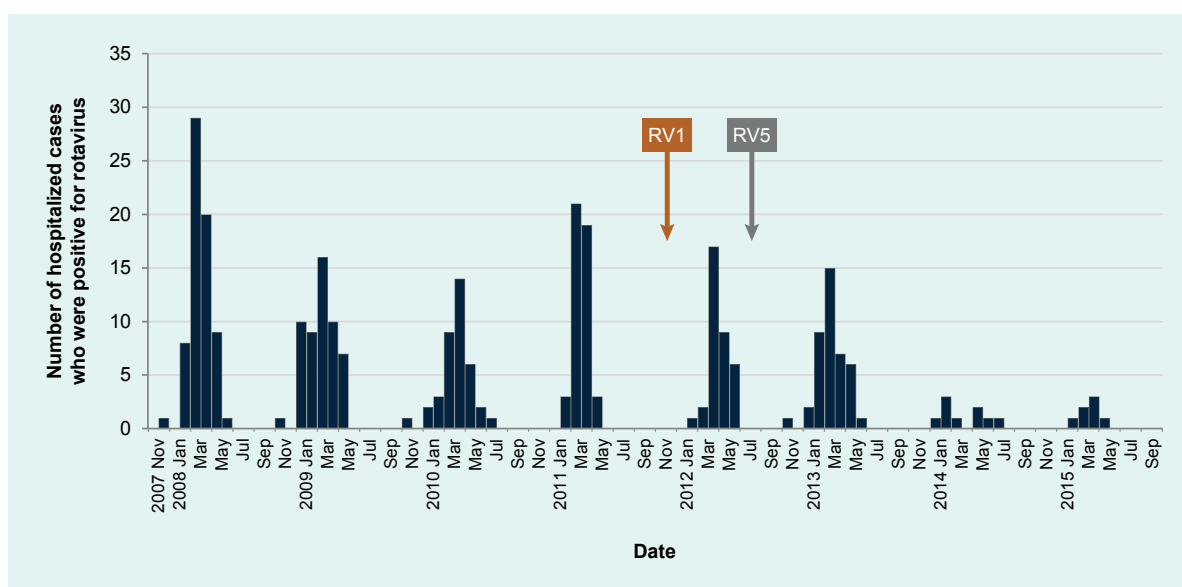
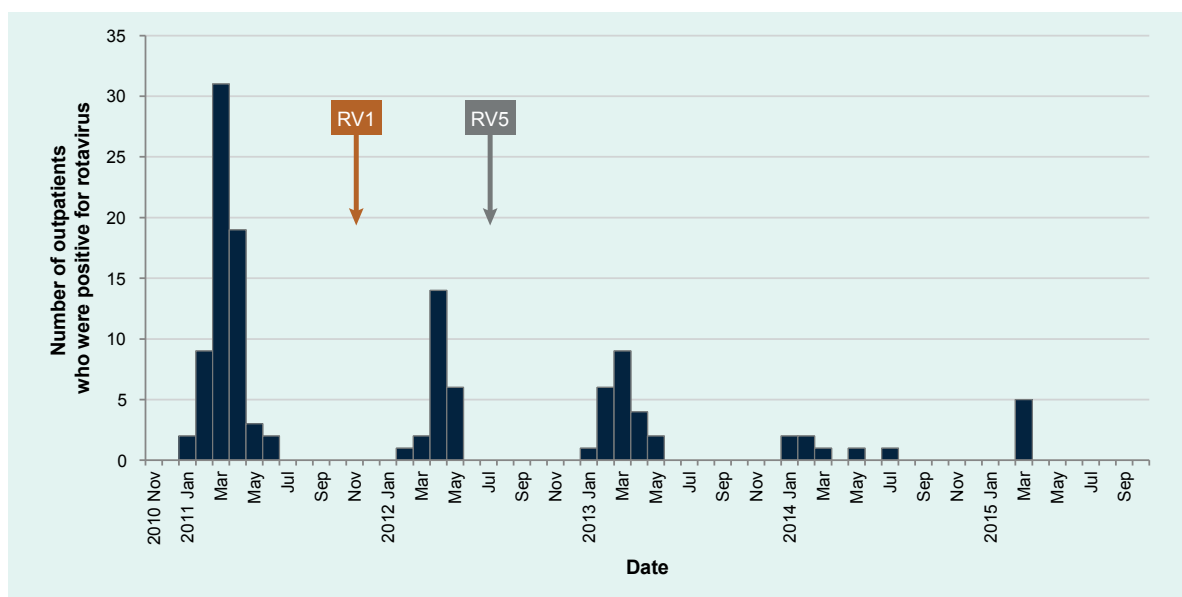
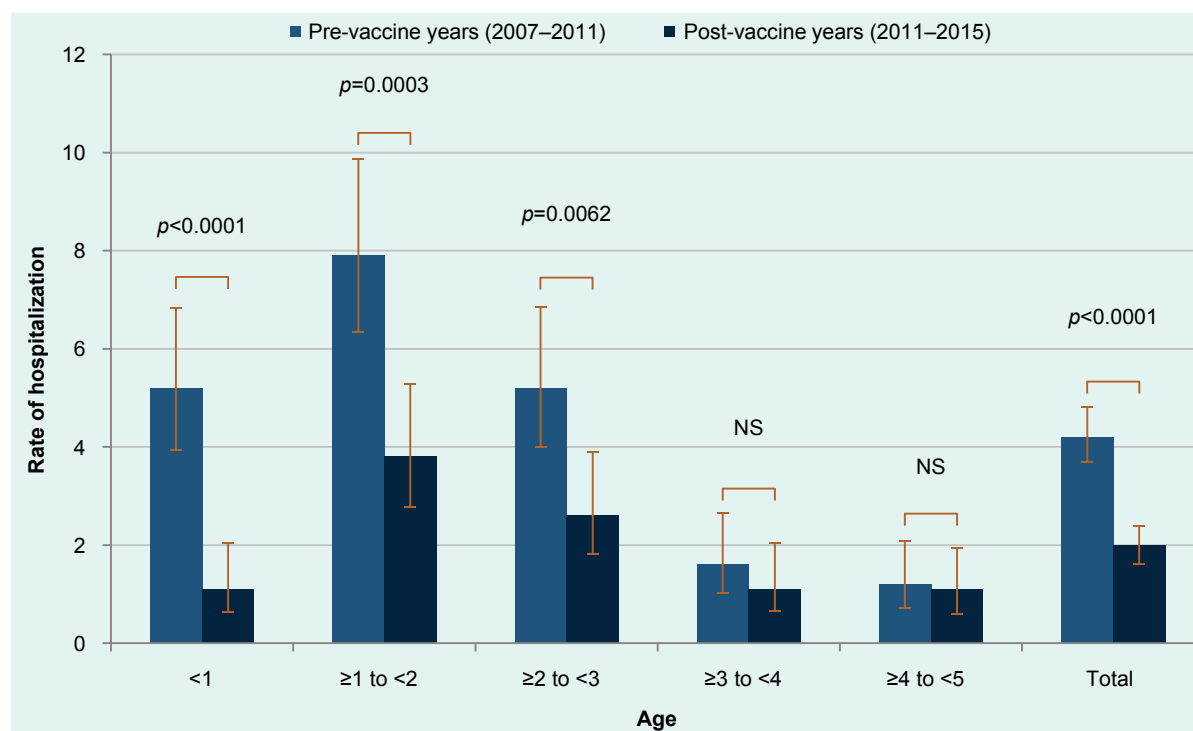


Figure 1b. Number of outpatient visits for rotavirus gastroenteritis



Arrows indicate the times when the vaccines were introduced. RV1 is the monovalent rotavirus vaccine, and RV5 is the pentavalent rotavirus vaccine.

Figure 2. Age distribution of hospitalization rate for rotavirus gastroenteritis



NS, not significant.

Bars indicate 95% confidence interval.

Trends in outpatient rotavirus gastroenteritis cases

Outpatient visits were surveyed for just one season in the pre-vaccine years (2010–2011), in which there were 66 rotavirus gastroenteritis diagnosed cases. In the four post-vaccine seasons (2011–2012, 2012–2013, 2013–2014 and 2014–2015), there were 23, 23, 7 and 5 diagnosed rotavirus cases, respectively. A very sharp decrease in the number of rotavirus-positive cases was observed in the 2013–2014 season (Fig. 1b).

Changes in genotypes

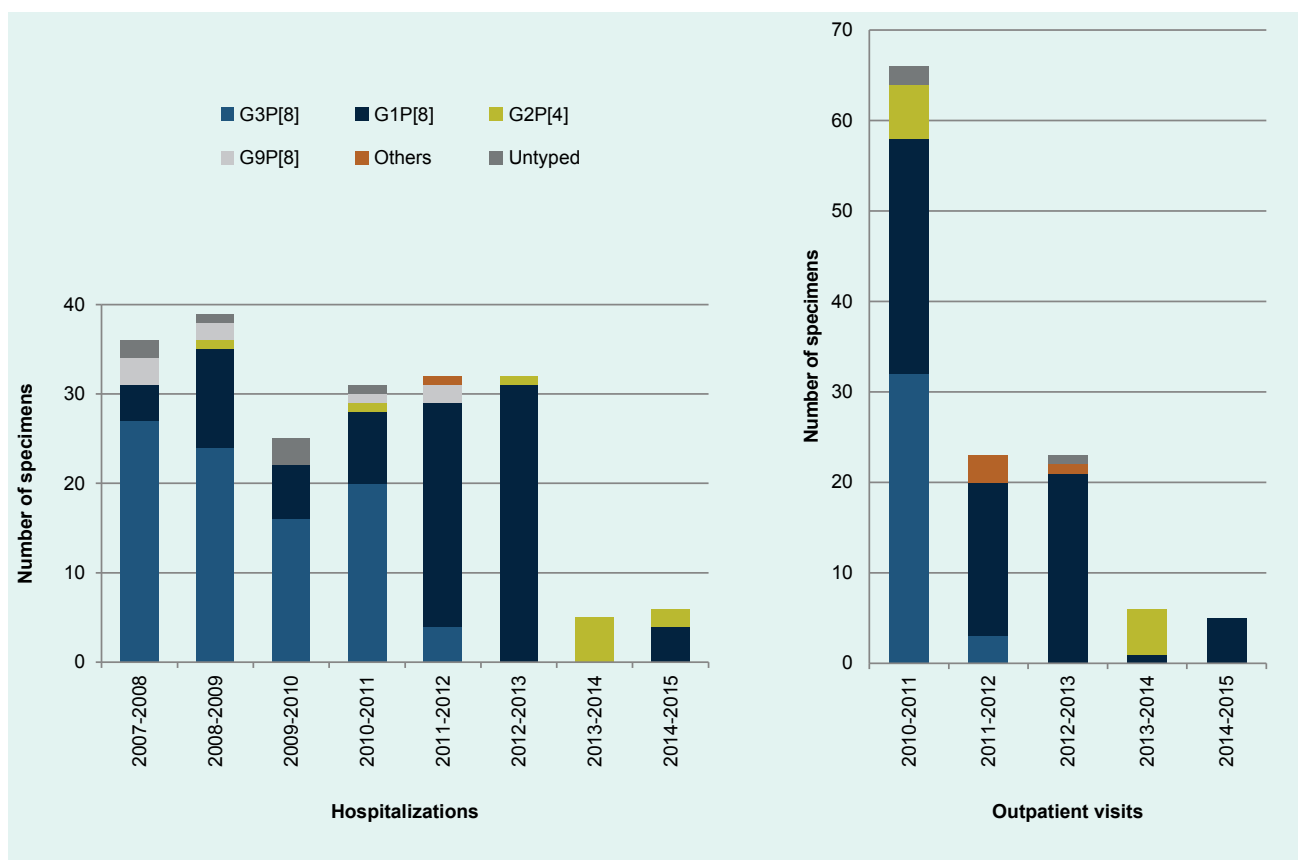
Of the 297 hospitalized patients, 206 (69.4%; 52.9–91.4%) were subjected to G and P typing using semi-nested PCR. Some stool samples were insufficient in quantity to investigate the genotype. From 2007 to 2011, the most dominant rotavirus genotype was G3P[8] (61.5–75.0%) followed by G1P[8] (11.1–28.2%) (Fig. 3). In 2011 to 2012 and 2012 to 2013, the most dominant rotavirus genotype was G1P[8] (78.1–96.9%). In 2013 to 2014, all five specimens tested had G2P[4]; in 2014 to 2015, G1P[8] (66.7%) was dominant from the six specimens tested.

Stool samples of all of the 123 outpatients were subjected to G and P typing (Fig. 3). In 2010 to 2011, the most dominant rotavirus genotype was G3P[8] (48.5%), and the second most dominant genotype was G1P[8] (39.4%). In 2011–2012 and 2012–2013, the most dominant rotavirus genotype was G1P[8] (73.9% and 91.3%, respectively). In 2013–2014, G2P[4] (83.3%) was dominant in the six specimens tested, and in 2014 to 2015, all five specimens tested had G1P[8].

Estimated rotavirus vaccine coverage

Vaccination histories were collected at the 18-month check-ups from January to March of 2014. During that time, of 555 children who were required to have an 18-month check-up in the city, 543 visited health centres (98% compliance). The first dose of rotavirus vaccine had been administered to 56.5% of the children (307 out of 543; 251 received RV1 and 56 received RV5). The second dose of rotavirus vaccine had been administered to 54.9% of the children (298 out of 543; 243 children received RV1 and 55 received RV5). The third dose of RV5 had been administered to 9.6% children (52 out of 543). Of the 543 children, 44.8% completed the two-dose series of RV1, and 9.6% completed the three-dose

Figure 3. **Changes of rotavirus genotypes of stools from hospitalized cases (left) and outpatient settings (right) in Tsu City, Japan**



series of RV5, giving the coverage of complete rotavirus vaccine series of 54.4%.

Rotavirus gastroenteritis among vaccinated cases

Ten cases of rotavirus gastroenteritis were reported among vaccinated children, including four hospitalized cases and six outpatients (Table 2). All these cases were fully vaccinated with two doses of RV1 vaccine. G1P[8] was found in five cases and G2P[4] in four cases. Genotyping was not performed for one case due to insufficient specimen.

DISCUSSION

We actively surveyed both hospitalized and walk-in patients for laboratory-confirmed rotavirus acute gastroenteritis in Tsu City, Mie, Japan before and after the introduction of rotavirus vaccine. The average hospitalization rate in the pre-vaccine years was 4.2 cases per 1000 person-years, which is comparable to

the reports from other developed countries in the pre-vaccine years: 2.7 cases per 1000 person-years in the United States of America, 3.7 to 13 cases per 1000 person-years in western Europe and 8.7 cases per 1000 person-years in Australia.¹⁰⁻¹⁵ Hospitalization rates and outpatient visits for rotavirus gastroenteritis have greatly decreased after vaccine introduction in Tsu City. The hospitalization rate declined by 85.7% from 4.2 in pre-vaccine years to 0.6 cases per 1000 person-years in the 2014–2015 season. In other words, 42 hospitalizations were prevented among children under 5 years old in Tsu City, assuming the incidence without vaccination remained the same as baseline. If we extrapolate our results to a national population, assuming the disease incidence and vaccine coverage in Japan is the same as in Tsu City, 18 770 children under 5 years old would be prevented from being hospitalized in Japan.

Similar to Tsu City, reduction in hospitalization due to rotavirus has been observed in the United States after introduction of RV5 into routine immunization in February 2006: by 31 December 2007, at least one dose of RV5

Table 2. Cases with vaccination history

Season	Age (month)	Sex	Inpatient or outpatient	Underlying condition	Vaccine type	Dose	Days from first dose to onset	Genotype
2011–2012	6	M	Inpatient	None	RV1	2	89	G1P[8]
2012–2013	9	M	Inpatient	None	RV1	2	221	G1P[8]
	10	F	Outpatient	None	RV1	2	233	G1P[8]
2013–2014	26	M	Inpatient	None	RV1	2	756	G2P[4]
	28	M	Outpatient	None	RV1	2	801	G2P[4]
	9	M		None	RV1	2	194	G2P[4]
	12	M		None	RV1	2	302	Untyped
2014–2015	21	F	Inpatient	None	RV1	2	569	G2P[4]
	34	M	Outpatient	None	RV1	2	972	G1P[8]
	34	M		None	RV1	2	993	G1P[8]

had been administered in 64% of children under 1 year old, and in 2008 to 2009, the hospitalization rate for rotavirus-coded diarrhoea declined by 60% from the baseline rates.¹⁶ In Japan, rotavirus vaccination was optional in 2016. It is available based on self-pay, and vaccine history is not kept by local government. Based on our vaccine coverage study in Tsu City, the coverage rate was 56.5% for the first dose of rotavirus vaccine and 54.4% for the complete series. Even with those coverage rates, a decrease in the number of patients both in hospital as well as outpatient clinic settings is apparent.

Significant decreases were observed among children under 1 year old, between 1 and 2 years old and between 2 and 3 years old after the introduction of rotavirus vaccines. On the other hand, incidence did not change significantly among children in the 3 years old or above age group. Taking into consideration that the vaccine was introduced in late 2011 in Japan, the majority of children older than 3 years were probably not vaccinated with rotavirus vaccine. In the United States, herd immunity effect was seen after the vaccine coverage increased.^{17,18} To obtain herd immunity effect from rotavirus vaccines in Japan, achieving higher vaccination coverage seems necessary and inclusion of the vaccine into the National Immunization Programme is one approach. Despite the significant reduction of hospitalization rates among children under 3 years of age, the hospitalization rate is still higher among children aged between 1 and 3 years compared to older children. This emphasizes the need to increase vaccination coverage in young children.

Rotavirus genotype G1 was the dominant type in Japan from the late 1980s to 2000. After that, G1 temporarily decreased and G3 became dominant. However G1 re-emerged and G3 decreased in 2004–2005.¹⁹ In Japan, the majority of rotavirus vaccines at this time are RV1 which contains one strain of live attenuated human rotavirus genotype G1P[8]. We analysed rotavirus genotypes from the stool sample collected in this study. The proportions of circulating genotypes between hospitalizations and outpatient visits were very similar. During our study period, the main circulating genotypes shifted from G3P[8] to G1P[8] in 2011–2012 to G2P[4] in 2013–2014 and then back to G1P[8] in 2014–2015, although only a few cases were identified in 2013–2015. Recent reports from Belgium, Brazil, Republic of Korea, Nicaragua and the United States showed that the percentage of rotavirus disease due to type G2P[4] rotavirus increased after vaccine introduction.^{16,20–24} However, the increase of G2P[4] was temporary in countries such as Brazil and Nicaragua, which is similar to what we observed in Tsu City. A study in 11 Latin American countries and Finland reported that the efficacy of RV1 against severe rotavirus gastroenteritis caused by type G1P[8] strains was 90.8% ($p < 0.001$) and against strains sharing only the P[8] antigen (G3P[8], G4P[8] and G9P[8]) was 87.3% ($p < 0.001$); efficacy against the fully heterotypic G2P[4] strains was 41.0% ($p = 0.30$).²⁵ Another study in six European countries also reported lower efficacy of RV1 against any rotavirus gastroenteritis caused by the G2 type (58.3%) compared to other G types, although the efficacy against severe

rotavirus gastroenteritis caused by the G2 type was as high as that for other G types (85.5%).²⁶ However, a study in the United States reported high efficacy (94%) of RV1 against G2P[4] disease.²⁷ Thus, it is difficult to conclude that the serotype shift we observed may be a representation of selective pressure of vaccine or decreased vaccine effectiveness over time or both. The finding could also be an artefact of small numbers. Since we continue our study at the same site, continuous monitoring of the genotype is important.

Our study has some limitations. First, we were unable to collect stool samples from all hospitalized acute gastroenteritis cases. We did not use enema and rectal swab to collect samples, and some patients who didn't provide stool specimens might have been missed, although we think the numbers are few. Second, this study is confined to just one city in Japan and is not nationally representative. Third, because rotavirus vaccine is optional in Japan at this time, it is difficult to assess accurate vaccine coverage in an area. However, very high attendance at 18-month check-ups in our area means that our estimated coverage rate should be relatively close to the actual coverage rate. Finally, this study is based on surveillance data of rotavirus gastroenteritis, and it is not a study to assess causality between vaccination and reduction in disease. There may have been unmeasured changes occurring during the study period which contributed to the decline in rotavirus gastroenteritis.

CONCLUSIONS

In summary, after the introduction of rotavirus vaccine in Japan in 2011, we observed a reduction in the incidence of rotavirus gastroenteritis hospitalizations and outpatient visits in Tsu City among children. To maximize the impact of vaccination and achieve herd immunity, we recommend including the rotavirus vaccine in the National Immunization Programme in Japan as a mean to improve vaccine coverage. Continued testing for genotypes is important in monitoring possible vaccine-induced selective pressure and informing use of vaccines.

Conflict of Interest

The corresponding author declares no conflict of interest associated with this manuscript. Takashi Nakano has received consulting fees and payment for lectures from

Japan Vaccine, MSD, Daiichi Sankyo, Tanabe-Mitsubishi, Takeda Pharmaceutical, Astellas Pharma, Denka Seiken and Sanofi. All other authors have no conflicts of interest to declare.

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